ISMB Oral Presentations

On-chip Brillouin spectrometer for 3D mechanical imaging

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Cell Mechanics Across Length Scales 1, July 15, 2026, 08:45 - 10:30

Brillouin spectroscopy provides a non-contact and label-free approach to probe the viscoelastic properties of materials through the analysis of light scattered by thermally induced acoustic phonons. Over the past decade, it has emerged as a powerful modality for three-dimensional mechanical imaging of biological systems at diffraction-limited resolution. However, the widespread adoption of Brillouin microscopy has been limited by the reliance on bulky, alignment-sensitive, and costly free-space detection systems that require sub-GHz spectral resolution and high suppression of elastically scattered light.

Here we present a fully integrated on-chip Brillouin spectrometer designed for compact and scalable 3D mechanical imaging. The device is implemented on a low-loss silicon nitride photonic platform and combines cascaded Mach-Zehnder interferometers with high-Q resonant structures to achieve sub-GHz spectral resolution within a footprint of approximately 1 x 2 cm. The scanning architecture enables selective acquisition over narrow spectral windows, allowing effective acquisition times down to ~10 ms for a single Brillouin peak. Direct comparison with state-of-the-art free-space VIPA spectrometers demonstrates comparable sensitivity and improved signal-to-background ratio under equivalent acquisition conditions. The integrated approach ensures intrinsic stability, reduced alignment requirements, and compatibility with fiber-coupled microscope interfaces. We validate the performance of the on-chip spectrometer through measurements in highly scattering media and demonstrate its applicability to Brillouin microscopy by acquiring three-dimensional mechanical maps of living cells and different mice organs. This work establishes a pathway toward portable, cost-effective, and robust Brillouin imaging systems, accelerating the translation of biomechanical phenotyping into life sciences, clinical research, and applied biophotonics.

Dynamic interactions between epithelial skin cells and a sensory cavity sculpt the growing olfactory orifice

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In vivo Mechanobiology 1, July 16, 2026, 08:45 - 10:30

During morphogenesis and in pathological conditions, gaps can form in the plane of epithelial barriers upon cellular forces that disrupt intercellular junctions. How the size of these epithelial holes further increases over time and what sets their shape remain poorly understood. Here we analyze the formation of the olfactory orifice (the nostril) in zebrafish, which opens and grows in the skin epithelium above a rosette of olfactory placode cells, allowing the sensory neurons to directly access odor cues. Using quantitative imaging and tissue-specific perturbations, we analyzed the dynamic remodeling of skin cells allowing the expansion of the orifice edge. We identified the sensory cavity located in the center of the placodal rosette as a crucial player that sets the size of the growing epithelial hole in the skin. We further showed that fine-tuning of actomyosin contractility within each tissue (skin and sensory cavity) exerts non-autonomous effects on the neighboring tissue, thereby shaping the nostril structure. This study uncovers dynamic cell behaviors and reciprocal tissue-tissue interplay that control the growth and shape of an epithelial hole in vivo.

Redirecting cancer cell invasion in glioblastoma using durotaxis as a bait.

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Mechanobiology in Disease and Mechanomedicine 2, July 13, 2026, 16:15 - 17:15

Glioblastoma (GB) is the most aggressive primary brain tumor and remains almost universally fatal. Its highly infiltrative nature prevents complete surgical resection and leads to inevitable recurrence. Despite decades of effort, standard chemoradiotherapy offers only limited benefit, and fewer than 5% of patients survive beyond five years. These limitations highlight the urgent need for therapeutic strategies that address the unique biological and physical properties of GB. Here we present a biophysics-based therapeutic approach that exploits durotaxis, or the ability of GB cells to migrate along stiffness gradients. For this, we engineered collagen-coated polycarbonate polyurethane scaffolds with defined mechanical properties designed to act as “mechanical traps” for tumor cells and redirect their migration away from the healthy brain tissue. Using in vitro 3D tumor resection models, we demonstrated that these scaffolds are highly infiltrated by multiple glioblastoma models, including human and murine cell lines, patient-derived organoids, and primary tumor cultures. In vivo, scaffold implantation resulted in progressive and selective tumor cell infiltration into the biomaterial, leading to an approximately 70% reduction in invasive tumor foci compared with controls. Importantly, this effect was stiffness-dependent as softer scaffolds matching physiological brain stiffness failed to limit invasion. Consistently, pharmacological and genetic disruption of durotaxis reduced scaffold colonization. Beyond limiting invasion, scaffold colonization also reshaped the tumor microenvironment, promoting T-cell infiltration and activation while reducing myeloid-driven immunosuppression, potentially through mechanotransduction. Altogether, these effects contributed to a marked increase in survival in GB in vivo preclinical models receiving radiotherapy and implanted with scaffolds. Overall, these findings demonstrate that glioblastoma invasion can be hijacked by exploiting durotaxis to create artificial stiffness niches for tumor cells. This work provides a proof of concept for a new “mechanotherapeutic” strategy and has paved the way for an upcoming clinical trial to test this approach in glioblastoma patients.

Quantification of cell-ECM 3D forces at the fiber level

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Advanced Tools for Multiscale Mechanobiology 1, July 14, 2026, 08:45 - 10:30

Quantifying cell-generated forces in 3D fibrillar hydrogels remains challenging due to the nonlinear, heterogeneous nature of collagen networks. Here, we introduce a data-driven 3D traction force microscopy (DDTFM) framework that reconstructs discrete collagen fiber architectures directly from confocal reflectance images and assigns mechanically calibrated fiber properties obtained through bulk shear rheology. Instead of modeling the extracellular matrix (ECM) as a homogenized continuum, we represent it as an interconnected fiber network and resolve deformation and force transmission at subcellular scales. In silico tests demonstrate that an inverse force recovery approach that imposes equilibrium of forces provides robust performance under noisy conditions. As proof of concept, we apply DDTFM to quantify the forces exerted by control and blebbistatin-treated human umbilical vein endothelial cells (HUVECs) embedded in a collagen hydrogel. This framework enables high-resolution mapping of cell-matrix mechanics in physiologically relevant 3D environments.

Capturing dynamic conformational change in proteins during gel network formation

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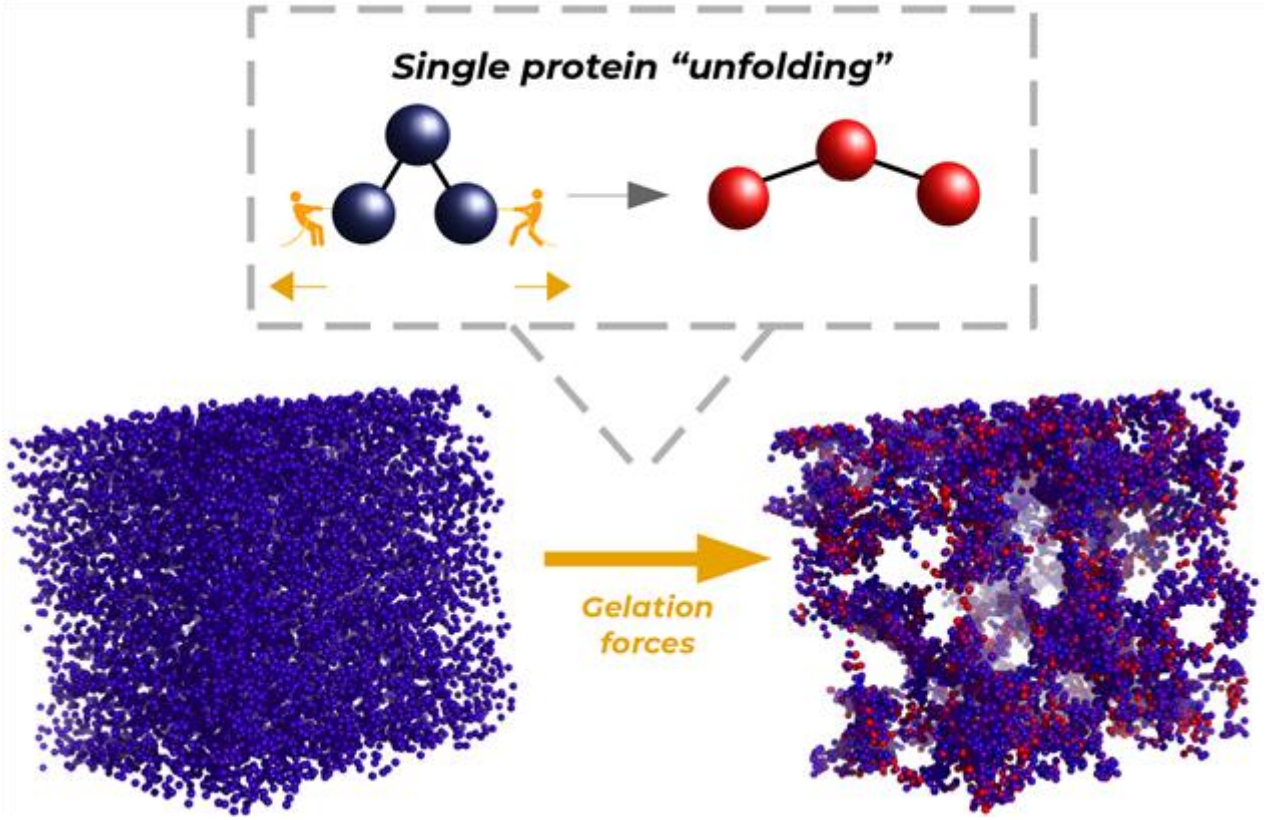
Mechanochemistry 2, July 15, 2026, 16:15 - 17:15

Protein gels are highly versatile systems that notably have multi-lengthscale behaviour and can be rationally designed. Through selection of their constituent protein building blocks they can be adapted to wound healing, tissue engineering and biosensing. There is a complex interplay between the behaviour of the individual building block and the bulk gel: when a protein in the gel undergoes conformational change, the bulk gel's structural and mechanical properties change. The converse is also true: bulk deformation can induce protein unfolding and presents a potentially complex mechanical response.

Though in-vitro experiments can map out individual protein and bulk gel characteristics well, the generic mesoscale formation and behaviour of a gel is less understood [1]. In-silico experiments have previously studied the force-lability of a few proteins or the network formation of a colloidal protein gel, but thus far there is no predictive, scalable mesoscale simulation that includes dynamic protein unfolding to our knowledge. We present a dynamic trimer model to represent protein unfolding and incorporate this into network formation simulations of over 104 proteins – this simple coarse-grained model bridges both scalability and dynamic unfolding in protein gel simulations. By varying protein concentration and energy barrier for protein unfolding, the force distribution in the network can be localised and a greater understanding can be developed of how conformational change affects a protein gel's structure and mechanical properties. Real-space data analysis allows us to locate precisely where unfolding is taking place and in what proportions. This gives us unprecedented access to the physical mechanisms underlying protein gel response and highlights the relevant parameters to control to produce bespoke gels for applications.

[1] Boroumand. Ahmad et.al, JCIS (2025), 699, 1.



Coordinated interplay between LRRC59 and nuclear transporters restrains the nuclear envelope repair machinery to safeguard genome integrity

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Nuclear Mechanobiology 2, July 14, 2026, 16:15 - 17:15

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Abstract
Nuclear envelope (NE) rupture is a hallmark of cancer cells, and mechanical stress drives persistent NE damage, resulting in genome instability and inflammation. NE repair relies on activation of the endosomal sorting complex required for transport (ESCRT)-III repair machinery by the LEMD2-CHMP7 compartmentalization sensor, but little is known beyond these core factors. Using convergent proximity proteomics, we have inventorised proteins mobilised to the NE upon assembly of LEMD2-CHMP7 and activation of ESCRT-III. Within this NE repairome, we identify LRRC59 as a critical regulator of LEMD2 accumulation at NE ruptures. We find that LRRC59, together with the nuclear transporters KPNB1 and XPO1, restricts the assembly of LEMD2-CHMP7 complexes to the site of rupture. Disruption of this regulatory axis escalates LEMD2-CHMP7 spreading across the NE, driving torsional DNA damage in ruptured nuclei and micronuclei. Thus, our work identifies a central regulatory layer of NE repair centered on LRRC59 and KPNB1. We propose that altered LRRC59 levels and deregulated nuclear transport coordinately compromise NE repair, driving genome instability and cancer development.

The role of spatial confinement in guiding primordial germ cell migration and fate specification

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Mechanobiology of Development and Tissue Engineering 2, July 15, 2026, 16:15 - 17:15

Primordial germ cells (PGCs) are the pluripotent progenitors of male and female gametes in metazoans. In vertebrates, they are initially specified around gastrulation, after which they migrate as single cells across diverse tissue contexts towards a group of mesodermal cells, associating with these cells to form sex-specific reproductive organs. During their migration, PGCs undergo epigenetic remodeling and differentiation into a mature germline fate. However, current understanding of the mechanochemical cues driving PGC maturation is limited. We propose that the physical architecture of embryonic tissue creates a highly confining environment during PGC migration, requiring germ cells to undergo drastic nuclear deformations to reach their destination effectively. Using zebrafish embryos, we show that PGCs migrate through narrow gaps between tissues and intercellular spaces. While migrating within this environment, PGC nuclei undergo dynamic nuclear shapes changes, indicating confinement-induced nuclear deformation.

To understand the role of this deformation in germ cell fate determination of human PGCs, we analyzed migration of embryonic stem cell-derived PGCs using a PDMS-based microchannel device. Using this in vitro model, we observe that PGCs migrate through highly confining (30 μm2) as well as non-confining (100 μm2) microchannels without any chemotactic cues. We also report a dramatic downregulation of the pluripotency factor NANOG, indicating that nuclear deformation alone is sufficient to alter germ cell fate. Going forward, we aim to utilize in vitro confinement tools, combined with in vivo studies in zebrafish, to gain a comprehensive understanding of the migratory environment of germ cells and the role it plays in maturation of the germline.

Using ECM viscoelasticity to regulate cardiomyocytes' beating dynamics in vitro.

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Cell Mechanics Across Length Scales 1, July 15, 2026, 08:45 - 10:30

Cardiomyocyte contraction is inherently a thresholded mechanical process, cycling between a diastolic relaxed phase at baseline tension (preload/pre-stress) and a systolic contracted phase at peak tension. These thresholds – and the beating dynamics between them – strongly influence contractile output and tissue-level function in cardiac regenerative approaches. Leveraging traction force microscopy on elastic and viscoelastic substrates, we outline a viscoelastic design framework to prescribe cardiomyocytes' diastolic/systolic tension set-points and the dynamics connecting them.

Firstly, we show how purely elastic ECM stiffness steers contractility in hPSC-derived cardiomyocytes cultured on polyacrylamide substrates spanning physiological-to-pathological moduli. Using semi-analytical elastic traction force microscopy (eTFM), we decompose cardiac microtissue beating into diastolic mechanical stress, systolic mechanical stress, and effective contraction (systolic minus diastolic). Increasing stiffness shifts both diastolic and systolic stresses to higher values while also increasing effective contraction. Effective contraction correlates with diastolic and systolic stress with minimal sarcomere-length change, supporting ECM stiffness regulation of cardiomyocyte beating primarily via baseline cardiomyocyte pre-stress. In multicellular cardiac microtissues, fibroblast–cardiomyocyte interactions tune baseline pre-stress at the supracellular mesoscale, corroborating a mechanically targetable axis in which material elasticity couples to cell-generated pre-stress in cardiac microtissue–hydrogel constructs.

Secondly, to move beyond the control of diastolic/systolic threshold towards tuning the temporal dynamics between these thresholds, we use semi-analytical viscoelastic traction force microscopy (veTFM). We show that cardiomyocytes can sample different effective elastic limits within a single beating cycle, linking diastolic/systolic set-points to the elastic modulus band that cardiomyocytes can access on a viscoelastic ECM. Contractility scales primarily with total viscous dissipation more than any single relaxation timescale, with certain dissipation regimes predicted to introduce post-systolic features and thereby alter cardiomyocyte beating dynamics.

Disentangling microenvironmental dimensionality and architecture in stem cell mechanobiology

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Nuclear Mechanobiology 1, July 14, 2026, 14:00 - 15:45

Mechanical regulation of cell state is central to mechanobiology, yet it is still largely investigated using flat culture models that fail to reproduce physiologically relevant force distributions. While three-dimensional (3D) cell culture systems are increasingly adopted, it remains unclear to what extent finely tuned microarchitectural features, rather than dimensionality per se, govern cellular mechanical state.
Here, we directly disentangle the roles of dimensionality and architecture in the regulation of mesenchymal stem cell (MSC) state. Optically accessible 3D microscaffolds were fabricated by two-photon polymerization and designed with either graded pore architectures (10×10×15, 20×20×15 and 30×30×15 μm^3) or isotropic pores (15×15×15 μm^3), providing distinct spatial distributions of mechanical constraints. MSCs cultured on flat substrates and within the two 3D architectures were compared.
Cellular responses were assessed through quantitative mechanobiological readouts. Confocal imaging of actin, lamins and vinculin was used to evaluate cyto- and nucleoskeletal organization and adhesion properties. FLIM probed metabolic state and chromatin compaction, while Brillouin microscopy enabled label-free mapping of intracellular mechanical properties.
Flat culture provided an incomplete description of cell behaviour. Importantly, 3D environments made of the same material but featuring different architectures elicited distinct cellular responses. The two 3D designs induced differences in cytoskeletal organization, chromatin structure, metabolic profile and intracellular stiffness, demonstrating that mechanically meaningful cell states in 3D systems critically depend on architectural design.
This architecture-resolved framework provides a basis for linking defined mechanical states to biological function and will be integrated with transcriptomic and proteomic analyses to investigate stemness maintenance and immunomodulatory potential, guiding the development of advanced biomedical platforms and devices.
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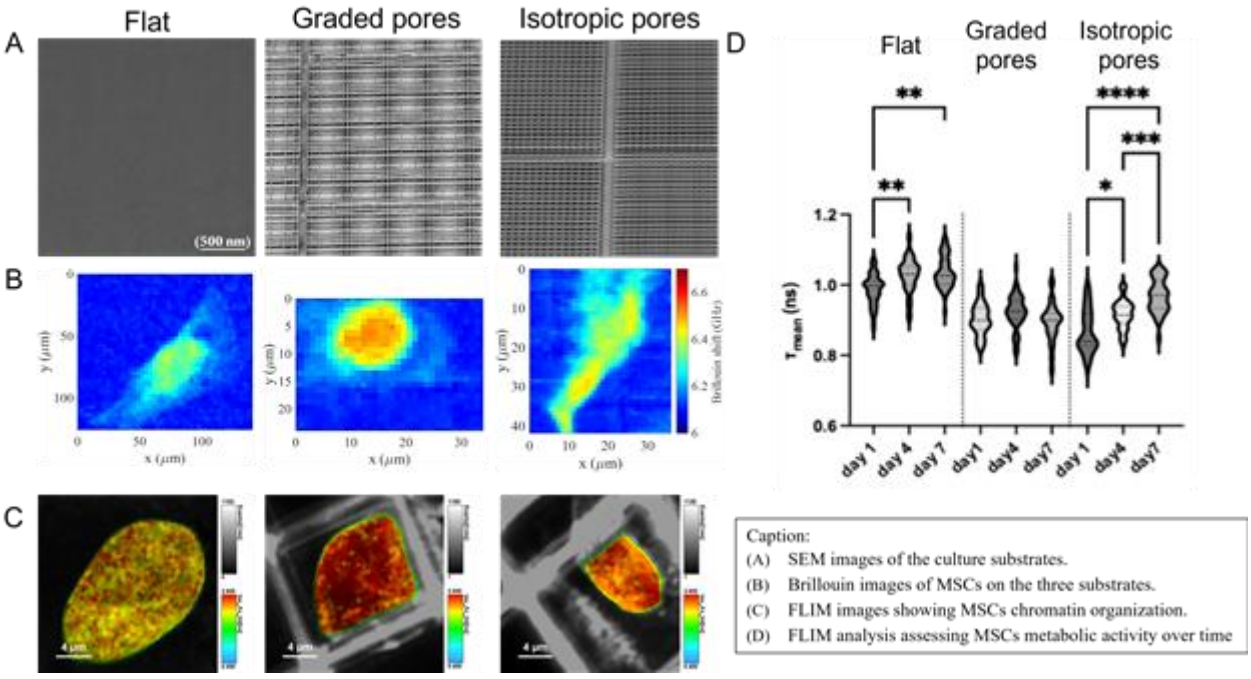

Caption:

(A) SEM images of the culture substrates.

(B) Brillouin images of MSCs on the three substrates.

(C) FLIM images showing MSCs chromatin organization.

(D) FLIM analysis assessing MSCs metabolic activity over time

Spatial and Temporal Regulation of Mechanical Homeostasis in the Outer Retina

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Mechanobiology of Ageing 1, July 15, 2026, 14:00 - 15:45

The organisation of multicellular systems fundamentally determines their function. Tissue mechanics has emerged as a key regulator of physiology and homeostasis, arising from cellular architecture and interactions with the extracellular environment. The concept of mechanical homeostasis describes how tissues maintain mechanical properties within an optimal range through dynamic cellular feedback loops. Across the lifespan, however, this balance is continually challenged by extracellular matrix remodelling and by shifts in cell death and proliferation. Post-mitotic tissues such as the retina offer a powerful model for investigating how mechanical homeostasis shapes physiological function, ageing, and disease.

To dissect mechanical homeostasis in the retina, we have combined stem-cell-based models with quantitative mechanobiological approaches to reconstruct and analyse the outer retina from the bottom up. Our earlier work revealed that the mechanical state of the retinal pigment epithelium (RPE) varies across visual angles, reflecting regional differences in basement membrane laminin composition, integrin engagement, and cellular workload. These adhesion-dependent properties, in particular traction forces, directly regulate RPE cells' capacity to support photoreceptors, linking tissue mechanics to visual function (Kozyrina A. and Piskova T. et al., EMBO Reports, 2025). More recently, we have modelled key aspects of outer-retinal ageing in vitro, including local extracellular matrix deformations (Reul F. et al., bioRxiv) and progressive reductions in RPE cell density (Piskova T. et al., bioRxiv). Each of these perturbations independently demonstrates that adaptation to time-related tissue remodelling challenges the mechanical homeostasis and drives functional decline, opening new perspectives for the diagnosis and treatment of age-related retinal diseases.

Together, these findings highlight mechanobiology as a unifying framework for understanding retinal ageing and pathology. By focusing on how tissues preserve mechanical equilibrium, rather than solely on end-stage failure, we can identify early vulnerabilities, mechanisms of resilience, and novel opportunities for therapeutic intervention.

Engineered mechanical heterogeneity through light-sheet grayscale volumetric bioprinting enables spatial and temporal control of cellular fate

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Advanced Tools for Multiscale Mechanobiology 1, July 14, 2026, 08:45 - 10:30

Introduction: Traditional biomaterials support long-term cell survival but typically are unable to provide the dynamic mechanical cues, particularly (visco)elasticity, that guide cell fate and tissue development. However, current biomaterial manufacturing methods offer limited control over mechanical heterogeneity in 3D and lack tools to analyse these properties with high spatial resolution. To address this, we introduce grayscaled light sheet volumetric bioprinting to achieve microscale, fully 3D spatial control of mechanical properties through grayscale-modulated light exposure. Using this approach, we aimed to achieve spatially defined and spheroid-position-driven (visco)elastic patterning, hypothesizing that grayscale-modulated crosslinking could regulate human mesenchymal stem differentiation via local mechanical cues and that Brillouin microscopy could track the spatiotemporal evolution of these properties.

Materials & Methods: Grayscaled light-sheet volumetric printing was used to create cell-laden gelatin methacryloyl-based hydrogels with controlled heterogeneous (visco)elasticity in the Pa to lower kPa range. Brillouin microscopy tracked (visco)elastic evolution at day 3, 6, and 20. Fate commitment was assessed by immunofluorescence. Nanoindentation measurements were conducted as a reference for obtained Brillouin shifts.

Results & Conclusion: Printed cellular environments with mechanical heterogeneity (Fig 1.) showed Brillouin shifts between 6.25±0.01 and 6.28±0.01 GHz, corresponding to elasticities of 0.2–2.0 kPa for softer and stiffer regions, respectively. Mechanical control was possible down to a length scale of 60 µm in cell-free and laden hydrogels. Differences in the 3D mechanical environment affected cellular behavior. Under dual osteogenic/adipogenic supplementation, stiff zones showed increased calcium accumulation, indicative of osteogenic commitment. Stiffness-patterned microenvironments, adaptively defined by spheroid position, modulated spheroid outgrowth within the soft environment. The herein introduced combination of grayscale Xolography for spatially and cell-position-driven controlled elasticity and Brillouin microscopy for spatiotemporal analysis of cell-material interactions, together with integrated in-situ microscopy for spheroid-aware fabrication of stiffness-patterned microenvironments, offers a unique platform opening new avenues for adaptive mechanobiological studies in 3D.

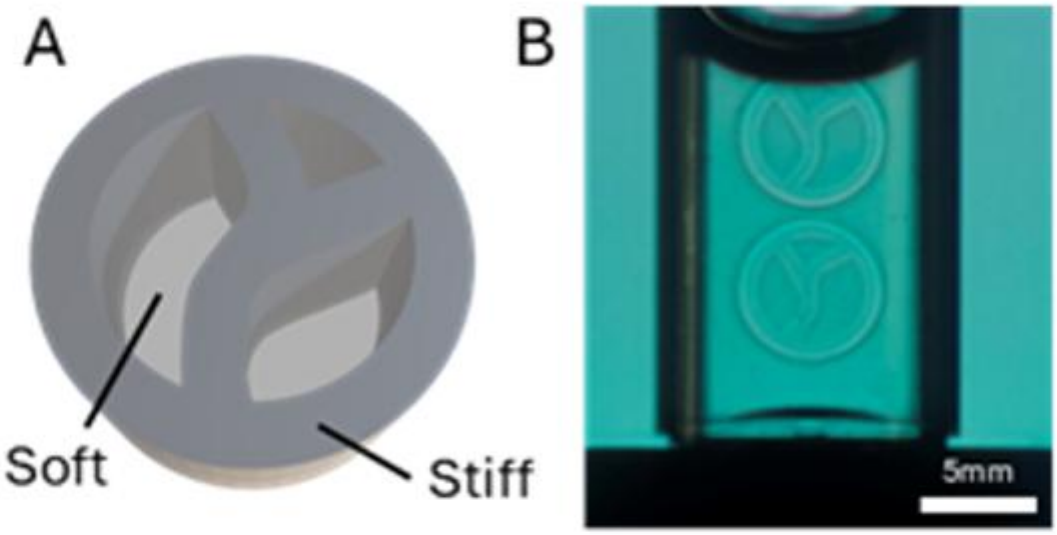

Figure 1. Greyscaled xclography print of a simplified trabecular structure. A) CAD model showing spatially defined stiff and soft regions. B) Schlieren image of the printed construct in a cuvette.

Metabolic stress tunes nuclear viscoelasticiy

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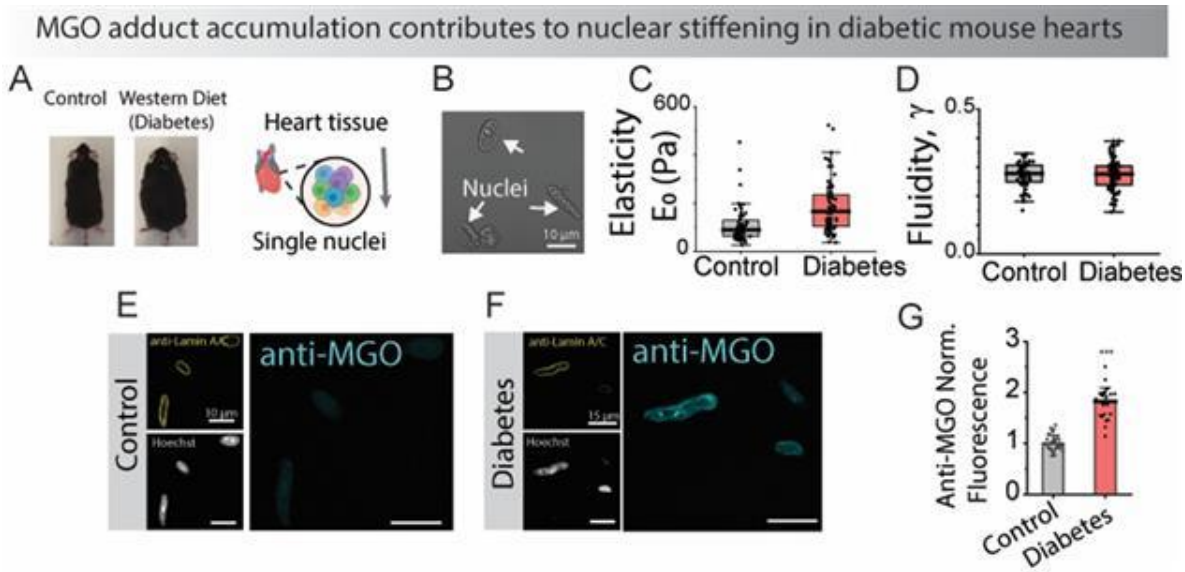
Nuclear Mechanobiology 1, July 14, 2026, 14:00 - 15:45

Cells constantly interpret mechanical cues to maintain tissue function. At the center of this process lies the nucleus, mechanically coupled to both the cytoskeleton and the extracellular matrix. Metabolic stress is known to alter extracellular matrix composition and stiffness, thereby reshaping the mechanical environment of tissues. Whether metabolic stress also directly modifies the mechanical behavior of the nucleus itself, however, remains unclear.
One major source of metabolic stress is glycation—a non-enzymatic covalent modification of proteins driven by reactive metabolites such as methylglyoxal (MGO), which accumulates in diabetes and aging. Here, we show that glycation stress fundamentally changes how the nucleus handles force. Using atomic force microscopy (AFM) combined with confocal imaging, we find that MGO-treated nuclei resist deformation but lose their ability to dissipate mechanical stress. Rather than adapting progressively to applied load, they accumulate strain and fail at high forces. This mechanically constrained behavior correlates with the accumulation of MGO-adducts on lamin A/C and chromatin, indicating that chemical modification of nuclear structural components reshapes nuclear mechanics at its core.
At the cellular level, metabolic stress reshapes force transmission to the nucleus. Glycated cells display nuclei that are flatter on stiff substrates compared to paired controls, consistent with enhanced nucleo-cytoskeletal mechanical coupling. Correspondingly, YAP mechanotransduction is altered: glycation increases YAP nuclear localization and enhances its responsiveness to substrate stiffness, indicating that metabolic stress amplifies the cellular response to mechanical cues. This mechanical phenotype is recapitulated in pathological contexts. Nuclei isolated from the myocardia of diabetic animals show increased stiffness that correlates with the accumulation of MGO adducts, demonstrating that glycation-associated nuclear stiffening is a feature of diabetic heart tissue.
Together, our findings reveal that metabolic stress does not simply perturb signaling, but it physically reshapes the nucleus, altering how cells sense and respond to force.



Specific adhesion and competition in cell migration and intercalation

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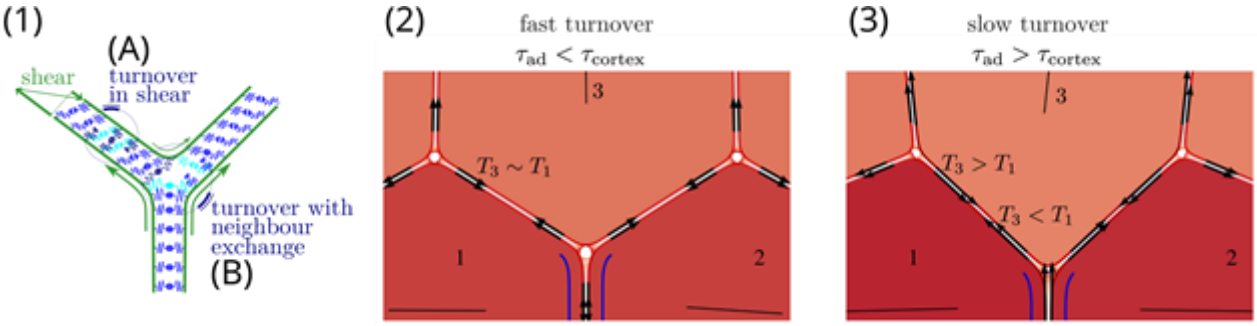
Mechanochemistry 2, July 15, 2026, 16:15 - 17:15

Living cells interact with their environment via specific adhesion, based on reversible intermolecular bonds forming between receptors on the cell surface and ligands populating the substrate—or other cells—with which they interact.

Bell and coworkers (Biophys J, 1984) have provided a thermodynamic framework which allows to determine the density of adhesions formed between two sites, depending on the distance separating them. This model has then mostly been used in the context where cell and substrate form parallel surfaces, and where bonds can form only along the shortest distance. However, especially in the context of shear between the surfaces (e.g, when the cell is sliding relative to it, Fig 1A), or in the case of a surface curvature radius comparable to binding distance (Fig 1B), a competition between sites has to be taken into account. This leads to a constrained numerical problem for which we propose an efficient algorithm using mathematical tools from optimisation theory.

The resulting algorithm allows us recapitulate force–distance curves while taking into account this competition for binding sites, and can be straighforwardly extended to nonlinear adhesion molecule rheologies, such as catch-bonds or slip-bonds (Etienne & Thibert, in preparation). It can then be used to investigate stochastic sliding friction, for instance in the context of cell migration, and cell neighbour exchange (T1) in the context of tissue morphogenesis.

In particular, we show how a comptetition of timescales between adhesion turnover and the viscoelastic relaxation of the contractile actomyosin cytoskeleton of epithelial cells can lead to an emergent effect, where slower subcellular dynamics lead to faster cell junction shrinkage during active T1 neighbour exchanges (Nestor-Bergmann et al, PLOS CB, 2022, Figs 2 & 3).



Mechanical activation of colon stem cells via magnetic and ultrasound stimulation

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In vivo Mechanobiology 2, July 16, 2026, 11:00 - 12:00

The colon tissue is continuously exposed to rhythmic physiological mechanical forces involved in intestinal transit. These pulsatile waves are transient and periodic, in contrast to the sustained mechanical pressure exerted by tumor growth. In previous work in mice, we demonstrated that 1kPa mechanical tumor growth pressure is an activator of the tumorigenic beta-catenin pathway, downstream of Ret activation (Fernandez-Sanchez et al., Nature 2015). This could be technically achieved by stabilizing in mouse colon conjunctive tissue ultramagnetic liposomes. We also showed that physiological pulsatile mechanical stress maintains the normal levels of mice colon stem cells Lgr5+ through activation of the mechanosensitive Ret kinase, thereby defining a new niche that Ret-dependently maintains homeostasis of the tissue (Nguyen et al., Communications Biology 2022). Conversely, when permanently stimulated by a magnetic mimicking-tumor growth analogue pressure, stem cell levels pathologically increase and undergo mechanically induced hyperproliferation and tumorigenic transformation. These findings identify Ret kinase as a mechanosensitive receptor that plays a central role in the interplay between mechanical cues and cell biology, thereby opening new therapeutic approaches to limit colorectal cancer progression. Consistently, systemic treatment with the chemotherapeutic agent Vandetanib, which inhibits Ret activation, reduced cancer stem cell production and decreased tumor burden in the mouse digestive tract.

Building on this work, we investigated whether ultrasound, generating both compressive and shear mechanical forces, could induce mechanical stimulation of colon cells via the mechanosensitive receptor Ret. Using low-intensity focused acoustic pressure, we succeeded in activating the Ret signaling pathway, increasing the level of mice colon stem cells and regulating cell proliferation (Zamfirov et al., Nature Biomedical Engineering 2024). Ultrasound-based modulation of mechanical signals thus represents a promising, non-invasive strategy to control cell behavior, with potential applications in regenerative medicine.

The Interaction with Nanotopographical Environment regulates nuclear mechanoresponse in mESCs via Histone Demethylase KDM3A

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Nuclear Mechanobiology 1, July 14, 2026, 14:00 - 15:45

Cell identity is traditionally viewed as a product of biochemical signalling, yet cells are exposed to defined physical landscapes, whose role in fate control remains unclear. In particular, how pluripotent stem cells integrate nanoscale extracellular cues into gene regulatory programs remains poorly understood. Here, we show that biomimetic substrate nanotopography acts as a potent regulator of naïve pluripotency in mouse embryonic stem cells (mESCs). Using supersonic cluster beam deposition, we generate substrates with defined nanotopography that recapitulate native features of extracellular matrix. We demonstrate that nanotopography induces a mechanically relaxed cell state characterised by reduced adhesion, cellular and nuclear softening, and altered nuclear architecture. These mechanical changes are coupled with chromatin remodelling, including reduced H3K27me3 and H3K9me2, redistribution of H3K9me3, and increased H3K4me3. Transcriptomic analyses reveal suppression of adhesion- and cytoskeleton-associated programs together with the activation of a naïve pluripotency transcriptional signature, including upregulation of Nanog. Mechanistically, we identify the H3K9 demethylase KDM3A as a mechanosensitive epigenetic regulator required for nanotopography-induced Nanog expression. Together, our findings uncover a novel mechanotransductive pathway directly linking extracellular nanotopography to chromatin state and pluripotency control

Active and passive contributions in the memory response of suspended microtissue to compression

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ECM Mechanobiology in Physiology and Disease 2, July 16, 2026, 11:00 - 12:00

Soft fibrous tissues are three-dimensional tissues which are shaped by interactions between fibroblasts cells and extra-cellular matrix (ECM). They form a continuous fibrous network within the body that provides strength to the organs, resisting against stretch, shear and compressive stresses they are subjected to. To realize this scaffold function they need to adapt their mechanical properties to those perturbations exerted at a variety of time-scales.
If transcription dependent mechanosensitive pathways can adapt the content of the ECM over the time scale of days, it is not well known whether and how these tissues adapt their mechanical properties at shorter time-scales (minutes to hours).
Here, using a novel setup of suspended microtissue, we investigate this question in the context of the response to compressive deformation. We find that those tissue stiffen in response to compression, in a timescale of minutes. Importantly, this stiffening is conserved over the time-scale of the perturbation applied, indicating a memory response to compression. We demonstrate that the collagenous ECM is responsible for this stiffening and controls the buffer period over which no stiffening is observed. However, cell mechanical activity, especially integrin dynamics, tends to balance this effect, by remodelling of the cell-ECM network. Those findings are backed by tissue-scale ablation experiments and by live imaging of the ECM and cell-ECM networks over compression.
Altogether, these findings underline the rapid remodelling of soft fibrous tissues in response to mechanical perturbation, which could have an impact in numerous physiological and pathophysiological contexts such as fibrosis.

Adipose-derived stem cells from Alzheimer's disease patients exhibit altered mechanotransduction associated with disease progression

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Mechanobiology of Ageing 2, July 15, 2026, 16:15 - 17:15

Emerging evidence suggests that disruption of mechanobiological cross-talk serves as a contributor to disease onset and progression. However, the mechanisms by which altered cell mechanics drive disease-related cellular dysfunction remain poorly understood.
In this study, utilizing Alzheimer's disease (AD) as a model system, we investigate whether intracellular accumulation of pathological hallmarks alters mechanical signal transmission and cellular behaviour. To address this, we employed adipose-derived stem cells isolated from patients with sporadic AD at distinct clinical stages, CDR1 (early AD) and CDR2 (advanced AD). Our findings demonstrate that AD cells exhibit increased cellular stiffness that correlates with disease progression, as assessed by Traction Force Microscopy and Brillouin microscopy. The mechanical alteration correlated with an abnormal mechanotransduction axis, including focal adhesions, actin-linking proteins, actin dynamics, and nucleoskeletal organization, culminating in proteostasis-related proteins dysfunction and disease progression.
Collectively, these findings suggest the presence of a mechanobiology feedback loop in which storage of pathological markers promotes cellular stiffening, impaired proteostatic mechanisms, and further drives Alzheimer's disease progression.

Mechanical strain of the intestinal epithelium directs absorptive lineage maturation

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Mechanobiology of Development and Tissue Engineering 2, July 15, 2026, 16:15 - 17:15

The intestinal epithelium is continuously subjected to a variety of mechanical forces, including extrinsic peristaltic contractions and intrinsic tensile forces generated by epithelial cell migration. Yet, how these mechanical cues influence the cellular processes underlying intestinal homeostasis remains poorly understood. We examined the impact of mechanical forces on intestinal cell dynamics by applying controlled external stretch to intestinal organoids, combined with high-throughput single-cell transcriptomic profiling and quantitative imaging. Our analyses reveal that prolonged cyclic mechanical strain alters the composition of differentiated intestinal cell populations. Specifically, we identify a strain-induced shift in the absorptive lineage towards a less mature state, with expansion of the population of early-stage enterocytes at the crypt–villus interface. This shift is associated with downregulation of transcriptional programs controlling enterocyte maturation within absorptive precursor populations. Our findings indicate that mechanical strain directs the maturation of the intestinal absorptive lineage, and highlight a role for mechanical forces in shaping intestinal epithelial composition and function. As the intestine serves as a paradigm for self-renewing tissues, our findings may define general principles by which tissue mechanics shape epithelial cell identity across organs.

Macromolecular order controls tissue-specific mechanical state transitions during gastrulation.

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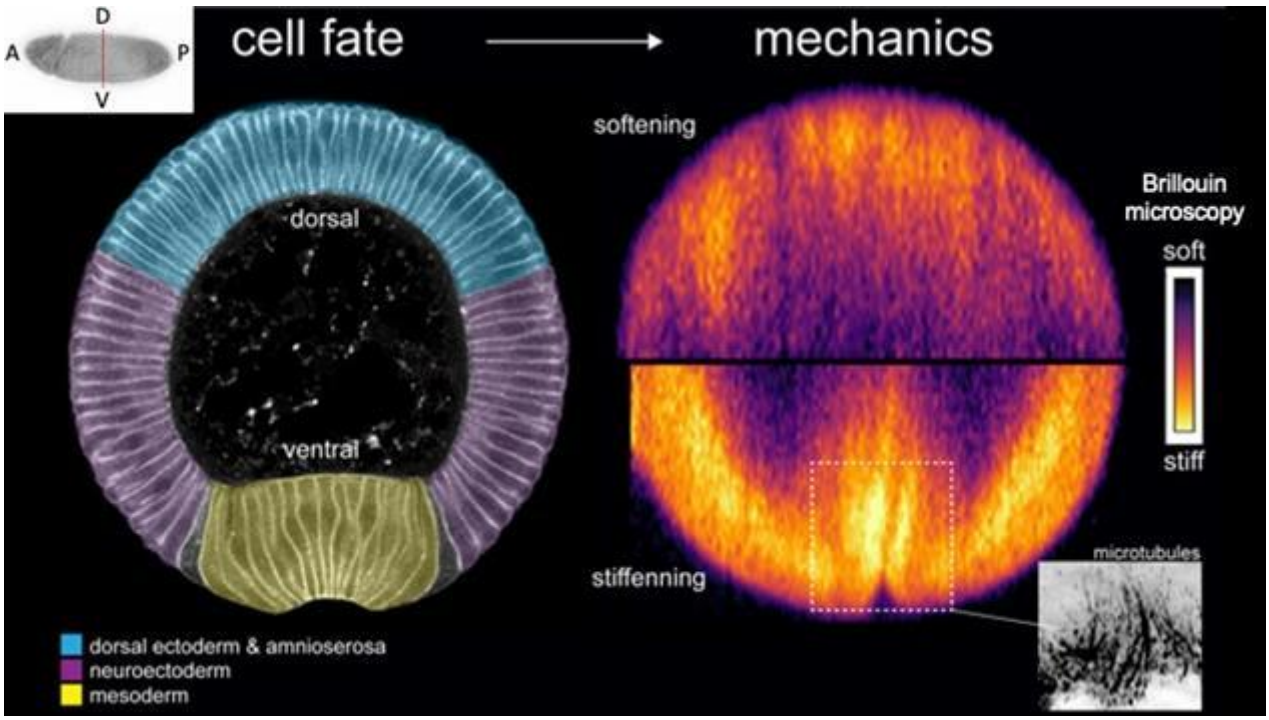
Mechanobiology of Development and Tissue Engineering 1, July 15, 2026, 14:00 - 15:45

During animal development, three-dimensional morphology emerges from the interaction between cellular forces and the material properties of cells, which determine their deformability. While force generation and transmission have been extensively characterised, how material properties are dynamically regulated across tissues within an intact, developing organism remains unresolved. Here, we employed line-scan Brillouin microscopy, a non-contact and label-free optical approach, to spatially and temporally map cell material properties across embryonic cell populations during Drosophila gastrulation. We identified tissue-specific mechanical state transitions. The mesoderm displayed a biphasic mechanical response, undergoing a transient stiffening during folding and invagination, followed by softening during epithelial-to-mesenchymal transition. In contrast, the ectoderm softened progressively during squamous morphogenesis from columnar precursors. Opposing mechanical trajectories therefore occurred concurrently but were associated with distinct morphogenetic programmes of the blastoderm. Our findings implicate microtubule order as a mechano-effector underlying these transitions. Mesodermal stiffening correlated in time and space with the alignment of tyrosinated, but not acetylated, microtubules. In the ectoderm, microtubules progressively reorganised: they became non-centrosomal, shortened along the apical-basal axis, and reoriented from a longitudinal (apical-basal) to a perpendicular alignment along the embryonic circumferential axis, consistent with increased longitudinal softening. Perturbing microtubule dynamics disrupted squamous morphogenesis, and preliminary data further indicated that interfering with microtubule turnover altered the ectodermal softening programme. To understand the role of these dynamic changes in material properties during morphogenesis, we performed physical modelling, which showed that a localised, transient increase in stiffness is required for tissue folding. Together, these findings support a model in which microtubule organisation regulates tissue-scale mechanical state transitions, linking macromolecular order to mechanical patterning in a developing embryo.


D
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cell fate
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softening
dorsal
ventral
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Brillouin microscopy
soft
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microtubules
dorsal ectoderm & amnioserosa
neuroectoderm
mesoderm

Endothelial Piezo1 Mechanosensing Orchestrates Adaptive and Maladaptive Trained Immunity in the Lung

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Immunomechanobiology 1, July 14, 2026, 14:00 - 15:45

The pulmonary endothelium forms a dynamic interface between circulating blood and tissue, continuously exposed to mechanical, infectious, and inflammatory stresses. Beyond serving as a passive barrier, endothelial cells (ECs) exhibit “trained” innate immunity, retaining memory-like functional adaptations after prior challenges. Yet the mechanisms that determine whether endothelial memory confers protection or drives chronic injury remain poorly understood. Here, we identify the mechanosensitive ion channel Piezo1 as a central regulator of endothelial immune training. Activation of Piezo1 during viral pneumonia induces sustained Ca^{2+} influx in pulmonary ECs, triggering Promyelocytic Leukemia (PML)-dependent transcriptional reprogramming and IFNβ–STAT1 signaling. Piezo1-mediated endothelial memory enhances antiviral defense upon homologous re-challenge but paradoxically increases susceptibility to secondary bacterial infection, particularly in females. Piezo1-deficient ECs (ΔEC-Piezo1) fail to develop antiviral memory yet are protected from heterologous bacterial injury, highlighting Piezo1’s role in defining the boundary between adaptive and maladaptive endothelial training. Mechanistically, Piezo1-driven Ca^{2+} signaling promotes PML SUMOylation and nuclear body assembly in aerocyte ECs, reshaping STAT1–STAT3 dynamics and driving neutrophil-dominated lung injury. Collectively, these findings reveal a mechanistic framework in which mechanical forces and inflammatory cues converge to orchestrate endothelial memory. Endothelial Piezo1 signaling is critical for antiviral protection but can also induce maladaptive, sex-biased vulnerability to secondary infections. Targeting the Piezo1–PML axis may therefore provide a novel strategy to modulate endothelial-trained immunity and improve outcomes following recurrent pulmonary infections.

This project is also supported in part by federal funds from the National Heart, Lung, and Blood Institute, National Institutes of Health, Department of Health and Human Services, under R01HL045638, and T32HL007829.

From matrix mechanics to mechanogenetics: regulating inflammation in post-traumatic osteoarthritis

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Immunomechanobiology 1, July 14, 2026, 14:00 - 15:45

Repairing damaged articular cartilage remains a major clinical challenge. Following joint injury, cartilage commonly degenerates into post traumatic osteoarthritis (PT-OA), resulting in loss of joint functionality and pain. PT-OA is characterised by persistent low-grade inflammation, extracellular matrix (ECM) degeneration, and altered chondrocyte mechanobiology. Although mechanical loading is essential for cartilage homeostasis, chondrocytes must continuously interpret dynamic mechanical, inflammatory and matrix-derived cues within a constantly evolving joint microenvironment. Failure of these adaptive responses is increasingly recognised as a key driver of degeneration and the failure of regenerative biomaterials. However, how matrix mechanics, mechanotransduction, and inflammatory signalling converge to shape chondrocyte behaviour remains poorly resolved. Here, we investigated PT-OA through a mechanobiology framework spanning biomaterials, mechanotransductive signalling and responsive therapeutics. Using cartilage ECM-inspired biomaterials with tunable viscoelastic and compositional properties, we examined how matrix context regulates nascent ECM deposition and early human articular chondrocyte responses, providing insight into how time-dependent biomaterial mechanics shape cartilage-relevant cell behaviour. In parallel, we investigated how Piezo1-mediated mechanotransduction modulates inflammatory signalling in chondrocytes. Using Yoda1-mediated Piezo1 activation in combination with PT-OA-relevant inflammatory stimuli, we characterised signalling responses under inflammatory and mechano-inflammatory conditions. Acute Piezo1 activation transiently engaged inflammatory and stress-associated signalling pathways. Unexpectedly, however, sustained combined Piezo1 and inflammatory stimulation altered downstream signalling responses over time and was associated with delayed vacuolisation and marked morphological changes, suggesting chondrocyte responses may not conform to current models of piezo1-driven inflammatory amplification alone. Finally, we discuss our progress towards NF-κB-responsive mechanogenetic systems designed to enable context-aware regulation of inflammation in PT-OA. Together, this work highlights how matrix context and mechanotransduction shape regenerative and inflammatory responses in cartilage, while moves towards establishing a framework for engineering responsive therapies informed by mechanobiological state.

Spatially controlled tissue properties foster epithelial invagination

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Mechanobiology of Development and Tissue Engineering 1, July 15, 2026, 14:00 - 15:45

Epithelial folding is an essential part of organogenesis and pathological development. While physical tissue properties crucially impact their development, little is known about the mechanical properties of folding epithelia. Here we use gastrulation in the chordate Amphioxus as a model for epithelial invagination. Tissue-scale micropipette-aspiration reveals spatial differences in bending modulus and visco-elastic tissue behaviour. We use a continuum model to demonstrate that these differences can foster invagination. Equivalent local differences in invaginating cell sheets across kingdoms indicates that this is a universal strategy to overcome geometrical constraints.

High-Throughput Confined Migration Reveals a Molecular Signature of Physical Confinement

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Advanced Tools for Multiscale Mechanobiology 1, July 14, 2026, 08:45 - 10:30

Physical confinement is a ubiquitous mechanical feature of tissues that strongly shapes cell migration in development, homeostasis, and disease. Although existing microfabrication approaches can model the extreme confinement cells encounter in vivo, these systems are typically low-throughput, closed, and difficult to integrate with downstream molecular analysis. Here, we present a high-density confinement platform that enables mechanobiology studies of migration through long, micron-scale channels at unprecedented scale. Using photolithography, thin-film PDMS replication, and iterative layer-by-layer plasma bonding, we generated porous membranes containing dense arrays of microchannels with tunable cross-sectional geometry and extreme aspect ratios. Integrated into custom 3D-printed inserts, this open-format system provides over three orders of magnitude more microchannels per well than existing platforms while remaining compatible with standard cell culture workflows, cell recovery, and in situ lysis. Using this platform, we observed striking confinement-dependent changes in cell morphology during transmigration and, for the first time, recovered sufficient numbers of post-migratory cells exposed to extreme confinement for chromatin accessibility and RNA-sequencing analyses. These data revealed distinct transcriptomic and chromatin accessibility states induced specifically by severe physical confinement, pointing to a previously inaccessible molecular signature of confined migration. By combining precise control over confinement geometry, high throughput, and scalable post-migration recovery, this platform creates a new opportunity to define how extreme physical confinement reshapes cell state and function, and to uncover mechanistic links between tissue architecture, migration, and disease.

Establishing a dynamic, subcellular understanding of mechanosensation using Drosophila antennal mechanosensors.

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In vivo Mechanobiology 2, July 16, 2026, 11:00 - 12:00

Specialized sensory cells use mechanically-sensitive ion channels to detect environmental forces. Molecular structures dynamically link external forces to these channels, sculpting cellular sensitivity. Mechanosensory cells can adaptively maintain or modulate the forces impinging on their ion channels, enabling responses to distinct components of external stimuli. Fundamentally, these processes underpin mechanical sensation and expand stimulus-response diversity; however, the mechanics of their molecular orchestration remain unclear. We would like to understand how interdependent molecular systems underlie tuning and feedback-adaptation in primary mechanosensory neurons.

Towards this end, we have established an in situ system that allows both precise control of mechanical stimuli and simultaneous, direct access to sensory cells. We achieve this using Drosophila antennal mechanosensors—diversely tuned, ciliated primary sensory neurons. Here, we piezoelectrically actuate the antenna to control the cell's native mechanical input. Then, deep-UV laser microdissection enables single-cell patch-clamp recording, or subcellular 2-photon calcium imaging. Using laser vibrometry as a complementary approach, we infer cellular mechanics by monitoring antenna-level changes during acute manipulations.

Using these techniques, we indeed find evidence for multiple cellular processes fine-tuning mechanosensory responses. Adaptation appears to be driven by force- or transduction-dependent feedback, and molecular players along the mechanosensory cilium show differential contributions. Interdependent active and passive components alter the forces experienced by mechanically-sensitive ion channels, ensuring they remain within stable operating ranges. These findings show how multiple processes can operate together to drive sensory responses, and our system offers new insights into subcellular specializations underlying mechanical sensitivity.

Investigating the effect of nanovibration on tumour models

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Sonomechanobiology 1, July 16, 2026, 08:45 - 10:30

Animal models have been widely used to study a variety of diseases, including cancer; however, they often fail to reflect the complexity of human pathology. Advances in 3D cell-based disease models are enabling more physiologically relevant representations of human disease and may provide in vitro alternatives to animal experiments.
Cells are known to respond to mechanical signals within their microenvironment. Previous studies applying nano-amplitude vibration to mesenchymal stem cells have demonstrated increased osteogenic differentiation [1, 2]. In contrast, cancer cells exhibit altered mechanosensitivity compared to their healthy counterparts, suggesting a potential basis for future diagnostic and therapeutic approaches [3].
Existing technologies, such as microfluidics, offer scalability and reproducibility while maintaining compact and efficient designs, enabling high-throughput testing for both diagnostics and therapeutics.
This study aimed to investigate the response of cancer cells to mechanical stimulation within a microfluidic environment. HCT116 cells were seeded into microfluidic devices, forming either 2D monolayers or 3D spheroids depending on device architecture and substrate treatment. The incorporation of hydrogels was also explored to assess the influence of matrix properties on cell response. Following cell adhesion or spheroid formation, devices were subjected to nanovibration at 1 kHz, 30 nm, and fixed after 24, 48 and 72 hours of stimulation. Analysis revealed that nanovibrated spheroids exhibited an increase in spheroid area, particularly when cultured within a hydrogel matrix. However, Ki-67 staining did not indicate a change in proliferation. Combined, it is hypothesised that nanovibrational stimulation modifies environmental attachment of cancer cells, indicating the potential utility of this platform for modelling cancer progression within increasingly fibrotic microenvironments.

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Extracellular Matrix Rigidity Drives Cytoskeletal and Epigenetic Remodeling in Microglia

Vaneeza Kausar[1], Sebastian Alvarado[1,2], Maral Tajerian[1,2]
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Immunomechanobiology 3 and Flash Talks S3b, July 14, 2026, 17:15 - 17:45

Microglia, the immune residents of the brain, are highly sensitive to their environment. They exhibit remarkable plasticity, adapting their morphology and function to meet environmental demands. Through the process of "glial education," environmental cues shape microglial identity by engaging epigenetic mechanisms that turn genes on and off. Microglia are surrounded by the extracellular matrix (ECM), a structure whose mechanical properties, particularly rigidity, change dynamically with aging and injury. Mechanical signals from the ECM can be transmitted to the nucleus, where they influence epigenetic states. These biomechanical shifts can alter glial education, yet how ECM rigidity drives epigenetic changes in microglia remains unknown. After showing that ECM rigidity shapes microglial morphology and engulfment, we now examine its molecular and epigenetic components, in particular, histone modifications and DNA methylation patterns. We hypothesize that microglia raised on different substrate rigidities develop distinct post-translational histone modification (PTM) profiles, shaped in part by cell-specific expression patterns. These PTMs are predicted to modulate chromatin accessibility and regulate the expression of key genes involved in microglial inflammatory responses and synaptic remodeling. To explore this, BV2 cells were cultured on collagen-coated PDMS substrates of varying stiffness (0.2, 2.0, 8, 16, 32, and 64 kPa). Phalloidin staining was used to visualize actin organization as an indication of cytoskeletal states influenced by underlying chromatin regulation. Mass spectrometry analysis of histone PTMs revealed pronounced stiffness-dependent shifts, including H3K79me (transcriptional activation), H3K36ac (enhancer activity), H3K122ac (DNA damage response), H1K25me (chromatin compaction), and rare modifications H3R49me and H3Q55me, which indicate lasting alterations to the chromatin landscape. This work establishes that ECM rigidity drives stiffness-dependent PTM remodeling, thereby linking biomechanical cues to the epigenetic regulation of microglial phenotypes. Future work will examine DNA methylome sequencing patterns and additional mechano-transduction pathways.

Single-Molecule Mechanosensing Beyond FRET Using Synthetic PEG Sensors in the ECM

Dr Alex Koch[1], Eldhose Skaria[1], Guillaume De Bo[1,2], Tom Jowitt[1], Andrew Gilmore[1], Sarah Woolner[1]
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Advanced Tools for Multiscale Mechanobiology 2, July 14, 2026, 11:00 - 12:00

Understanding molecular-scale forces is central to mechanobiology, yet directly measuring force transmission within the extracellular matrix (ECM) remains challenging. Genetically encoded Förster Resonance Energy Transfer (FRET)-based tension sensors are difficult to express in extracellular environments and are intrinsically limited to small distance changes. To overcome these constraints, we are developing synthetic mechanosensors that report force-induced conformational changes via fluorescence and correlation-based readouts.

We have synthesised and optimised a dual colour PEG-based mechanosensor, establishing an efficient, modular synthesis pathway that preserves fluorescence brightness while maintaining water solubility. We have demonstrated, via a FRET readout, that this mechanosensor responds to incorporation within a hydrogel, validating our sensor's ability to report distance in a mechanically tuneable 3D environment.

To extend the range of distance beyond FRET, we are developing fluorescence cross-correlation spectroscopy (FCCS) as a distance-based readout, where force-induced separation of the two fluorophores measurably decreases cross-correlation. Preliminary measurements support the feasibility of this approach, enabling us to quantify distance changes over tens to hundreds of nanometres, beyond the current range of FRET.

Taking our sensor beyond conventional fluorescence readouts, we have also synthesised a DNA-PAINT compatible version of our mechanosensor, replacing fluorophores with DNA docking strands. Thus, enabling nanoscale localisation and multiplexed detection for force sensing applications in fixed tissues.

Together, these advances establish a modular mechanosensor platform that bridges single-molecule force sensing, synthetic ECM integration, and multi-application fluorescence imaging. This work lays the foundation for quantitative force measurements across length scales inaccessible to traditional FRET-based approaches.

What we learned from 6000 patient blood samples measured with deformability cytometry: age, biomarkers, and disease mechanotypes

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Immunomechanobiology 2, July 14, 2026, 16:15 - 17:15

Deformability cytometry (DC) is a label-free microfluidic imaging technique that quantifies mechanical and morphological properties of single cells at rates of up to 1000 cells/s directly from brightfield images.

Here, we analyse >6000 whole-blood samples from a clinical cohort spanning newborns to adults. We employed an automated analysis pipeline combining image-derived feature extraction with clustering and classification of the main blood cell populations, replacing manual gating.

Using this framework, we established age-dependent baselines of cell size, deformation and Young's modulus for the major blood cell classes and identified systematic developmental trends over the first 18 years of life. We then correlated DC-derived features with routine clinical biomarkers, including C-reactive protein (CRP), interleukin-6 (IL-6), procalcitonin (PCT), ferritin and white blood cell counts. Specific mechanotypes, particularly of neutrophils, monocytes and lymphocytes, showed associations with these markers and provided information beyond simple cell counts. Notably, neutrophils, which are among the earliest cellular responders during acute infection, exhibited pronounced mechanotype changes, including an increase in cell size with rising IL-6 levels, supporting the idea that physical phenotyping may help detect infection at an early stage.

Finally, by stratifying samples according to clinical information and diagnostic groups, we identified disease-related mechanotype patterns across a range of infectious and inflammatory conditions. These included, for example, differences between acute gastrointestinal infections and chronic inflammatory bowel disease, as well as distinct signatures associated with Epstein–Barr virus and cytomegalovirus. These results show that deformability cytometry captures clinically relevant biophysical phenotypes of blood cells and highlight its potential as a complementary approach for blood-based diagnostics and immune state profiling.

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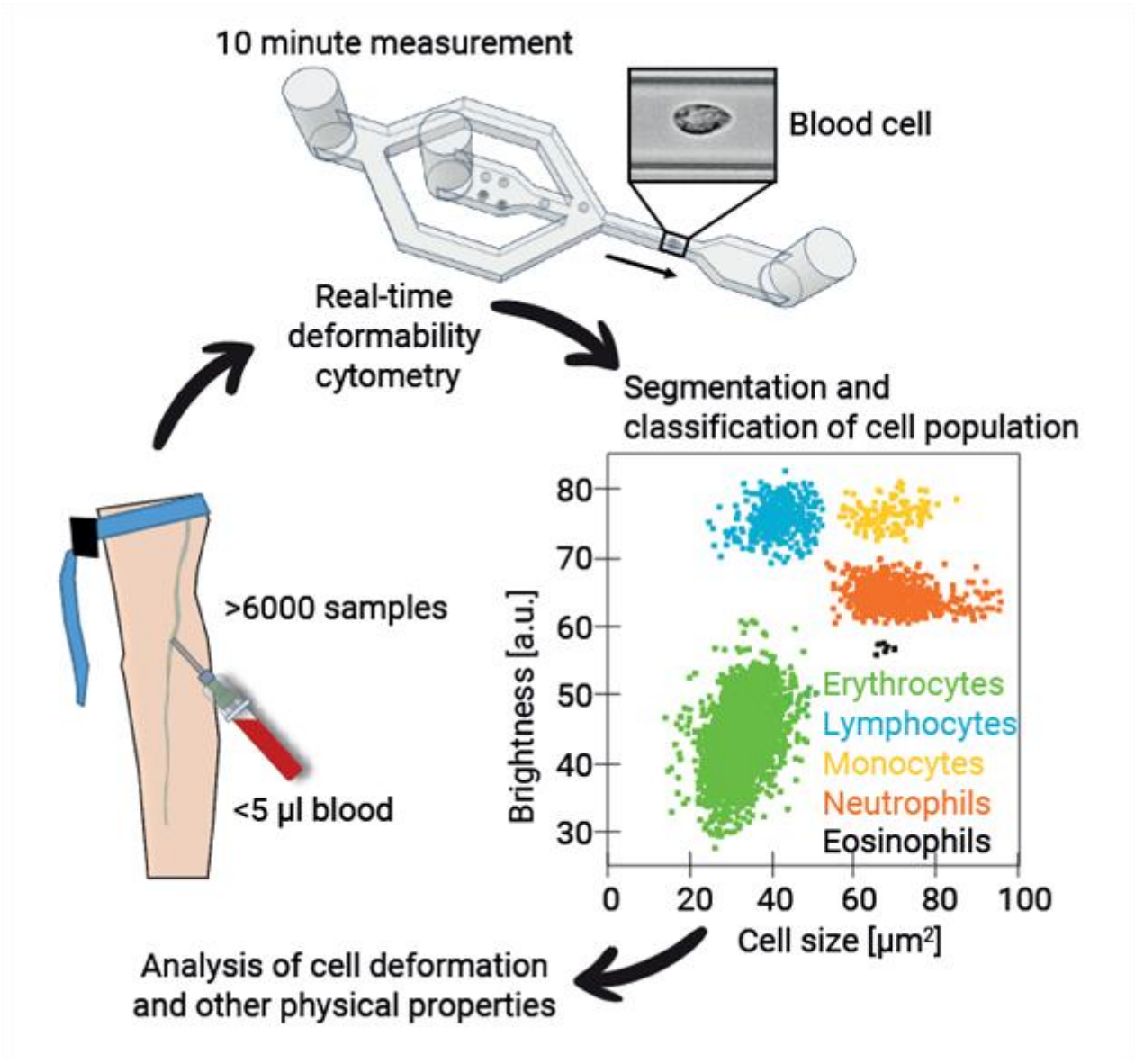
[2] Toepfner et al., eLife (2018)
[3] Kubánková et al., Biophys. J. (2021)
[4] Kaliman et al., Biophys. J. (2025)


10 minute measurement
Blood cell
Real-time
deformability
cytometry
Segmentation and
classification of cell population
>6000 samples
<5 µl blood
Brightness [a.u.]
80
70
60
50
40
30
0
20
40
60
80
100
Cell size [µm²]
Erythrocytes
Lymphocytes
Monocytes
Neutrophils
Eosinophils
Analysis of cell deformation
and other physical properties

Mechano-metabolic interplay in bladder cancer invasion

Prof. Malgorzata Lekka[1], Sara Metwally[1], Dorota Gil[2], Justyna Śmiałek-Bartyzel[1], Joanna Pabijan[1]
[1]The Henryk Niewodniczanski Institute of Nuclear Physics, Polish Academy of Sciences, Poland, [2]Jagiellonian University Medical College, Poland

Mechanobiology in Disease and Mechanomedicine 1, July 13, 2026, 14:00 - 15:45

Mechanical cues from the extracellular matrix (ECM) are central regulators of tumor progression, influencing cytoskeletal organization, adhesion signaling, and metabolism. How cancer cells integrate mechanical stimuli with metabolic pathways across stages of malignancy remains poorly understood. Building on our early biomaterial-based studies using chitosan, which showed that altered cellular mechanics seems to be linked to reduced energy production, we investigated mechano-metabolic coupling in bladder cancer models representing benign (HCV29), low-invasive (HT1376), and highly invasive (T24) phenotypes. We examined the effects of increased environmental viscosity on single-cell mechano-metabolism. Elevated viscosity reduced mitochondrial activity and ATP levels without affecting viability, indicating metabolic stress independent of cell death. HCV29 cells recovered metabolic activity upon return to standard conditions, unlike HT1376 and T24 cells, highlighting cell-line-specific mechanometabolic resilience. High-viscosity environments also induced cytoskeletal reorganization, including stress fiber formation in less viscous media and actin aggregates in highly viscous alginate, accompanied by altered mechanotransduction. Furthermore, to model heterogeneous tumor microenvironments, we engineered collagen–hyaluronan hydrogels with tunable stiffness. Matrix stiffening reprogrammed spheroid architecture, motility, and metabolic signaling in a stage-dependent manner. In compliant matrices, invasion relied on MMP-2–mediated ECM remodeling, whereas in rigid environments, proteolytic motility was suppressed, revealing a critical stiffness threshold that dictates the invasive strategy. Adhesion and metabolic markers indicated distinct mechano-metabolic coupling across phenotypes, reflecting stage-specific adaptation to mechanical stress.
Collectively, our results integrate early biomaterial-induced metabolic perturbations with modern concepts of ECM-driven tumor plasticity, establishing a framework in which cancer cells link mechanical sensing to metabolic regulation. They underscore mechano-metabolic interactions as key determinants of behavior and invasion, highlighting potential therapeutic strategies targeting mechanical and metabolic vulnerabilities (this work was supported by the National Science Center (Poland), project NCN-OPUS no UMO-2021/41/B/ST5/03032).

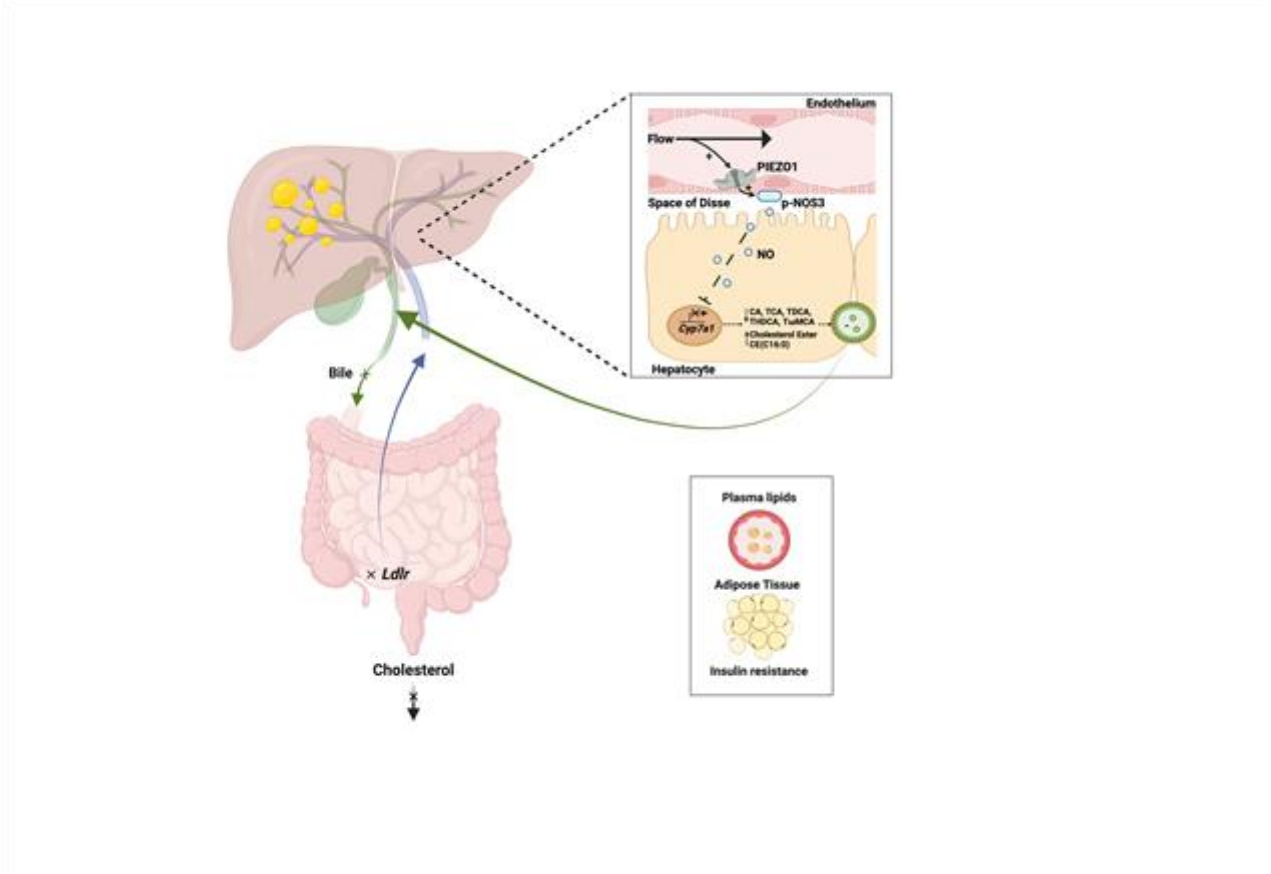
Endothelial force sensing signals to parenchymal cells to regulate lipid metabolism

Associate Professor In Integrative Liver Biology Laeticia Lichtenstein[1], Chew Cheng[2], Mouath Bajarwan[2], Shaili Patel[3], Charalampos Konstantinou[3], David Beech[2]
[1]University Of Leeds, School Of Food Science And Nutrition, United Kingdom, [2]Department of Hepatobiliary and Transplant surgery St James Hospital Leeds, United Kingdom, [3]University of Leeds, Faculty of Medicine, United Kingdom

In vivo Mechanobiology 1, July 16, 2026, 08:45 - 10:30

How cardiovascular activity interacts with lipid homeostasis is incompletely understood. We postulated a role for blood flow acting at endothelium in lipid regulatory organs. Transcriptome analysis was performed on livers from mice engineered for deletion of the flow-- sensing PIEZO1 channel in endothelium. This revealed unique up-regulation of Cyp7a1, which encodes the rate-- limiting enzyme for bile synthesis from cholesterol in hepatocytes.

Consistent with this effect were increased gallbladder and plasma bile acids and lowered hepatic and plasma cholesterol. Elevated portal fluid flow acting via endothelial PIEZO1 and genetically enhanced PIEZO1 conversely suppressed Cyp7a1. Activation of hepatic endothelial PIEZO1 channels promoted phosphorylation of nitric oxide synthase 3, and portal flow-- mediated suppression of Cyp7a1 depended on nitric oxide synthesis, suggesting endothelium-- to-- hepatocyte coupling via nitric oxide. PIEZO1 variants in people were associated with hepatobili-
ary disease and dyslipidemia. The data suggest an endothelial force sensing mechanism that controls lipid regula-tion in parenchymal cells to modulate whole-- body lipid homeostasis.



The atypical adhesion protein PINCH-3 controls TGFβ-driven matrix biogenesis in glioblastoma

Alexander Loftus[1], Ben McKinnel[1], Marianna Romano[1], Alessia Reyes[1], Rose Winchester[1], Maarten Van Den Ancker[1], Andrew Jackson[1], Alexander von Kriegsheim[1], Adam Byron[2], Neil Carragher[1], Margaret Frame[1]
[1]Institute of Genetics and Cancer, University of Edinburgh, United Kingdom, [2]Division of Molecular and Cellular Function, School of Biological Sciences, Faculty of Biology, Medicine and Health, University of Manchester, United Kingdom

ECM Mechanobiology in Physiology and Disease 2, July 16, 2026, 11:00 - 12:00

Glioblastoma is a lethal cancer that, despite arising in the normally soft and sparsely fibrous brain, frequently develops a rigid, fibronectin-rich extracellular matrix (ECM) associated with invasion, post-surgical recurrence and poor patient outcome. How GBM cells establish this mechanically aberrant matrix environment remains unclear. Here, we identify PINCH-3, an atypical and previously uncharacterised paralogue of the adhesion protein PINCH-1 expressed in a subset of patient-derived GBM cells, as a driver of fibronectin matrix biogenesis. PINCH-3 is incorporated into the ILK/PINCH/Parvin (IPP) adhesion complex, rewiring its output towards TGFβ signalling and a Smad2-dependent transcriptional programme that promotes fibronectin expression and fibrillar ECM assembly. This matrix assembly programme supports formation of tensin-3-positive and mechanotransductive fibrillar adhesions, consistent with enhanced cell–matrix coupling and the capacity for force-dependent ECM organisation and signalling. Mechanistically, the unique terminal extensions of PINCH-3 bind the endocytic trafficking receptor LRP1 and latent TGFβ-binding proteins, promoting TGFβ/Smad2 activation. Loss of PINCH-3 or LRP1 reduces Smad2 activity and fibronectin fibrillogenesis, while exogenous TGFβ rescues these defects, supporting a model in which a PINCH-3–LRP1 complex regulates TGFβ availability upstream of Smad2. Together, these findings reveal an unexpected mode of adhesion complex plasticity that enables GBM cells to construct a fibronectin-rich, mechanically permissive tumour matrix in the brain.

Mechanical response of epithelial tissues to curvature

Marine Luciano[1]
[1]University Of Mons, Belgium

Mechanobiology of Development and Tissue Engineering 1, July 15, 2026, 14:00 - 15:45

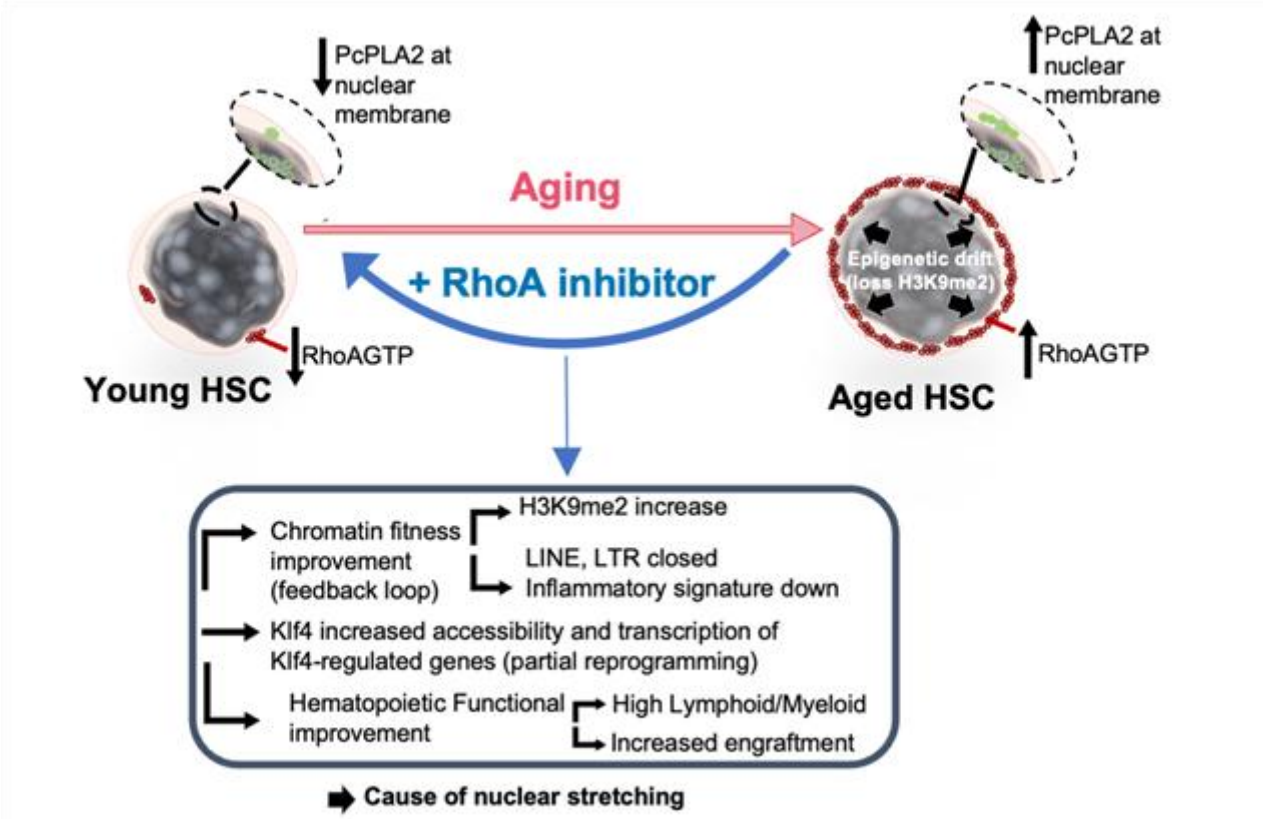
The optimal functioning of many organs relies on the curved architecture of their epithelial tissues. Yet, how epithelia detect and integrate changes in curvature remains poorly understood. A first challenge was therefore to engineer physiologically relevant curved epithelial tissues in vitro. Using curved polyacrylamide-based hydrogels that faithfully replicate the geometry and curvature range of human body structures, we demonstrated that epithelial monolayers actively sense curvature through coordinated redistribution of cytoskeletal tension and nuclear mechanoadaptation. We showed that curvature induces spatial gradients of contractility, reshapes nuclear morphology, and modulates YAP subcellular localization and chromatin organization. Using bowl-shaped microwells reproducing lobular geometries, we further demonstrated that epithelial tissues reorganize their actin cortex according to curvature amplitude, modulating YAP localization and nuclear architecture.
Because organ-level curvature often spans multiple length scales, we next developed a hybrid system coupling wavy hydrogels to an inducible rolling PDMS multilayer, generating tunable tubular structures with corrugated inner surfaces that enable the study of epithelial mechanical and functional responses to rapid anisotropic curvature changes across length scales. We found that curvature at distinct length scales differentially regulate cellular alignment, nuclear morphology and positioning, revealing a hierarchical integration of geometric cues.
In vivo, epithelial tissues are also exposed to dynamic curvature fluctuations. To address how epithelia sense and adapt to time-varying curvature, we developed a pneumatically actuated microfluidic device that applies cyclic concave–convex deformations to epithelial monolayers cultured on an ultrathin PDMS membranes. Using confluent epithelial monolayers, we showed that cyclic curvature modulation elicits geometry-dependent mechanoresponsive signaling, including dynamic changes in YAP subcellular localization, highlighting the temporal dimension of curvature sensing.
Together, these findings establish curvature as a multiscale and dynamic regulator of epithelial mechanics, linking geometry to cytoskeletal organization, nuclear architecture, and mechanotransduction pathways.

Targeting RhoA nuclear mechanoactivity rejuvenates aged hematopoietic stem cells

Dr. Eva Mejia-Ramirez[1,2,3], Pablo Iáñez Picazo[4,5], Barbara Walter[1,2], Sara Montserrat-Vázquez[1,2], Francesco Affuso[1,2], Stefan Wieser[6], Fabio Pezzano[7], Lloïc Reymond[7], Jorge Castillo-Robles[2,3,8], Francesca Matteini[1,2], Loris Mularoni[2], Dídac Macià[4], Ángel Raya[2,3,8,9], Verena Ruprecht[6,7,9], Yi Zheng[10], Paula Pertrone[4,11], MCarolina Florian[1,2,3,9]
[1]Stem Cell Aging Group, Regenerative Medicine Program, The Bellvitge Institute for Biomedical Research (IDIBELL), L'Hospitalet de Llobregat, Barcelona, Spain, [2]Program for advancing the Clinical Translation of Regenerative Medicine of Catalonia, P-CMR[C], Spain, [3]Center for Networked Biomedical Research on Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN), Spain, [4]ISGlobal, Barcelona, Spain, [5]Universitat Pompeu Fabra (UPF), Spain, [6]University of Innsbruck, Innsbruck, Austria, [7]Center for Genomic Regulation (CRG), The Barcelona Institute of Science and Technology, Barcelona, Spain, [8]Stem Cell Potency Group, Regenerative Medicine Program, The Bellvitge Institute for Biomedical Research (IDIBELL), L'Hospitalet de Llobregat, Barcelona, Spain, [9]The Catalan Institution for Research and Advanced Studies (ICREA), Barcelona , Spain, [10]Division of Experimental Hematology and Cancer Biology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, United States, [11]Digital Health Unit, Barcelona Supercomputing Center, Spain

Mechanobiology of Ageing 1, July 15, 2026, 14:00 - 15:45

Mechanical alterations contribute to the decreased regenerative capacity of hematopoietic stem cells (HSCs) upon aging. RhoA is a key regulator of mechanosignaling, but its role in mechanotransduction in stem cell aging remains unclear. Here we demonstrate that RhoA is activated by increasing nuclear envelope (NE) tension by cell confinement and by osmotic shock. Interestingly, our data show that aged HSCs experience physiologically higher intrinsic NE tension and RhoA activation. We show that pharmacological inhibition of RhoA activity lowers NE tension in aged HSCs. Feature image analysis of HSC nuclei reveals that an aged dependent chromatin remodeling is responsible of higher NE tension levels upon aging. Moreover, our data show that RhoA inhibition restores youthful levels of the heterochromatin marker H3K9me2 in aged HSCs and decreases chromatin accessibility and transcription at retrotransposons. Finally, we demonstrate that RhoA inhibition in aged HSCs upregulates Klf4 expression and transcriptional activity, improving aged HSC regenerative capacity and lympho-myeloid skewing in vivo. Together, our data outline an intrinsic RhoA-dependent mechanosignaling axis in HSCs, which can be pharmacologically targeted to restore aged stem cell function.


PcPLA2 at nuclear membrane
Aging
+ RhoA inhibitor
RhoAGTP
Young HSC
PcPLA2 at nuclear membrane
Epigenetic drift (loss H3K9me2)
RhoAGTP
Aged HSC
Chromatin fitness improvement (feedback loop)
H3K9me2 increase
LINE, LTR closed
Inflammatory signature down
Klf4 increased accessibility and transcription of Klf4-regulated genes (partial reprogramming)
Hematopoietic Functional improvement
High Lymphoid/Myeloid
Increased engraftment
Cause of nuclear stretching

Advanced hydrogel-based micropillar arrays to study mechanoregulation of brain myelination

Emad Moeendarbary[1]
[1]University College London, United Kingdom, [2]BioRecode LTD, United Kingdom
Mechanobiology in Disease and Mechanomedicine 1, July 13, 2026, 14:00 - 15:45

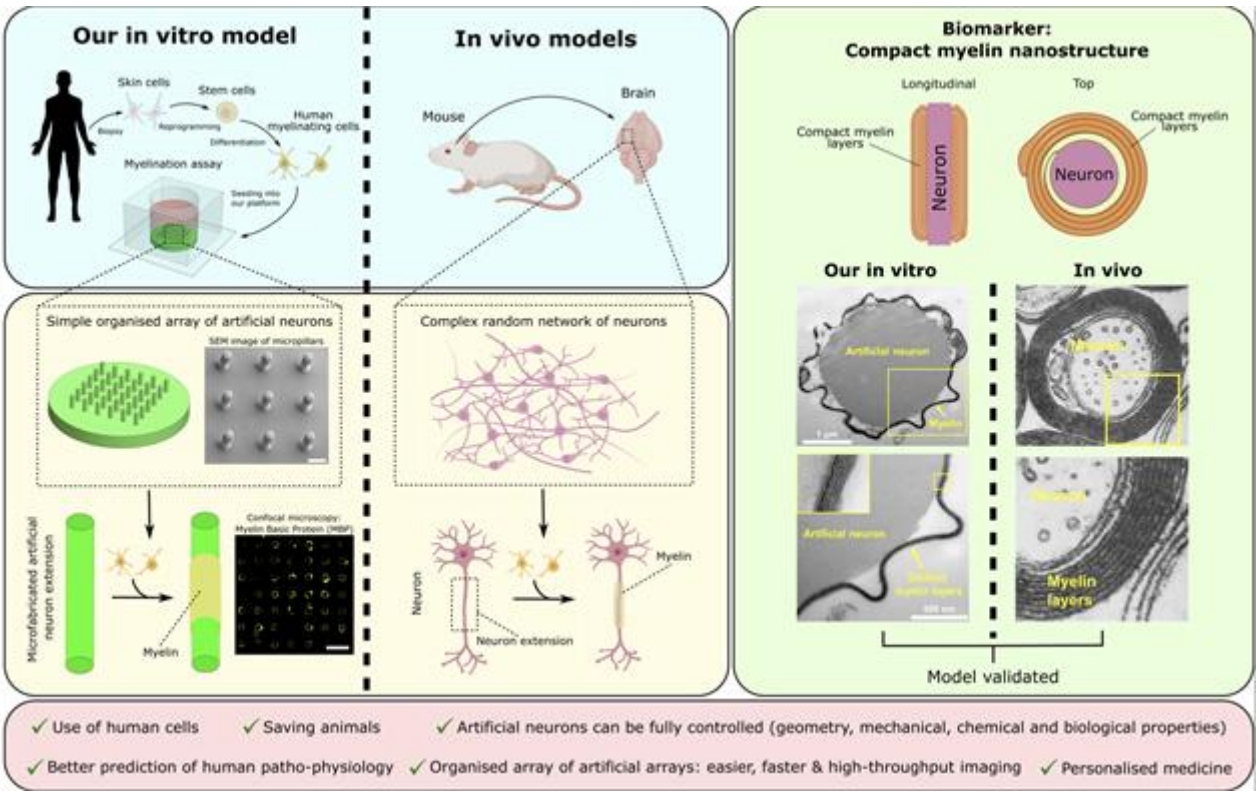
In this work, I will present a biomimetic mechanobiology platform designed to dissect how physical cues regulate central nervous system myelination. Oligodendrocytes are highly mechanosensitive cells, yet most in vitro systems rely on rigid substrates that fail to replicate the softness and three-dimensional architecture of axons. This mechanical mismatch limits our understanding of how axonal biophysics instructs myelin formation.

To address this, we engineered a fully hydrogel-based micropillar array that mimics axon-like geometry while allowing independent control of stiffness, diameter, and spacing within physiologically relevant ranges. Using polyacrylamide pillars spanning 0.5–50 kPa and diameters of 3–10 μm, we systematically decoupled geometric and mechanical parameters to determine how each regulates oligodendrocyte differentiation and myelin wrapping.

I will show that soft, axon-mimetic substrates support robust, multi-layered compact myelin formation, validated by confocal and transmission electron microscopy. Myelination increases with pillar diameter, recapitulating in vivo axon calibre dependence, while stiffness modulates wrapping efficiency in a diameter-dependent manner. Notably, supraphysiological stiffness enhances apparent myelination, highlighting how rigid platforms may artificially inflate pro-myelinating responses.

Transcriptomic profiling further reveals that three-dimensional axon-mimetic architecture promotes a mature oligodendrocyte gene signature, with upregulation of myelin-related and extracellular matrix pathways and suppression of proliferative programs. Importantly, I will demonstrate that drug responses are stiffness-dependent, suggesting that mechanical context critically shapes pharmacological outcomes and may explain discrepancies between preclinical screening and clinical translation.

Together, this work establishes a scalable and physiologically relevant mechanobiology platform that decouples axonal stiffness and geometry, enabling systematic interrogation of the physical regulation of myelination. This approach provides new insight into the mechanical code of myelin formation and improves the predictive power of remyelinating therapeutic discovery.



✓ Use of human cells ✓ Saving animals ✓ Artificial neurons can be fully controlled (geometry, mechanical, chemical and biological properties)

✓ Better prediction of human patho-physiology ✓ Organised array of artificial arrays: easier, faster & high-throughput imaging ✓ Personalised medicine

Tuning the force: magnetic nanoparticles for modulating cell behaviour

Christian Castro-Hinojosa[1], Pablo Martínez-Vicente[1], Susel Del Sol-Fernández[1], Yilian Fernández-Afonso[1], Lucía G. Recaredo[1], Raluca M. Fratila[1], María Moros[1]
[1]Instituto de Nanociencia y Materiales de Aragón, Spain

Mechanochemistry 1, July 15, 2026, 14:00 - 15:45

Magnetic nanoparticles (MNPs) are widely used in nanomedicine due to their unique properties, including their size and their responsiveness to external magnetic fields. These features enable MNPs to exert traction forces remotely. When targeted to cell membranes, MNPs can apply localized pulling forces, offering a versatile platform for precise cellular manipulation. The use of magnetic fields to modulate cell behaviour provides several advantages over other techniques such as optogenetics, as they can penetrate deep tissues and deliver a wide range of forces without causing damage to biological samples.

Our recent research focuses on using MNPs to stimulate E-cadherins on the cell surface, enabling remote modulation of intracellular signaling. We present a nanoplatform based on MNPs functionalized with E-cadherin fragments for targeted stimulation of cellular cadherins, key adhesion proteins that link extracellular mechanical cues to intracellular signaling, including the Wnt/β-catenin pathway, a key regulator of cell proliferation, differentiation, and tissue morphogenesis. Histidine-tagged cadherin fragments consisting in the whole extracellular domain of the E-cadherin were produced in HEK cells after lentiviral transduction and functionalized on MNPs through metal-affinity binding (MNP@cadherin). This ensures oriented immobilization, high stability, and preservation of the bioactive conformation, which is essential to enable specific interactions between MNP-cadherins and cellular cadherins.

Upon exposure to a weak, low-gradient magnetic field using a custom-designed stimulator, E-cadherin-functionalized MNPs transmitted localized mechanical forces to membrane-bound cadherins, triggering E-cadherin–mediated mechanotransduction. This stimulation led to β-catenin release from membrane complexes, nuclear translocation and activation of Wnt target genes, as confirmed by transcriptomic profiling and a Wnt-responsive luciferase reporter assay. These molecular events translate into functional results, including enhanced cell proliferation and accelerated wound closure.
This technology represents a novel approach for probing mechanobiology, opening new venues for therapeutic strategies.

Mechanical regulation of long-range chemical signaling in the developing Xenopus laevis brain

Sudipta Mukherjee[1,2,5], Eva Pillai[2,3,4], Niklas Gampl[1,5], Ross McGinn[1,2,5], Katrin Mooslehner[1,2,5], Julia Becker[1,2,5], Alexander Winkel[2], Amelia Thompson[2], Kristian Franze[1,2,5]
[1] Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, [2]PDN, University of Cambridge, UK, [3]Cell Biology and Biophysics Unit, European Molecular Biology Laboratory, Germany, [4]Developmental Biology Unit, European Molecular Biology Laboratory, Germany, [5]Max-Planck-Zentrum für Physik und Medizin, Erlangen, Germany

In vivo Mechanobiology 1, July 16, 2026, 08:45 - 10:30

Developmental processes rely on both chemical and mechanical signals, but how these two signals interact is still poorly understood. We here identified a crosstalk between tissue stiffness and long-range chemical signaling in vivo, using the developing Xenopus laevis brain as a model system. Knocking down Piezo1, a mechanosensitive ion channel, either in the brain tissue or in retinal ganglion cells (RGCs) growing through the brain both led to axon pathfinding errors. Piezo1 knockdown in the neuroepithelium led to decreased expression of the chemical guidance cues semaphorin3A and slit1 as well as to a decrease in brain tissue stiffness. Tissue softening observed in Piezo1 knockdown embryos was mediated by a decrease in the cell-cell adhesion proteins NCAM1 and N-cadherin. Downregulating NCAM1 and N-cadherin-mediated cell-cell adhesions recapitulated the Piezo1 knockdown phenotype, resulting in both decreased brain tissue stiffness and reduced Sema3A expression. Tissue stiffness turned out to be a critical regulator of the expression of sema3A and slit1 both in vitro and in vivo. Decreased environmental stiffness reduced the expression of both chemical guidance cues, while increasing tissue stiffness initiated their ectopic expression. As Sema3A and Slit1 are diffusible cues that act over large distances, local mechanical signals may impact cell function far away from the actual stimulus. Due to the conserved nature of the molecules investigated, the phenomenon is likely relevant across diverse biological systems.

Rate of applied ultrasound pulse may be as important as ultrasound pressure in predicting osteoblast cell responses to LIPUS

Andrea Orthodoxou[1], Margaret Lucas[1], **Helen Mulvana**[1]
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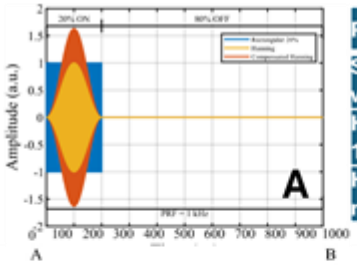
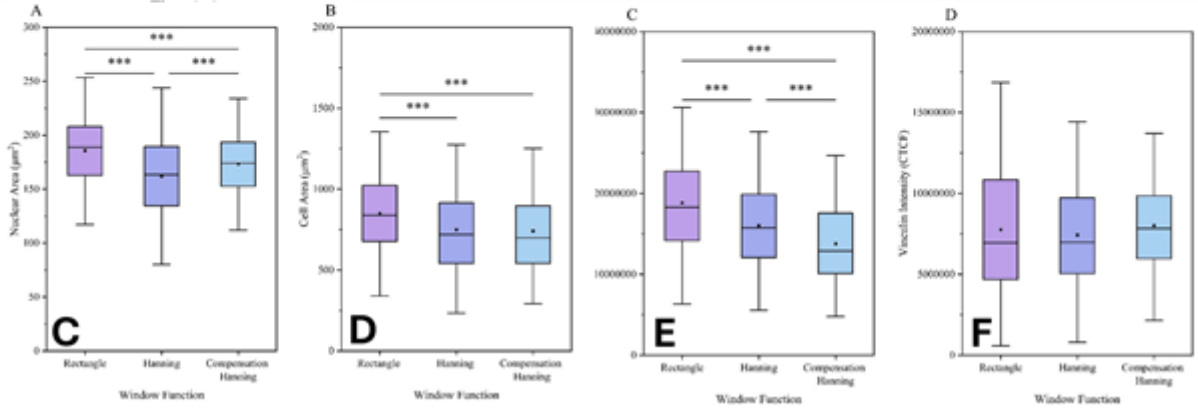
Sonomechanobiology 1, July 16, 2026, 08:45 - 10:30

Low intensity pulsed ultrasound (LIPUS) can mechanically modulate cellular activity for therapeutic benefit, for example to promote fracture repair [1]. However, the underlying biological mechanisms and thus reliable exploitation remain poorly understood. Our previous work showed conventional LIPUS descriptors (e.g. spatial-average-temporal-average intensity, ISATA) inadequately predict bioeffects, whereas ultrasound pressure may better indicate the forces influencing membrane tension [2]. Here, we use windowing to investigate how force application rate affects cellular responses.
Laser Doppler vibrometry (PSV-500, Polytec) was used to quantify mylar substrate displacement in optically and acoustically transparent submersible culture cassettes during LIPUS under three windowing schemes (A): LIPUS_RECT (rectangular envelope), LIPUS_HAN_I (Hanning windowed, ISATA-matched at 60 mW/cm^2), and LIPUS_HAN_P (Hanning windowed, peak-pressure matched at 160 kPa). LIPUS was delivered with planar single-element transducer (A302S, Panametrics) driven with signal generator and power amplifier to produce a 1 MHz sinusoid pulsed at 1 kHz, 20% duty cycle. Identical pulses were applied to MG63 seeded cassettes placed at transducer focus in outgassed water, and mechanosensing responses assessed via nuclear and cellular morphology and actin/vinculin expression [2]. Membrane displacement at 1 kHz (pulse repetition) was up to four times greater than at 1 MHz (carrier), with amplitudes (B): 4.17±0.3 nm (LIPUS_RECT), 6.92±0.76 nm (LIPUS_HAN_I), 2.62±0.54 nm (LIPUS_HAN_P). Despite LIPUS_RECT delivering an intermediate displacement, it elicited the strongest mechanosensing response, as shown by increased nuclear and cell area and elevated actin expression (C-F). These data reinforce that ISATA and pressure are inadequate predictors of LIPUS bioeffects, that low frequency displacement is sufficient to activate mechanotransduction, and suggest strain rate, rather than absolute membrane tension, may dominate regulation of cellular responses as has been demonstrated in other cell types [3].

[1] Harrison, et al., Ultrasonics, 70: 45-52, 2016.
[2] Orthodoxou, et al., Ultrasonics, 107945, 2026.
[3] Mcknight, et al., Ann Biomed Eng 31: 239–249, 2003



Pulse Shape B	Displacement @ 1 MHz	Displacement @ 1 kHz
Standard LIPUS (rectangular window)	1.22 ± 0.08 nm	4.17 ± 0.3 nm
Hanning: pressure-matched 160 kPa	1.26 ± 0.1 nm	2.62 ± 0.54 nm
Hanning: ISATA- matched 60 mW/cm2	1.67 ± 0.2 nm	6.92 ± 0.76 nm

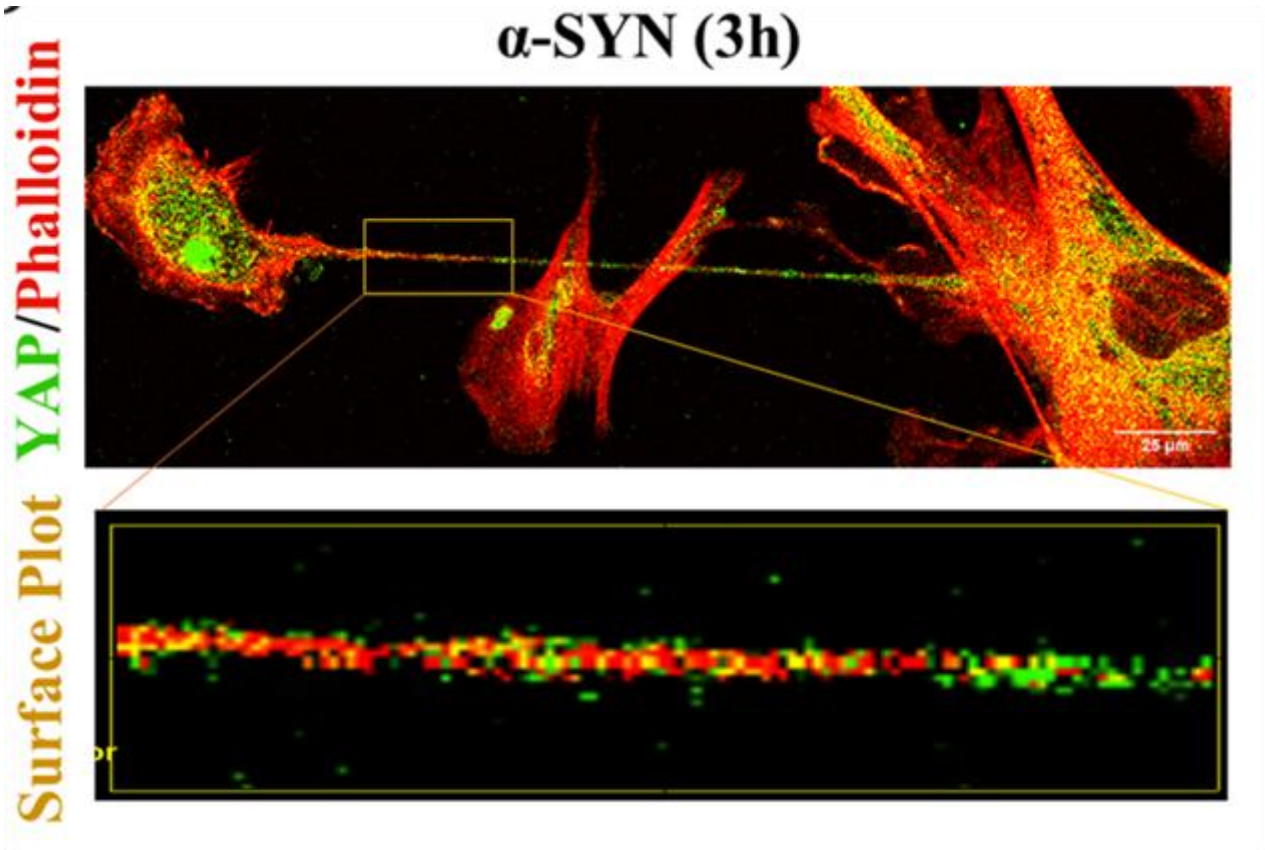


Mechanical Signaling Protects Astroglia from α-Synuclein-Induced Senescence via tunneling nanotubes

Dr Sangeeta Nath[1], Suchana Chatterjee[1], Ashok Ravula[2], Anirudh Sreenivas BK[1], Abinaya Raghavan[1], Sivaraman Padavattan[3], Sreenath Balakrishnan[2]
[1]Manipal Institute of Regenerative Medicine, Manipal Academy of Higher Education, India, [2] Indian Institute of Technology Goa, India, [3]Department of Biophysics, National Institute of Mental Health and Neurosciences, India

Mechanobiology of Ageing 1, July 15, 2026, 14:00 - 15:45

Astroglia can counteract the harmful effects of α-synuclein protofibrils (α-SYN) and reverse premature cellular senescence by promoting tunneling nanotubes (TNTs). TNTs are nano-sized, open-ended, actin-rich membrane channels connecting neighboring cells, enabling transfer of organelles and cytoplasmic materials. Cytoskeletal remodeling, especially via actin signaling, is key to TNT formation. However, the mechanism behind this recovery is unknown. This study is the first to examine TNT–mediated mechanical stability in senescent astroglial recovery. We demonstrate that disruption of Lamin A/C in α-SYN-treated senescent cells reduces actin-cytoskeleton stress, as measured by nucleus flatness index and isometric scale factor from quantitative microscopy. ROCK (Rho-associated kinase) inhibition, which is crucial for reducing actin-cytoskeleton tension, promotes TNT. Small molecules like Cytochalasin-D, Nocodazole, and Jasplakinolide, which inhibit TNTs by altering actin tension other than ROCK-pathway, cannot reverse senescence. RNA-sequence heatmaps reveal changes in senescence, integrin, and ROCK-pathway genes; STRING links these to the Hippo pathway. Experiments show that cytosolic YAP translocation, a key regulator of the Hippo pathway, is vital for TNT formation and actin-based stability in U87-MG astrocytoma and primary astrocytes. Interestingly, we observe many instances in which TNTs form between cells with low actin tension and Hippo-signaling on and those with relatively higher actin tension and Hippo-signaling off. The most notable observation is the high abundance of YAP inside the TNTs, which seems to colocalize with actin, as shown by the surface plot image of α-SYN-treated TNTs. The study reveals that TNTs maintain mechanical stability through Lamin A/C integrity and actin tension in α-SYN-senescent astroglia, and protect against α-SYN toxicity, reversing premature senescence.


α-SYN (3h)
YAP/Phalloidin
Surface Plot
25 μm

Mechanoprotective Strategies to Rejuvenate Ageing Endothelium

Timo Zadegh Nazari-Shafti[1]
[1]Baylor College of Medicine, United States

Mechanobiology of Ageing 3 and Flash Talks 5b, July 15, 2026, 17:15 - 17:45

Age-related endothelial dysfunction critically contributes to vascular frailty, thrombosis, and graft failure, yet how to preserve or even rejuvenate aged endothelial monolayers remains unresolved. Building on our previous work showing that anisotropic micro-topographies restore adherens junction integrity and proliferation in senescent endothelial cells, and that a novel endothelial damage inhibitor (EDI) preserves the integrity of human saphenous vein graft endothelium during clinical handling, this talk will present new data that integrate biochemical and biomechanical strategies to stabilize ageing endothelium in surgically and device-relevant settings. Using primary human venous endothelial cells and patient-derived graft tissue, we combine controlled hypothermic stress, defined topographical cues, and pharmacological EDI exposure to dissect how junctional remodeling, focal adhesions, and YAP-mediated mechanotransduction jointly govern barrier function and survival in ageing cells. Quantitative imaging and functional assays reveal complementary roles of EDI and anisotropic substrates in maintaining connectivity while promoting controlled proliferation under clinically relevant stress conditions. Together, these findings highlight a mechano protective framework for improving long-term endothelialization of cardiovascular implants and vein grafts in older patients, and illustrate how mechanobiology of ageing can inform translational design of next-generation graft preservation solutions and pro-endothelial implant surfaces.

Ultrasound stimulation as a mechanism of influencing cell behaviour in hepatic tissue engineering

Ekaterina Panova[1], S Vlach[1], M.S. Massaro[1,2], R. Palek[3], J. Sevcik[1,3], L. Cervenkova[1], L. Bolek[2], V. Liska[1,3], V. Moulisova[1]
[1]Biomedical Center, LFP UK, Czech Republic, [2]Department of Biophysics, LFP UK, Czech Republic, [3]Department of Surgery, LFP UK, Czech Republic

Sonomechanobiology 1, July 16, 2026, 08:45 - 10:30

Porcine liver decellularized matrix scaffold is a promising biomaterial for liver tissue engineering and regenerative medicine (1). Exposure to acoustic waves is one strategy to enhance scaffold recellularization results (2). This study investigates the effect of ultrasound stimulation on various cell types, with the prospective goal of establishing an effective cell echanotransduction stimulation mechanism in the context of hepatic tissue engineering.

Decellularised pig liver tissue cubes were seeded with HUVEC and hMSC cells in separated monocultures. Scaffolds were exposed to 1 MHz ultrasound pulse for 5 minutes after cell seeding and collected for analysis after 24 hours and 7 days of culture. Cell behaviour was assessed via Live-dead and immunofluorescence (imaging adhesion marker: Integrin-β1). Ultrasound cell stimulation showed preservation of the viability in HUVECs and increased viability in case of hMSC cells. It also increased hMSC and HUVEC Integrin-β1expression, showing enhanced cell adhesion. Altogether, the method increases mesenchymal cell affinity for the scaffold even after a short exposure period and influences endothelial cells distribution within scaffold.
Work supported by Charles University projects Cooperatio “Surgical disciplines” (COOPERATIO-207043), NU22J-06-00058 (Ministry of Health, Czech Republic), National Institute for Cancer Research (Programme EXCELES, No. LX22NPO5102), “Integration of biomedical research and healthcare in the Pilsen metropolitan area” No. CZ.02.01.01/00/23_021/0008828) co-funded by EU, and the SVV project of Charles University No. 264773.
(1) Massaro M.S. et al., Mater. Sci. Eng., C, 2021
(2) Rabiet L et al., Sci. Rep. 2024

Dynamic encoding of mechanical input by Piezo1 integrates force magnitude, stimulus history and multicellular coordination

Periklis (Laki) Pantazis[1]
[1]Imperial College London, United Kingdom

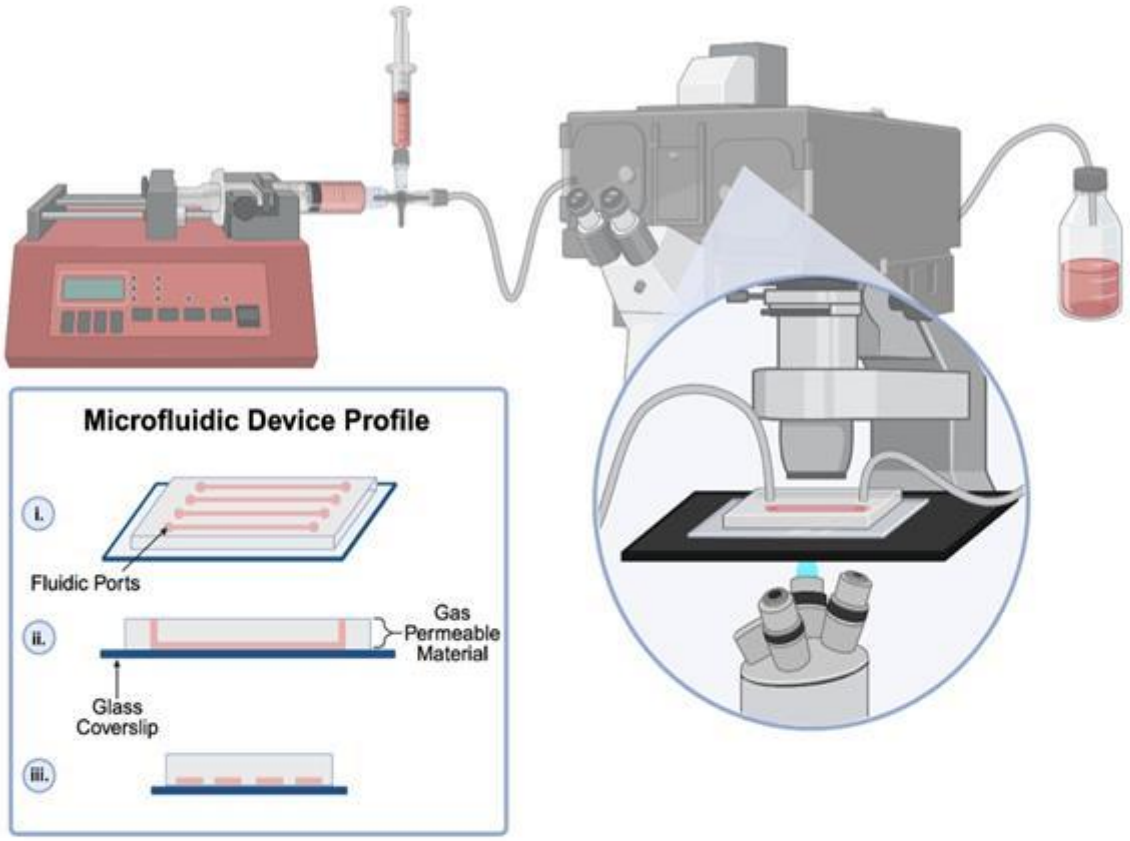
Cell Mechanics Across Length Scales 2, July 15, 2026, 11:00 - 12:00

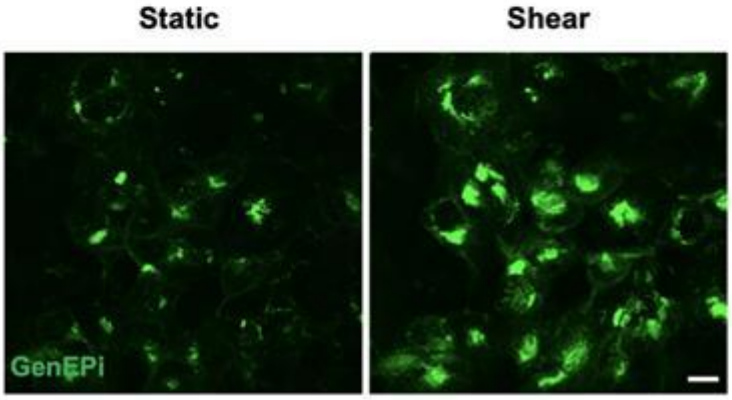
Cells in living tissues experience complex, dynamic mechanical cues, yet how mechanosensitive ion channels encode both force magnitude and stimulus history across multicellular populations remains poorly defined.

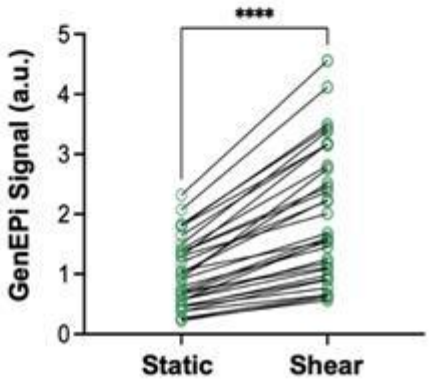
Here we present a microfluidic live-imaging platform that delivers precisely defined laminar fluid shear stress to confluent monolayers while enabling high-resolution, real-time readout of Piezo1 activity. Using XLGenEPi, an inducible genetically encoded sensor reporting Piezo1 channel opening, we track mechanotransduction dynamics simultaneously at single-cell and population scales under physiologically relevant flows.

We uncover a striking biphasic activation program: shear triggers an initial burst of robust, highly synchronous Piezo1 activity across the monolayer, followed by progressive attenuation and desynchronisation during continued or repeated stimulation. Importantly, this transition is force-dependent—higher shear accelerates the loss of coordination—and even modest shear produces measurable signal depression over time, revealing adaptive encoding below saturating loads. Across shear regimes, Piezo1 output scales with stimulus magnitude and exhibits history-dependent kinetics, indicating that Piezo1 is not a simple on/off switch but a dynamic encoder of mechanical information. We are now leveraging this platform to define the cellular mechanisms that govern the emergence, stability and breakdown of coordinated responses under flow.

Together, our work reveals how Piezo1 converts tissue-level forces into evolving patterns of mechanochemical signalling, providing a quantitative framework to dissect mechanotransduction dynamics in health and disease.


Microfluidic Device Profile
i.
Fluidic Ports
ii.
Gas
Permeable
Material
Glass
Coverslip
iii.


Static
Shear
GenEPi


****
GenEPi Signal (a.u.)
0
1
2
3
4
5
Static
Shear

Piezo1 links Fibroblasts and Inflammation in Atrial Fibrillation

Ramona Emig[1], Manuel Koch[1], Pia Iaconianni[1], Peter Kohl[1], Ursula Ravens[1], Dr Remi Peyronnet[1]
[1]Institute of Experimental Cardiovascular Medicine, University Heart Center Freiburg – Bad Krozingen, Medical Center and Faculty of Medicine, University of Freiburg, Germany

Immunomechanobiology 2, July 14, 2026, 16:15 - 17:15

Atrial fibrillation (AF) is associated with atrial dilatation, fibrotic remodelling, and inflammation. Mechanical stretch is known to trigger structural and functional remodelling, and fibrosis alters tissue mechanics that are sensed and actively responded to by cardiac cells. In AF, inflammation secondary to atrial dilatation is often considered an additional driver of fibrotic remodelling. However, how mechanical stimulation of fibroblasts influences inflammatory cell behavior, and whether this interaction further modifies tissue mechanics, remains poorly understood.

The cation non-selective stretch-activated channel Piezo1 is upregulated in atrial fibroblasts isolated from patients with AF compared to those in sinus rhythm. Piezo1 functions as a mechanosensor in these cells and contributes to interleukin-6 (IL-6) secretion. RNA sequencing revealed that siRNA-mediated reduction of Piezo1 decreases expression of pro-inflammatory cytokines, including CCL2 and IL-8. As soluble mediators, these cytokines may contribute to mechanically induced modulation of inflammatory processes, such as immune cell recruitment from the circulation.

To assess whether human atrial fibroblasts modulate immune cell behavior in a paracrine, Piezo1-dependent manner, we performed in vitro co-culture experiments. Transient knockdown or overexpression of Piezo1 in atrial fibroblasts demonstrated that Piezo1 levels correlate with the ability of fibroblasts to attract THP-1 monocytes in transwell migration assays. Similar effects were observed for primary human neutrophil migration. Monocyte recruitment was primarily mediated by CCL2, whereas neutrophil migration depended on IL-8.

Together, these findings suggest that elevated Piezo1 expression in atrial fibroblasts promotes immune cell recruitment via paracrine signalling. As Piezo1 is upregulated in AF, this might be a novel mechanism, potentially linking mechanical alterations in atrial tissue to enhanced atrial inflammation, and thereby contributing to disease progression.

Age-associated mechanical reinforcement impairs phagocytosis in the retinal pigment epithelium

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Mechanobiology of Ageing 2, July 15, 2026, 16:15 - 17:15

To function properly, tissues maintain a fine-tuned balance of forces and mechanical characteristics, which we refer to as mechanical homeostasis. In postmitotic tissues, such as the retinal pigment epithelium (RPE), compensatory proliferation is not available, potentially turning cell turnover during ageing into a challenge to mechanical homeostasis. The ageing RPE undergoes pronounced structural remodelling, yet it remains unknown if this restructuring may be an adaptation to cell loss and if it impacts the mechanical homeostasis and function of the monolayer.

To address these questions, we established a reductionist in vitro model of age-associated cell loss by inducing large-scale apoptosis in stem cell-derived RPE monolayers. This cell density reduction recapitulates key structural features of the aged RPE, including reduced cell height, shortened apical microvilli and reorganisation of the actin cytoskeleton. The remodelled tissue acquires a new mechanical homeostasis, characterized by tissue stiffening as per nanoindentation, reinforced cell-cell junctions and elevated overall contractility. These age-like monolayers show impaired vision-supporting function of photoreceptor outer segment (POS) phagocytosis – internalizing reduced number of fragments of larger size, while displaying less apical actin ruffling and apicolateral deformation during phagocytosis. Transcriptomic analysis reveals broad changes in actin-associated genes, including nucleators, bundlers and membrane linkers. Pharmacological modulation of actin nucleators shows that Arp2/3- and formin-dependent actin remodelling differentially control particle number and size during phagocytosis, linking actin cytoskeletal dynamics to functional output.

Together, our results show that age-related structural remodelling in the postmitotic RPE as an adaptation to cell loss establishes a new state of mechanical homeostasis, where actin dynamics are redirected toward tissue reinforcement at the expense of plasticity required for phagocytosis. These findings highlight how age-associated cytoskeletal adaptation, independently of additional stressors, can compromise tissue function supporting the notion of mechanical ageing.

STIFFNESS-DRIVEN TRACTION FORCES PROMOTE COLLAGEN ALIGNMENT AND DIRECTIONAL MIGRATION IN 3D BREAST CANCER MODELS

Raquel Ruiz-Mateos Brea[1,2], Pablo Blázquez Carmona[1,3], Elías Núñez Ortega[1], David Morón Ortega[1], Esther Reina Romo[1,2], José Antonio Sanz Herrera[1,2]
[1]Universidad de Sevilla, Spain, [2]Instituto de Biomedicina de Sevilla, Spain, [3]Universidad de Cádiz, Spain

ECM Mechanobiology in Physiology and Disease 1, July 16, 2026, 08:45 - 10:30

Cancer cell mechanics have gained attention for evaluating metastatic potential and malignant phenotypes. Evidence suggests that elevated traction forces correlate with the heightened migratory and invasive capabilities of metastatic cells. Furthermore, extracellular matrix (ECM) stiffness has also been identified as a crucial factor of cancer progression, highlighting the importance of mechanobiology in developing novel cancer therapeutic strategies.
In this study, we employed 3D Traction Force Microscopy (TFM) to quantify the contractile forces exerted by MDA-MB-231 breast cancer cells encapsulated within collagen gels designed to mimic both physiological and tumoral mechanical environments. Using confocal microscopy, we captured 3D images of cells and collagen fibers at 24- and 48-hour intervals, complemented by continuous 48-hour time-lapse imaging. These datasets were processed using the TFMLab MATLAB toolbox and custom computational models, allowing the simultaneous quantification of ECM remodeling—specifically fiber density, alignment, and tunnel formation— alongside cellular mechanical parameters and migration. Preliminary results elucidate a complex interplay between cellular traction and matrix microarchitecture. Notably, we observed a localized densification of collagen fibers near the cell surface that intensified over time. Furthermore, traction forces scaled proportionally with ECM stiffness and were linked with fiber alignment, tunnel formation and migratory directionality, providing deeper insight into how cell-matrix interactions drive the mechanobiological progression of metastasis.

Mechanical forces drive nuclear-cytoskeletal remodeling and Ephrin-mediated adaptation in leukemic cells.

Cristina Scielzo[1], Marco Cellani[1], Marta Sampietro[1], Matteo Pitton[2], Riccardo Pinos[1], Margherit Pauri[1], Federica Barbaglio[1], Lydia Scarfò[1], Silvia Farè[3]
[1]Irccs, Hospital San Raffaele Milano, Italy, [2]Policlinico San Donato (IRCCS), Italy, [3]Politecnico di Milano, Italy

Nuclear Mechanobiology 2, July 14, 2026, 16:15 - 17:15

Chronic Lymphocytic Leukemia (CLL) is characterized by the dynamic trafficking of malignant $CD5^+$ B cells between peripheral blood and lymphoid tissues, where microenvironmental cues sustain survival, proliferation, and drug resistance. While the role of mechanotransduction has been extensively investigated in solid tumors, its contribution to hematologic malignancies remains poorly understood. Here, we integrate approaches including mechanical confinement, stiffness-tuned substrates, kinome profiling, and 3D bioprinting to dissect how physical forces influence CLL cell behavior. Using microfabricated confinement systems with channel heights ranging from 1–6 µm, we demonstrate that CLL cells can withstand extreme compression without loss of viability but display markedly limited nuclear spreading compared to healthy B cells. Basally, CLL nuclei are smaller and less deformable, consistent with reduced expression of lamin A and B2 and an altered organization of the actomyosin cytoskeleton. Kinome profiling under confinement revealed activation of multiple adaptive signaling pathways, including PI3K/AKT, cAMP, and Ephrin receptor cascades, indicating a contractility-dependent mechanoadaptive response. To more closely mimic physiological tissue conditions, we cultured CLL cells on PDMS substrates spanning 0.5–8 kPa or embedded them in 3D bioprinted hydrogels recapitulating lymphoid tissue rigidity. Cells exposed to higher stiffness (8 kPa) exhibited enhanced ERK/AKT/mTOR signaling and selective upregulation of Ephrin receptors, including EphA2 and EphA10. Interestingly, stiffness-induced Ephrin activation was distinct between malignant and healthy B cells, suggesting aberrant mechano-sensing in CLL. In 3D bioprinted scaffolds, CLL cells underwent transcriptional reprogramming of genes involved in homing, cytoskeletal dynamics, and survival, which correlated with increased resistance to both chemotherapeutic and targeted agents relative to conventional 2D cultures. Collectively, these findings highlight nuclear–cytoskeletal alterations and Ephrin receptor signaling as central mediators of mechanical adaptation in CLL. Our data support a model in which microenvironmental stiffness and physical confinement contribute to leukemic persistence, potentially promoting therapy resistance and disease progression

Mechanochemical regulation of a clathrin- and dynamin-independent endocytic pathway

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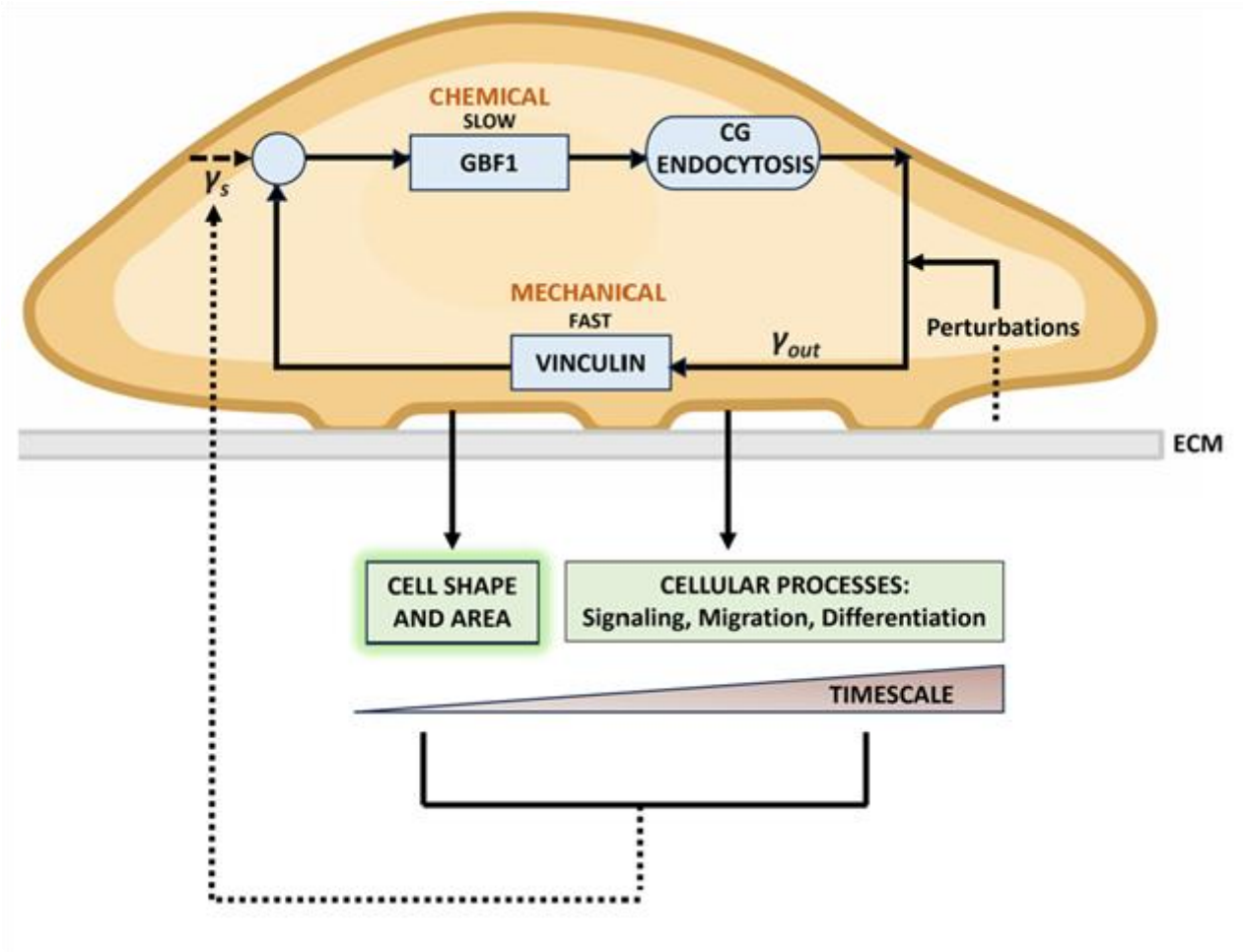
Cell Mechanics Across Length Scales 2, July 15, 2026, 11:00 - 12:00

Multiple endocytic pathways regulate the uptake of extracellular material and modulate plasma membrane properties. Acute changes in membrane tension are buffered by the high-capacity, ARF1-regulated, dynamin- and clathrin-independent CLIC/GEEC (CG) pathway of endocytosis1. Previous work identified a mechanochemical feedback circuit linking integrin-based sensing of extracellular cues to membrane tension regulation. In this circuit, focal adhesion-associated mechanotransducer vinculin negatively regulates Arf1 GTPase via its GEF, GBF1, to control CG endocytosis, thereby providing the necessary negative feedback for tensional homeostasis2. However, the mechanism underlying this regulation remains poorly understood.
Using domain-deletion constructs and point mutants of vinculin, we show that the vinculin tail rather than the head domain forms a core module that suppresses CG endocytosis. This inhibitory function requires Src-dependent phosphorylation and intact actin and phosphatidylinositol 4,5 phosphate binding sites in the vinculin tail, indicating that both post-translational modification and mechanical engagement are needed to license vinculin's CG-inhibitory activity.
Because vinculin activation is governed by forces at the cell-matrix adhesions, we asked whether extracellular mechanical and chemical cues could modulate CG endocytosis via this axis. Measuring bulk fluid uptake across substrates of varying chemistry and stiffness, we find that CG endocytosis is tuned by the microenvironment in a vinculin-dependent manner. Loss of vinculin or disruption of its phosphorylation state blunts CG pathway sensitivity to these cues. Thus, vinculin functions as a mechanochemical integrator that couples adhesion-based force sensing to the regulation of CG pathway. Ongoing work explores how vinculin-dependent control of endocytosis links microenvironmental mechanics to membrane tension homeostasis.

1. Thottacherry JJ, et. al. Spoiled for Choice: Diverse Endocytic Pathways Function at the Cell Surface. Annual Review of Cell and Developmental Biology. 2019;35(1):55-84.

2. Thottacherry JJ, et. al. Mechanochemical feedback control of dynamin independent endocytosis modulates membrane tension in adherent cells. Nature Communications. 2018;9(1).


CHEMICAL
SLOW
GBF1
CG
ENDOCYTOSIS
V_s
MECHANICAL
FAST
VINCULIN
V_{out}
Perturbations
ECM
CELL SHAPE
AND AREA
CELLULAR PROCESSES:
Signaling, Migration, Differentiation
TIMESCALE

Comparing Microbubble-Induced Deformation in Stiff and Soft Cells using High-Speed Imaging and Digital Image Correlation

Sam Sloan[1,2], Oliver Pattinson[1,2], Aya Ben Issa[1], Simon Tilley[2,4], Eleanor Stride[3], Janos Kanczler[1], Fabrice Pierron[5], Dario Carugo[3], Nicholas Evans[1,2]
[1]Centre for Human Development, Stem Cells and Regenerative Medicine, Bone and Joint Research group, University of Southampton , United Kingdom, [2]Bioengineering Sciences Group, Institute for Life Sciences, University of Southampton, United Kingdom, [3]Botnar Research Centre, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences (NDORMS), University of Oxford , United Kingdom, [4]Trauma and Orthopaedics, University Hospital Southampton, United Kingdom, [5]MatchID NV, Belgium

Sonomechanobiology 2, July 16, 2026, 11:00 - 12:00

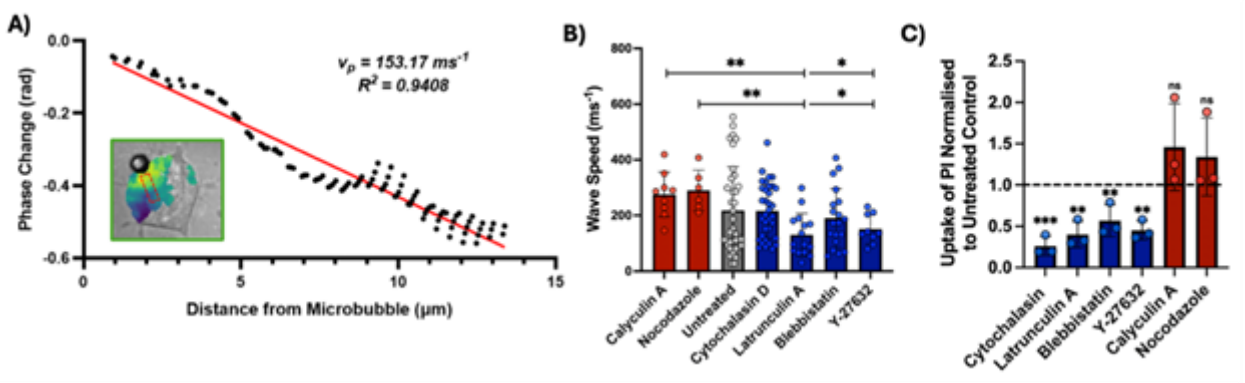
Ultrasound-stimulated microbubbles can transiently permeabilise cells and enhance targeted therapeutic delivery (sonoporation), but efficacy varies markedly between different tissue types. One potentially important factor is the relationship between tissue mechanical properties, microbubble dynamics and hence microbubble–cell interactions. This relationship, however is poorly understood, especially at megahertz loading rates. To address this question, we tested the hypothesis that the material properties of the cell determine microbubble-induced deformation dynamics and sonoporation.

MG63 cells incubated with agents that soften or stiffen cells prior to imaging at 5 Mfps using a Shimadzu HPV-X and microbubble-induced cell deformation was quantified using digital image correlation (DIC) [1] and FFT to map displacement amplitude and phase change (Figure1A). For sonoporation measurements, a cell impermeable dye, propidium iodide (PI), was added with microbubbles and cells were exposed to focused ultrasound at, 0.3MPa 1MHz, PRF=1kHz, DC=30%) in a bespoke device [2] before imaging and quantification for % of cells dye-positive.

Deformation propagated significantly further into the cells treated with stiffening agents compared to cells treated with softening agents (pooled data; 3.31±0.92μm vs. 2.44±0.46 μm; $p<0.0001$). This was also true when comparing untreated cells with either softening or stiffening agents (2.44±0.46 μm vs. 2.85±0.69μm; $p=0.01$ and 3.31±0.92μm vs 2.85±0.69μm; $p=0.019$). This correlated with a significant increase in sonoporation rate and wave-propagation speed in cells treated with stiffening agents compared with those treated with softening agents. This remained true when comparing untreated cells with either softening or stiffening agents (Figure1B&C).

These results indicate that cell stiffness influences the degree of deformation induced by microbubbles oscillating at MHz frequencies and the likelihood of sonoporation, with softer cells experiencing more localised deformation and less membrane permeabilisation.

[1] O.Pattinson et al. doi:10.1021/acsbiomaterials.3c00757 (2023)
[2] M.Gray et al. doi:10.3791/61989 (2021)


A)
v_p = 153.17 ms^{-1}
R^2 = 0.9408
Phase Change (rad)
Distance from Microbubble (µm)
B)
Wave Speed (ms^{-1})
Calyculin A
Nocodazole
Untreated
Cytochalasin D
Latrunculin A
Blebbistatin
Y-27632
C)
Uptake of PI Normalised to Untreated Control
Cytochalasin
Latrunculin A
Blebbistatin
Y-27632
Calyculin A
Nocodazole

Remodeling of chromatin under low intensity diffuse ultrasound

Dr Anuradha Subramanian[1], Sandra Noriega[2]
[1]Universiy of Alabama-Huntsville, United States, [2]University of Nebraska-Lincoln, United States
Sonomechanobiology 2, July 16, 2026, 11:00 - 12:00

A variety of mechanotransduction pathways mediate the response of fibroblasts or chondrocytes to ultrasound stimulation. In addition, regulatory pathways that co-ordinate stimulus-specific cellular responses are likely to exist. In this study, analysis was confined to the hypothesis that ultrasound stimulation (US) influences the chromatin structure, and that these changes may reflect a regulatory pathway that connects nuclear architecture, chromatin structure and gene expression. Murine fibroblasts seeded on tissue culture plates were stimulated with US (5.0 MHz (14 kPa), 51-s per application) and the thermal denaturation profiles of nuclei isolated from fibroblasts were assessed by dynamic scanning calorimetry (DSC). When compared to the thermal profiles obtained from the nuclei of non-stimulated cells, the nuclei obtained from stimulated cells showed a change in peak profiles and peak areas, which is indicative of chromatin remodeling. Independently, US was also observed to impact the histone (H1):chromatin association as measured indirectly by DAPI staining. Based on our work, it appears plausible that US can produce a remodeling of chromatin, thus triggering signal cascade and other intracellular mechanisms.

Neuronal mechanosensing in a neurodevelopmental disorder' model

Chiara De Cesari[1], Nicoletta di Leo[1], Laura Andolfi[1], Sara Carpi[1], Sara Chiarugi[1], Noa Ndimurwanko[2], Francesco Greco[2], Laura Marchetti[3], Ype Elgersma[4], Silvia Russo[5], Liam A. McDonnell[2], Marco Cecchini[1], **Ilaria Tonazzini**[1]
[1]Nanoscience Institute, National Research Council (CNR), Italy, [2]Fondazione Pisana per la Scienza, Pisa, , Italy, [3]Dept. Clinical Genetics, Erasmus Medical Center, Netherlands, [4]Dept. of Pharmacy, University of Pisa, Italy, [5]Laboratory of Medical Cytogenetics and Molecular Genetics, IRCCS Istituto Auxologico Italiano, Italy

Cell Mechanics Across Length Scales 1, July 15, 2026, 08:45 - 10:30

The mechanosensing of physicochemical extracellular stimuli orchestrates the wiring and plasticity of the brain, however little is known about these processes in neurodevelopmental disorders. Ubiquitin ligase E3A (UBE3A) plays a key role during neurodevelopment - its loss leads to Angelman Syndrome (AS), while its increase to autism spectrum disorders - but its exact role in the brain remains unclear. Nano/micro-structured substrates (micrograting- GRs) are able to induce biomimetic directional stimuli, via focal adhesions constrain and mechanotransduction process, to neuronal cells in vitro, and consequently to tune/test neuronal responses to topographical cues (e.g. radial-glia migration).
We here investigate neuronal mechanotransduction, guidance, and migration in UBE3A-deficient (AS) cell models in vitro (neuroblastoma cells, HEKs, primary murine neurons, human inducible-neurons), by exploiting GR substrates. We found deficits in topographical contact guidance for all the AS cells tested on GRs. The intracellular localization of Piezo2 channels was also differently regulated by polarization in AS cells. The migration of AS neurons was also lightly impaired, particularly at the level of neurite dynamics and in response to specific directional cues. Moreover, proteomic analysis of the content of small neuronal extracellular vesicles showed significant differences in the levels of proteins involved in cell-cell/matrix adhesion, and cytoskeleton processes between wild-type and AS samples. In parallel, we demonstrated reduced microtubules' polymerization in AS neurons. Finally, by in utero electroporation, we confirmed that UBE3A loss causes delayed pyramidal neuron migration in the murine cortex in vivo.
In conclusion, GR substrates can be exploited as platforms to investigate in vitro the behaviour of neurons, at the molecular level, resembling specific in vivo physical cues. These results support the view that defects in early neuronal mechanosensing and cytoskeleton dynamics may lead to defective neuronal connectivity and, ultimately, impaired plasticity in AS neurodevelopmental disorders.

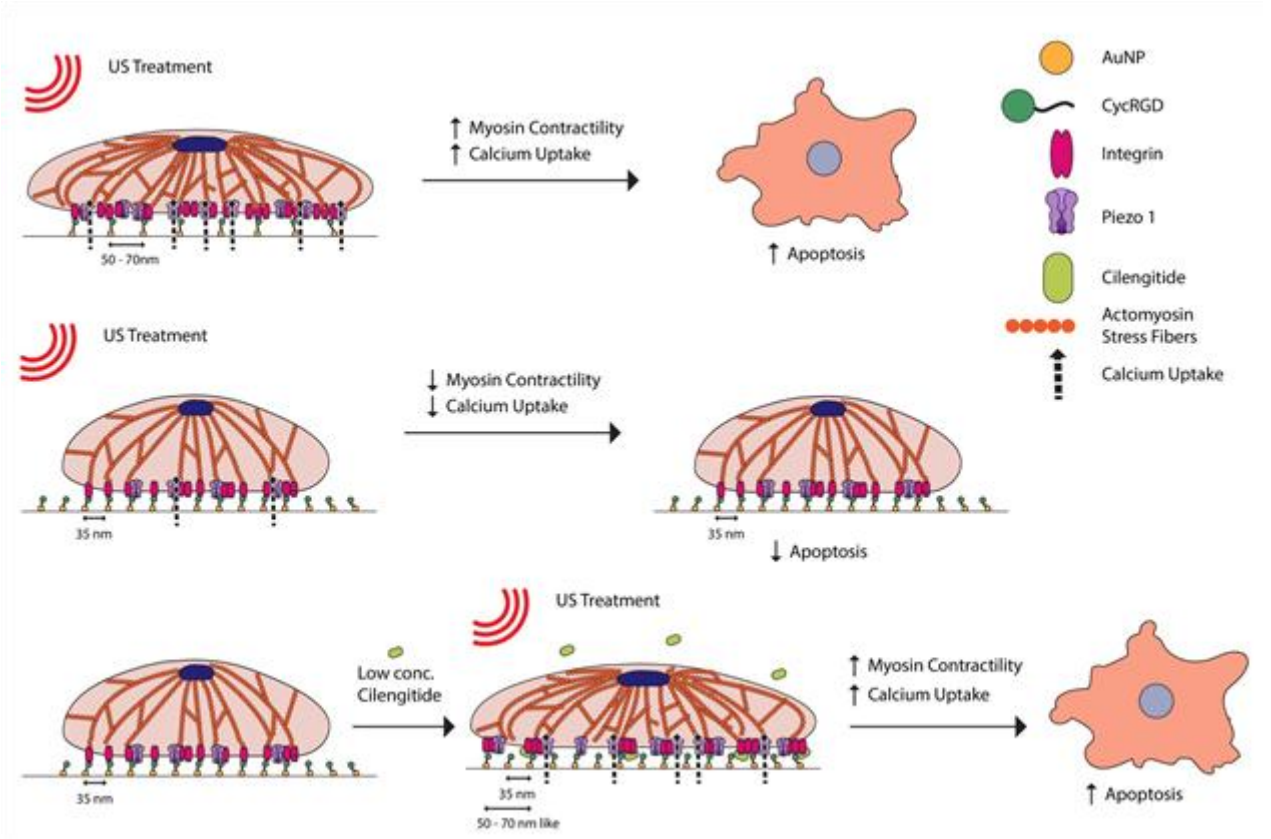
Nanoscale Ligand Spacing Regulates Mechanical Force-Induced Cancer Cell Killing

S Manasa Veena[1], Chen Dixiao[2], Akshay Kumar[1], Rudra Pratap[1], Jennifer L. Young[2], Ajay Tijore[1]

[1]Indian Institute Of Science, Bengaluru, India, [2]Mechanobiology Institute, National University of Singapore, Singapore

Mechanochemistry 1, July 15, 2026, 14:00 - 15:45

Cancer cells sense and respond to the extracellular environment, with differences in nanoscale ligand spacing affecting their behavior. Emerging reports show that stretch/ultrasound-mediated mechanical forces promote apoptosis (mechanoptosis) by increasing myosin contractility. Since myosin contractility is critical for nanoscale-ligand spacing-regulated cell behavior, we study the effect of ligand spacing on mechanoptosis. Gold nanoparticle arrays were created with 35, 50, and 70 nm spacings and functionalized with cyclic-RGD peptide. Interestingly, the highest level of apoptosis was observed on 50 and 70 nm ligand spacing, where increased myosin contractility and peripheral Piezo1 channel localization causing calcium influx were observed. Perturbing cell-matrix interactions by nanomolar doses of Cilengitide (cyclic RGD pentapeptide) increases mechanoptosis on 35 nm ligand spacing to similar levels observed on 50 and 70 nm. Thus, nanoscale-level changes in binding domains regulate mechanoptosis through cell-matrix mediated mechanotransduction, and the synergistic action of ultrasound and Cilengitide can ultimately be applied to enhance tumor treatment.



Cell Adhesion and Extracellular Matrix Assembly on Viscoelastic Substrates

Jonah Voigt[1], Jens Timmer[2], Elisabetta Ada Cavalcanti-Adam[1]
[1]University of Bayreuth, Germany, [2]ETH Zürich, Switzerland

ECM Mechanobiology in Physiology and Disease 1, July 16, 2026, 08:45 - 10:30

The mechanical properties of the extracellular matrix (ECM) are important regulators of cell behaviour, governing proliferation, migration, differentiation, and tissue remodelling. While ECM stiffness has been widely studied as a determining factor of mechanotransduction, increasing evidence also highlights the importance of matrix viscoelasticity, particularly time-dependent stress relaxation, in guiding cell responses, as biological tissues exhibit diverse viscoelastic properties tailored to their physiological functions. However, disentangling the respective contributions of stiffness and viscoelasticity in vitro remains challenging, particularly in the stiff regime relevant to load-bearing tissues and disease states. Here, we introduce silicone-based elastomer substrates of equal stiffness (~80kPa) but distinct stress relaxation profiles to decouple these effects. They are convenient to use, providing stable mechanical properties and straightforward coating with ECM proteins without the need for chemical cross-linkers. With them, we investigated how substrate stress relaxation regulates cellular mechanosensing and cell-mediated ECM remodelling under physiologically relevant stiff conditions, and are currently exploring the influence of viscoelasticity on the secretion and assembly of the ECM. Increased substrate stress relaxation was found to lead to enhanced fibronectin reorganization, focal adhesion maturation, and traction force generation at equivalent fibronectin surface densities. Cells cultured on substrates of higher stress relaxation were found to have greater nuclear to cytosolic localization of YAP and formed β1-integrin-enriched adhesions, correlating with the formation of fibrillar-like fibronectin structures. The results showcase that by simply tuning the stress relaxation behaviour of the substrates, ECM organization and assembly can be directed without the need for additional biochemical cues, providing insight into mechanically regulated tissue-remodelling.

Interplay between Target Rigidity and Geometry Governs Phagocytic Outcomes

Youri Peeters[1], Philip Pietryszek[2], Laura de Laporte[2], Daan Vorselen[1]
[1]Department of Cell Biology & Immunology, Wageningen University & Research, Wageningen, Netherlands, [2]DWI – Leibniz Institute for Interactive Materials, RWTH Aachen University, Germany

Immunomechanobiology 1, July 14, 2026, 14:00 - 15:45

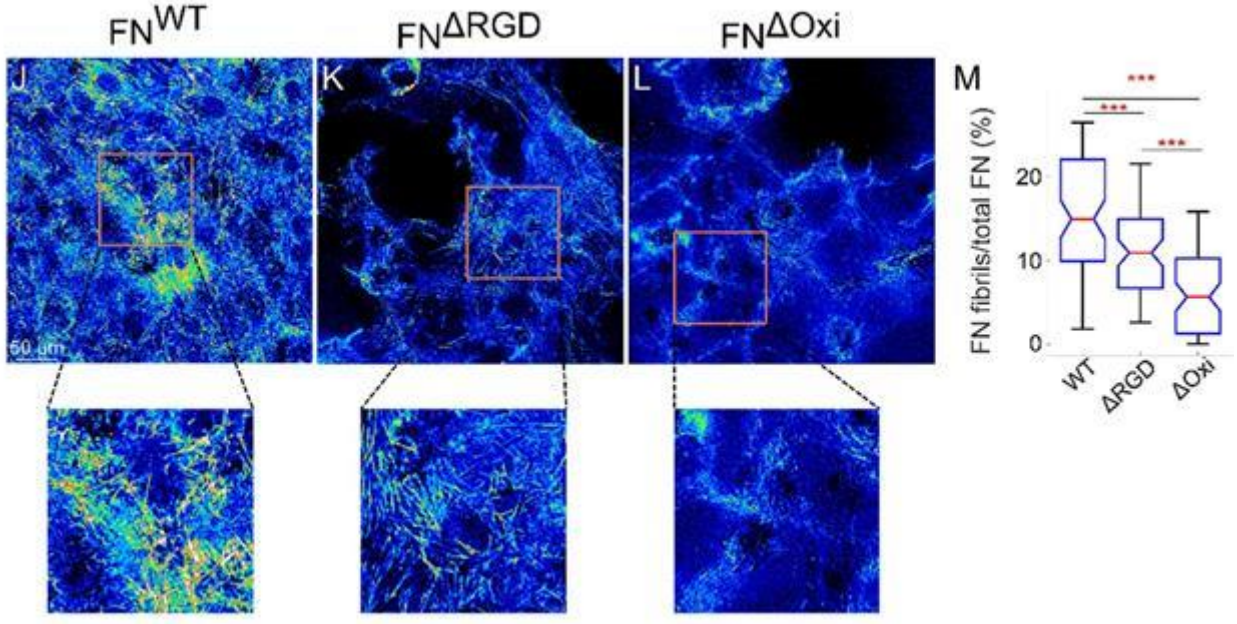
Immune cells encounter an enormous variety of threats, from small rigid bacteria to malleable cancer cells and irregularly shaped microplastics. Macrophages are frequently the first to encounter these targets and respond by eating them through phagocytosis. While recent research has shown that physical properties (size, geometry, stiffness) are key regulators of phagocytosis in isolation, potential interplay between properties has not been considered. We combine development of controlled hydrogel microspheres and rods, phagocytic assays, and quantitative imaging and biophysical approaches to investigate such interplay. We reveal that stiffer microspheres are phagocytosed more efficiently than softer ones in an integrin-dependent manner. Surprisingly, and in stark contrast to spheres, uptake of microrods is more efficient for softer than stiffer rods. Rigidity dependence of rod uptake persists up to unusually high stiffness (~1 MPa) and is integrin-independent. Bending of fully internalized microrods suggests that the overall bending flexibility of rods regulates phagocytosis. Strikingly, live-cell imaging experiments reveal minimal bending of soft microrods during phagocytic engulfment, suggesting that rigidity-dependence arises post-internalization, during intracellular maturation of phagosomes. Indeed, endosome labeling reveals that internal membranes around rigid rods are leaky, correlating with poor acidification and degradation of internalized particles. Together, these results show a complex interplay in regulation of innate immunity by biophysical cues and may ultimately offer new insights to intervene with macrophage functions therapeutically.

Inhibiting Enzyme-Mediated Fibronectin Fibrillogenesis – A Novel Route For Fibrosis Inhibition

Maher Abu Saleh[1], Noa Lavi[1], Anas Odeh[1], Tina Shogan[1], Lavi Coren[1], Ido Mizrahi[1], Shelly Zaffryar-Eilot[1], Elisabeth Nadjar-Boger[1], Ilanit Boyango[2], Marwan Dawood[2], Emily Avitan-Hersh[2], Peleg Hasson[1], Haguy Wolfenson[1]
[1]Technion - Israel Institute Of Technology, Israel, [2]Department of Dermatology, Rambam Health Care Center, Israel

ECM Mechanobiology in Physiology and Disease 1, July 16, 2026, 08:45 - 10:30

Fibrosis is a detrimental condition that is estimated to be involved in ~35% of all deaths in the developed world. It results from dysregulated repair of damaged tissue, wherein fibroblasts that trans-differentiate into myofibroblasts excessively deposit and crosslink extracellular matrix (ECM) proteins. Impaired signaling and high tissue stiffness create a vicious feed forward loop that maintains myofibroblasts in a continuously activated state, gradually disrupting tissue architecture and impairing organ function.
Disrupting this loop is challenging since its components also mediate normal wound healing, highlighting the need to attenuate rather than fully block them. Key players in this cycle are the lysyl oxidases, a family of five secreted ECM modifying enzymes (LOX, LOXL1–4) that oxidize collagens and elastin, facilitating their crosslinking. One or more family members are involved in all fibrotic processes, and hence identifying a mechanism that modulates their activity could inhibit fibrosis.
Fibronectin (FN), one of the most important ECM proteins in fibrosis, is essential for fibroblast-to-myofibroblast transition and collagen deposition. FN is secreted as a closed dimer but becomes functional only in its fibrillar form. We recently demonstrated that a crucial step preceding the known integrin mediated FN fibrillogenesis is the oxidation of FN by lysyl oxidases at three specific lysines, and that blocking this oxidation abrogates fibrillogenesis. Based on these findings, we generated two miniproteins containing these oxidation sites as inhibitors of lysyl oxidases and FN fibrillogenesis.
We show that the miniproteins are oxidized by lysyl oxidases, disrupt FN fibrillogenesis, reduce cell spreading, and inhibit fibroblast-to-myofibroblast transition. In vivo, topical application to full thickness mouse wounds markedly reduced scarring and myofibroblast accumulation. Further, the miniproteins reverted myofibroblasts from Morphea patients to a non-activated state. Because lysyl oxidases upregulation and FN deposition occur in essentially all fibrotic reactions, these inhibitors hold great promise for future therapeutic use.



Force-induced membrane remodeling in health and disease

Huanghe Yang[1]
[1]Duke University School of Medicine, United States
Mechanobiology in Disease and Mechanomedicine 1, July 13, 2026, 14:00 - 15:45

PIEZO1 is a key mechanosensor at the cell surface that converts mechanical forces into intracellular signals, yet the downstream pathways that transduce forces to specific cellular signals remain incompletely defined. Here, I summarize our discovery and characterization of a mechanotransduction cascade linking PIEZO1 to TMEM16F, a Ca^{2+}-activated lipid scramblase that catalyzes passive phospholipid flip-flop and rapidly remodels membrane lipid asymmetry with broad implications for development and disease. First, we show that PIEZO1 is expressed in placental trophoblasts, where it is essential for trophoblast fusion, placental development, and fetal survival, extending its established role in angiogenesis. Mechanistically, PIEZO1-mediated Ca^{2+} influx activates TMEM16F, driving externalization of phosphatidylserine (PS), a critical “fuse-me” signal that promotes trophoblast fusion. Second, we demonstrate that the PIEZO1-TMEM16F axis is conserved in red blood cells (RBCs), where mechanical forces trigger membrane remodeling events including PS exposure and microparticle release. Because PS functions as an “eat-me” signal, a procoagulant surface, and a cue for cell-cell interactions, this mechanosensitive remodeling promotes RBC clearance, coagulation, and adhesion to the endothelium. Notably, this cascade is exaggerated in hereditary xerocytosis and sickle cell disease (SCD) due to hyperactive PIEZO1, providing a molecular explanation for the long-standing observation of elevated PS exposure in sickle RBCs, an important pathogenic feature of SCD. Finally, we identify benzbromarone, an antigout drug, and cannabidiol (CBD), a non-psychoactive cannabis-derived compound, as inhibitors of PIEZO1 that potently disrupt this cascade and prevent force-induced RBC membrane remodeling. Together, these findings support a unifying model in which the PIEZO1-TMEM16F pathway serves as a general mechanism for mechanosensitive membrane remodeling across cell types. Pharmacological targeting of this axis may offer a therapeutic strategy to treat diseases driven by hyperactive mechanotransduction.

Electrical and Mechanical Characterization of Mono- and Bilayers of hiPSC Cardiomyocytes

Tomaso Zambelli[1], Xinyu Zhang[1], Margherita Burattini[2], Michele Miragoli[2]
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Advanced Tools for Multiscale Mechanobiology 2, July 14, 2026, 11:00 - 12:00

The coordinated electrical and mechanical coupling of cardiomyocytes is essential for proper cardiac pump function, yet this balance is disrupted in life-threatening pathologies. Human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs) have emerged as a powerful platform for personalized disease modeling, as they recapitulate key pathological features such as impaired electrical conduction and altered mechanical behavior.

Here, we employ hiPSC-CMs carrying mutations associated with Brugada syndrome (BRU) and dilated cardiomyopathy (DCM), organized in a bilayer configuration to both validate experimental methodologies and better approximate the physiological microenvironment. Electrical activity was characterized using high-density CMOS-based microelectrode arrays (HD-MEAs), while mechanical function was quantified through video-based analysis under β-adrenergic stimulation.

We introduce a dual methodological framework. First, high-throughput in-plane (xy) mechanical measurements were obtained using a novel optical tracking system (OPT) alongside confocal reference-free traction force microscopy (cTFM), enabling precise quantification of cardiac kinematics. Second, atomic force microscopy (AFM) with FluidFM probes was integrated with these approaches to extend the analysis into three dimensions (xyz), providing insight into cell–cell mechanical coupling.

This multimodal platform enables the detection of electromechanical latency between cell layers and reveals disease-specific alterations associated with inherited cardiomyopathies. Beyond identifying pathological phenotypes, the system allows quantitative assessment of pharmacological responses, highlighting its potential as a scalable tool for translational research and drug screening.

Nuclear force feedback as rheostat for actomyosin tension control

Emily Goodall[1], Keyi Xie[1], Thomas Waring[1], Lorna Young, Iakowos Karakesisoglou, **Tobias Zech**[1]
[1]University of Liverpool, United Kingdom

Nuclear Mechanobiology 1, July 14, 2026, 14:00 - 15:45

Cells react to the application of mechanical force with an increase in actomyosin contractility and experience higher tension on cell-matrix adhesions and the nucleus. Yet how cells avoid having damaging levels of actomyosin tension is not known. Rnd3/RhoE, an atypical small GTPase, influences actin cytoskeletal organisation through negative regulation of RhoA activity. By compressing or cyclically stretching primary fibroblasts to increase cytoskeletal tension we found that Rnd3 moves from the nucleus to the cytosol in a mechano-sensitive manner to maintain actomyosin tension homeostasis. We have identified an interaction between nuclear Rnd3 and the LINC complex member Sun2. The LINC complex couples the inner nuclear membrane to the cytoskeleton. Upon increased actomyosin tension and nuclear force coupling, Sun2 is rapidly phosphorylated and degraded, releasing Rnd3 from the nucleus to down-regulate forces tearing on the nucleus. Therefore, we propose that actomyosin contractility is tuned by nuclear force sensing to determine an optimal cell response to the extracellular matrix conditions. In cases where this response is impaired due to defective nuclear force coupling, dysregulated RhoA activity leads to cell and nuclear damage. Relieving the increased cytoskeletal tension in -for example- progerin expressing Hutchinson Gilford Progeria Syndrome (HGPS) patient cells by using clinically approved ROCK inhibitors led to increased proliferations rates and viability.

ISMB Flash Presentations

Characterisation of TRPV channel mechanosensitivity: implications for vasopressin neuron osmosensing

Phoebe Adler[1], Yuanyuan He[1], Michael Perkinson[1], Colin Brown[1], Martin Fronius[1]
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Flash Talks 5a, July 15, 2026, 17:15 - 17:45

Body fluid homeostasis is maintained by the hormone vasopressin, which is synthesised by magnocellular neurons in the hypothalamic supraoptic nucleus and paraventricular nucleus, and is secreted into the circulation from the posterior pituitary gland. Vasopressin secretion increases in response to hyperosmotic-induced cell shrinkage via activation of an N-terminal variant of the transient receptor potential vanilloid 1 (ΔN-TRPV1) channel. In addition to ΔN-TRPV1, vasopressin neurons express TRPV2 and TRPV4. However, the function of TRPV2 and TRPV4 in vasopressin neurons is unknown. Therefore, this project aimed to determine the role of TRPV2 and TRPV4 in response to mechanical force that mimics cell shrinkage.
Single-channel cell-attached patch clamp recordings were made from HEK293T cells lacking the mechanosensitive channel, PIEZO1, transfected with ΔN-TRPV1 (n=26), TRPV2 (n=30), or TRPV4 (n=42). For mechanical stimulation, positive and negative pressure steps of ±10, ±20, and ±30 mmHg were applied to the cell membrane using a high-speed pressure clamp. Cells transfected with PIEZO1 were used as a positive control (n=27) and untransfected cells were used as a negative control (n=24).
ΔN-TRPV1 and TRPV2 were not spontaneously active, whereas TRPV4 was spontaneously active with a conductance of 117 ± 3 pS. PIEZO1 exhibited robust activation in response to positive and negative pressure. By contrast, ΔN-TRPV1, TRPV2, and TRPV4 did not respond to positive or negative pressure. Similarly, endogenous channels in untransfected cells did not respond to positive or negative pressure. These findings suggest that ΔN-TRPV1 might require heteromeric assembly with TRPV2 and/or TRPV4 for functional activity, indicating that osmotic activation of vasopressin neurons might be mediated by heteromeric TRPV channels. Accordingly, recordings of putative TRPV heteromers are ongoing.

Mechanical Control of Nuclear Lamina Dynamics Governs Mesenchymal Stromal Cells' Fate

Mr Yusuf Ayten[1], Monica P Tsimbouri[1], Vineetha Jayawarna[2], Richard, O.C. Oreffo[3], Manuel Salmeron-Sanchez[2], Catherine C Berry[1], Matthew J Dalby[1]
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Mechanobiology of Ageing 3 and Flash Talks 5b, July 15, 2026, 17:15 - 17:45

Mesenchymal stromal cells (MSCs) are highly sensitive to their physical microenvironment, and their phenotype is tightly regulated by surface mechanics (Xu et al., 2023; Carthew et al., 2022; Cao et al., 2023). In their native niche, MSCs maintain an intermediate intracellular tension—between osteoblasts and adipocytes—required for functional stability (Lee et al., 2023; Chiarini et al., 2022). During in vitro expansion and ageing, this balance is lost, leading to cytoskeletal disruption, altered nuclear mechanics, and senescence (Danielsson et al., 2023; Coscarella et al., 2023). Bioengineered laminin-presenting poly(ethyl acrylate) (PEA) surfaces can restore this physiological tension by re-establishing controlled cell–matrix interactions (Xu et al., 2023; Carthew et al., 2022).

The nuclear lamina, particularly Lamin A/C, acts as a mechanosensitive regulator linking intracellular tension to chromatin organisation (Miroshnikova & Wickström, 2021; Briand & Collas, 2020). Lamin A/C dynamics are governed by farnesylation, caspase-6-mediated cleavage, and phosphorylation, which regulate its mobility between the lamina and nucleoplasmic pool (Dubik & Mai, 2020; Pavlov et al., 2021; Bianchi et al., 2020). High cytoskeletal tension stabilises Lamin A/C at the nuclear periphery, increasing nuclear stiffness and chromatin compaction (Saito et al., 2025; Leconte et al., 2024). In contrast, restored physiological tension promotes Lamin A/C phosphorylation and nucleoplasmic redistribution, enhancing chromatin plasticity (Wintner et al., 2020; Park et al., 2021).

The nucleoplasmic Lamin A/C pool, regulated by lamina-associated protein 2α (LAP2α), is associated with euchromatin and supports transcriptional adaptability (Naetar et al., 2020; Sidorenko et al., 2022). Here we hypothesise that by modulating Lamin A/C distribution, bioengineered surfaces can regulate chromatin accessibility, histone modifications, and gene expression, thereby regulating MSC proliferation, survival, and senescence (Park et al., 2022; He et al., 2022). Collectively, restoring physiological intracellular tension through engineered microenvironments provides a strategy to reprogram nuclear mechanics and preserve MSC regenerative potential.

Contact percolation governs collective motility via mechano-chemical feedback in heterogeneous breast cancer

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Flash Talks S4, July 15, 2026, 12:00 - 12:30

Breast cancer progression is driven by dynamic changes in tissue mechanics that promote phase transitions toward collective cell movement, immune activation, and invasion. While these processes have been mainly investigated in model systems of genetically identical cells, breast carcinomas are intrinsically heterogeneous, comprising cell populations with distinct genetic and mechanical properties. How this heterogeneity shapes collective dynamics and tumor progression remains poorly understood. Here, we interpret our experimental data through contact percolation theory to uncover a mechano-chemical switch underlying the emergence of collective flocking motility in heterogeneous breast cancer tissues. Using engineered mixtures of motile RAB5A-expressing cells and immotile control cells, we show that system-spanning clusters of fluidized RAB5A cells induce an abrupt morphodynamic switch in neighboring control cells, enabling them to acquire polarized protrusions and full-scale flocking-like motility. Theoretical modeling supports a mechanism by which local cell composition governs this transition and the onset of coordinated, system-wide movement, in a process that depends on RAC1-driven protrusive activity. Mechanistically, control cells in mixed monolayers above the percolation threshold exhibit activation of an E-cadherin-dependent EGFR-MAPK signaling axis, whereas E-cadherin silencing suppresses MAPK activation, impairs protrusion alignment, and disrupts flocking. This transition is accompained by collective mechanical remodeling, as control cells progressively soften and become more elongated as the fraction of neighboring RAB5A cells increases, consistent with enhanced tissue fluidization. In parallel, control cells activate a STAT1-dependent inflammatory program, fostered by the combined action of paracrine signaling and contact-dependent amplification. Together, these findings support a model in which contact percolation and mechano-chemical coupling contribute to dynamic tissue reorganization, inflammatory reprogramming, and invasive behavior in heterogeneous breast cancer.

Heterodimeric Coiled Coils as a Modular Toolkit for Single-Receptor Force Sensing at the Cell-Matrix Interface

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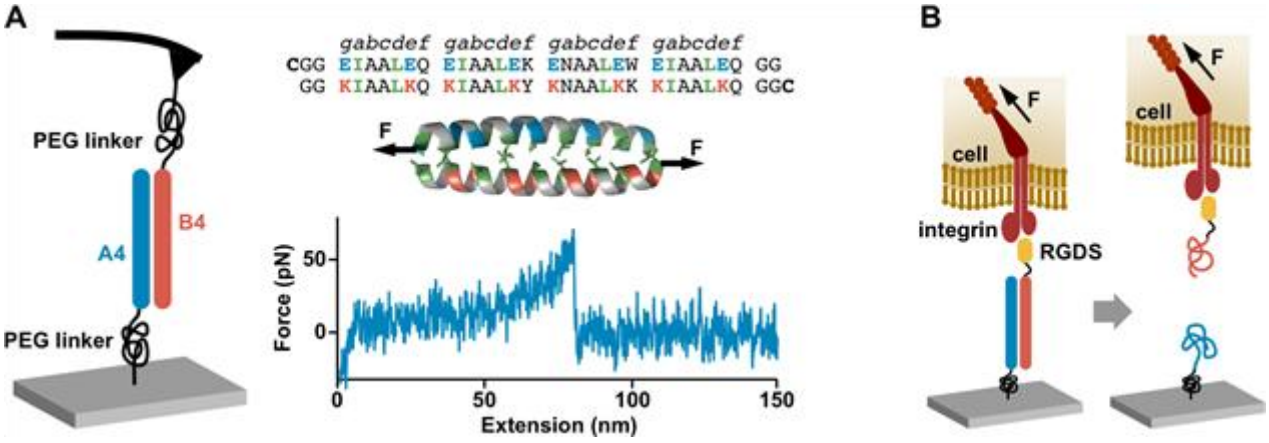
[1]Johannes Kepler University, Austria, [2]Max Planck Institute of Colloids and Interfaces, Germany
Flash Talks S2, July 14, 2026, 12:00 - 12:30

Molecular-scale forces transmitted across individual receptor-ligand bonds play a central role in how cells sense, interpret and respond to their environment. Directly quantifying molecular forces during early cell-matrix interactions, however, remains challenging. Molecular force sensors (MFSs) provide access to single-molecule forces, but commonly used platforms such as DNA-based MFSs rely on multistep chemical functionalization and are limited to forces below ~65 pN.

Here, we introduce heterodimeric coiled coils (CCs) as a new protein-based building block for the design of MFSs. Coiled coils are ubiquitous mechanical motifs in cytoskeletal and extracellular matrix proteins, made of self-assembling α-helices that wind into superhelical structures. Using atomic force microscope (AFM)-based single-molecule force spectroscopy (SMFS), we established sequence-structure-MECHANICS relationships for de novo designed CCs with lengths between three and five heptads (Fig. 1A). We show that mechanical stability depends on CC length, helix stability, hydrophobic core packing and, most importantly, on the pulling geometry, which provides a powerful handle to tune rupture forces while preserving thermodynamic and kinetic stability.

Based on this molecular calibration over a wide range of loading rates, we developed a modular library of CC-based MFSs. RGDS-functionalized CC-MFSs were used to fabricate mechanoresponsive surfaces that set the maximum forces transmitted through individual integrin-ligand bonds during early cell adhesion (Fig. 1B). In 2D fibroblast cultures, all CC-MFSs supported initial cell attachment within 30 minutes after seeding. However, between 60 and 120 minutes pronounced differences in cell spreading, morphology and cytoskeletal organization emerged depending on the dynamic mechanical stability of the underlying CC-MFS, demonstrating force discrimination at the single-receptor level. Ongoing work aims to extend the accessible force range and to incorporate fluorescence-based readout schemes, further expanding the applicability of CC-based MFSs for probing cell-matrix interactions at the molecular scale.



Injectable Synthetic Niches for Mechanobiological Regulation of Mesenchymal Stem Cells

Cristina Cortesi[1], Giovanni Buccioli[1], Leonardo Cherubin[1], Claudio Conci[1], Chiara Martinelli[1], Bianca Maria Colosimo[2], Davide Moscatelli[1], Emanuele Mauri[1], Alessandra Nardini[3], Rebeca Martinez Vazquez[3], Manuela Teresa Raimondi[1], Emanuela Jacchetti[1]
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Flash Talks 5c, July 15, 2026, 17:15 - 17:45

Mesenchymal stem cell (MSC)-based therapies are often characterized by differentiation and consequent loss of immunomodulatory properties following transplantation. High-resolution three-dimensional (3D) scaffolds [1] have shown to preserve MSC stemness by providing finely tuned biophysical cues, consistent with the physiological mechanobiological regulation of the stem cell niche. However, the scaffolds fabrication on rigid substrates precludes their injectability. Conversely, injectable bioprinted scaffolds [2] lack sufficient resolution to precisely control cell fate. This work aims to develop injectable microscaffolds capable of preserving MSC stemness and enhancing immunomodulatory factors secretion.
Highly-porous 3D microscaffolds, designed as concentric interconnected polyhedra, were fabricated via two-photon polymerization of IP-S (Nanoscribe, GmbH) and SZ2080 photoresists, employing Quantum X Shape system (λ=780nm, 25x objective, NA0.8) and a custom setup (λ=1030nm, 100x objective, NA1.4)[1]. Confocal microscopy was performed using A1R+ Nikon microscope (40x objective, NA1.15) to assess MSC viability (Calcein-AM/Ethidium Homodimer-I), proliferation, and cytoskeletal (SiR-Actin) and nuclear (Hoechst33342) morphology. Compression finite element analyses (FEA) (Abaqus, Dassault Systèmes) were performed to evaluate stress distribution and displacement across different scaffold configurations, materials and loading conditions.
Microscaffolds fabricated across both setups and both photoresists support robust cell colonization, with excellent viability (~95%) and proliferation (1.7 rate over three days). MSCs exhibited well-developed actin cytoskeleton organization (Fig.1), indicating active mechanosensing. The graded architecture of the scaffolds provides precise biophysical cues to cells, while significantly influencing structural compressive performance. However, FEA simulations confirmed that all scaffold configurations sustain pressures of at least 0.5MPa, ensuring mechanical stability under physiological conditions typical of soft tissues [3]. By optimizing scaffolds detachment after cellularization, floating synthetic-niches were obtained without compromising cell viability, highlighting their potential for minimally invasive injection for regeneration therapies.

[1] Jacchetti et al., 2021, DOI:10.1038/s41598-021-81920-2
[2] Du et al.,2025, DOI:10.1039/d5mh00930h
[3] Metzger et al.,2015, DOI:10.1016/j.jbiomech.2015.07.028

Acknowledgments
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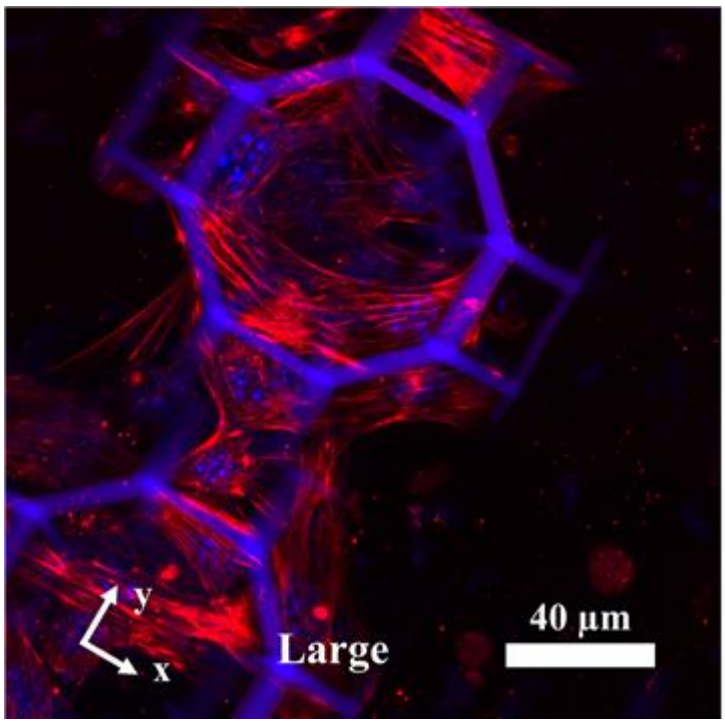

Actin Staining

SiR-Actin kit

Nuclei Staining

Hoechst 33342

Scaffold

Viscoelasticity in the integrin-growth factor crosstalk for bone regeneration

Finlay Cunniffe[1], Ziyuan Luo[1], Eonan Pringle[1], Marco Cantini[1]
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Flash Talks 5c, July 15, 2026, 17:15 - 17:45

The extracellular matrix (ECM) is a dynamic environment with biophysical (e.g. viscoelasticity) and biochemical properties (e.g. growth factors, GF) that drive cell fate. Mimicking this complexity has become a focus of tissue engineering strategies involving mesenchymal stem cells (MSCs) for bone regeneration. Crucially, synergy between these properties has been shown, with matrix stiffness regulating the activity of key osteogenic GF BMP-21. However, these studies disregard the time-dependent viscoelastic behaviour of native tissues, which has been shown to greatly impact cell responses2. Here, we aim to study how viscoelasticity affects the activity of an osteogenic GF-mimetic peptide (DWIVA) that has, thus far, demonstrated inconsistent osteogenic potential3. We first developed a dynamic platform utilising supported lipid bilayers functionalised with DWIVA and an adhesive ligand, RGD, to study cell responses to viscosity. Through this we established that a dynamic environment, when sufficient cell-generated forces are permitted, is crucial to unlocking the osteogenic potential of DWIVA. This was seen to be due to the local rearrangement of surface ligands which permits the colocalisation of cell adhesive and GF machinery. We then furthered this work in viscoelastic hydrogel systems made from either polyacrylamide or poly(ethylene glycol)-norbornene (PEGNB), which were used for assessment of adhesion, differentiation and signalling responses. While we observed no changes in early adhesive or mechanotransductive responses as a result of DWIVA functionalisation, crucially, viscoelasticity promoted the expression of osteogenic markers, including osterix and osteocalcin, on otherwise non-osteogenic soft (1-3 kPa) gels. Finally, we designed a novel DWIVA-loaded 3D PEGNB hydrogel and demonstrate that a bottom-up approach of increasingly complex mechanobiology models can be used to facilitate the design of clinically-suitable vehicles for promoting bone regeneration from MSCs.

1 Crouzier et al. (2011) Adv. Mater. 23(12)
2 Chaudhuri et al. (2016) Nature Mater. 15(3)
3 Oliver-Cervello et al. (2020) Adv. Healthcare Mater. 10(7)

MagPiezo: a Magnetogenetic Platform for Remote Activation of Endogenous Piezo1 Channels in Endothelial Cells

Susel Del Sol Fernández[1,2], **Mariarosaria De Simone**[2], Yilian Fernández-Afonso[2,6], Daniel Garcia-Gonzalez[3], Pablo Martínez-Vicente[2,4], Thomas S van Zanten[2,5], Raluca M. Fratila[2,5], Maria Moros[2,5]

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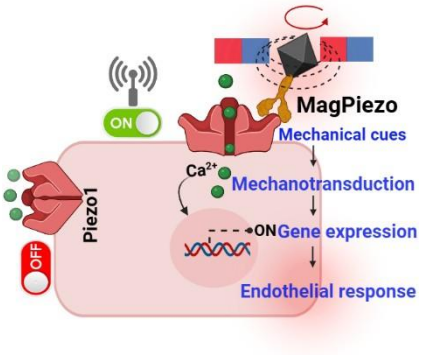
Mechanochemistry 1, July 15, 2026, 14:00 - 15:45

This study introduces MagPiezo, a novel magnetogenetic platform designed to enable remote and targeted manipulation of endogenous Piezo1 channels without genetic modification in vitro. MagPiezo integrates a custom-built magnetic applicator and 19 nm octahedral mixed ferrite nanoparticles (MFs) with enhanced magnetocrystalline anisotropy, engineered to selectively target Piezo1 channels. The application of a low intensity (< 40 mT), low frequency (0.5 Hz) magnetic field is sufficient to generate wireless torque forces in the piconewton range capable of gating Piezo1 channels in vitro. Remarkably, MagPiezo induces robust responses in endothelial cells, including calcium influx, cytoskeletal reorganization and transcriptional activation. Unlike other magnetogenetic tools, MagPiezo avoids the need to assemble the magnetic nanoparticles (MNPs) into bigger beads to reach the opening threshold and does not need to genetically engineer Piezo1 channels. Moreover, it uses low magnetic field intensities and frequencies, enhancing its potential for in vivo translation. Therefore, MagPiezo is a powerful platform for manipulating Piezo1 channels and dissecting mechanotransduction events in vascular biology, paving the way for new strategies to modulate mechanoreceptors.



Role of epigenetic modifications in the establishment of mechanical memory

Lucile Diot[1], Léa Mayeur[1], Julie Gauchoux--Bruna[1], Séverine Lecourt[2], Stéphane Dayot[1], Jean-Philippe Morretton[1], Camille Lobry[2], Nadia Elkhatib[1], Guillaume Montagnac[1]
[1]Inserm U1279, Gustave Roussy, University Paris-Saclay, France, [2]Inserm, Saint Louis Hospital, France

Flash Talks S3a, July 14, 2026, 17:15 - 17:45

Mechanical memory is defined by the persistent effect of past environment rigidity on cell adaptation to a new environment. Different mechano-sensitive signaling pathways have been implicated in mechanical memory. However, it is currently unknown how past information about substrate stiffness is stored inside the cell. Here, we report that the histone demethylase KDM7a controls mechanical memory of cell division by regulating H3K27 demethylation in a nuclear membrane tension-dependent manner. We observed that KDM7a was overexpressed in cells cultured on a soft substrate and was required to encode memory of a past soft substrate. On soft environments, reduced nuclear membrane tension controlled KDM7a recruitment at the nuclear envelop and H3K27 demethylation. Conversely, KDM7A localized to the nucleoplasm on stiff environments and H3K27 was methylated. These differences of histone methylation was maintained once cells primed on a soft substrate were transferred to a stiff secondary environment. Manipulation of nuclear membrane tension revealed that KDM7A localization was controlled by tension. We propose that information about substrate rigidity is encoded and stored in the epigenome through nuclear membrane tension-regulated H3K27 methylation dynamics.

Mechanobiological Modulation of human primary T-Cells by Immunosuppressive Drugs

Dr Alysson Duchalet[1], Mar Alcaraz-Hurtado[1], Miguel Fribourg[2,3], Andra Cristina Dumitru[1]
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Immunomechanobiology 3 and Flash Talks S3b, July 14, 2026, 17:15 - 17:45

In organ transplantation, graft survival depends on a delicate balance between regulatory and effector T-cells accessing the transplanted tissue. While immune signaling guides this process, graft infiltration also requires T-cells to arrest on endothelium and traverse micron-scale tissue barriers. Clinical graft outcomes show marked variability in T-cell infiltration, with distinct subsets differentially accessing the graft despite being present in circulation, pointing to underexplored mechanical determinants of tissue entry. Whether immunosuppressive therapies reprogram the mechanical state of T-cells and thereby influence their access to the graft remains unknown.

Here, we use atomic force microscopy (AFM) to define a multidimensional mechanical fingerprint of primary human $CD4^+$ T-cells and to determine how immunosuppressants reshape this mechanical state. Across healthy donors, we uncover subset-specific heterogeneity in primary T-cell mechanics, revealing intrinsic differences in baseline mechanical fitness. Treatment with frontline immunosuppressants tacrolimus and prednisolone induces a robust stiffening of $CD4^+$ T-cells, whereas changes in cellular fluidity are selectively triggered by tacrolimus.

Upon receptor activation, T-cells follow a characteristic mechanical trajectory, marked by an initial stiffening phase followed by recovery toward a mechanical equilibrium. Tacrolimus overrides this activation-induced mechanical remodeling by accelerating recovery and imposing an early equilibrium, effectively resetting the mechanical setpoint of the cell.

To identify the mechanistic basis of this drug-imposed mechanical state, we combined AFM with confocal microscopy and functional network–guided analysis of cytoskeletal and nuclear components. The most consistent and predictive changes occur at the level of the nucleoskeleton. Lamin B2 intensity and spatial distribution closely mirror drug-induced mechanical adaptations, identifying lamin B2 as a key mediator of T-cell mechanical regulation.

Together, these findings reveal that immunosuppressants do not only suppress signaling but actively reprogram T-cell mechanics with nuclear remodeling emerging as a key mechanistic contributor. This mechanobiological perspective provides new insight into T-cell infiltration in transplantation and immune-mediated disease.

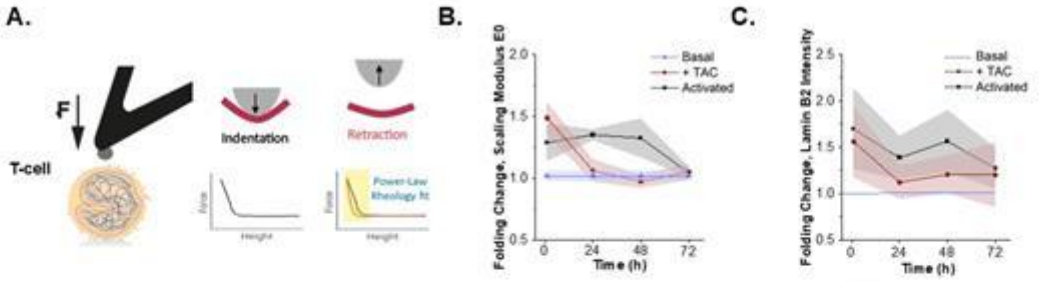

Figure. AFM and confocal microscopy uncover mechanical and nuclear changes during CD4⁺ T-cell CD3/CD28 activation under tacrolimus (TAC) pre-exposure.

Schematic representation of an individual T-cell indented by an AFM probe. Scaling modulus E0 is extracted from force-distance curves using a custom-written analysis routine implementing a power-law rheology model[1-3] **B.** Temporal evolution of E0 after exposure to TAC 0.1 µM or vehicle for 2H prior to CD3/CD28 activation. Basal curve represent a control condition without prior TAC pre-exposure or activation. Data are normalized to CTRL baseline. Shadowed area represent the Standard Error (SE) to the mean of three different healthy donors. **C.** Relative Lamin B2 fluorescence intensity quantified by Confocal microscopy after CD3/CD28 activation with and without TAC 0.1 µM 2H exposure. Data are normalized to basal and shadowed area represent the SE to the mean of two different healthy donors. Gisbert, V.G. et al., Small (2023).

[1]Gisbert, V.G et al., Small (2023)
[2]Garcia, P.D. et al., Nanoscale (2020)
[3]Garcia, P.D. et al, Nanoscale (2018)

Establishing Schizosaccharomyces pombe as a model system to investigate the molecular underpinnings of cellular adaptations to mechanical loading

Ms Phoebe Dunbabin[1], Dr Kate Poole[1]
[1]University Of New South Wales, Australia

Flash Talks 5a, July 15, 2026, 17:15 - 17:45

S. pombe is a non-motile, rod-shaped unicellular eukaryote with highly invariant shape characteristics that divides symmetrically during mitosis. This symmetrical division results from the formation of a septum at the centre of the growing cell, a process regulated by the force balance of the microtubule cytoskeleton. While the role of microtubules in cell division has been well-characterised in S. pombe, less is known about the force-sensing molecules in these cells and how they may influence microtubule assembly. We have identified several candidate force-sensing molecules in S. pombe, including ion channels involved in osmoregulation belonging to the TRP family, homologues of bacterial mechanosensitive channels and structural analogues of channels involved in mechanotransduction at the cell-substrate interface in mammalian cells. These putative force-sensors were cloned to assess whether they mediate mechanically activated currents when heterologously expressed in a mammalian system lacking endogenous mechanically activated (MA) ion channels. Microtubule assembly and the subsequent formation of the divisional septum in S. pombe is a process governed by mechanical forces. We therefore investigated how these cells respond to changes in mechanical loading, applied using simulated microgravity. Microgravity disrupted the precision of septum placement during cell division, resulting in increased divisional asymmetry. To investigate the role of S. pombe MA ion channels in signalling changing mechanical load, deletion strains will also be exposed to simulated microgravity. We hypothesise that channel deletion will either restore divisional symmetry, as cells no longer possess the molecules responsible for sensing changes in mechanical loading, or exacerbate the asymmetry, if MA channels are required for an adaptive response. By identifying MA ion channels in S. pombe, this project seeks to expand its applications as a model system for studying mechanotransduction, while also promoting the use of microgravity as a unique environment to explore the relationship between mechanical force and cell behaviour.

Interfacing nanotechnology and mechanobiology: magnetic nanoparticle tools for magnetogenetic actuation of cell membrane mechanoreceptors

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Flash Talks 5a, July 15, 2026, 17:15 - 17:45

The ability to remotely modulate intracellular pathways using physical stimuli such as light, electric or magnetic fields has opened new avenues for fundamental and applied biomedical research. Magnetic fields are particularly attractive in this context, as they can penetrate deeply into tissues (unlike light). The use of magnetic fields in combination with magnetic nanoparticle (MNP) actuators represents an emerging platform for the remote manipulation of cellular functions, known as magnetogenetics. MNPs can generate heat or mechanical forces upon exposure to external magnetic fields, enabling the activation of intracellular pathways linked to force- or temperature-sensitive membrane receptors.
One of the main research lines in our laboratory is focused on developing tools for remote activation of membrane mechanoreceptors, such as E-cadherins or mechanosensitive ion channels (Piezo1, TRPV4), using suitably functionalized MNPs and customized magnetic field applicators. This requires attaching MNPs on cell membranes using strategies that maximize their membrane residence time. Here, we present two approaches for living cell membrane labelling with MNPs: 1) a universal strategy based on bioorthogonal chemistry (strain-promoted azide-alkyne [3+2] cycloaddition – SPAAC) and 2) a specific strategy targeting E-cadherins. In the case of SPAAC, we introduce azide artificial reporters on cell membranes by metabolic glycoengineering or lipid insertion, followed by covalent reaction with MNPs functionalized with strained alkyne probes. For targeting cellular E-cadherins, we immobilize recombinant E-cadherin fragments on the MNP surface in an oriented manner using a one-pot metal affinity binding protocol developed in our group. These strategies can provide non-invasive tools for the mechanobiology community, allowing to apply mechanical forces to specific molecular targets with high spatial and temporal precision and to directly probe mechanotransduction pathways.
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Mechanical regulation of neuroepithelial development

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Flash Talks 6b, July 16, 2026, 12:00 - 12:30

During embryonic development, initially flat neuroepithelial tissues remodel themselves into complex 3D structures such as the brain or retina. This process is driven by intrinsically generated forces that depend on the cells' mechanical environment. However, how accumulated tension in the tissue feeds back on individual cells to influence their fate or migration patterns is not well understood. To address this, we downregulated the cellular force sensor Piezo1 in zebrafish and Xenopus laevis embryos, thereby reducing local mechanosensing capabilities. Piezo1 downregulation led to impaired retinal lamination, deformed retinae and nuclear rounding. Additionally, live imaging of Piezo1-deficient zebrafish eye primordia revealed defects in retinal progenitor migration during optic cup morphogenesis. These finding suggest that Piezo1 activity contributes to coordinating force generation and tissue level tension in the developing neuroepithelium, thus leading to nuclear and tissue shape changes. Combining laser ablation to locally perturb force propagation with direct measurement of tissue tension will clarify how Piezo1-dependent mechanical feedback links nuclear shape, cell fate decisions and tissue morphogenesis.

Adaptor-mediated recruitment of three dyneins to dynactin enhances force generation

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Flash Talks S4, July 15, 2026, 12:00 - 12:30

Cytoplasmic dynein is an essential microtubule motor protein that powers organelle transport and mitotic spindle assembly. Its activity depends on dynein-dynactin-cargo adaptor complexes, such as dynein-dynactin-BicD2 (DDB), which typically function with two dynein motors. We show that mechanical tension recruits a third dynein motor via an auxiliary BicD2 adaptor binding the light intermediate chain of the third dynein, stabilizing multi-dynein assemblies and enhancing force generation. Lis1 prevents dynein from transitioning into a force-limiting phi-like conformation, allowing single-dynein DDB to sustain forces up to ~4.5 pN, whereas force generation often ends at ~2.5 pN without Lis1. Complexes with two or three dyneins generate ~7 pN and ~9 pN, respectively, consistent with a staggered motor arrangement that enhances collective output. Under load, DDB primarily takes ~8 nm steps, challenging existing dynein coordination models. These findings reveal adaptive mechanisms that enable robust intracellular transport under varying mechanical demands.

Bridging perinuclear actin to the nucleus: new insights into cytoskeletal-nuclear integration

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Flash Talks S3a, July 14, 2026, 17:15 - 17:45

The interaction of actin filaments with the nuclear envelope is essential for diverse cellular processes, including cell migration, nuclear positioning, and transcriptional control. The main studied mechanism that links F-actin to the nucleus is the LINC complex. Recently, the formation of a perinuclear actin rim has been identified in various cell types in response to external force or migration cues. This rim affects transcription and cell motility capabilities, operates independently of the LINC complex, and relies on the activation of the actin nucleator INF2 by calcium influx. However, it is not clear how the rim is coupled with the nuclear envelope.
Here we show that the perinuclear actin rim is sensitive to elevated levels of lamin B1 but not lamin A, suggesting a physical link between the nuclear lamina and the cytosolic perinuclear actin rim. In search of potential coupling factors, we found that the nuclear membrane protein Emerin, which has an actin-binding domain, is not required for the perinuclear actin rim formation. Interestingly, we identified that Ezrin-Radixin-Moesin (ERM) proteins, traditionally known for linking F-actin to the plasma membrane, are also localized to the nuclear envelope. Overexpression of ERM proteins increased the perinuclear actin rim levels, while knockdown of ERM proteins reduced the rim levels. These results suggest that the ERM proteins are part of a lamin B-sensitive mechanism that links F-actin to the nuclear envelope in an alternative mechanism to the LINC complex.

Failed apoptotic extrusion drives an epithelia-intrinsic inflammation program

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Immunomechanobiology 3 and Flash Talks S3b, July 14, 2026, 17:15 - 17:45

Apical extrusion is an epithelia intrinsic surveillance mechanism that removes unfit or apoptotic cells in an immunologically silent manner whilst preserving barrier integrity. Apoptotic extrusion is a mechanically active process, where neighbour cells generate compressive forces on the apoptotic cell, through cortical contractility and lamellipodial activity. E-cadherin is necessary for this process, and disruption of E-cadherin adhesion and/or mechanotransduction compromises extrusion, with apoptotic cells being retained in the epithelium. Importantly, this led to upregulation of IL-8 expression in neighbour cells to elicit acute inflammatory responses.

In this study we used single cell RNA sequencing to further define neighbor cell responses when apoptotic extrusion failed. Apoptosis was induced with etoposide in Caco-2 cells, and extrusion inhibited by E-cadherin RNAi. The analysis of the dataset identified a distinct cluster corresponding to putative immediate neighbours in the failed extrusion model. These cells display significant upregulation of the TNF signalling pathway, which is strongly implicated in the pathogenesis of Crohn's disease and show an increased similarity to scRNA analysis of Crohn's disease patients' biopsies compared to the controls.

Together, our transcriptomic and functional validation data support a model in which defective apoptotic extrusion drives pro-inflammatory signalling in epithelial neighbours of apoptotic extrusion. Therefore, impaired extrusion may represent a previously unrecognized epithelia-intrinsic mechanism contributing to chronic inflammation in Crohn's disease. To directly assess clinical relevance, we will perform RNAscope analysis on intestinal biopsies from Crohn's patients to evaluate the spatial expression of candidate inflammatory targets identified in our single-cell dataset. We hypothesize that failed apoptotic extrusion constitutes an epithelial-intrinsic trigger of inflammation, providing a mechanistic bridge between barrier dysfunction and TNF-driven pathology in Crohn's disease.

Remodelling the bone marrow niche: A 2.5D in vitro platform for discovery.

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Flash Talks 6a, July 16, 2026, 12:00 - 12:30

The bone marrow (BM) niche integrates biochemical and mechanical cues that regulate hematopoietic stem cell (HSC) maintenance, yet recreating these interactions in vitro remains difficult because HSCs rapidly differentiate under standard culture conditions. There is a clear need for simple, mechanically relevant systems that preserve stromal function while allowing controlled interrogation of niche-driven regulation in both healthy and malignant haematopoiesis.
Here, we establish a 2.5D BM niche model based on soft, fibronectin-functionalised, degradable poly(ethylene glycol) (PEG) maleimide hydrogels overlaid onto mesenchymal stromal cells (MSCs). This configuration introduces defined mechanical confinement while retaining the advantages of a 2D interface: easy access for imaging and intact MSC paracrine signalling. Using confocal imaging, we quantified canonical niche-associated markers (NESTIN, SCF, CXCL12, ALCAM, LepR), YAP1 localisation, Ki67 expression, VINCULIN organisation, and extracted projected cell area. Functional readouts included primary HSC maintenance by flow cytometry, MOLM13 proliferation quantified by AlamarBlue, and MSC-mediated support of MOLM13 determined by flow cytometry.
MSCs overlaid with the FN PEG hydrogel consistently upregulated niche-associated markers and remained LepR positive. They were smaller in size, consistent with mechanical confinement, and displayed reinforced focal adhesions with increased VINCULIN density and an increased adhesion footprint. Notably, MSCs maintained total YAP1 even under ROCK inhibition, suggesting a stabilised cytoskeletal state not solely dependent on tension-regulated YAP dynamics. They remained largely quiescent in 2% FBS and re-entered the cell cycle only upon exposure to proliferation media. Functionally, mechanically primed MSCs supported a higher proportion of primitive HSCs compared with 2D controls and enhanced MOLM13 proliferation.
Together, these findings show that a simple hydrogel overlay is sufficient to drive MSCs toward a niche-like stromal phenotype through confinement, strengthened adhesion architecture, stabilised YAP signalling and controlled proliferation. This accessible, tunable 2.5D system provides a mechanistically relevant platform for studying stromal mechanobiology and improving human-relevant haematopoietic culture models.

Assessing the differential impact of RAS mutations on tissue mechanics and tumour formation

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Flash Talks 6b, July 16, 2026, 12:00 - 12:30

Human RAS genes encode three isoforms: KRAS, NRAS, and HRAS. In cancer, RAS proteins are often mutated at hotspot codons G12, G13, and Q61. Studies have shown that different RAS isoforms and point mutations exhibit distinct mutation frequencies across cancer types, which may be attributed to their unique signalling and functional properties.

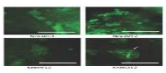
However, these differences have not yet been fully examined from a mechanobiological perspective. Hyperactivated RAS has been shown to increase cell contractility, which is linked to multiple tumorigenic processes, including dysregulated cell division, live-cell extrusion, and metastasis. The extent to which different RAS mutations alter the physical properties of cells during early tumorigenesis, however, remains to be elucidated.

We adopted a targeted microinjection system that delivers RAS-mutant RNA to a fate-restricted cell in developing Xenopus laevis embryos. This injected single cell generates a clonal tumour cell cluster in the epithelium of early gastrula stage embryos, allowing live imaging and laser ablation to study the mechanical properties of cancerous cells and their surrounding wild-type cells. Furthermore, we then grow the embryos to early tadpoles where the clonal clusters become induced tumour-like structures (ITLS), enabling the study of early tumorigenesis in complex tissue environments. This study focuses on four RAS variants: KRAS^G12V, KRAS^G12D, NRAS^G12V, and NRAS^Q61K. Preliminary data show that different RAS variants generate ITLS with distinct sizes, compositions, and intracellular RAS localisation patterns.

Laser ablation and western blot experiments indicate that KRAS^G12V and KRAS^G12D significantly increase junctional tension in tissues and are associated with elevated MAPK and PI3K/AKT pathway activity, whereas NRAS^Q61K does not increase junctional tension and is associated only with MAPK hyperactivation.

These results suggest that distinct RAS mutations exert differential tumorigenic and mechanical effects during early tumorigenesis, potentially explained by their variant-specific signalling profiles.

2. Different RAS proteins have different cellular localisation

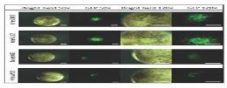


GFP+ intracellular partition

GFP at peripheral membranes

We observed an increase of GFP-positive signal in the cytosol of injected tumour cells at stage 28 (red arrow) compared to other RAS mutants (white arrow). Scale bars are 100µm.

4. Differences in early oncogenic clusters

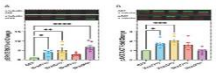


Bigger and irregularly contoured Kras mutant clusters

Smaller and peripherally localised Nras mutant clusters

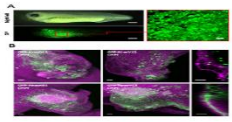
At stage 10, in GFP-KrasD12- and GFP-KrasV12- injected embryos, cell clusters were generally bigger in size and located in the centre of the neuroectoderm (white arrow) or the midbrain (yellow arrow). In GFP-NrasQ61- and GFP-NrasV12-injected embryos, cell clusters were generally smaller in size and located on the edge of the neural tube (white arrow). Scale bars are 100µm.

5. Differences in signalling pathway activation downstream of RAS variants



(A) All RAS variants except for NrasV12 hyperactivate the MAPK pathway.
(B) Only NrasV12 hyperactivates the PI3K/Akt pathway while Nras variants do not. We are currently using WB to look at the activation of downstream effectors of PI3K/Akt in RAS variants. We are also testing the effects of RAS inhibitor Ulixertinib and the AKT inhibitor Capivasertib on Xenopus embryos. *p < 0.05, **p < 0.01, ***p < 0.001

3. Different RAS tumour cells might have different fates

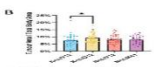


Injection of control SFP RNA into a single A4 blastomere results in a large proportion of fluorescent cells differentiating into melanocytes with a characteristic dendritic morphology. Scale bars are 500 µm (left panel) and 50 µm (right panel).

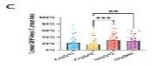
Confocal images of whole-mount stained ITLS showing that KrasV12 tumours are characterised by sheets of tumour cells with apical-out polarity, whereas cells in other mutants are not. Scale bars are 50µm.

1. Different RAS variants produce subtly different tumours in terms of shape and cell contact

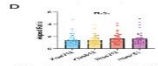
Demonstration image of how we calculated the ITLS (isolated tumour-like structure) area.



A higher mean ITLS area as a percentage of body area was observed in GFP-KrasD12-injected embryos compared to that of GFP-KrasV12-injected ones.

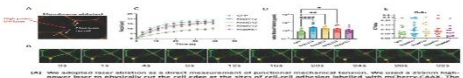


Nras-mutant ITLS had a significantly higher percentage of within which GFP signals colocalise to tumour area, when compared to KrasD12.



Dot plot showing the mean length/width ratios of ITLS between all RAS mutant groups were not significantly different from each other. *p < 0.05, **p < 0.01, ***p < 0.001

6. Mechanical differences between different RAS variants



(A) We adopted laser ablation as a direct measurement of junctional mechanical tension. We used a 200mW high-power laser to physically cut the cell edge at the sites of cell-cell adhesion labelled with mCherry-CAAX. The junction could be then visualised as the outwards recoil of the vertices following ablation. SY coordinates of the two vertices were tracked using the Fiji plugin TrackMate. Initial recoil velocity was calculated as the first derivative of the fitted curve.
(B) Cropped region of confocal time lapse stills showing laser ablation at a cell edge in a GFP-KrasV12 cluster.
(C) Recoil measurements.
(D) Initial recoil velocities within KrasV12 clusters ($p < 0.001$), KrasD12 clusters ($p < 0.01$) and NrasV12 clusters ($p < 0.01$) were significantly higher than in GFP clusters (pooled) (tests with Dunn's tests).
(E) K values showed no significant differences between groups (Kruskal Wallis with Dunn's tests), suggesting that initial recoil velocity can act as an indicator of local junctional tension.

Recurrent mechanical stress in periorbital skin is associated with accelerated aging in vivo and is reproduced in an in vitro cyclic strain model

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Mechanobiology of Ageing 3 and Flash Talks 5b, July 15, 2026, 17:15 - 17:45

Aging of the skin is a complex, multifactorial biological process driven by both intrinsic and extrinsic influences. Although exposed to similar aging factors, individual facial sites display markedly different aging phenotypes, illustrated by the earlier onset of wrinkle formation in the periorbital area compared with the cheek. As the periorbital area is subjected to continuous mechanical strain from facial expression, we hypothesized that mechanical stress might be a major determinant of its accelerated aging phenotype. To investigate this, we conducted an in vivo study with 88 female subjects (aged 18–78 years) and compared skin samples of the periorbital site and the cheek, a facial site exposed to lower levels of mechanical strains. Consistent with our hypothesis, we detected differential expression of mechanosensitive genes in the periorbital site, accompanied by differences in skin structure and accelerated cellular aging. Metabolic, mitochondrial and translational pathways were downregulated in the periorbital site, in parallel with accelerated biological aging demonstrated by transcriptomic age clock analysis. Intriguingly, even young subjects (< 30 years old) showed accelerated molecular aging in the periorbital site, consistent with mechanical stress as an underlying contributor. To validate the role of continuous mechanical strain in periorbital skin aging, we employed an automatic, uniaxial stretch system (STREX ST-1440) to apply cyclic mechanical strain (CMS) to primary skin cells. Transcriptomic profiling of cells subjected to in vitro CMS revealed overlapping signatures with those observed in vivo, including suppression of mitochondrial and translational pathways, thus further linking the in vivo molecular alterations to mechanical stress. In summary, our study proposes mechanobiological processes as a central determinant of site specific skin aging, explaining why periorbital skin ages more rapidly than adjacent sites. Targeted modulation of mechanotransduction pathways may thus form the basis for future interventions to counteract mechanical stress-induced skin aging.

Optogenetic construction of de novo integrin-adhesion complexes reveals role for biocondensation in adhesion nucleation

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Flash Talks S2, July 14, 2026, 12:00 - 12:30

Integrin-adhesion complexes (IACs) form spontaneously in cells on extracellular matrix substrates, allowing them to sense matrix composition and transduce force. However, IACs often do not form uniformly across a cell, which begs the question: What is required to nucleate an adhesion, and what factors enable the stabilization of an IAC once it has formed? Many factors have been suggested to promote formation and the subsequent stabilization of IACs. It is difficult to explicitly test these factors in vivo as IACs undergo constant remodeling. Here, we employ optogenetics to explicitly test the ability of talin in different activity and phase states to nucleate and stabilize IACs in regions where none are present. We find that fusion of intrinsically disordered regions directly to talin enhances its adhesion nucleation potential and allows new adhesions to be produced in response to optogenetic talin clustering. Similarly, expression of factors previously shown to enhance biocondensation in vitro, such as paxillin, the paxillin N-terminus, or unfolding of talin, allows for adhesion nucleation and biocondensation of talin. We show that these biocondensates of talin can cluster and activate integrins even in the absence of extracellular matrix. By applying optogenetic activation to regions of the cell with or without ventral actomyosin, we demonstrate actomyosin engagement promotes the formation and stability of adhesions. These results are corroborated by theoretical modelling which shows that phase separation of talin is enhanced by differential clutch formation in the presence of actomyosin thus enabling peripheral adhesion formation and stability. This work establishes a model in which increased cooperativity of talin enables IAC nucleation through talin biocondensation, which clusters and activates integrins. In addition to these findings, we generate multiple optogenetic tools that enable local nucleation or enhancement of IACs.

CapG is a mechanoresponsive transcriptional co-regulator of cancer cell invasion programs.

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Flash Talks S3a, July 14, 2026, 17:15 - 17:45

Mechanical forces are increasingly recognized as central regulators of cancer behavior, promoting invasion and therapy resistance through the induction of force-responsive molecular pathways. These effects are particularly relevant in solid tumors that experience elevated mechanical stress, such as pancreatic ductal adenocarcinoma (PDAC) and glioblastoma (GBM). Although morphologically and mechanistically different, both develop within physically challenging microenvironments, where elevated intratumoral pressures and tissue stiffness can impact signaling pathways that promote invasion, including epithelial-to-mesenchymal transition (EMT). Identifying force-responsive elements driving these processes across highly invasive epithelial and non-epithelial tumors will thus provide valuable insight into potential therapy targets.

Using comparative proteomics studies of invasive and non-invasive GBM cell lines, we identified significantly elevated levels of actin-capping protein CapG in the nuclei of highly invasive cells. We find that CapG subcellular localization changes in response to cell density and to mechanical stimuli, increasing in its nuclear localization upon higher force loads, similar to the behavior of prototypical mechanosensitive regulator YAP. Furthermore, we find that Lamin A/C acts as a retention factor for this protein's nuclear localization. Importantly, we find that nuclear CapG interacts with EMT-associated transcription factors and regulates expression of hallmark EMT genes. Finally, we confirm in patient samples that elevated expression and nuclear localization of CapG correlate with PDAC progression and Lamin A levels, and are associated with -nuclear- biomechanical properties, EMT and TGFβ signaling gene upregulation in infiltrating tumor regions.

Taken together, our findings implicate CapG in a novel mechanosensitive pathway that drives invasive behavior in PDAC and GBM, highlighting a potential new therapeutic avenue for these malignancies.

Measuring the pushing force exerted by cytoskeleton proteins using optical tweezers.

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Flash Talks S2, July 14, 2026, 12:00 - 12:30

A cell's ability to interact with its environment through membrane protrusions is fundamental to interpretation and navigation of complex 3D environments of extracellular matrices (ECM). Membrane protrusions can take various forms (filopodia, lamellipodia, blebs) with actin machinery engaging with the cell membrane, pushing it forward and retracting it when required. During migration, protrusions can interpret various signals, matrix stiffness, pore sizes or chemokine gradient, allowing the cell to travel the path of least resistance. Assuming that these protrusions can exert not only pulling but pushing forces to probe/deform/displace the ECM, the global aim of the project is to measure these pushing forces and identify the mechanisms producing them.
Using beads trapped by an optical tweezers, membrane tethers are pulled from adherent cells and the dynamics of the cytoskeleton components can be studied. Additionally, the forces applied by the cell to the bead during this process can be measured and the presence of pushing forces can be identified.
Furthermore, in an aim to understand the mechanisms leading to the growth of Actin into the tethers we investigate if coating the beads with different proteins plays a role. Interestingly, our preliminary results indicate that, actin grows into the pulled tether when fibronectin or concanavalin A coated beads are used. However, length of the tether potentially dictates the type of growth, continuous from the base or patchy throughout the tube, and the forces exerted on the bead. Finally, we observe that microtubules polymerize into the membrane tethers only when Actin is depolymerized using Latrunculin B, this also allows us to measure the force that MTs can exert on their environment inside a cell and their dynamics in protrusions.

Chemo-mechanical characterisation of engineered bone marrow niches using correlative Brillouin and Raman spectroscopy

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Flash Talks S2, July 14, 2026, 12:00 - 12:30

The bone marrow (BM) niche is a dynamic mechano-chemical environment that regulates haematopoietic stem cell maintenance, cancer evolution and dormancy. Capturing these processes in human-relevant models requires non-invasive technologies capable of resolving both mechanical and biochemical changes over time. Here, we develop a correlative Brillouin–Raman micro-spectroscopy platform for label-free chemo-mechanical characterisation of engineered BM niches.
Both techniques rely on inelastic light scattering but probe distinct regimes: Brillouin scattering detects GHz-frequency shifts arising from interactions with acoustic phonons and reports on viscoelastic properties, whereas Raman scattering measures THz vibrational modes linked to molecular composition. The large spectral separation of these signals enables their collection within a shared optical pathway, providing complementary, high-content information beyond conventional endpoint assays.
We apply Brillouin microspectroscopy to a 2.5D BM niche model comprising mesenchymal stromal cells interfaced with synthetic PEG-fibronectin hydrogels with a controlled degradability rate, implemented in miniaturised PDMS devices. Focusing on microenvironmental mechanics provides an effective strategy to monitor niche evolution, capturing subtle, time-dependent changes driven by coordinated cell-mediated remodelling. Brillouin mapping confirms spatial mechanical homogeneity within developed niche-on-chip models and detects time-dependent changes driven by cell-extracellular matrix interactions. Degradable and non-degradable matrices show distinct mechanical evolution over one week, highlighting the sensitivity of our system to progressive remodelling of the cellular environment. These results illustrate the strength of Brillouin spectroscopy as a robust mechanical readout for optimisation of niche-on-chip systems.
Ongoing work focuses on integrating Raman spectroscopy to complement mechanical measurements with biochemical information, enabling correlative tracking of dynamic processes within engineered BM niches. Future developments will include automated acquisition to improve throughput. Together, this platform provides a scalable, non-invasive framework for studying mechanobiological processes in human-relevant models.
This work was supported by a UKRI EPSRC (EP/X036049/1).

Mechanical and Transcriptional Responses of Breast Cancer Cells to Microfluidic- Induced Rapid Deformations and Monolayer Stretching

Mona Makkieh[1,5], Alessandra A. Passeri[2,5], **Davide Lazzari**[1,5], Stefano Marchesi[1], Andrea Disanza[1], Leonardo Donati[3], Rafal Salem[1], Sabata Martino[3], Daniele Fioretto[2], Maurizio Mattarelli[2], Giorgio Scita[1,6], Silvia Caponi[4,6], Brenda Green[1,6]
[1]IFOM- AIRC Institute of Molecular Oncology, Italy, [2]University of Perugia- Department of Physics, Italy, [3]University of Perugia- Department of Chemistry, Biology, and Biotechnologies, Italy, [4]National Research Council of Italy, Italy, [5]Equal Contribution, [6]Corresponding Co-authors
Flash Talks S2, July 14, 2026, 12:00 - 12:30

Mechanical forces and physical properties play a fundamental role in regulating cellular processes, such as cytoskeletal remodeling, gene expression, and cell behavior, with profound implications for both physiological functions and disease. Despite major advances in the characterization of 3D cell mechanics, significant technical challenges remain in capturing the dynamic coupling between mechanical and biochemical processes. To address these limitations, we developed Brillouin–Raman Microspectroscopy on-a-Chip, which enables high resolution analysis of mechano-chemical responses in complex live 3D biological systems under controlled deformation. This contact-free, optical method combines Brillouin and Raman microscopy within microfluidic devices, providing a unique correlative approach to overcome current limitations in probing cellular mechanics and biochemical responses in live multicellular models.
Applying this platform to breast tumor spheroids, we reveal that rapid, cyclical mechanical deformations, mimicking in vivo stresses, significantly impacts tumor physiology. These responses are accompanied by global spheroid stiffening, as precisely quantified by Brillouin spectroscopy and confirmed by elevated phalloidin levels. Remarkably, repeated deformation imprints a form of mechanical memory in these collective systems, which result in enhanced invasiveness.
The controlled spheroid deformations trigger rapid nuclear shape changes and robust transcriptional reprogramming, marked by a significant upregulation of the early stress response master regulator ATF3. ATF3 is a transcription factor that that is activated rapidly and transiently and can exert either cell-protective or cell-detrimental effects, depending on the nature and duration of the stress. To investigate ATF3 as a mechano-responsive element in breast cancer progression, we employed multiple mechanical perturbation paradigms, including spheroid deformation, hypo- and hypertonic treatments, and monolayer stretching. Consistent with previous reports implicating ATF3 in oncogenic behavior and enhanced invasive potential, our data reveal that prolonged and repeated mechanical stress induces a form of mechanical memory, associated with changes in chromatin remodelling.

YAP/TAZ deficiency in megakaryocytes impairs actomyosin function and increases platelet formation

Noemie Brassard-Jollive[1], Ines Guinard[1], Julie Boscher[1], Laurie Ruch[1], Josiane Weber[1], Nungruthai Nilsri[2], Catherine LEON[1]
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Flash Talks 6b, July 16, 2026, 12:00 - 12:30

Platelet production relies on megakaryocytes (MKs), located in the bone marrow, a soft but highly confined environment. MKs extend proplatelets through vessel wall, that elongate in the bloodstream to release platelets. We previously showed that stiff substrate and 3D confinement negatively controlled proplatelet extension through activation of RhoGTPases and actomyosin. To investigate the mechanisms, we used a mouse model of myelosuppression induced by 5-fluorouracile that promotes loss of confinement and ectopic platelet release. Transcriptomic analyses revealed down regulation of the hippo-Yap pathway. Although it is widely accepted that YAP/TAZ are indispensable to relay mechanical inputs in various pathophysiological contexts, their involvement in MK differentiation and platelet production remained unexplored. Using a 3D culture model in soft gel, we observed preferential YAP nuclear relocation in MKs compared to the liquid culture. Mice deficient for YAP/TAZ in the megakaryocytic lineage (Yap/Taz-/-; Pf4-Cre) (DKO) presented a 20% increased platelet count. Under regenerative conditions, this higher platelet count was up to 48%, associated with a 12% decreased platelet volume. To identify the mechanisms, we performed transcriptomic analysis and observed in DKO MKs a number of differentially expressed genes related to actin cytoskeleton. Accordingly, MK spreading onto stiff substrate (90 kPa) was defective in DKO MKs, associated with a decreased podosome density, confirming impaired cytoskeleton reorganization upon adhesion, while conversely proplatelet formation was increased on the stiff substrate. Altogether, these data suggested that absence of YAP/TAZ alter MK capacity to adequately respond to stiffness and restrain proplatelet formation. Furthermore, absence of YAP/TAZ promoted the presence of abnormally shaped, elongated MKs with “worm-like” morphology and deformed nucleus. These elongated shapes are likely promoted by anormal actomyosin cytoskeleton activity and stabilized by microtubules. In conclusion, we found that YAP/TAZ plays a role in controlling the capacity of MK to normally adapt to stiffness and control platelet formation.

In vivo nuclear envelope adaptation during cell migration across confining embryonic tissue environments

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[1]Department of Physiology, Development and Neuroscience, University Of Cambridge, United Kingdom

Flash Talks 6b, July 16, 2026, 12:00 - 12:30

In physiology and in disease, cells often migrate through narrow spaces, such as leukocytes undergoing diapedesis or cancer cells during dissemination. Cultured cells under physical confinement have been shown to experience mechanical stress due to deformation of the nucleus. Nuclear deformation can lead to loss of nuclear integrity and DNA damage, and it has been proposed to underlie cancer initiation and progression. In vivo, the consequences of physical confinement on physiological, developmental cell migration remain so far unexplored. Here, we use the zebrafish neural crest as an in vivo model to address how multipotent embryonic cells respond to physical confinement during developmental migration. By measuring the extracellular space from head to tail along the embryonic body axis, we found that the level of tissue scale confinement increases along the antero-posterior axis. We found that neural crest experience dramatic nuclear deformation during their migrating between adjacent tissues, which quantitatively scales with tissue confinement. By using complementary genetic and mechanical strategies to ablate the surrounding tissue, we observe a rescue of nuclear deformation in vivo. Surprisingly, we found that while deformation of the NC nucleus causes stretching of the nuclear envelope, it does not cause DNA damage even upon extreme deformations. Instead, cells adapt, by decreasing both their DNA damage and LaminB2 levels upon entering confined spaces. In summary, we establish the neural crest as a physiological framework uncovering a dynamic adaptation to tissue confinement in vivo.

Signals from the mechanosensitive ion channel Piezo1 involved in the activation of the metalloproteinase

Christine Lux, Alessa Pabst, Aaron Babendreyer, Stefan Düsterhöft, **Andreas Ludwig**

Flash Talks 5a, July 15, 2026, 17:15 - 17:45

We have demonstrated that mechanical activation of the ion channel Piezo1 can enforce the activity of the metalloproteinase ADAM17 in various cell types leading to increased shedding of surface molecules. ADAM17 is well known to be regulated via the adapter molecule iRhom2, but it remains unclear how Piezo1 mediated signalling can tune this regulation. Cell stimulation with the Piezo1 agonist Yoda1 or the PKC agonist PMA leads to activation of several kinases including ERK1/2. In coprecipitation studies with transfected HEK293 cells we found that ERK1/2 can associate with tagged iRhom2 and that bound ERK1/2 is phosphorylated when cells are stimulated with Yoda1 or PMA. Notably, this cell stimulation is also associated with increased binding of iRhom2 to 14-3-3 protein which is known to strongly depend on phosphorylation of the target proteins. Removal of potential phosphorylation sites in the iRhom2 N-terminus abrogates 14-3-3 binding but does not affect ERK1/2 binding. Moreover, inhibition of ERK1/2 kinase was found to abrogate 14-3-3 protein binding. Notably, the removal of phosphorylation sites in iRhom2 could well suppress PMA induced ADAM17 activation but had only a modest effect on Piezo1 induced ADAM17 activity as measured by a substrate cleavage assay. The results demonstrate that Piezo1 and PMA induce activation of ERK1/2 bound to iRhom2 leading to phosphorylation dependent recruitment of 14-3-3 to iRhom2, but the extent to which this regulatory pathway impacts ADAM17 activity seems to be different for both stimuli. Finally, we studied the effect of ERK1/2 inhibition on ADAM17 in endothelial cells. Yoda1 treatment induced ERK1/ 2 phosphorylation and ADAM17 activation which was measured in terms of JAM-A or TNFR shedding. This response could be suppressed in part by the ERK1/2 inhibitor indicating that the ERK1/2 pathway is involved but not sufficient to explain ADAM17 regulation by Piezo1 signaling.

Biomechanical Vulnerability of Oral Cancer Cells Enables Low-Frequency Ultrasound Treatment

Rashmita Luha[1], Ajay Tijore[1]
[1]Indian Institute Of Science, India

Flash Talks 6c, July 16, 2026, 12:00 - 12:30

Achieving selective and efficient targeting of cancer cells while preserving the normal cells remains a crucial obstacle in oral cancer therapies, which compromises patients' quality of life. Here, we present a non-invasive approach using low-frequency ultrasound (US) to exploit the biomechanical vulnerabilities of patient-derived oral cancer cells, thereby promoting selective apoptosis. Cancer cells are subjected to optimized US parameters, revealing selective induction of cancer cell apoptosis (mechanoptosis) without harming normal cells. Reduced expression of the mechanosensory protein Tropomyosin 2.1 (Tpm2.1) in oral cancer cells, due to elevated levels of MicroRNA-21 (miR-21), correlates with heightened sensitivity to US treatment. Furthermore, mechanistic studies demonstrate that US disrupts actomyosin contractility by disassembling myosin IIA fibers, thereby impairing the migration and invasion of cancer cells. Remarkably, a study using an elastomeric platform for coculture of patient-derived cancer and cancer-associated fibroblast (CAF) cells shows a significant reduction in CAFs' ability to infiltrate and compartmentalize the tumor core as well as encapsulate the tumor upon US treatment. Our findings thus provide a foundation for developing a non-invasive US treatment for oral cancer and opening avenues for broader application in superficial malignancies.

Investigating cell-material interaction for the study of cell migration induced by substrate space-time warping

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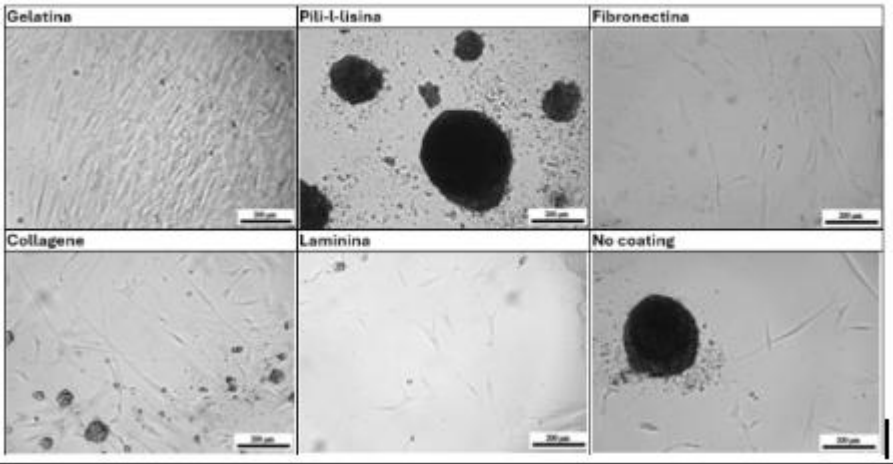
[1]Department of Information Engineering, University of Pisa , Fucecchio, Italy, [2]Research Centre "Enrico Piaggio", University of Pisa, Italy

Flash Talks S4, July 15, 2026, 12:00 - 12:30

Cell–material interactions regulate adhesion, migration, and tissue organization, yet the influence of substrate biochemical functionalization remains poorly standardized, particularly in soft systems. Current studies compare only a few coatings, using heterogeneous metrics, preventing quantitative cross-study comparisons. This gap is especially relevant for adipose-derived mesenchymal stem cells (ADSCs), a clinically promising and mechanoresponsive cell population, widely used in regenerative medicine and organ-mimetic models. We, systematically, investigate ADSC adhesion dynamics (as monolayers and spheroids) on soft substrates functionalized with five coatings, with the long-term goal of enabling controlled cell migration through cell-induced substrate warping as a contactless guidance strategy. ADSCs were seeded (31250 cells/cm^2) on 5 mg/mL agarose-20 mg/mL dextran gels coated with gelatine (50 mg/mL), collagen (100 µg/mL), fibronectin (10 µg/mL), laminin (100 µg/mL), poli-l-lysine (100 µg/mL) and on culture plates as control. Cells were monitored through live bright-field images taken every two minutes for one hour, starting two hours after seeding and every two hours for three days. To determine the optimal cell number allowing for spheroid formation, different cell numbers (5,000-200,000 cells) were cultured for 48 hours on low-adhesion wells to promote aggregation and then transferred to non-coated substrates. Imaging was performed to assess morphology at 10x magnification, using a bright field microscope. Spheroid diameter and roundness were quantified analysing images with ImageJ. The results demonstrate coating-dependent differences in cell morphology and adhesion behaviour (Fig.1a) and a cell number-dependent increase in spheroid size, sphericity, and cohesion (Fig. 1b). These preliminary findings, show that substrate coating significantly modulates cell adhesion. Ongoing quantitative analyses of shape descriptors, migration velocity, and adhesion kinetics will provide standardized metrics linking substrate chemistry to cell dynamics. This unified dataset will support computational modelling and the development of advanced in vitro systems for the study of cell migration as a function of substrate space-time warping.

a)


Gelatina
Pili-l-Lisina
Fibronectina
Collagene
Laminina
No coating

b)

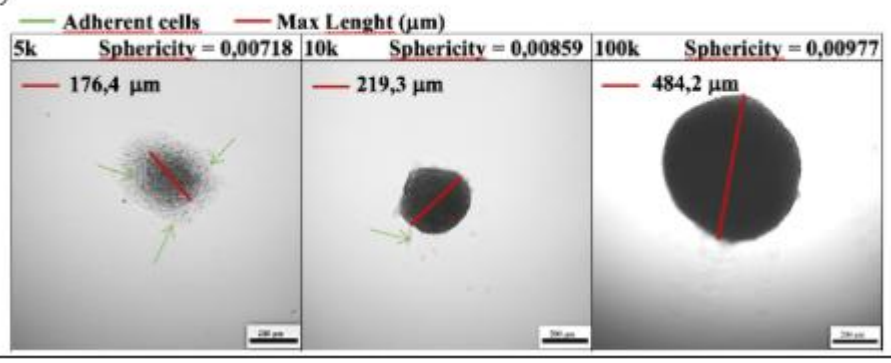

Adherent cells
Max Lenght (µm)
5k Sphericity = 0,00718
176,4 µm
10k Sphericity = 0,00859
219,3 µm
100k Sphericity = 0,00977
484,2 µm

Photo-responsive hydrogels with tunable stiffness for cell mechanobiology

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Immunomechanobiology 3 and Flash Talks S3b, July 14, 2026, 17:15 - 17:45

Chronic liver diseases lead to approximately 2 million deaths each year. Fibrosis—driven by the excessive deposition of extracellular matrix produced by activated hepatic stellate cells—is the primary risk factor for hepatocellular carcinoma. Despite its clinical relevance, effective antifibrotic treatments remain limited and often burdened by significant side effects. Immune-based cell therapies, especially those involving macrophages, offer a promising avenue for liver regeneration; however, their therapeutic impact has so far been limited, likely because current strategies fail to induce a durable, antifibrotic macrophage state.
This work aims to overcome this limitation by developing a new therapeutic approach that “primes” macrophages through mechanical stimulation. The strategy exploits mechanical memory, a long-lasting cellular program that persists even after mechanical cues are removed. To achieve this, we engineered a light-responsive hydrogel composed of chitosan, a highly biocompatible natural polymer, cross-linked with azobenzene functionalized genipin to enable on-demand modulation of stiffness. This platform aims to deliver precisely controlled spatiotemporal mechanical cues to macrophages, steering them toward an anti-inflammatory phenotype and ultimately offering a promising route to restore liver functionality.

Investigating the mechanical effects of microbubble cavitation with high-speed imaging

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Flash Talks 6c, July 16, 2026, 12:00 - 12:30

The aim of this study was to observe and quantify the direct mechanical effects of microbubble cavitation on healthy vs. malignant tissue.

UPPL1541 tumours were implanted into the bladders of mice. After three weeks, the mice were culled then transcardially perfused with 2ml of phospholipid-coated microbubbles. The implanted tumours, and additional healthy tissue were then excised. 100um thick slices of these tissues were imaged with a high-speed camera at 10 Mfps, under ultrasound exposure (200 cycle pulses, 0.5MHz centre frequency, 1MPa peak negative pressure).

Analysis of microbubble oscillation amplitude and tissue strain indicated a notably higher stiffness of tumour compared to healthy tissue. This is consistent with quasistatic measurements. Microbubbles were also observed moving from blood vessels into the surrounding tissue, suggesting that extravasation of intact microbubbles can occur.

The direct mechanical effects of cavitation are likely important contributors to their therapeutic effects in drug delivery as well as ablative applications. The significant extravasation of microbubbles into tumour tissue potentially provides an explanation for ultrasound mediated treatments remaining effective in poorly vascularised tumours.

The authors would like to thank James Choi for providing invaluable advice on this project. Funding for this project was provided by EPSRC.

Characterisation of Tumour Cell Biomechanics using High-Throughput Microfluidic Devices

Orlaith McSweeney[1], María José Gómez-Benito[2], Irish Senthilkumar[1], Bart Smeets[3], Eoin McEvoy[1]
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Flash Talks S4, July 15, 2026, 12:00 - 12:30

INTRODUCTION

Personalised treatment requires mechanistic insight into heterogeneous tumour cell behaviour, such as identifying biomarkers for chemoresistance. This study presents a microfluidic cell aspiration platform, integrated with computational modelling, to characterise heterogeneity in active tumour cell biomechanics.

METHODS

We developed a high-throughput system for cell membrane aspiration within custom microfluidic devices, by controlling pressure gradients (ΔP) across microchannels. PDMS chips with 5-15μm microchannels were fabricated via photolithography and plasma-bonded to coverslips. We developed computational fluid dynamics (CFD; COMSOL) models to predict how geometry and boundary conditions govern ΔP (Fig.1A). Chips were interfaced with pressure controllers (Fluigent) to impose ΔP in a 0.6-1kPa range. We seeded T47D cells stained with BioTracker490 membrane dye ($1x10^6$ cells/ml) within the device and monitored aspiration into microchannels over time (Fig.1B). ImageJ was used to measure cell diameters pre-aspiration and aspiration lengths. We developed finite element (FE) models incorporating active cortical, cytoplasmic and nuclear regions (Abaqus, Fig.1B), to capture non-linear, viscoelastic behaviour, calibrated to experimental timescales (Fig.1E). Finally, models were extended to multicellular models (Mpacts, Fig.1F) to parse heterogeneity across larger length scales.

RESULTS

CFD modelling revealed device designs and conditions to ensure gradual ΔPs across microchannels (Fig.1A). Optimal cell aspiration occurred in 6-9μm channels, with aspiration length increasing with channel width and ΔP (Fig.1D). Result variability reflected heterogeneity in cell size and stiffness (Φmean: 12.09±3.09μm). FE modelling uncovered the time-dependent interplay between non-linear cortex and nucleus stiffness in governing aspiration length arising from biomechanical heterogeneity (Fig.1C). While stiff cells are more readily aspirated when smaller, softer cells exhibit greater aspiration lengths when larger due to a transition from an elasticity-limited to a volume-limited response.

DISCUSSION

This coupled experimental-computational platform enables quantitative characterisation of non-linear tumour cell biomechanics. This framework can be extended to provide novel characterisation for biomechanisms of chemoresistance, multicellular spheroids, and patient-derived tissue.

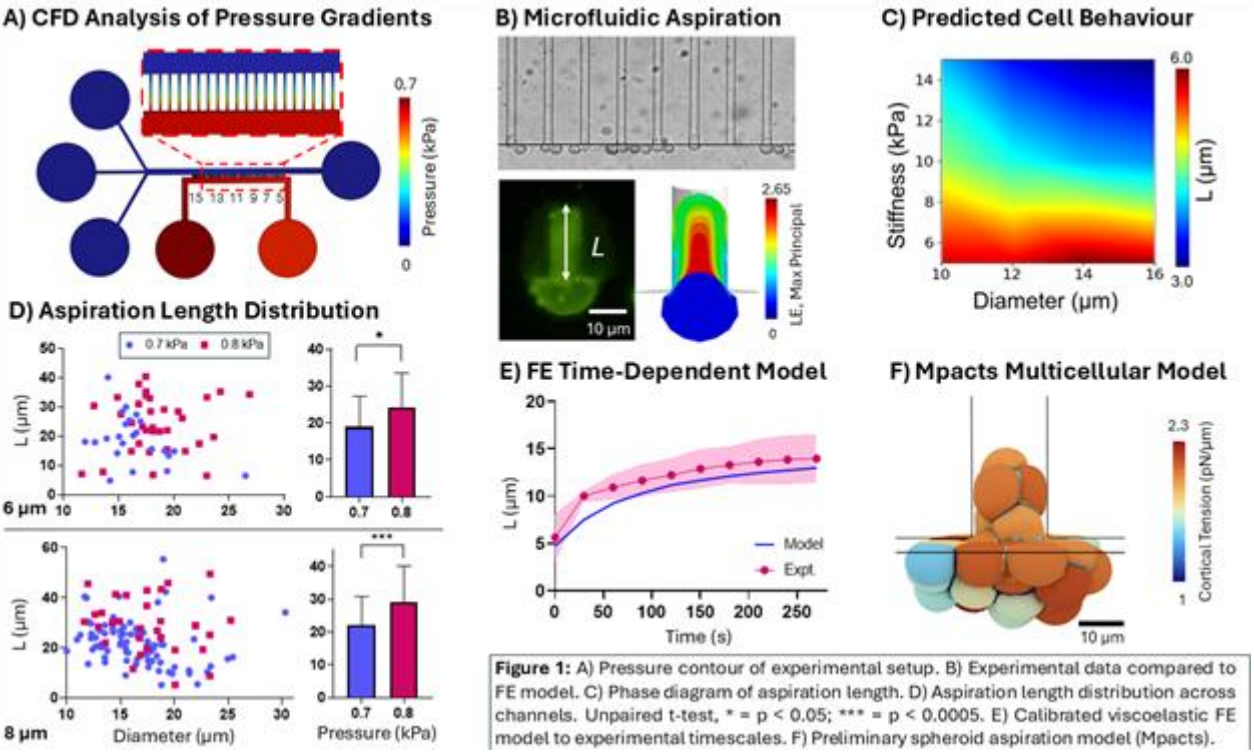

Figure 1: A) Pressure contour of experimental setup. B) Experimental data compared to FE model. C) Phase diagram of aspiration length. D) Aspiration length distribution across channels. Unpaired t-test, * = $p < 0.05$; *** = $p < 0.0005$. E) Calibrated viscoelastic FE model to experimental timescales. F) Preliminary spheroid aspiration model (Mpacts).

Inhibiting mechanotransduction as a novel approach for cancer therapy

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[1]Institute for Bioengineering of Catalonia (IBEC)), Spain, [2]Institute for Research in Biomedicine (IRB), Spain, [3]King's College London, United Kingdom

Flash Talks S1, July 13, 2026, 17:15 - 17:45

Increased tissue stiffness is a hallmark of many solid tumours, driving tumour progression. This occurs through mechanotransduction, the process by which cells sense and respond to mechanical signals. Our lab has identified a key interaction between two proteins, essential for mechanotransduction. This interaction is triggered by force-induced unfolding of a target protein, which occurs only in stiff tissues. Hence, we propose a novel therapeutic approach that targets mechanotransduction by inhibiting the stiffness-induced unfolding of the target protein. This innovative approach provides a new angle to cancer therapy and novel insights into the role of mechanical signals in disease progression. With this aim, we have identified peptide hits that can increase the mechanical stability of the target protein upon binding to it. This in turn inhibits target protein unfolding and subsequent mechanotransduction events important for cancer progression. The peptide hits have been thoroughly validated in various in vitro assays. In cellulo, transient expression of peptide hits in fibroblast decreased focal adhesions (FAs), cell spreading and the nuclear to cytoplasmic ratio (N/C) of the mechanosensitive transcription factor YAP on stiff substrates. Peptide hits had no effect on soft substrates, indicating a specific inhibition of mechanotransduction. Currently, we are expanding the functional characterisation of the biological activity of the peptide hits in fibroblasts and pancreatic cancer cells and in vivo.
Overall, our goal is to demonstrate a clear mode of action of the peptide hits on cancer cells, fibroblasts, and in a pancreatic cancer mouse model. This study will lead to a first-in-class mechanoinhibitor drug like candidate, with potential applications in cancer (with a focus on pancreatic cancer) and other conditions characterized by mechanical stress, such as fibrosis.

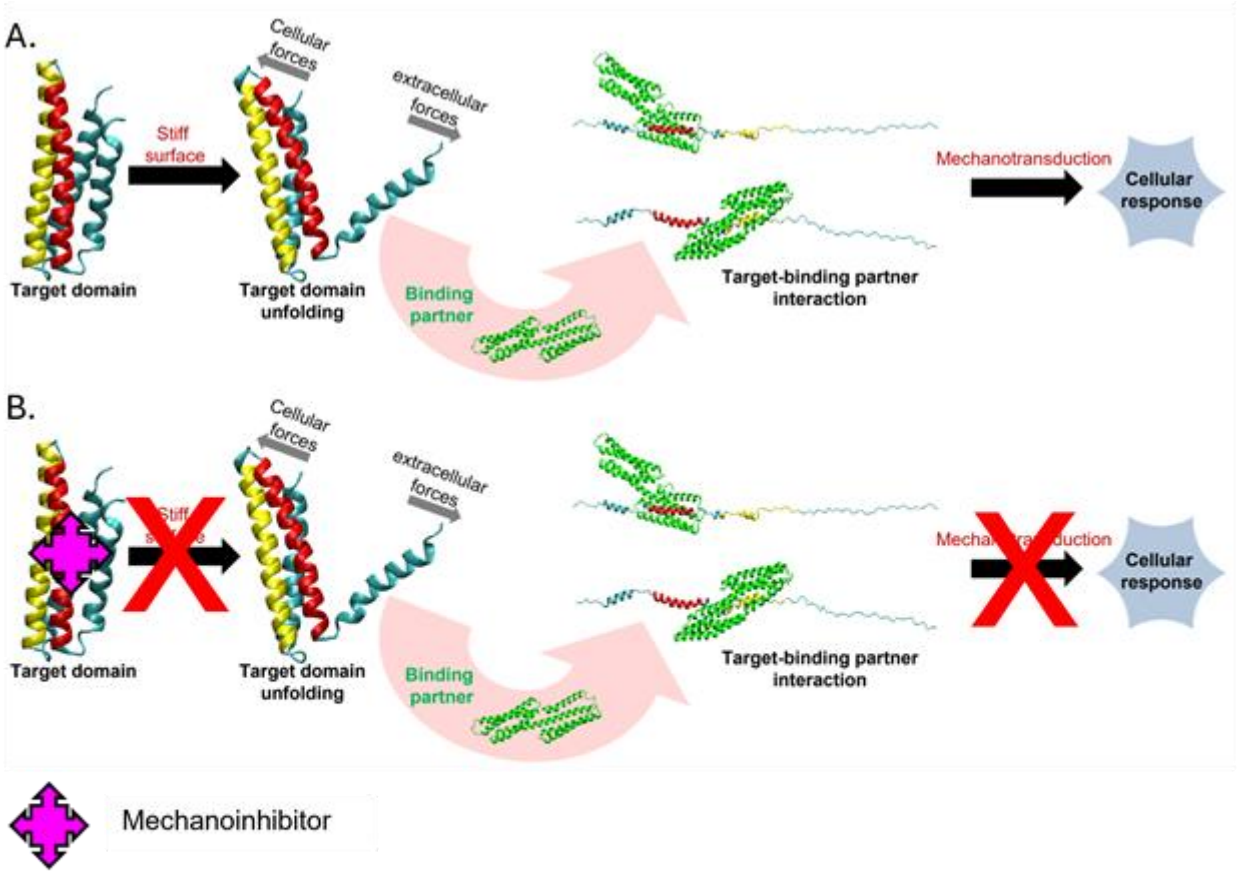


Fig. 1: Schematic of the project concept. **A.** In stiff environment, cells and tissues exert forces that lead to unfolding of the target protein Talin R3 and opening of cryptic binding sites. Binding of Talin to its partner Vinculin leads to a cascade of events in the process called mechanotransduction. Finally, the mechanical cues are transduced into biochemical signals, results in cellular responses that promote tumor progression. **B.** The mechanoinhibitor (magenta inset) bind to the surface of our target, mechanically reinforcing and increases its stability. Subsequently hinders the unfolding of the target blocking mechanotransduction events.

Strain Rate Impacts Biological Properties and Membrane Tension of Cells in Xenopus laevis Epithelia

Dr Iona Norwood[1], Natasha Cowley[1], Irwin Phanada[1], Raphael Thuret[1], Oliver Jensen[2], Patrick Caswell[1], Sarah Woolner[1]
[1]Division of Cell Matrix Biology and Regenerative Medicine, University of Manchester, United Kingdom, [2]Department of Mathematics, University of Manchester, United Kingdom
Flash Talks S2, July 14, 2026, 12:00 - 12:30

Cells within our tissues are constantly subjected to internal and external mechanical forces and must detect and respond to these forces appropriately through the process of mechanotransduction. These mechano-responses play a key role in maintaining tissue homeostasis, morphogenesis, and the prognosis of many common diseases, such as cancer.

The exact method by which cells can detect forces is not yet fully understood. Direct detection of changes in the membrane tension has provided one potential mechanism for sensing forces applied to a tissue. Moreover, membrane tension shown to be involved in regulating processes such as cell fate determination and cell migration.

In this work, we demonstrated that the downstream responses of cells to a force of the same magnitude can be influenced by the rate at which that force has been applied. For instance, fast stretches are associated with the promotion of mitotic entry and the alignment of the mitotic spindle with the axis of stretch. Interestingly, we found that following a slow stretch, there was no increase in the proportion of cells entering mitosis, whereas the mitotic spindles still aligned with the axis of stretch. A vertex model-based analysis pipeline was used to quantify differences in the physical and geometric properties of cells and tissues following different strain rates.

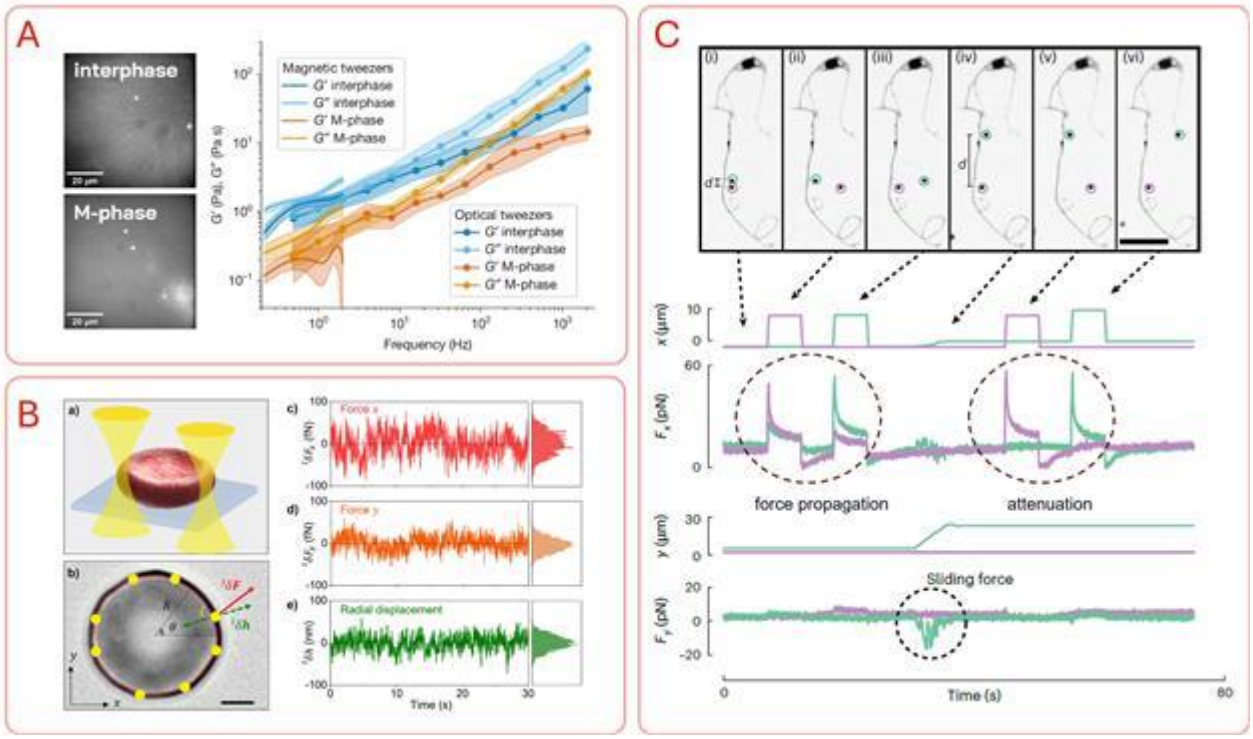
To test the possibility that directly detecting changes in membrane tension may regulate the mechanoresponse of tissues under different strain rates, we developed a protocol using the fluorescent membrane tension probe, Flipper-TR, to quantify membrane tension in tissues subjected to different rates of stretch. This has revealed differences in the ways membrane tension adapts in response to the application of fast or slow stretch. Flipper-TR was also used to detect increase in membrane tension of cells in tissues after treatment with MβCD and the induced expression of constitutively active ezrin.

Subcellular viscoelasticity and dynamic force generation quantified with optical tweezers

Oriol Nos Aguila[1], Frederic Català-Castro[1]
[1]IMPETUX, Spain

Flash Talks 6b, July 16, 2026, 12:00 - 12:30

Mechanical forces sculpt cells and tissues, regulate migration and intracellular transport, organize subcellular architecture, and provide cues for mechanoresponsive and behavioral processes. Different parts of the cell therefore display distinct mechanical signatures that are dynamically modulated across space and time during cell physiological processes. For example, cytoplasmic viscoelasticity is mechanically coupled to cytoskeletal scaffolding for cell and nucleus integrity, but is downregulated during the mitotic phase to allow chromosome segregation (Fig. 1A, Brugués Lab, DOI: 10.1038/s41586-025-09915-x). While the membrane cortex shapes the outer scaffold of the cell, membrane flickering enables active remodeling of red blood cells, allowing them to adapt to extreme confinement (Fig. 1B, Monroy Lab, DOI: 10.1002/advs.202514778). Similarly, the actin–spectrin cortex underlying axonal membranes precisely tunes the range of membrane tension propagation, supporting the function of neuronal proprioceptors and mechanosensors. (Fig. 1C, Krieg Lab, DOI: 10.1038/s41567-025-03037-x). Together, these examples illustrate how subcellular materials —plasma membrane, cortex, filament networks, and chromatin— respond to mechanical stress through regulated viscoelasticity, active force generation, and energy dissipation. In this talk, we will review how optical force spectroscopy can reveal the physics behind these examples using SENSOCELL, our multi-trap optical tweezers platform.



BAF mobility tunes nuclear mechanics to enable confined invasion in glioblastoma

Sarah Peeters[1,2], Hera Kim[2], Romy Timmer[2], Isa Decuypere[1], Lucie Ergot[3], Michelle Joy-Immediato[2], Cecilie Petterson Oksvold[2], Marlies Verschuuren[1], Sarah De Beuckeleer[1], Liam De Cock[1,2], Tessa Nuyttens[1], Jorrit De Waele[2], Matthieu Piel[4], Frederik De Smet[5], Hua Hu[2], Sylvain Gabriele[3], Winnok De Vos[1], Coen Campsteijn[2]
[1]University Of Antwerp, Belgium, [2]University of Oslo, Norway, [3]University of Mons, Belgium, [4]Institut Curie and Institut Pierre Gilles de Gennes, France, [5]KULeuven, Belgium

Flash Talks S3a, July 14, 2026, 17:15 - 17:45

Glioblastoma (GBM) is the most common and aggressive primary brain tumours in adults, characterized by extensive invasion, high cell heterogeneity and pronounced cellular plasticity. Invasive GBM cells are exposed to substantial mechanical forces, as they need traverse a biomechanically challenging microenvironment, shaped by elevated intracranial and intratumoural pressures, and spatial confinement through a dense extracellular microenvironment. How these biomechanical stresses influence invasion, how cells adapt to such constraints, and whether these adaptations ultimately drive tumour aggressiveness remain unclear. To investigate this, we first showed that GBM nuclei experience pervasive biomechanical stress in patient tissue and GBM cell lines, manifested by nuclear dysmorphia and frequent loss of nuclear envelope (NE) integrity. Using a panel of GBM cell lines, we showed a link between nuclear morphology, nuclear fragility and mechano-resilience. The ability of cancer cells to withstand mechanical force strongly correlated with their invasive capacity in a 3D collagen matrix, connecting mechanical resilience to tumour aggressiveness. Through proximity proteomics, we identified an NE-associated mechano-regulatory hub selectively enriched in invasive GBM cells, consisting of lamin A/C, Leucine-Rich Repeat-Containing protein 59 (LRRC59), and the BAF-targeting Vaccinia-Related Kinase 2 (VRK2). This mechano-adaptative module converged on barrier-to-autointegration factor (BAF), a critical chromatin-NE tether and first responder to NE rupture. Consistent with this, perturbation of these regulators or complementary disruption of BAF function altered BAF mobility, increased nuclear stiffness, and abolished 3D invasion of GBM cells. Collectively, these findings demonstrate that precise control of BAF dynamics at the NE-chromatin interface is essential for the transient nuclear deformations required for confined migration. Our work uncovers an NE-centric mechano-adaptive protein hub that is required for GBM invasion and reveals a selective vulnerability that could be exploited to curb GBM invasiveness.

TRPA1 and Piezo1 mediate stretch-induced increase in atrial Ca2+-spark rate

Dr Remi Peyronnet[1]
[1]Institute for Experimental Cardiovascular Medicine, Germany

Flash Talks 5a, July 15, 2026, 17:15 - 17:45

Stretch modulates atrial electrophysiology and promotes the initiation and maintenance of atrial fibrillation. In ventricles, stretch-induced arrhythmic behavior has been linked to increased spontaneous sarcoplasmic reticulum (SR) Ca^{2+} release via ryanodine receptors ("Ca^{2+} sparks"), mediated in part by cation non-selective stretch-activated channels (SACNS) that enhance Ca^{2+} influx. However, the molecular mechanism underlying this mechano-sensitive response in atrial cardiomyocytes remains unclear. We aimed to determine whether diastolic stretch enhances SR Ca^{2+} release in single atrial cardiomyocytes and to identify the molecular pathway involved.

Freshly isolated rabbit left atrial cardiomyocytes were attached to glass micro-rods using MyoTak and axially stretched. Confocal imaging was used to assess SR Ca^{2+} release following pacing (1 min, 2 Hz), at resting sarcomere length (SL ≈ 1.79 ± 0.01 µm) and during sustained axial stretch (~12% SL increase) in the absence of electrical stimulation.

Sustained stretch increased diastolic Ca^{2+} spark rate. This effect was abolished in Na^{+}/Ca^{2+}-free solution despite unchanged SR Ca^{2+} content (caffeine exposure experiments), indicating involvement of transmembrane cation influx. Streptomycin, a non-selective SACNS blocker, prevented the stretch-induced increase in Ca^{2+} spark rate. Piezo1 activation (Yoda1) elevated baseline Ca^{2+} spark rate and further enhanced it with stretch. TRPA1 activation (AITC) markedly increased baseline Ca^{2+} spark rate but did not augment the stretch response. In contrast, TRPA1 inhibition (A967079 or HC-030031) abolished the stretch-induced increase. Disruption of microtubules (colchicine), but not reactive oxygen species scavenging (N-acetylcysteine), prevented the stretch effect.

Thus, axial stretch enhances diastolic SR Ca^{2+} release in atrial cardiomyocytes via a mechanism involving transmembrane Na^{+}/Ca^{2+} flux, specifically through TRPA1, requiring intact microtubules but independent of redox signaling. Disease-related alterations in the microtubule network, stretch-activated channel expression, and/or channel gating may alter this mechano-sensitive response and contribute to arrhythmogenesis.

Impact of Matrix Viscosity on Astrocyte Morphology and Reactivity in 3D Tissue Models

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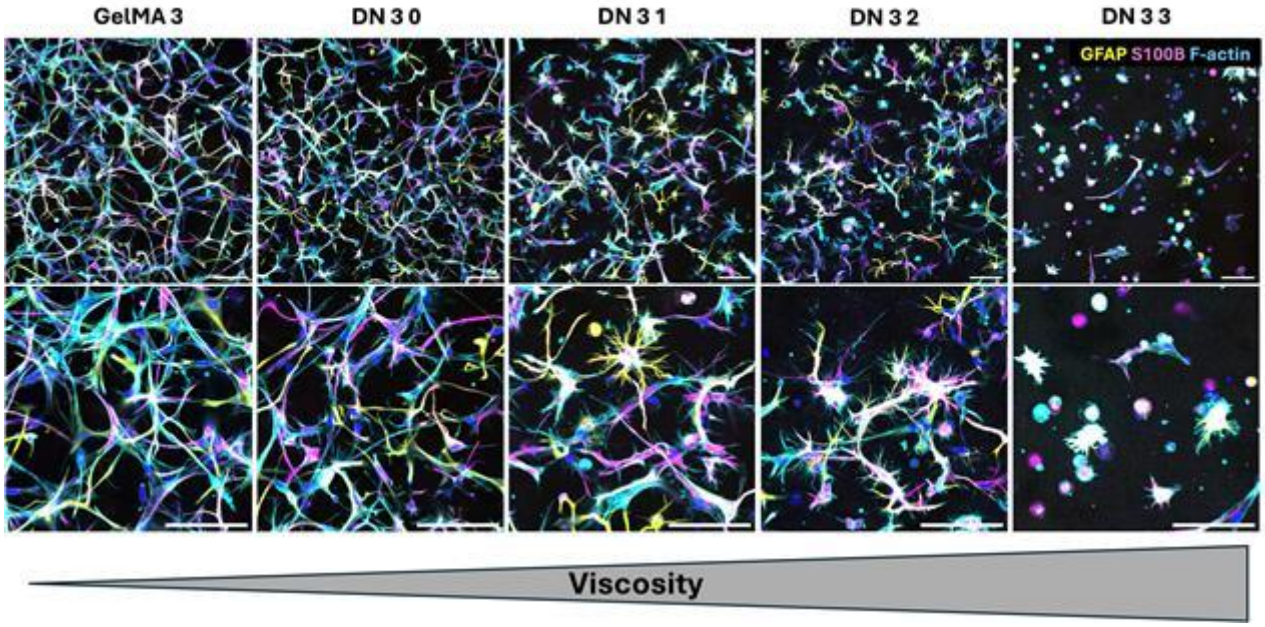
Flash Talks 5c, July 15, 2026, 17:15 - 17:45

The extracellular matrix (ECM) provides biochemical and mechanical cues that regulate cellular behaviour, with astrocyte-ECM interactions playing a key role in neural homeostasis. ECM composition and elasticity are key factors guiding astrocyte phenotype and function; however, the influence of ECM viscosity has not been investigated. This study uses engineered models to investigate how changes to biomaterial stress-relaxation guide the morphology and reactivity of human astrocytes.

Primary human astrocytes were encapsulated within double-network hydrogels with tunable viscoelastic properties composed of a covalent network of gelatin-methacryloyl and a reversible-covalent network of gelatin-adipic acid dihydrazide and dextran-aldehyde. After 7 days, the astrocyte-laden hydrogels were imaged via confocal microscopy (GFAP, S100b and F-actin) or processed for transcriptomic analysis through RT-qPCR.

Modulating the biomaterial's viscosity allowed access to striking astrocyte morphologies that have not previously been observed in vitro. We observed a morphological transition along the viscosity axis, ranging from elongated (low-viscosity) to highly branched astrocytes (high-viscosity), with the latter exhibiting a reactive-like phenotype, characterised by increased process length, number and ramification complexity. We observed decreases in the area and perimeter of nuclei, correlating with nuclear morphologies previously observed in reactive astrocytes. RT-qPCR analysis revealed that astrocytes cultured in high-viscosity hydrogels maintained their levels of GFAP, S100b, ALDH1L1 and SLC1A2, with an upregulated expression of reactivity markers ICAM1, C3 and IL-6. The absence of inflammatory stimuli in the culture media suggests that the pro-inflammatory state was guided by the stress-relaxation of the biomaterial.

Our findings highlight the importance of matrix viscosity in modulating the morphology and phenotype of human astrocytes, with further studies ongoing to characterise the transcriptomic, epigenomic, and functional changes. Understanding the mechanistic basis underpinning astrocytes' transduction of stress-relaxation cues will provide novel insights into astrocyte-ECM interactions and may facilitate improved in vitro models and novel therapies for treating astrocyte-implicated pathologies.


GelMA 3
DN 3 0
DN 3 1
DN 3 2
DN 3 3
GFAP S100B F-actin
Viscosity

Distinct Roles of Matrix Viscoelasticity and Degradation in Governing Collective Spheroid Responses in 3D environments

Theodora (dora) Rogkoti[1], Apeksha Shapeti[2], Jorge Barrasa-Fano[2], Marco Cantini[1], Hans Van Oosterwyck[2], Manuel Salmeron-Sanchez[1,3,4]
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Flash Talks 6a, July 16, 2026, 12:00 - 12:30

The extracellular matrix (ECM) is both viscoelastic, exhibiting time-dependent mechanical responses, and degradable through cell-secreted enzymes, properties that enable continuous tissue remodelling. Prior research has shown that enhanced ECM viscoelasticity and degradation can elicit similar responses in single cells, such as increased spreading and migration. In native tissues, however, cells exist in collectives that interact both with their environment and each other. In this context, the distinct contributions of viscoelasticity and degradation in regulating multicellular mechanobiology remain unclear.
To address this, human mesenchymal stem cell spheroids were embedded in newly engineered PEG-based hydrogels with independently tuneable stiffness, stress relaxation, and degradability. Spheroid morphology, mechanics, and contractility were assessed using Brillouin and 3D Traction Force Microscopy to determine how these matrix properties govern collective behaviour in 3D.
In soft 3D matrices, slow stress-relaxation rates restricted spheroid spreading, whereas fast-relaxing and degradable matrices promoted extensive protrusive outgrowth supported by paxillin-rich adhesions. Matrix degradation emerged as the dominant regulator of spheroid outgrowth, producing spheroids with significantly larger areas and reduced circularities compared to viscoelasticity alone. Brillouin microscopy, used to measure spheroid mechanics non-invasively, revealed that increased spheroid spreading correlated with lower Brillouin frequency shifts, indicating a mechanically softer spheroid core. In stiffer matrices, enhanced stress relaxation did not alter spheroid morphology or stiffness, while degradation facilitated protrusion formation and reduced spheroid stiffness. Finally, traction force microscopy showed that spheroids in stiffer hydrogels generated smaller matrix displacements but higher traction forces than those in softer hydrogels, consistent with force generation against a more resistant environment. Irrespective of stiffness or degradation, spheroid-generated displacements and forces significantly increased over time and exhibited consistent polarisation across opposite spheroid poles, suggesting internally balanced force organisation irrespective of morphology. Together, these findings reveal the complex interplay between matrix stiffness, viscoelasticity and degradability in governing collective cell responses in 3D.

The role of the LINC complex in the nuclear and cytoskeletal response to mechanical stress

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Flash Talks S3a, July 14, 2026, 17:15 - 17:45

Skeletal muscle cells are continuously subjected to mechanical loading, necessitating robust mechanotransduction pathways to maintain cellular integrity and genome organization. The Linker of Nucleoskeleton and Cytoskeleton (LINC) complex, comprising Nesprins and SUN proteins, is central to this process by physically coupling the nuclear lamina to the cytoskeleton. However, the precise mechanisms governing force transmission and structural adaptation between these compartments remain incompletely understood. In this study, we used multiple geometrical confinement platforms—including the AgarSqueezer, a 6-well confiner, and 2D micropatterned lines—to investigate remodelling of C2C12 and A8820 skeletal muscle cells under controlled mechanical compression.
Our results demonstrate that mechanical stress induces significant nuclear morphological shifts, characterized by increased aspect ratios. While severe compression (2 µm) typically reduces nuclear solidity, mature myotubes exhibit greater structural resilience than myocytes, likely due to a reinforced microtubule network. Notably, Lamin A/C-deficient cells display a unique "solidity recovery" under load, which we attribute to the compensatory recruitment of H3K9me3-marked heterochromatin to the nuclear periphery, providing temporary structural reinforcement. Furthermore, we observed that mechanical stress triggers the recruitment of SUN1 and Lamin A/C to the nuclear envelope, even under moderate confinement (5 µm), which precedes major morphological deformation. This nuclear adaptation is mirrored in the cytoskeleton by a twofold increase in focal adhesion density, indicating a heightened state of intracellular tension and mechanical coupling. These findings elucidate how the LINC complex coordinates nuclear and cytoskeletal reorganization to preserve muscle cell function, providing critical insights into the mechanobiology of muscular dystrophies.

Decoding how dynamic extracellular matrix mechanics drives invasion in 3D mammary tissues

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Flash Talks 6a, July 16, 2026, 12:00 - 12:30

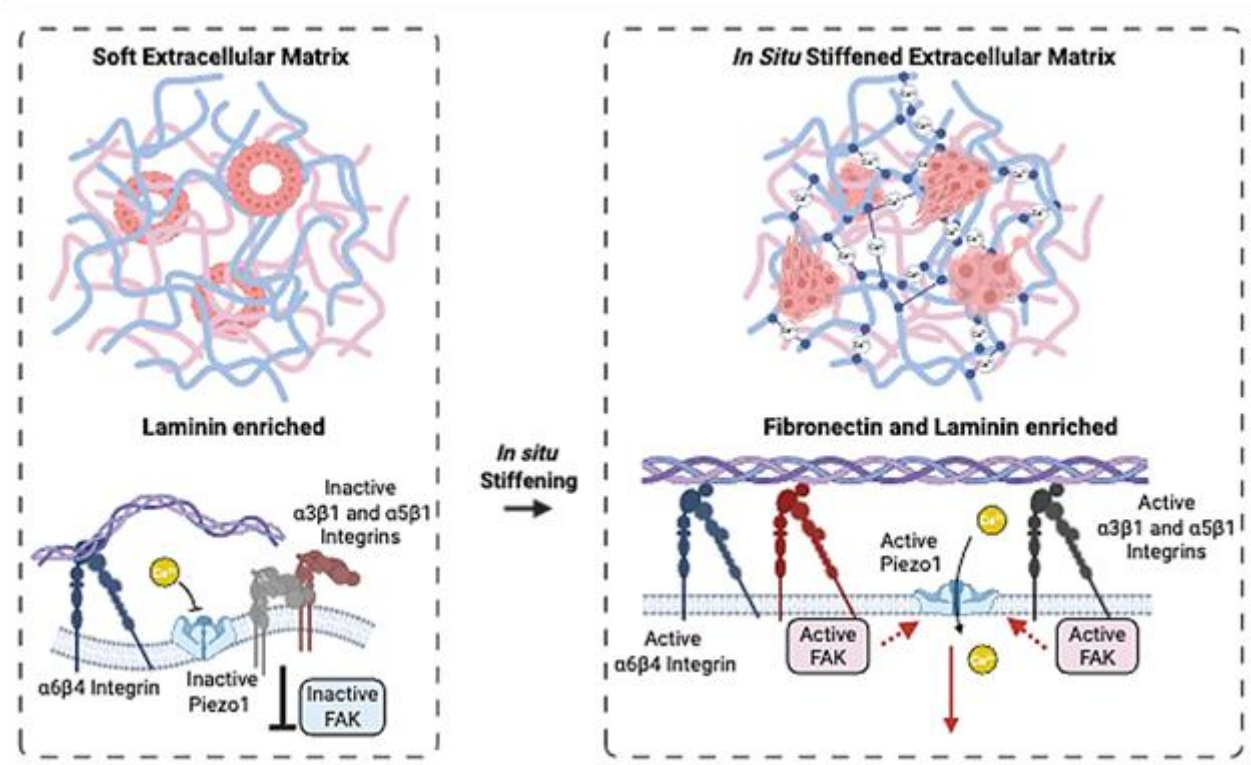
Tissue stiffening is a hallmark of cancer progression, yet how fully formed epithelial structures respond to mechanical cues within their native extracellular matrix (ECM) remains poorly understood. We adapted an interpenetrating network (IPN)–based hydrogel system to enable in situ stiffening around mature mammary acini, preserving three-dimensional tissue architecture while allowing independent control of matrix mechanics.

Stiffening alone drives invasion through two temporally distinct phases: a rapid priming phase characterized by basement membrane disruption and fibronectin secretion, followed by a delayed invasion phase involving fibronectin remodeling, laminin re-deposition and acinar proliferation. Mechanistically, α3β1- and α5β1-integrin–FAK signaling activates the mechanosensitive ion channel Piezo1 to regulate ECM remodeling and invasion. Integrin-mediated adhesion stabilization supports force transmission and matrix deformation, while Piezo1-dependent calcium signaling coordinates cytoskeletal dynamics underlying invasive behavior.

These findings establish that mechanical remodeling of the ECM is sufficient to drive invasion in three-dimensional mammary tissues through coordinated mechanotransduction and matrix remodeling.

Ongoing work extends these models to investigate how additional matrix properties, including viscoelasticity, porosity and ECM composition, influence invasion patterning and epithelial plasticity. Preliminary observations suggest that variations in matrix mechanical behavior can shift invasion phenotypes and spatial organization of epithelial cell states.

Together, this work highlights the importance of dynamic ECM mechanics in regulating tumor invasion and establishes engineered 3D tissue models as powerful platforms to dissect tumor–microenvironment interactions.


Soft Extracellular Matrix
Laminin enriched
Inactive
α3β1 and α5β1
Integrins
α6β4 Integrin
Inactive
Piezo1
Inactive
FAK
In situ
Stiffening
In Situ Stiffened Extracellular Matrix
Fibronectin and Laminin enriched
Active
α3β1 and α5β1
Integrins
Active
Piezo1
Active
α6β4 Integrin
Active
FAK
Active
FAK

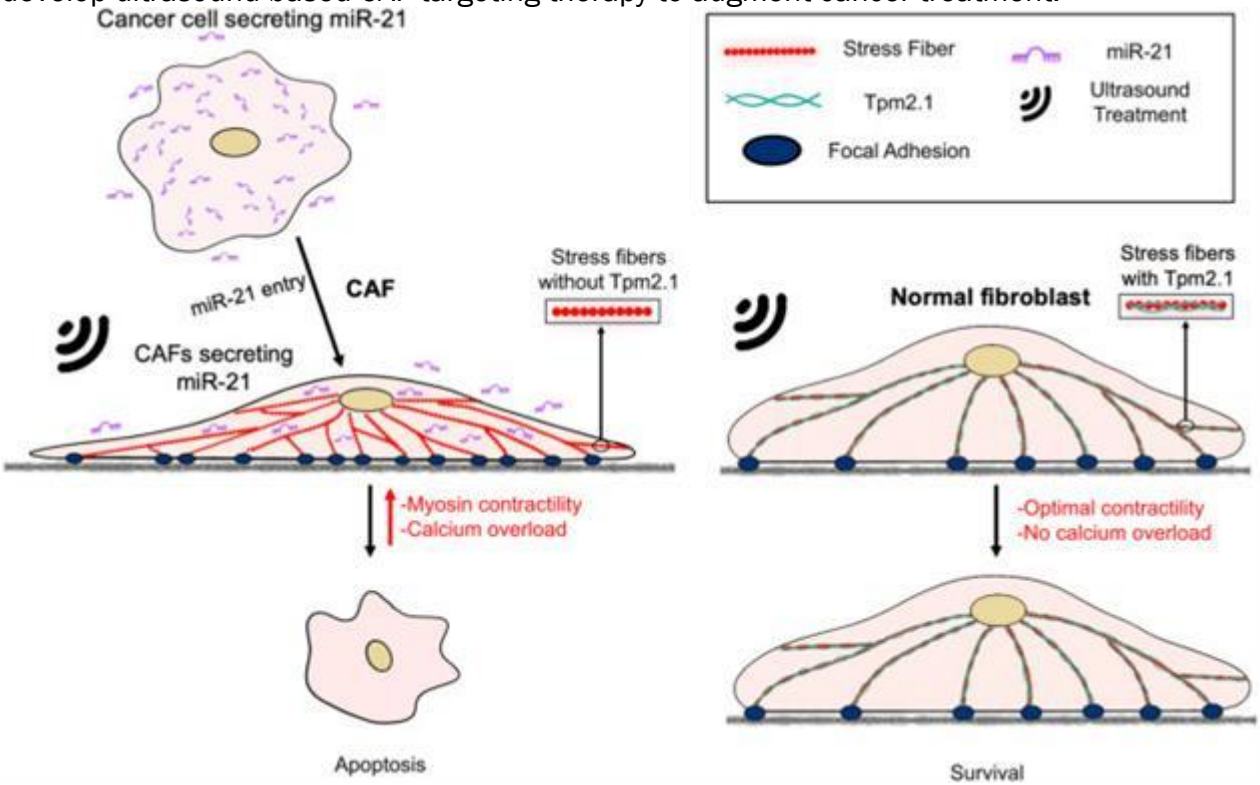
Selective killing of cancer-associated fibroblasts by ultrasound-mediated

mechanical forces

Gomathi Sankar[1], Ajay Tijore[1]
[1]Indian Institute of Science, India

Flash Talks 6c, July 16, 2026, 12:00 - 12:30

Recent studies show that stretch/ultrasound (US)-generated mechanical forces cause selective apoptosis in several cancer cells, tumor organoids, and animal models without damaging normal cells. Cancer-associated fibroblasts (CAFs) are an integral tumor microenvironment (TME) constituent. They display altered biomechanical properties similar to cancer cells, such as matrix secretion and its remodeling, chemokine secretion, and high contractile force generation. We thus test the effect of US-mediated mechanical forces on patient-derived CAF survival. Surprisingly, US treatment causes CAF apoptosis (mechanoptosis) through a calcium-activated apoptotic pathway but not in normal fibroblasts. MicroRNA-21 (miR-21) secreted by primary cancer cells suppresses the mechanosensory cytoskeletal protein tropomyosin 2.1 (Tpm2.1) in CAFs. This Tpm2.1 depletion in CAFs is responsible for mechanoptosis. Interestingly, normal fibroblasts behave similarly when Tpm2.1 was depleted. Further, 3D gel contractility and migration assay confirm that a prolonged US treatment disrupts myosin IIA-mediated contractility, which CAFs primarily use to support cancer invasion. Since US treatment causes mechanoptosis and reduces contractility, this approach could be used to develop ultrasound-based CAF targeting therapy to augment cancer treatment.



A mechanobiological perspective on primary brain cancers

Dylan Fowler[1], Mark Jackson[2], Carsten Schulte[1]
[1]Department Of Biomedical Engineering, University Of Strathclyde, United Kingdom, [2]School of Cancer Sciences, University of Glasgow, United Kingdom

Flash Talks S1, July 13, 2026, 17:15 - 17:45

In recent years, it became increasingly evident that genetics cannot explain the intricate complexity of aggressive primary brain cancers, such as glio- (GB) and medulloblastoma (MB), but that mechanobiological aspects heavily contribute to their pathophysiology. Understanding how the extracellular matrix (ECM) nanoarchitecture affects cancer cells is thus of significant relevance to identify new levers for therapeutic approaches.
In this context, we are developing biomaterials that we optimised for advanced bioimaging and experimental throughput harnessing electrospinning and e-beam lithography. We use these substrates that mimic primary brain ECM as faithfully as possible to dissect the impact of mechanotransductive processes on GB and MB cell pathophysiological capabilities and therapeutic resistance. Mechanobiological characterisations comprise techniques, such as deformability cytometry, Brillouin spectroscopy, and super-resolution microscopy. These experiments are integrated with the study of the role of potential mechanotransductive key regulators informed by deep analyses of patient genomic data (e.g., TCGA, IvyGAP, and cbioportal) to ensure clinical relevance.

Spatial localization of chromosome territories are altered in cells cultured on softer matrices

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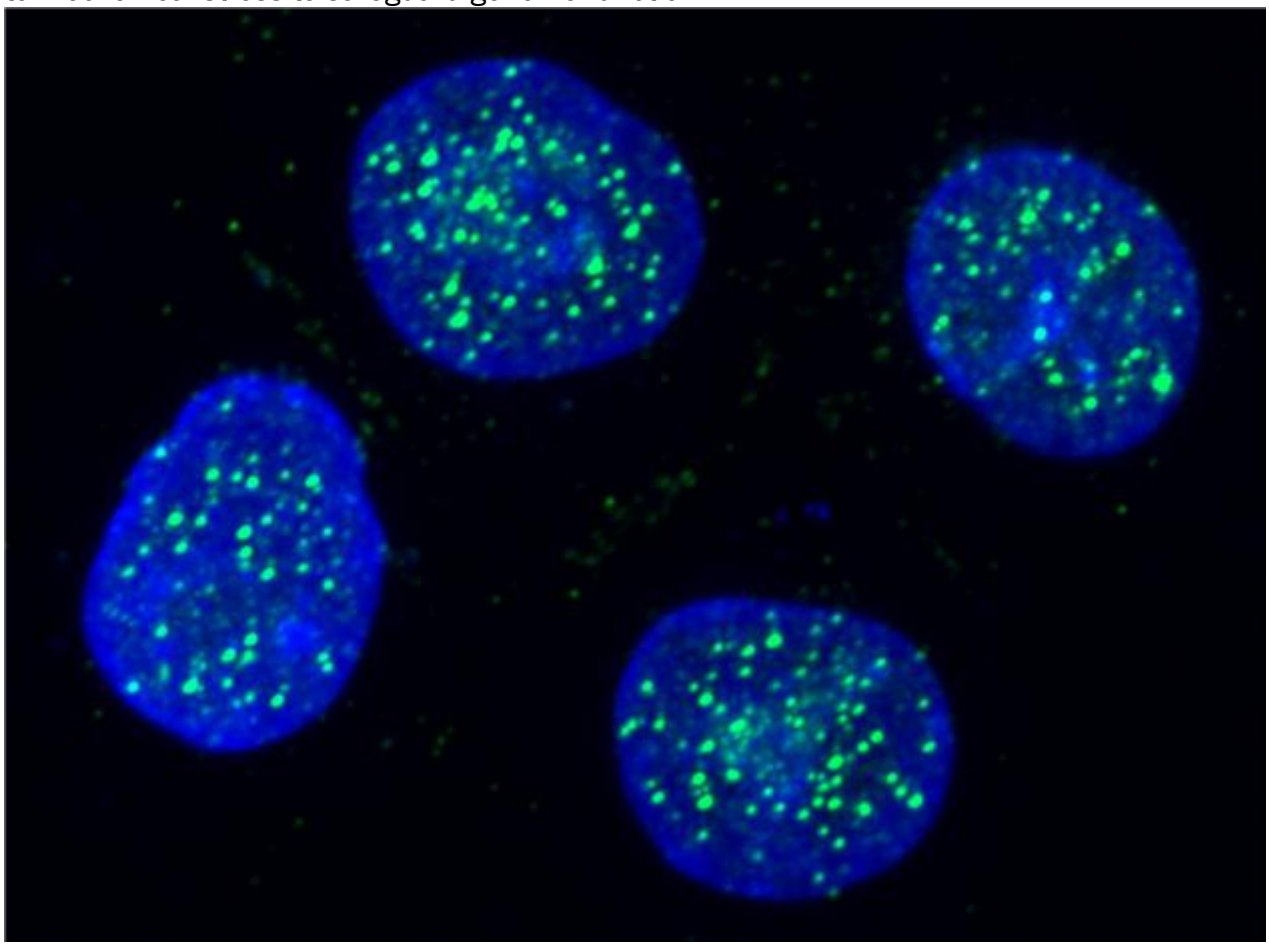
Flash Talks S3a, July 14, 2026, 17:15 - 17:45

Chromosomes are non-randomly organized within the interphase nucleus into specific sub-volumes known as Chromosome Territories (CTs). Generally, gene-rich chromosome territories reside in the nuclear center while gene-poor territories occupy the periphery. To determine the molecular mechanisms driving this organization, we exposed cells to softer hydrogel substrates (2–55 kPa) and compared them to rigid glass controls (~1 GPa). On softer substrates, cells showed increased surface area and a significantly altered transcriptome. Crucially, the invariant positioning of CTs was disrupted. This reorganization was linked to the mislocalization of the LINC complex and lamins into the nuclear interior, as well as changes in the distribution of histone marks. We identified Emerin phosphorylation as the critical relay for these mechanochemical signals; inhibiting this phosphorylation prevented CT movement. Our recent studies reveal an altered organization of telomeres in cells cultured on softer matrices. Collectively, these results highlight the inherent plasticity of the nucleus and its ability to adapt to mechanical stress to safeguard genome function.



Origin-Specific Mechanical Signatures Define Endothelial Cell Behavior in 2D and 3D Microenvironments

Apeksha Shapeti[1], Janne de Jong[1], Elizabeth A.V. Jones[2], Rozenn Quarck[3], An Zwijsen[2], Eva Faurobert[4], Hans Van Oosterwyck[1,5]
[1]KU Leuven, Biomechanics Section, Belgium, [2]Department of Cardiovascular Sciences, Center for Molecular and Vascular Biology, KU Leuven, Belgium, [3]Clinical Department of Respiratory Diseases, University Hospitals of Leuven and Laboratory of Respiratory Diseases and Thoracic Surgery (BREATHE), Belgium, [4]Univ. Grenoble Alpes, Institute for Advanced Biosciences, France, [5]KU Leuven, Prometheus, Belgium

Flash Talks 5c, July 15, 2026, 17:15 - 17:45

Endothelial cells (ECs) exhibit structural and transcriptomic diversity based on the organ or vascular bed of origin, yet their mechanical heterogeneity and its impact on vascular behavior remains poorly defined. Because mechanosensing, force generation, and matrix interactions regulate angiogenesis, barrier function, and tissue repair, understanding origin-dependent mechanobiology is essential. We integrated RNA sequencing with 2D (single-cell and monolayer) and 3D (sprouting) mechanobiology assays to define mechanical signatures—cytoskeletal organization, adhesion, degradation, and force generation—of HUVECs and microvascular ECs from the brain, lungs, and dermis. We identified distinct mechanical strategies employed by each EC type. HUVECs and brain ECs invaded 3D matrices through filopodia-guided exploration and moderate matrix degradation, with HUVECs additionally showing coordinated pMLC activation and β1-integrin–rich adhesions. Lung ECs were minimally degradative, thereby limiting invasiveness. Dermal blood ECs displayed a hyper-mechanical phenotype with strong matrix degradation, abundant filopodia, robust actin fibers, and high cell–ECM forces—traits likely reflecting adaptation to their stiff native microenvironment. In contrast, dermal lymphatic ECs were highly contractile but showed little degradation or filopodia formation, resulting in poor invasion, consistent with the lower mechanical demands of basement membrane-lacking lymphatic vessels. RNA-seq analysis further revealed that cell-type-specific differences in β1-integrin and MMP expression recapitulate the observed variation in adhesion and matrix degradation, linking the functional heterogeneity identified in the 3D sprouting assay in underlying gene expression programs. We show that EC mechanical phenotypes are strongly origin-specific and shaped by native microenvironments. Selecting appropriate ECs is critical for physiologically relevant mechanobiology and for improving the design, interpretation and translation of vascular studies.

Engineered 3D Collagen Scaffolds Reveal Mechanobiological Drivers of Breast Cancer Invasion in Obese Microenvironments

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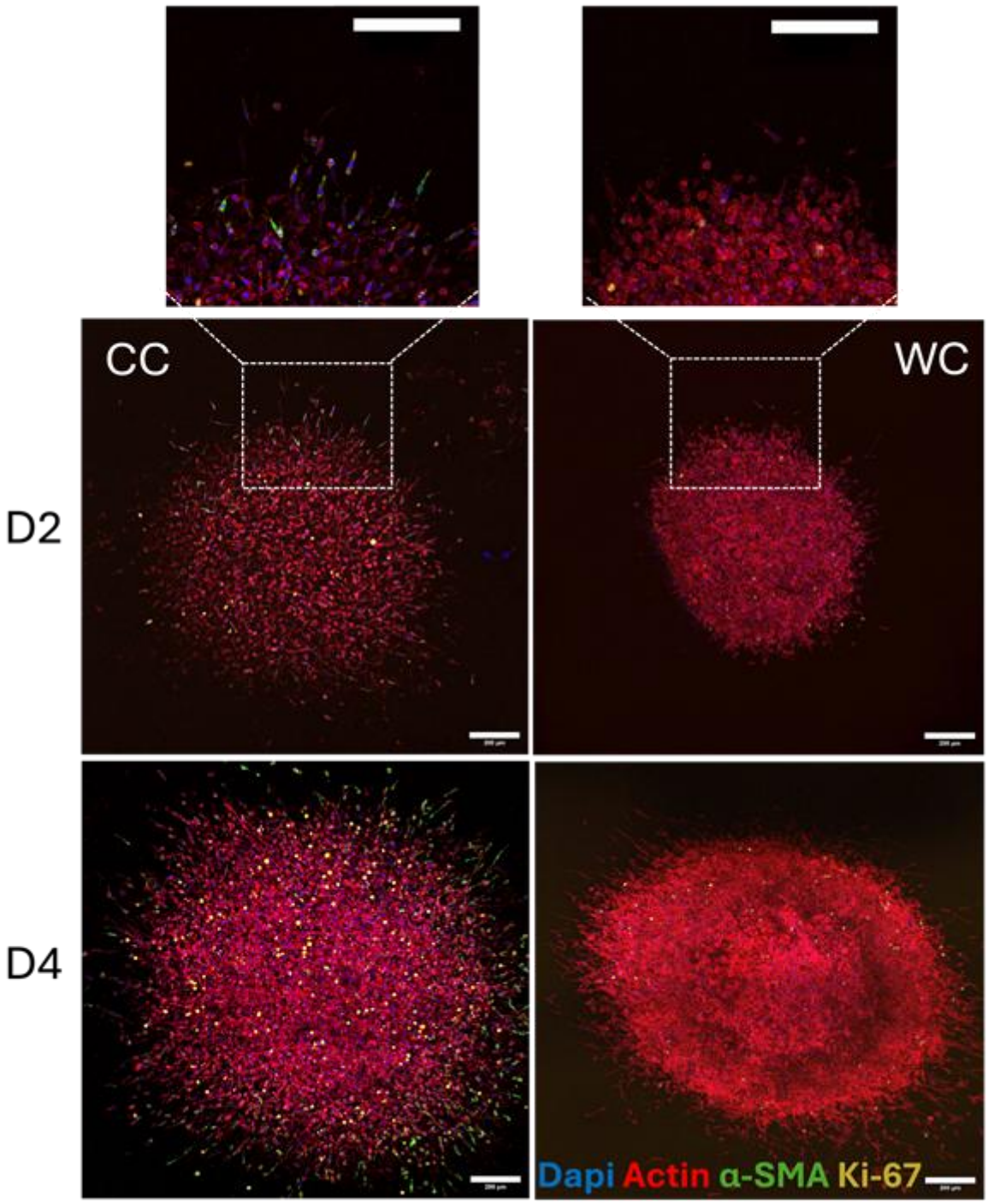
[1]University Of Glasgow, United Kingdom, [2]Tufts University, United States

Flash Talks 6a, July 16, 2026, 12:00 - 12:30

Obesity is associated with significantly poorer breast cancer outcomes, yet the relative contributions of biochemical and mechanical alterations in the obese tumour microenvironment remain poorly understood. We engineered an in vitro 3D platform comprising fibrillar collagen scaffolds tuned to replicate the architecture and stiffness of both lean and obese mammary microenvironments. Breast cancer cell spheroids were incorporated to simulate tumours, enabling examination of the biochemical and mechanobiological drivers of invasion, using conditioned medium from lean and obese adipocytes.

Our findings reveal that the secretome of obese adipocytes significantly enhances invasion and growth of cancer cell spheroids, with invasion depth increasing 1.5-fold in obese-mimicking scaffolds compared to lean-mimicking scaffolds, demonstrating that biochemical and mechanical cues act synergistically to potentiate tumour invasion. We also identified specific ECM remodelling enzymes (MMPs) released by obese adipocytes that facilitate this accelerated invasion.

These results demonstrate the critical role of combined biochemical and mechanical dysregulation in obesity-driven breast cancer progression, suggesting that targeting abnormal ECM degradation may offer novel therapeutic strategies for mitigating cancer progression in obese patients. Crucially, our findings establish that matrix mechanics and structure are not merely a passive context but an active driver of tumour mechanosensing, positioning mechano-related changes of the ECM as a tractable therapeutic target in obesity-associated breast cancer.


CC
WC
D2
D4
Dapi Actin α-SMA Ki-67

Matrix Rigidity Controls Hemidesmosomes

Feifei Yan[1], Sara Göransson[1], Jianjiang Hu[1], Staffan Strömblad[1]
[1]Karolinska Institutet, Sweden

Flash Talks 6a, July 16, 2026, 12:00 - 12:30

Hemidesmosomes links adhesion to the basement membrane with intermediate filaments. However, potential mechanoregulation of hemidesmosomes has remained unclear. Here we show that hemidesmosomes in breast cancer cells are controlled by the stiffness of the basement membrane. Notably, Tensin-4 expression is upregulated by stiff ECM at the protein level in multiple breast cancer cells. Importantly, while Tensin-4 localizes in focal adhesions in cells on glass, at a stiffness resembling breast cancer, hemidesmosomes predominantly localizes in hemidesmosomes and is essential for their formation, as well as for the keratin intermediate filament network. Disruption of hemidesmosomes or the keratin network abrogates a stiffness-induced malignant phenotype in breast cancer cells. Our findings define a novel mechanoresponse pathway linking matrix stiffness to control of hemidesmosomes via regulation of Tensin-4, offering new insights into the interplay between the matrix mechanics, cell adhesions and breast cancer cell behavior.

Cagging of membrane-to-cortex attachment can trigger cellular symmetry breaking

Srishti Dar[1], Ruben Tesoro Moreno[1,6], Ivan Palaia[2,3], Anusha B. Gopalan[1,5,6], Zachary Gao Sun[4,7], Léanne Strauss[1,6], Richard R. Sprenger[8], Julio M. Belmonte[9], Sarah K. Foster[1], Michael Murrell[7], Christer S. Ejsing[1,8], Anđela Šarić[3], Maria Leptin[10], Alba Diz-Muñoz[1]
[1]Cell Biology and Biophysics Unit, EMBL Heidelberg, Germany, [2]King's College London, United Kingdom, [3]Institute of Science and Technology Austria, Austria, [4]Physics Department, Yale University, United States, [5]Light Microscopy Core Facility, Johannes Gutenberg University, Germany and Microscopy Core Facility, Institute for Molecular Biology, , Germany., [6]Heidelberg University, Faculty of Biosciences, Germany, [7]Systems Biology Institute, Yale University, United States, [8]Department of Biochemistry and Molecular Biology, VILLUM Center for Bioanalytical Sciences, University of Southern Denmark, Denmark, [9]Department of Physics, North Carolina State University, United States, [10]Developmental Biology Unit, European Molecular Biology Laboratory, Germany

Flash Talks S4, July 15, 2026, 12:00 - 12:30

Cell surface mechanics are the main functional driver of cell migration, differentiation and proliferation. The link between membrane fluidity and membrane to cortex attachment affecting cytoskeleton architecture has been poorly explored in vitro and in vivo. Recent data from the laboratory has shown the importance of membrane fluidity and the effect of membrane-to-cortex attachment protein size on actin network dynamics in vitro, supporting a direct crosstalk between linker size, membrane fluidity and actin network dynamics. Here we explore the effect of linker length in the actin cortex and plasma membrane in vivo.
To that end, we engineered membrane to cortex linkers with diverse predicted lengths (25 and 50nm, corresponding to those of endogenous proteins and their dimers) and explored their behavior in cells. The expression of linkers of ≥25nm in length leads to symmetry breaking, whereby a patch rich in both the linkers and actin is formed. Longer versions in addition generate cell-scale protrusions resembling uropods in migrating immune cells. All these phenotypes can be recapitulated with endogenous overexpression of membrane-to-cortex attachment proteins, suggesting, the mechanics of both synthetic and endogenous linkers are similar. The polarization and the formation of uropod-like structure is lost upon actin polymerization inhibition, suggesting that a feedback mechanism exists between linker polarity and the actomyosin cortex. Altogether our data shows that linker length can effectively increase its Kon, by caging molecules within the underlaying actin cortical mesh. This work showcases how the coupling of membrane mechanics to polymer physics can lead to unexpected cellular morphogenesis and aid migration.

Small Molecule Therapies To Rescue Gap Junctional Intracellular Communication And Overcome Stiffness-Induced Chemoresistance

Charlotte Turner[1], Raja Vadivelu[1], Brian Harkin[1], Eoin McEvoy[1]
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Flash Talks S1, July 13, 2026, 17:15 - 17:45

INTRODUCTION

Breast cancer (BC) is the leading cause of cancer death in women globally. Matrix stiffening, reduced cell proliferation, and a loss of functional gap junction (GJ) expression are associated with BC progression. Here we investigate how these factors could influence chemosensitivity in BC and identify pathways to mitigate such chemoresistance.

METHODS

T47D cells were cultured in supplemented RPMI. Low passage (LP) and high passage (HP) cells fall between P1-10 and P11-20 respectively. Single cells seeded into gelatin-mTG hydrogels spontaneously formed spheroids over 12 days. Samples received 24-hour treatment with GJ-modulators ATRA, dipyridamole, or resveratrol in DMSO prior to chemotherapeutic doxorubicin (DOX). Calcein diffusion was tracked between connected cells to characterise GJ functionality.

RESULTS

Spheroids exhibited stress-dependent growth, with those encapsulated in stiff hydrogels (sfH) significantly smaller and compact than spheroids in soft hydrogels (stH) (Figure1.A-B). stH-spheroids reduced in size following treatment with doxorubicin, while no significant differences were observed for sfH-spheroids (Figure1.C), suggesting mechanosensitive resistance.
Cx43 expression and function was significantly higher in LP compared to HP T47D cells, largely diffuse in the cytoplasm in both cases. Following HP treatment with GJ-modulators, Cx43 was significantly increased. ATRA and dipyridamole pushed Cx43 expression to the membrane, specifically increasing concentrations at the cell-cell interfaces (Figure1.D-E).
DOX treated sfH-spheroids decreased in size when treated in combination with ATRA, dipyridamole, or resveratrol, compared to chemotherapy alone (Figure1.F).

DISCUSSION

T47D cells cultured under higher mechanical stress developed smaller, more compact spheroids, regulated via mechanosensitive pathways. Increased cell density and lower proliferation interfere with chemotherapy diffusion and sensitivity. As T47D cells mature through passages, they appear to lose GJ expression which may compound chemoresistance, but GJ assembly was overcome through treatment with small molecule drugs. Overall, we utilised combinational therapy to enhance gap junctional intercellular communication, promoting chemotherapy diffusion and sensitivity in BC spheroids.

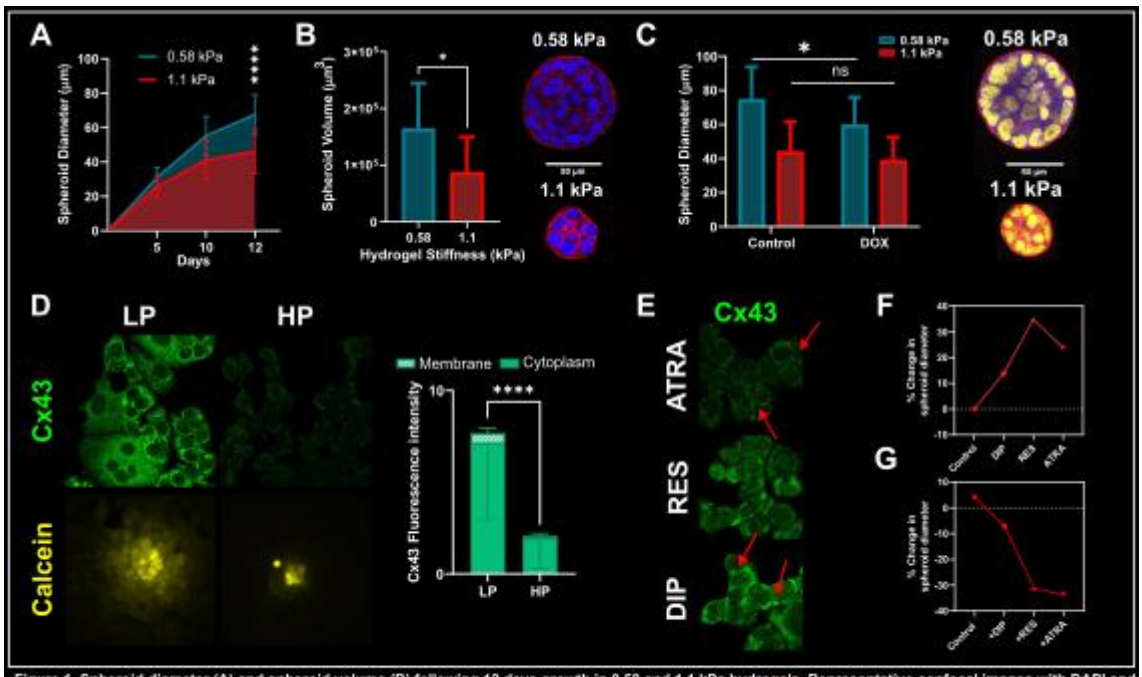

Figure 1. Spheroid diameter (A) and spheroid volume (B) following 12 days growth in 0.58 and 1.1 kPa hydrogels. Representative confocal images with DAPI and FITC staining. C) Spheroid diameter following treatment with doxorubicin (DOX) and representative images. D) Cx43 immunofluorescence localisation and calcein transfer in low passage and high passage T47D cells. E) Cx43 staining following 24hr treatment of HP T47D cells with all-trans retinoic acid (20µM), resveratrol (20µM), or dipyridamole (60µM). Red arrows indicate examples of Cx43 at the cell-cell interfaces. F) Change in spheroid size in 1.1kPa hydrogels following treatment with GJ therapies. G) Change in spheroid size in 1.1kPa hydrogels after 24 hr treatment with GJ therapies followed by 72hrs of doxorubicin.

Tissue-engineered outer retina model to study the influence of extracellular matrix on retinal cell interactions

Vasudha Turuvekere Krishnamurthy[1,2], Laura Klasen[2,3], Ramin Nasehi[2,3], Lisa Jungbluth[1], Eva Miriam Buhl[5], Alice Podesta[6], Si-Ting Wu[1], Björn Kampa[6], Laura De Laporte[2,3,4], Jacopo Di Russo[1,2]

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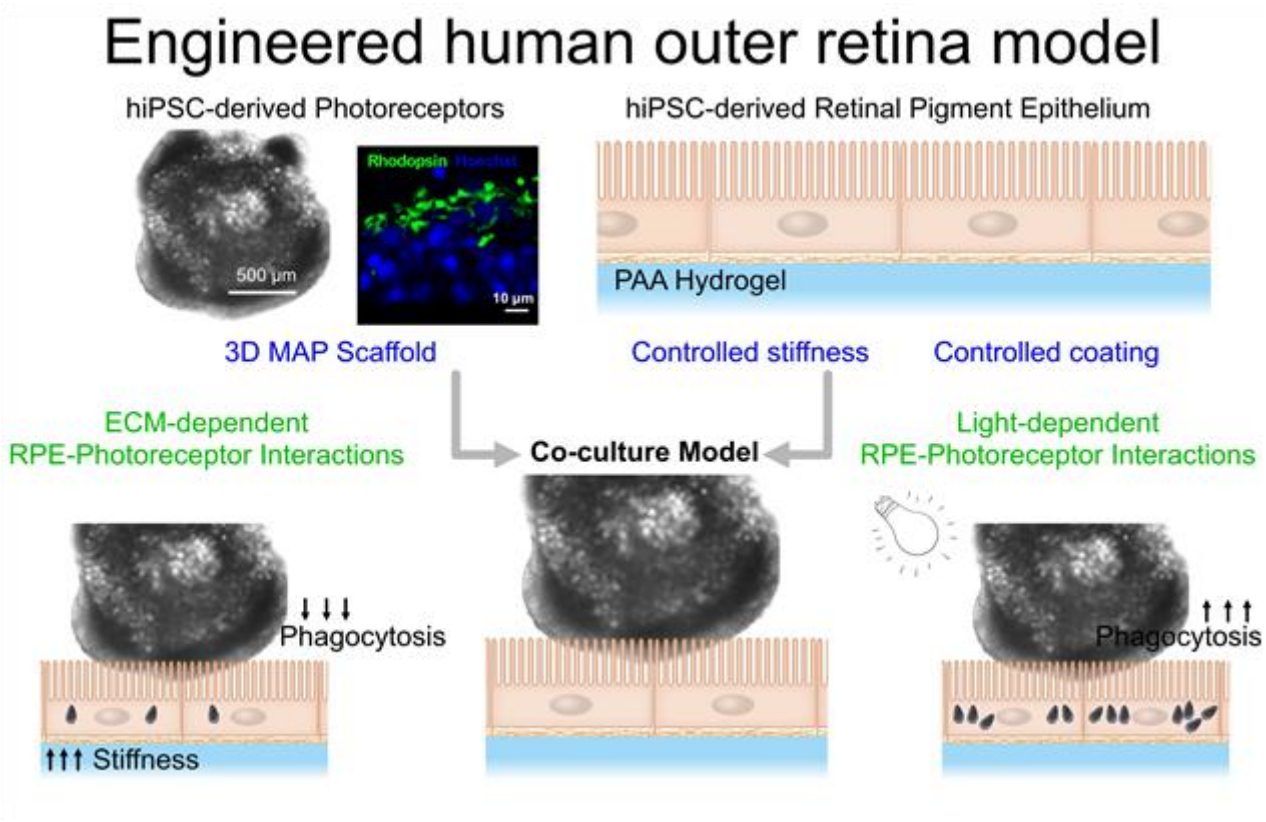
Flash Talks 5c, July 15, 2026, 17:15 - 17:45

Outer retinal degeneration is a leading cause of vision loss and is strongly influenced by age- and disease-associated changes in the extracellular matrix (ECM). The outer retina represents a mechanically and biochemically specialised niche in which ECM properties regulate photoreceptor (PR)-retinal pigment epithelium (RPE) interactions. However, current human retinal organoid models fail to reproduce this microenvironment and lack a mature, functional outer retina.

To address this gap, we developed a human-relevant co-culture system that recapitulates ECM-RPE-PR interactions and enables controlled perturbation of ECM biochemical and mechanical cues. Human induced pluripotent stem cells (hiPSCs) were differentiated into mature PRs within three months, significantly faster than conventional retinal organoid protocols, by assembling cells into a 3D microporous annealed particle (MAP) scaffold composed of spherical poly (ethylene glycol) microgels. The PR MAP scaffolds were co-cultured with stem cell-derived RPE on ECM-mimicking hydrogels.

PRs formed light-responsive outer segments displaying the “eat-me” signal, phosphatidylserine, confirmed by pSIVA staining. When co-cultured with hiPSC-derived RPE on tunable hydrogels, PR outer segment fragments were efficiently phagocytosed and localised to endosomes. Phagocytosis was reduced by MERTK receptor inhibition, confirming specificity. Following dark-to-light transition, phagocytosis increased, consistent with in vivo behaviour. Finally, increasing ECM stiffness to mimic age- and disease-associated tissue stiffening reduced phagocytic efficiency, consistent with earlier findings obtained using porcine outer segment fragments. Collectively, this human-based in vitro model enables mechanistic studies of how ECM changes associated with ageing and disease regulate RPE-photoreceptor interactions, providing a new platform for investigating outer retinal mechanobiology.

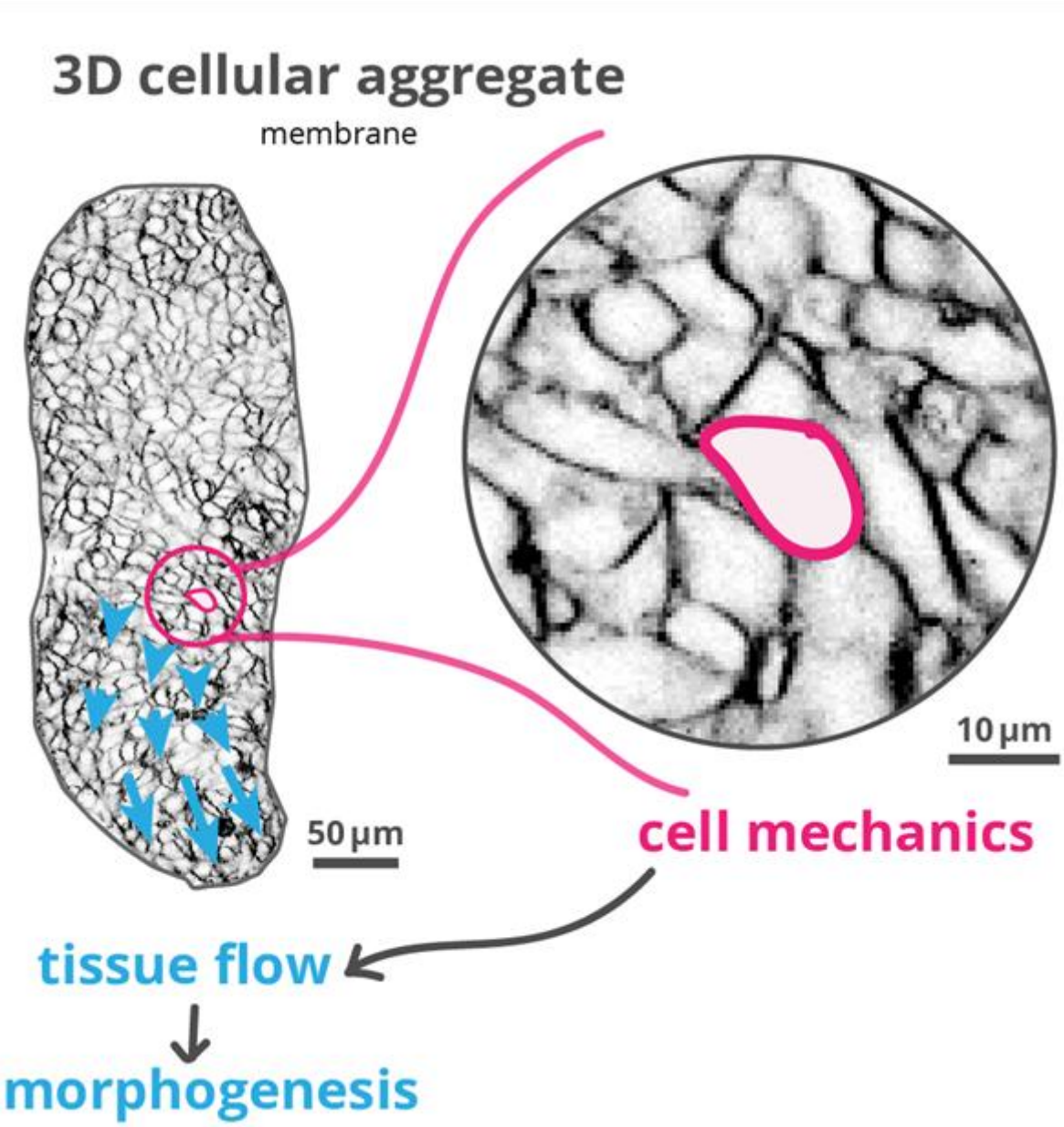

Engineered human outer retina model
hiPSC-derived Photoreceptors
hiPSC-derived Retinal Pigment Epithelium
500 µm
Rhodopsin
10 µm
PAA Hydrogel
3D MAP Scaffold
Controlled stiffness
Controlled coating
ECM-dependent
RPE-Photoreceptor Interactions
Co-culture Model
Light-dependent
RPE-Photoreceptor Interactions
Phagocytosis
↑↑↑ Stiffness
Phagocytosis

Morphogenesis across scales: the role of cell surface mechanics in regulating tissue fluidity during gastruloid development

Marta Urbanska[1], Wiktoria Brdej[1], Tianyin Hu[1], Ewa Paluch[1]
[1]University of Cambridge, United Kingdom

Flash Talks 5c, July 15, 2026, 17:15 - 17:45

During early embryonic development, pluripotent cells differentiate, change shape, and rearrange spatially to form the blueprint of the adult body. While the molecular pathways controlling developmental morphogenesis have been studied extensively, the role of physical properties of cells and tissues in this inherently mechanical process has only recently been brought into focus. Gastruloids—three-dimensional aggregates of mouse embryonic stem cells—have emerged as a robust model system that recapitulates key features of early post-implantation mouse development, including anterior-posterior patterning and body axis elongation. To address the mechanisms underlying gastruloid elongation, we investigate the role of cell surface mechanics in this process. We have shown that gastruloid elongation is inhibited by maintaining high cellular plasma membrane tension through expression of constitutively active ezrin (ezrinCA), an actin-membrane linker protein. We further show that ezrinCA expression does not abolish mesodermal lineage commitment, indicating that the morphogenetic defect is not primarily a result of arrested developmental progression. Using gastruloid fusion as an assay to probe tissue-level mechanics, we find that ezrinCA expression impairs the fusion dynamics of the spherical aggregates at the onset of elongation. This strongly suggests that maintaining high membrane tension leads to decreased tissue fluidity. We are currently investigating how changes in cell surface mechanics control tissue-level viscoelastic properties and drive gastruloid elongation. Our work sheds light on the interplay between cell surface mechanics and morphogenetic movements in developing gastruloids, and more broadly on how mechanical properties of single cells influence tissue fluidity.


3D cellular aggregate
membrane
10 µm
50 µm
cell mechanics
tissue flow
morphogenesis

CHEMOTHERAPY EXPOSURE DISRUPTS CELL JUNCTION AND CYTOSKELETAL ASSEMBLY IN COMPACT AMOEBOID-LIKE TUMOUR CELL CLUSTERS

Dr Raja Vadivelu[1], Charlotte Turner[1], Eoin McEvoy[1]
[1]School of Science and Engineering, Biomedical Engineering, University Of Galway, Ireland
Flash Talks S1, July 13, 2026, 17:15 - 17:45

Introduction
Chemoresistance in triple-negative breast cancer (TNBC) cells is strongly linked to poor clinical outcomes. This study examines how different levels of cancer cell plasticity in TNBC contribute to phenotypic shift induced drug resistance. Repeated switching between mesenchymal–amoeboid transition (MAT) and its reverse, amoeboid–mesenchymal transition (AMT), ultimately deform into amoeboid phenotype, adopting a rounded, blebbing morphology and form compact clusters. Consequently, they differently alter cell–cell adhesion mechanics through the regulation of cytoskeletal-associated junctional protein localization. The recruitment of this junctional protein mediating chemoresistance via altered cell mechanics remains unexplored.

Methods
Anoikis-resistant mouse triple-negative breast cancer 4T1 cells were isolated from viable floating (F) cell colonies cultured in T75 flasks using RPMI medium. Floating cells were serially collected and re-plated to generate successive passages (F(i+1)) until F-6, F-9, and F-12 populations were obtained (Fig 1a). Selected passages of F cells on non-adhesive hydrogels formed 3D compact cell clusters and were exposed to chemotherapeutic doxorubicin (DOX). The subcellular localization of Cx43, ZO-1, and vinculin was assessed by immunocytochemistry followed by confocal microscopy.

Results
Proliferation was observed to increase with F-population index, with morphologies reflecting amoeboid -like cells (Fig 1b). These cells successfully formed compact clusters on non-adhesive hydrogels (Fig 1c). While DOX (5μM) treatment reduced cell viability in F-6 clusters, F-12 clusters were highly chemo-resistant (Fig 1d). Noticeably, we observed that DOX exposure in F-12 clusters leads to a loss of junctional CX43, ZO-1, along with vinculin delocalization [Fig 1e (ii -iv)].

Discussion
Our observation revealed that the redistribution of CX43 and ZO-1 from membrane to cytoplasmic localization potentially compromise cellular connectivity and affect drug permeability. In addition, dispersed vinculin destabilizes cell-cell adhesion. Collectively, disruption of cell–cell junction components and the loss of adhesion integrity impede intracellular transport, restricting drug penetration and promoting chemoresistance.

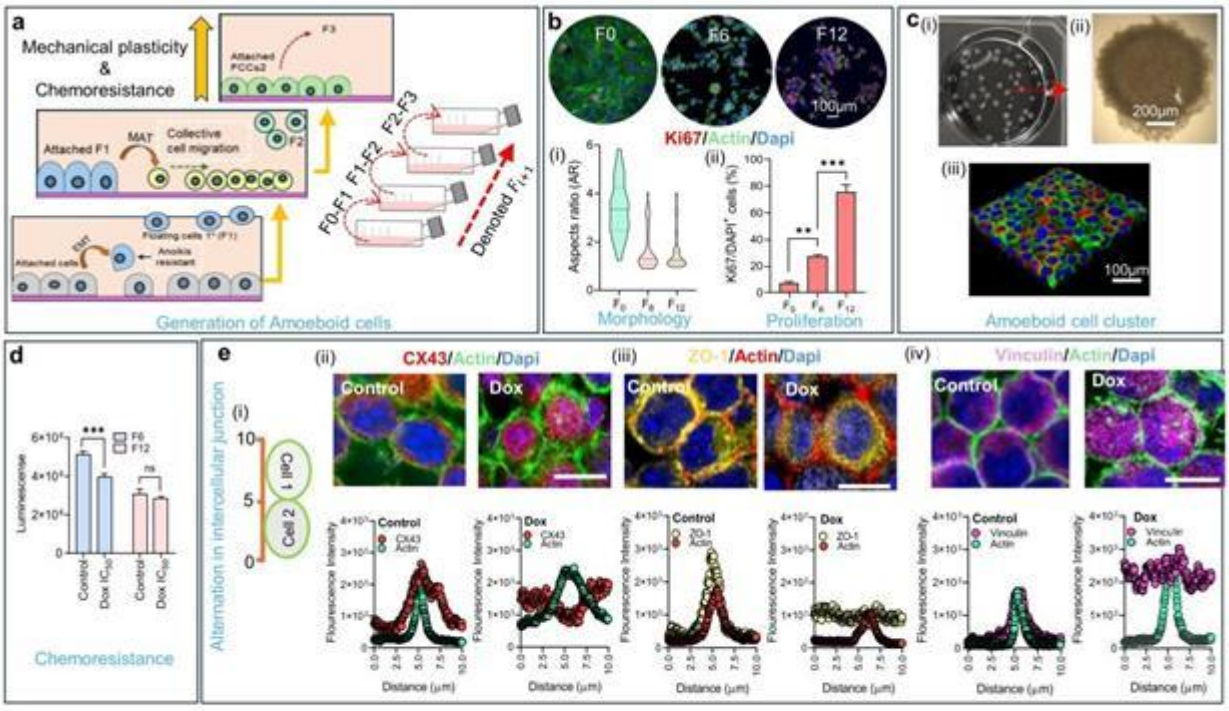


Figure 1 [**a**] Schematic showing phenotypic transition from EMT to MAT through anoikis resistant floating cells [**b**] (i) Adoption of rounded amoeboid morphology and (ii) increase cell proliferation F0 > F12. [**c**] 3D F-12 amoeboid cell clusters (i) Stereomicroscopy image (ii) Brightfield (iii) Confocal Z-stack ; [**d**] Cytotoxic effect of Dox Ic_{50}. [**e**] (i) Schematic diagram showing intracellular region between two cells (ii) Doxorubucin (Dox) induced localization of Cx43 and Z0-1 and Vinculin in F-12 (Scale bar = 5µm).

3D degradable hydrogels unlock enhanced contractility of osteoarthritic chondrocytes

Nele Vaes[1], Maxim Vovchenko[1,2], Jorge Barrasa-Fano[1], Apeksha Shapeti[1], Rocío Castro-Viñuelas[3,4], Laurens Kimps[1], Christ Glorieux[2], Ilse Jonkers[3,4,5], Hans Van Oosterwyck[1,6]
[1]Biomechanics Section, Department of Mechanical Engineering, KU Leuven, Belgium, [2]Laboratory for Soft Matter and Biophysics, Department of Physics and Astronomy, KU Leuven, Belgium, [3]Human Movement Biomechanics Research Group, Department of Movement Sciences, KU Leuven, Belgium, [4]Skeletal Biology and Engineering Research Centre, Department of Development and Regeneration, KU Leuven, Belgium, [5]Institute for Physics-Based Modeling for In Silico Health, KU Leuven, Belgium, [6]Prometheus Division of Skeletal Tissue Engineering, KU Leuven, Belgium

Flash Talks 6a, July 16, 2026, 12:00 - 12:30

Osteoarthritis (OA) drives phenotypic changes in chondrocytes and disrupts extracellular matrix composition and mechanics. While the importance of mechanical loading in OA etiology is generally accepted, the impact of OA on active cell-generated forces, central to cell-matrix interaction, remains insufficiently understood. Here, we systematically compared the force generation capacity of human OA and non-OA articular chondrocytes and examined how cell culture dimensionality (2D versus 3D) and matrix degradability shape the force generation capacity. Through traction force microscopy (TFM) and high-resolution immunostaining, we found that OA modifies the expression and organization of key proteins involved in force exertion and transmission in both 2D and 3D cultures. Strikingly, only in a 3D degradable hydrogel environment, did these changes translate into increased contractile activity. This elevated contractility by OA chondrocytes is accompanied by enhanced protrusive activity, increased F actin and myosin levels and augmented actomyosin engagement. Additionally, F-actin, β1 integrin and fibronectin redistributed towards the protrusions. Altogether, these alterations may underlie the increased cell-matrix interactions observed in OA chondrocytes. Contrary to this, OA chondrocytes did not exhibit increased contractility when cultured on 2D hydrogel substrates. These findings show that the ability to identify OA-driven mechanobiological changes depends strongly on both the degradability and dimensionality of the culture environment. In conclusion, our findings underscore the importance of 3D degradable environments for revealing disease-associated shifts in chondrocyte force generation and emphasize the importance of selecting appropriate model systems for OA mechanobiology research.

Bioengineering breast cancer dormancy in the bone marrow niche

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Flash Talks S1, July 13, 2026, 17:15 - 17:45

Breast cancer recurrence is frequently driven by dormant disseminated tumour cells that persist within the bone marrow niche and later reactivate. To address this challenge, we are developing a bioengineered platform that models and detects dormancy using bioactive metabolites delivered via lipid nanoparticles.

In 2D studies with MCF-7 breast cancer cells, treatment with bioactive metabolites reduced expression of the proliferation marker Ki-67 and increased expression of dormancy-associated markers p27 and COUP-TFI, confirming induction of a quiescent phenotype. We further demonstrate that lipid nanoparticles can be efficiently loaded with these metabolites and are readily internalised by MCF-7 cells, enabling controlled delivery.

Building on this, we are engineering a 3D bone marrow–mimetic niche in which breast cancer micrometastases are embedded within a highly compliant hydrogel matrix (<1 kPa), recapitulating the soft mechanical environment of marrow. The model incorporates haematopoietic and mesenchymal stem cells to support long-term maintenance of dormancy and stemness, capturing key cellular and mechanobiological interactions.

Importantly, these systems are designed as technologies to detect and study recurrence by identifying cues that trigger reactivation, such as infection-induced inflammation. By integrating the model into microwell-based chip platforms, we enable high-throughput screening of microenvironmental and inflammatory stimuli. This approach provides a powerful tool to uncover mechanisms of dormancy escape and supports the development of improved diagnostic strategies and personalised therapies aimed at preventing fatal breast cancer recurrence.

Investigating nanovibration-induced mechanical stimulation on the differentiation and stemness of patient-derived glioblastoma cells.

Kirsty Weighill[1,2,3], Natividad Gomez-Roman[1], Peter Childs[2,3]
[1]Strathclyde Institute of Pharmacy and Biomedical Science, University Of Strathclyde, United Kingdom, [2]Strathclyde Biomedical Engineering, University of Strathclyde, United Kingdom, [3]Centre for the Cellular Microenvironment (CeMi), University of Strathclyde, United Kingdom

Flash Talks 6c, July 16, 2026, 12:00 - 12:30

Glioblastoma (GBM), a malignant primary brain tumour, has inevitable recurrence in all patients due to resistant glioblastoma stem cells that repopulate the tumour following treatment. Nanovibration is a novel, potential, therapy that mechanically stimulates cells, influencing cell behaviour .e.g. mesenchymal stem cell differentiation, that could potentially target resistant glioblastoma stem cells. This study aims to investigate how nanovibration at 1 kHz±30 nm and 20 kHz±40 nm influences glioblastoma cells, focusing on differentiation from their stem cell state.

Patient-derived glioblastoma cells (E2/G7) were cultured in stem-cell enriched conditions (STEM), media containing foetal bovine serum promoting differentiation (DIFF) and STEM conditions plus nanovibration (NANO) at 1 kHz and 20 kHz (out with human hearing range therefore clinically applicable). Differentiation and stemness was investigated by western blot from 2D and 3D (AlvetexTM scaffolds) and the neurosphere formation assay (NFA), following nine days of nanovibration.

Western blot analysis showed nanovibration at 1 kHz/20 kHz has no effect on E2 cell differentiation in both 2D and 3D, with STEM and NANO cells expressing similar levels of GFAP (glial differentiation marker) and SOX-2 (stem cell marker). DIFF cells showed significantly increased GFAP compared to STEM and NANO for E2 cells at 1 kHz in 2D and 1 kHz/20 kHz in 3D ($p<0.01$) and E2 cells at 20 kHz in 2D ($p<0.05$). DIFF cells also showed a significantly reduced SOX-2 compared to STEM and NANO for E2 cells at both frequencies in 2D ($p<0.01$) and 3D ($p<0.001$). Neurosphere formation assay revealed nanovibration at 1 kHz/20 kHz does not alter stemness in E2 or G7 cells with no significance between STEM and NANO response.

Nanovibration at 1 kHz/20 kHz has no effect on the differentiation or stemness of E2/G7 patient-derived glioblastoma cells. Future work will investigate nanovibration of E2/G7 spheroids embedded in a hydrogel for further 3D studies.

Mechanochemical feedback couples cranial neural crest migration and neural tube morphogenesis via mechanosensitive fibronectin remodelling

Kai Weissenbruch[1], Roberto Mayor[1]
[1]University College London, United Kingdom

Flash Talks 6b, July 16, 2026, 12:00 - 12:30

Cranial neurulation and collective migration of cranial neural crest cells are two major processes during embryonic morphogenesis. Although often considered distinct and functionally independent, spatiotemporal overlap exists between both to a various degree across many species. Using Xenopus laevis as a model, we show that collective cranial neural crest migration is a prerequisite for cranial neural tube closure. Neural crest delamination and invasion into extracellular matrix, secreted by the cranial mesoderm, leads to fibronectin remodelling along the neural crest-neural plate border. The emerging fibronectin sheet not only segregates neural crest and neural plate but is also necessary for neural tube morphogenesis. Mechanistically, neural crest cells express the membrane-bound matrix metalloproteinase MMP14, which is necessary and sufficient for this fibronectin remodelling. Thus, the mechanism depends on spatially localised MMP14 activity, facilitated by collective neural crest cell movement, rather than diffusion. Finally, our data reveal that the neural crest-specific expression of MMP14 is mechanosensitive and amplified by compressive forces. Strikingly, such forces arise in vivo due to neurulation itself, as the bending motion of the neural folds spatially confines neural crest cells between the underlying mesoderm and the superficial ectoderm.

ISMB Poster Presentations

A Computational Model of Vascular Smooth Muscle Cell Mechanosensitivity, Mechanotransduction and Phenotype Modulation for the Multiscale Modelling of Arterial Failure in Ageing and Genetic Disease

Mr. Yousof Mohamad Assaad Abdel-Raouf[1], Lauranne Maes[1,2], Nele Famaey[2], Patrick Sips[3], Julie De Backer[3,4], Patrick Segers[1]
[1]Institute of Biomedical Engineering (IBME- BioMMedA), Universiteit Gent, Belgium, [2]Department of Mechanical Engineering, KU Leuven, Belgium, [3]Center for Medical Genetics Ghent, Department of Biomolecular Medicine, Universiteit Gent, Belgium, [4]Department of Cardiology, University Hospital, Belgium

E-Poster Session Tuesday lunch, July 14, 2026, 13:00 - 13:50

Arterial failure is a common consequence of ageing and connective tissue disease, and is hypothesized to be linked to phenotype switching of vascular smooth muscle cells (VSMCs) that occupy the spaces between elastic lamellae in the media of the large elastic arteries. Different factors, including hypertension, changes in the extracellular matrix (ECM), and inflammation, can disrupt the mechanosensitivity of these cells, which modulate into aberrant phenotypes, triggering a cascade that can lead to full arterial disease. We have previously shown that numerical biomechanical models accounting for phenotype plasticity due to disrupted mechanosensitivity and remodelled ECM can recoup clinical biomarkers of disease including medial degradation, fibrosis, increased stiffness and aneurysm. Our model also reports that early intervention increases likelihood of recovery and late intervention yields negative outcomes past a point-of-no-return. However, given the multiscale nature of this phenomenon, that work focused largely on tissue-scale remodelling of biomechanical constituents, and the mechanosensitive aspect of the cells was considered phenomenologically. Here, we demonstrate a numerical model to account for mechanosensitive and mechanotransduction mechanisms. This work, models the molecular clutch, actin dynamics, nuclear mechanics and the most prominent genetic circuits of developed VSMCs, including signalling of the YAP/Taz, MRTF-A/B, myocardin and KLF4 genes, downstream of the FAK-Src and Rhoa-GTP/Rac1-GTP pathways. This model shows cells expressing the highest contractile phenotype at substrate stiffness 10-20 pN/nm, and dominance of the synthetic phenotype outside those ranges. As previously implemented, we will couple the outcomes of the changes in ECM stiffness and forces on cell phenotype expression – namely the contractile, synthetic, degradative, and osteochondrocytic phenotypes – with remodelling of microstructural constituents like collagen, glycosaminoglycans, and elastin. While there are still pathways and mechanisms unaccounted for, this model offers a more mechanistic reflection of the biomechanical origins of phenotype modulation, and an opportunity to bridge the multiscale gap.

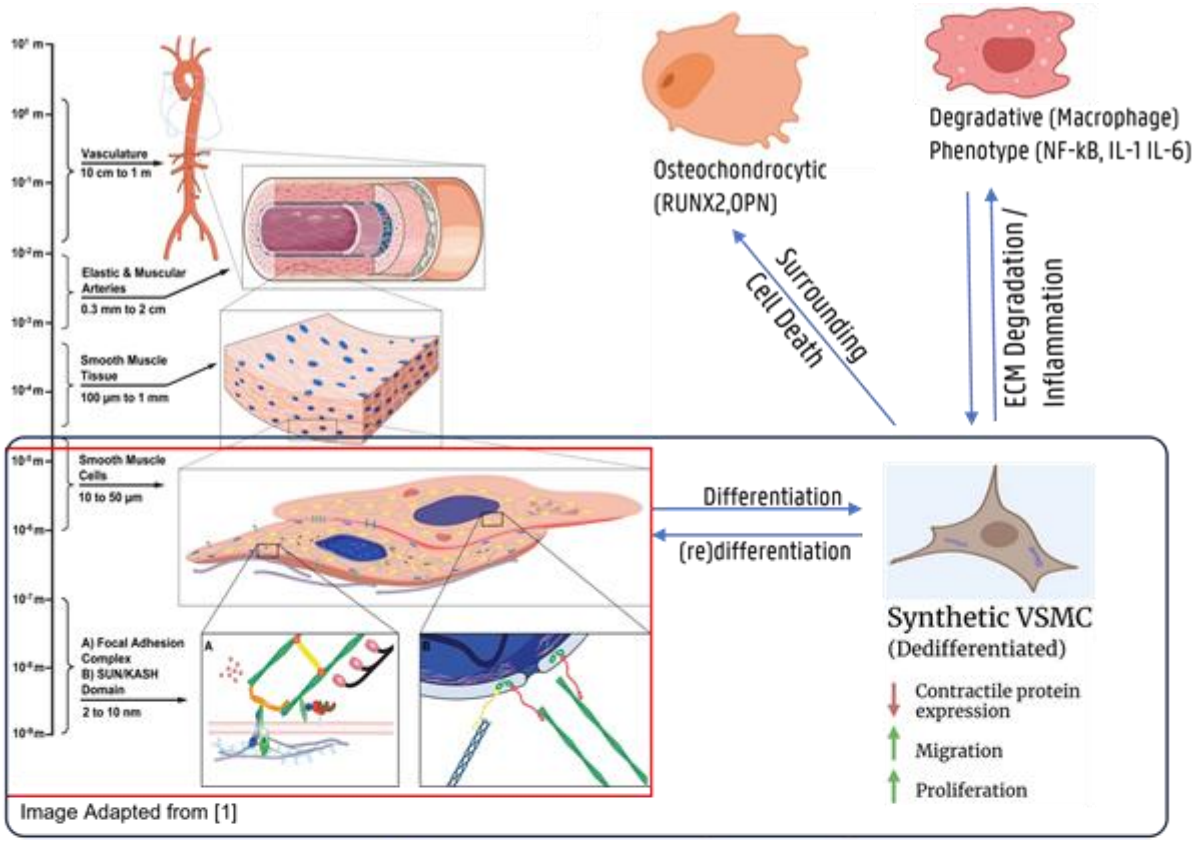
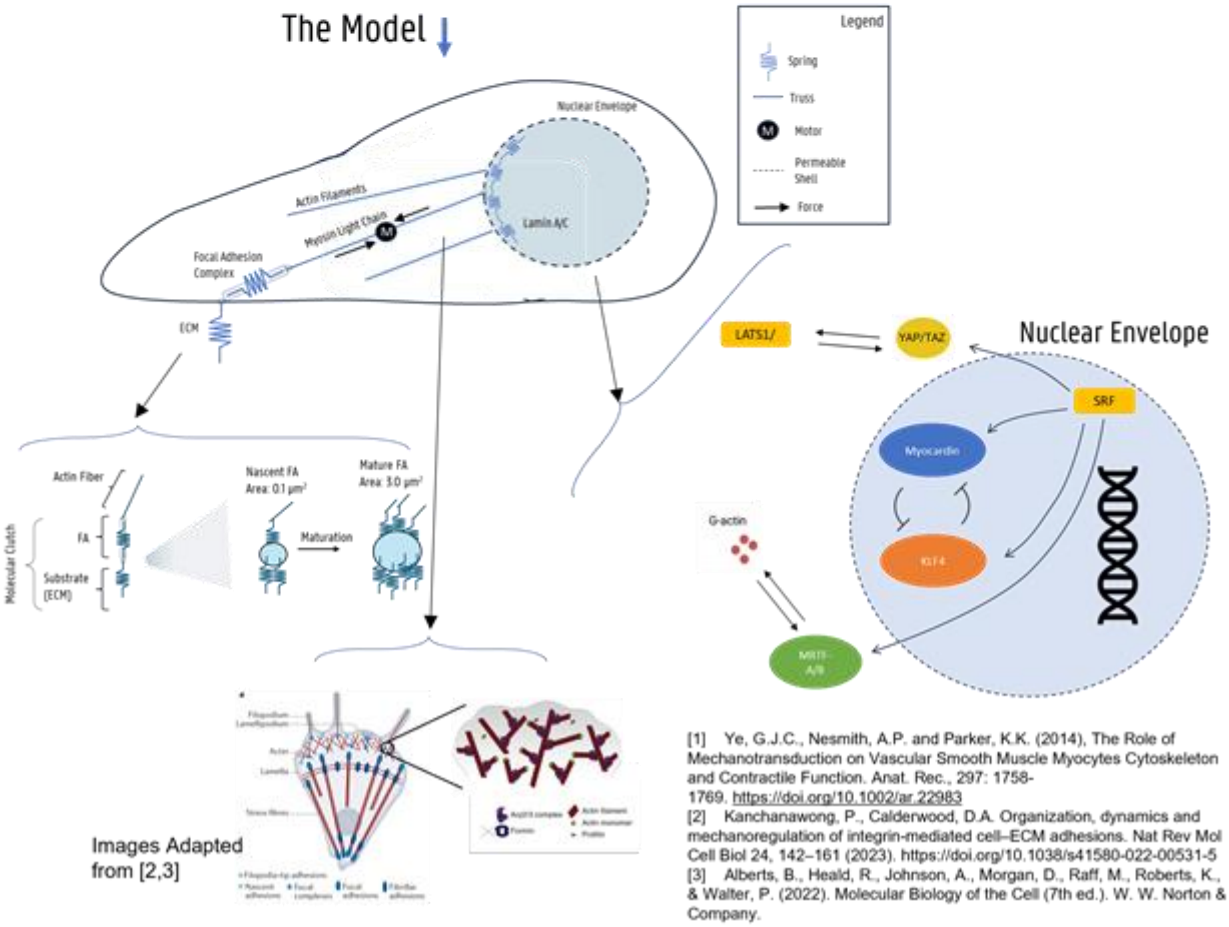


Image Adapted from [1]

The Model



Images Adapted from [2,3]

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The Effects of Nanovibration on Cellular Yield in Serum-Free Conditions for Cultivated Meat

Charlotte Adams[1], Melanie Jimenez[1], Stuart Reid[1], Peter Childs[1]
[1]University Of Strathclyde, United Kingdom

E-Poster Session Wednesday Lunch, July 15, 2026, 13:00 - 13:50

The field of cultivated meat implements tissue engineering and cell culture techniques to produce products that are comparable to traditional meat. Interest in cultivated meat is growing, with over $3 billion of investment since 2013 [1]. However, multiple challenges remain, most significantly, the high production cost. The first cultivated hamburger produced in 2013 was estimated to cost $330 000 [2]. Since then, production costs have decreased year-on-year, but further reductions are necessary to ensure the global success of cultivated meat. One of the key strategies toward this goal is to increase cell yield, thus maximising the production per batch.

Previous research suggests that mechanical stimulation can drive increases in proliferation [3]. Vibration is a versatile method of mechanically loading cells that has demonstrated increased proliferation in a range of cell types. Notably, mesenchymal stem cells and periodontal ligament fibroblasts, with up to 110% increases in proliferation [4]. However, there is still no clear consensus, as to the most effective vibration parameters for increased yield (Figure 1).

In this work, DF-1 embryonic chicken fibroblasts were exposed to 7 days of 30 nm vertical vibration at frequencies ranging from 100 Hz to 10 kHz. Nanoamplitude vibration was delivered via a bespoke bioreactor that implements piezo actuators to facilitate vibration. The resulting changes in proliferation were measured via cell count at multiple time points with morphological assessment also carried out to assess changes to cytoskeletal organisation. Throughout stimulation, cells were cultured in a previously established serum-free media composition [6].

This work provides the first characterisation of the impact of vibrational parameters on cultivated-meat relevant cells, and in the absence of FBS. Validating, for the first time the effects of nanovibration without the presence of FBS, thus opening a new avenue for larger scale food bioprocessing.

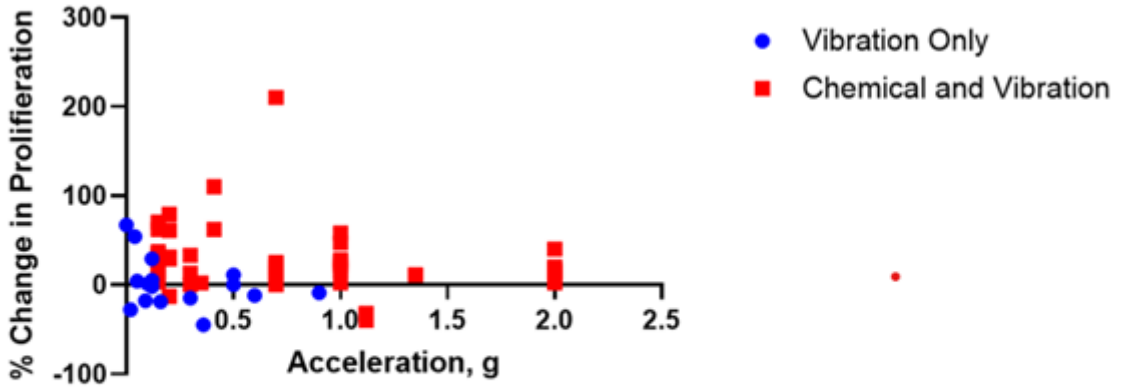

Figure 1. Collated results of published studies investigating the effects of vibration on cell proliferation. Studies implementing vibration as a sole stimulus, and studies implementing vibration in combination with a specific media have been separated. Results were collated from a comprehensive review of studies involving vibration conducted in 2025 [5]. Key search terms 'vibration' and 'proliferation'

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CellQ-Twin: A Soft Robotic Platform for Multiaxial and Rhythmic Cell Culture

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E-Poster Session Tuesday lunch, July 14, 2026, 13:00 - 13:50

Mechanobiology research requires precise and physiologically relevant mechanical stimulation platforms to interrogate how cells convert physical forces into biochemical responses. However, many existing cell-stretching systems remain costly, mechanically rigid, or limited in waveform programmability, restricting their integration into routine biological workflows [1]. We present CellQ-Twin, a pneumatically driven soft-robotic platform designed to deliver scalable, programmable multiaxial strain across multiwell culture formats.

The system employs elastomeric membranes actuated via independently controlled pneumatic chambers to generate radial and non-equibiaxial strain profiles. Membrane strain fields were characterised using finite-element modelling and validated experimentally through digital image correlation, demonstrating uniform strain delivery (≤1% error) up to 10% per axis at 1 Hz. The platform is incubator-compatible, supports live-cell imaging, and enables repeatable rhythmic stimulation across six wells simultaneously.

To evaluate biological compatibility, collagen-coated PDMS membranes were subjected to 0%, 2%, or 10% cyclic strain (1 Hz) for 8 hours and compared to static culture on tissue-culture plastic. Bone marrow mesenchymal stromal cells were seeded (50,000 cells per well), imaged pre- and post-stimulation to quantify morphological adaptation, and assessed for viability. Culture supernatants were analysed for cytokines and adhesion molecules via ELISA and multiplex assays, and RNA was harvested to examine mechanosensitive gene expression. Cells adhered robustly to collagen-coated PDMS and remained viable under cyclic loading, with strain-dependent morphological and molecular responses observed.

By combining quantitative strain-field validation, independent biaxial control, and compatibility with downstream molecular assays, CellQ-Twin provides a versatile and accessible cell stretching platform for systematic investigation of force-regulated cellular behaviour.

References:

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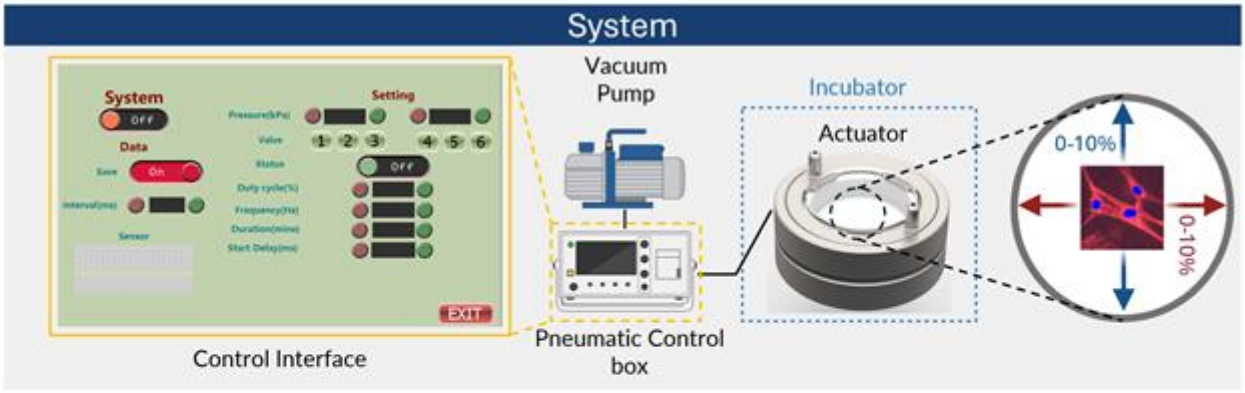
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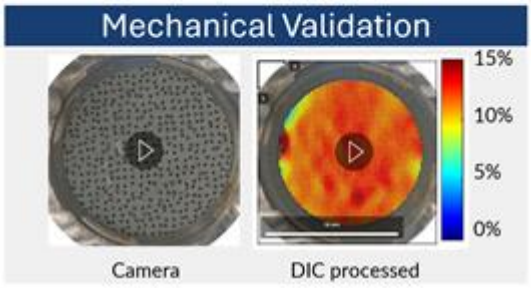
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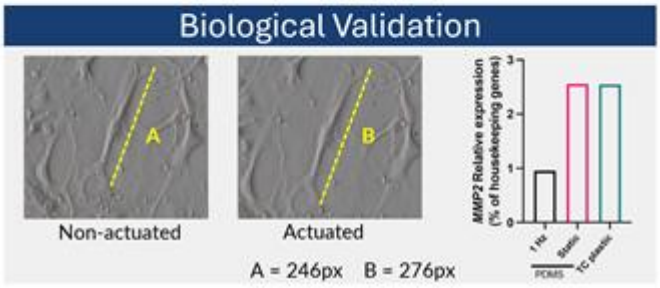
Biological Validation
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B
Non-actuated
Actuated
A = 246px B = 276px
MMP2 Relative expression (% of housekeeping genes)
1 Hz
Static
TC plastic
PDMS

The characterisation of the difference between human and mouse pancreatic cells under biomechanical stress

Alfin Alexander[1], Alicja Wilczynska-Obszanska[1], Monika Jakubowska[1]
[1]Malopolska Centrum Biotechnology (mcb), Jagiellonian University, Poland

E-Poster Session Wednesday Lunch, July 15, 2026, 13:00 - 13:50

Numerous studies have sought to develop in vitro pancreatic cancer models using human or mouse pancreatic cancer cell lines. Although these cell lines are widely employed in preclinical pancreatic cancer research, differences in their responses have rarely been addressed, despite their potential impact on data acquisition and interpretation. Notably, the biomechanical characteristics of the pancreatic tumour microenvironment - which is significant for disease progression and therapy - remains often overlooked in in vitro studies. To address this gap, we conducted research to characterise the distinct properties of human and mouse pancreatic cancer cell lines, as well as primary stromal cells (e.g., pancreatic stellate cells), under biomechanical stress. Human PANC-1 cells and mouse KPCY pancreatic cancer cells (the latter tagged with yellow fluorescent protein, YFP) were co-cultured with species-matched pancreatic stellate cells (hPSCs or mPSCs, respectively). Biomechanical stress was introduced by culturing cells as 3D spheroids (solid compression stress) and as 2D monolayers exposed to a shear stress of 10 dyn/cm^2 via fluid flow. Spheroid samples underwent (immuno)histological staining, while PCR analysis of gene expression was performed on both spheroids and 2D cultures. Hematoxylin-eosin staining and immunohistochemistry revealed distinct spatial cell organisation in human versus mouse 3D co-cultures, particularly regarding the distribution of collagen I and III in PANC-1/hPSC and KPCY/mPSC spheroids. PCR analysis further demonstrated that biomechanical stress modulates vimentin gene expression in both KPCY monocultures and KPCY/mPSC co-cultures. These findings will be complemented by additional experimental techniques developed during my doctoral studies.

Sequential Mechanical Stimulation Dynamically Regulates Calcium response in DRG Neurons

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Mechanically-activated ion channels are central mediators of sensory transduction in dorsal root ganglion (DRG) neurons. While atomic force microscopy (AFM) and optical tweezers allow controlled mechanical stimulation at the single-cell level, they typically deform relatively large membrane regions and associated underneath structures, limiting the investigation of localized mechanotransduction. Fluidic Force Microscopy, which integrates AFM-based force control with microfluidic pressure delivery, enables spatially confined positive or negative pressure to be applied to the plasma membrane of the same cell within a single experiment, allowing directional and sequential stimulation with high precision.

Here, we investigated mechanosensitive calcium responses in mouse DRG neurons cultured for 24h or 48h after isolation. A microchanneled, tipless cantilever was positioned on the neuronal soma under controlled contact force, and intracellular calcium dynamics were monitored during sequential stimulation protocols: negative followed by positive pressure (−40/−80mbar → +40/+80mbar) and the reverse order (+40/+80mbar → −40/−80mbar). Calcium responses strongly depended on pressure magnitude, polarity, sequence, and culture time. At 40mbar, negative followed by positive stimulation did not significantly alter the proportion of responsive cells at either 24h or 48h. In contrast, when positive pressure (+40mbar) was applied first, the subsequent negative stimulus (−40mbar) failed to evoke calcium responses in both conditions, indicating sequence-dependent inhibition. At 80mbar, this effect was more pronounced. Negative-first stimulation (−80mbar) elicited robust responses to both stimuli, particularly at 48h. However, when positive pressure (+80 mbar) preceded negative stimulation, the second response was abolished at 24h and partially recovered at 48h, suggesting time-dependent modulation or mechanical adaptation.

These findings demonstrate that mechanosensitive channel activity in DRG neurons is governed not only by force amplitude but also by the order and polarity of mechanical inputs. Sequential mechanical cues dynamically shape neuronal responsiveness, potentially through changes in membrane prestress conditions or membrane–cytoskeleton coupling.

Uncovering how cellular connections and mechanical inputs impact gene regulation during embryonic development

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During embryonic development, a population of apparently identical cells gives rise to differentiated cell types with specific functions, typically associated with well-defined morphologies. For example, stem cells generally exhibit a rounded geometry with a large, relaxed nucleus, whereas differentiated cells acquire more complex geometries.
Evidence suggests that changes in the extracellular matrix (ECM) are transmitted directly to the cell membrane and nuclear envelope, activating specific cell fate transcriptomic programmes. However, the mechanisms by which cells sense mechanical changes and coordinate them with gene regulation and nuclear geometry remain poorly understood. Although single-cell omics are essential for studying cellular heterogenicity, a previous cell dissociation step is required, disrupting the rapid and reversible mechano-regulated processes. To overcome this limitation, we utilized ditiobis-succinimidyl propionate (DSP) as a genomic fixator prior to cell dissociation. To identify genes whose expression is modulated by cell connections and geometries (cellular connexome), we compared early zebrafish embryos under two conditions: fresh dissociated cells and DSP-fixed-embryos dissociated cells. Our bulk and single-cell RNA-seq data reveal that the DSP-fixed cells retain higher expression levels of genes related to cell-cell and cell-ECM contacts. Furthermore, transcription factors, intermediate filaments and ion channels are better preserved in DSP-fixed cells, suggesting their mechanosensitivity and relationship with the cellular connexome. Comparative analysis of the identified clusters in the sc-RNAseq shows that clusters with the largest transcriptomic differences correspond to populations with long and rapid migration movements during epiboly. We are currently validating components of this cellular connexome via in situ hybridization, GFP fusion proteins of TFs to track in vivo dynamics, and CRISPR-Cas9 knockouts for functional analysis.
Optimization of this DSP-based fixation protocol enables unprecedented resolution in assessing how cellular connections and mechanical states regulate gene expression, including at the single-cell level, and in identifying key components of the cellular connexome during embryonic development.

Enlightening mechanics: high-throughput automated spheroid stiffness mapping in lab-on-a-chip devices with Brillouin microscopy

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Mechanical properties of biological tissues and cellular assemblies provide critical insights into their functional state and often act as early indicators of disease, complementing or preceding biochemical changes visible with conventional fluorescence microscopy. To model these systems in vitro, spheroids embedded in viscoelastic hydrogels are widely used as they mimic the native three-dimensional tissue microenvironment and preserve cell-to-cell interactions. Developing reliable, high-throughput methods to probe spheroid mechanics could therefore open new opportunities for diagnostics and disease monitoring.

Brillouin microscopy is well-suited for this task, as it is non-invasive, label-free and offers mechanical contrast based on the inelastic scattering of photons off spontaneous, thermally-induced acoustic vibrational modes. The resulting Brillouin frequency shift (BFS) depends on the local sound velocity within the material. Consequently, Brillouin micro-spectroscopy enables microscale resolution visualisation of the longitudinal storage and loss moduli, correlated to sample stiffness and viscosity, respectively.

We propose integrating Brillouin microscopy with a novel viscoelastic hydrogel lab-on-a-chip platform, encapsulating mesenchymal stem cell (MSC) spheroids within a microfluidic device, modelling a bone marrow niche. To complement this, we develop Python-based software, which enables sample identification in automated, high-throughput experiments and quantification of both gel and spheroid BFS within the devices as a proxy to their mechanics. Furthermore, we apply Brillouin microscopy to establish a reproducible viscoelastic niche within the microfluidic devices and track the spatial and temporal evolution of the mechanical state of MSC spheroids and the surrounding hydrogel.

While Brillouin microscopy is a promising technique for probing mechanics of biological systems, fully leveraging its potential requires improved standardisation, increased throughput, and tighter control of the measurement environment. We believe that this system establishes a mechanobiology-ready platform, potentially opening new pathways for translational applications of Brillouin microscopy in diagnostics, for example, by distinguishing the mechanical signature of healthy and pathological bone marrow models.

Interaction between Lamin A/C and Src mechanosensors in the nucleus of osteosarcoma cells: implications for diagnosis, prognosis and therapy

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Mechanotransduction is the process by which cells can convert extracellular mechanical stimuli into biochemical changes within a cell. In cancer cells, this mechanism can be completely deregulated, thereby participating in cancer onset, progression and metastatization. In our previous work, we demonstrated that SaOS-2 osteosarcoma cancer cells, commonly recognized as low aggressive osteoblast-like cells, exhibit high nuclear Lamin A/C expression compared to more-aggressive osteosarcoma cell lines. Interestingly, the nuclear content of Src, a tyrosine-kinase involved in key cellular processes such as cell proliferation, migration and mechanosensing, has the same behaviour of Lamin A/C and decreases as osteosarcoma cell aggressiveness increases. Based on literature evidence about the importance of lamins phosphorylation, we tested whether Src interacts with Lamin A/C in the nucleus of SaOS-2 cells. Here, we demonstrated a tight relationship between Lamin A/C and Src in SaOS-2 cell nuclei, assessed by advanced imaging-based microscopy techniques. With confocal laser scanning and STED microscopy, a statistically significant co-distribution between the two proteins was observed, especially in the nuclear rim rather than in the nuclear matrix. To deepen the Src-Lamin A/C colocalization at the nanoscale level, we used the time-domain fluorescence lifetime imaging microscopy (FLIM), a sensitive molecular imaging method to detect protein-protein interactions, combined with Forster's resonance energy transfer (FRET) detection (FLIM-FRET technique), demonstrating a close relationship between Src and Lamin A/C in the nuclear compartment of osteosarcoma cells. These findings suggest to consider osteosarcoma as a mechanopathology, thereby opening to new therapeutic approaches for patients. Understanding how the physical microenvironment influences cancer cell signalling will lead to the improvement of strategies to target the deregulated mechano-sensitivity of osteosarcoma cells.

Brillouin Microscopy: A Tool for 3D Imaging in Mechanobiology

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In recent years, Brillouin imaging has rapidly advanced, finding new application areas thanks to its capability to measure mechanical parameters in three dimensions and on live samples. We present initial results obtained with our newly developed Brillouin microscope, which integrates this technology with existing optical imaging methods.
We showcase several examples, including single-cell measurements and tissue sample analyses. Its 3D capability makes this method particularly valuable for 3D cell culture applications, with initial results on complex organoids being presented. Additionally, there is a growing number of applications in plant physiology, and we will share results using the Arabidopsis root model system.
In summary, Brillouin microscopy is a versatile tool that can visualize differences in mechanical properties, quantify them, and observe dynamic events on time scales relevant to developmental biology.

The role of the plasma membrane in mechanochemical regulation of signalling

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The cell membrane serves as a crucial interface between the outside environment, allowing the cell to sense and respond to it. In this context the generation of membrane domains (active emulsions)[1] mediated by actin-driven nanoclustering of Glycosyl Phosphatidyl Anchored Proteins (GPI-APs) at the cell surface plays an important role in generating a distinct chemical environment in the membrane. These nanoclusters are triggered by β1 integrin signalling leading to the activation of the RhoA-Formin axis, and actomyosin activity. Mechanochemical activation of vinculin downstream of integrin leads to this nanoclustering, and is required for cell spreading and migration[2]. Ongoing work from our laboratory suggests that these actively generated GPI-AP nanodomains are necessary for the activity of various RhoGTPases. We propose that this allows the cells to sense and encode the mechano-chemical environment of the cell and integrate it at the plasma membrane, translating these cues into a physiological response. We have been investigating this process across scales. At the molecular scale, the ability of myosin1 to bind actin is inhibited by a competing actin binder, tropomyosin[3] and promoted by vinculin. We hypothesize that activated vinculin thus gates the interactions between actin and myosin1 for the generation of GPI AP nanoclusters. Further, the plasma membrane may utilize these clusters at the mesoscale for physiological activities such as spreading and migration through a the small GTPase, Rac1. Finally, we propose that at the cellular scale this mechanosensitive clustering machinery may template Rac1 activity in response to mechanical stimulus, to effect durotaxis.

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Understanding Cellular Mechanobiological Response and Contractile Dynamics in Cardiac Tissue Mimics Following Injury

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Cells continuously sense and adapt to the mechanical and biochemical properties of their environment, a process central to both tissue homeostasis and injury response. In the heart, tissue wounding, such as in myocardial infarction, leads to extensive cardiomyocyte (CM) death, creating a non-contractile wound embedded in a uniquely challenging environment: the surrounding myocardium remains rhythmically self-contractile, while adult CMs have minimal regenerative capacity. Cardiac fibroblasts (cFBs) are recruited during the subsequent wound-healing response, driving extracellular matrix deposition and ultimately fibrotic scar formation. How CMs and cFBs interact mechanobiologically within this heterogeneous, contracting wound remains insufficiently understood.
To this end, we established a 2D in vitro wound closure model using collagen coated polyacrylamide hydrogels to support co-culture of CMs and cFBs. Laser ablation was employed to generate standardized supracellular wounds within confluent monolayers, allowing real-time microscopic analysis of cellular dynamic behaviour during the response to injury. Immediately following ablation, we observed distinct patterns of acute cell death: CM-cultures displayed minimal debris, whereas cultures with cFBs exhibited greater debris and stronger substrate attachment. Over time, non-myocytes demonstrated migration into the wound area, with higher directed migration closer to the center of the wound. Interestingly, CMs at the wound border displayed coordinated contractile behavior immediately post-injury. Their combined contractions were preferentially oriented away from the wounded region, in stark contrast to remote control areas where no directional preference was observed. Together, these findings illuminate early post-injury cellular behavior in a dynamic, self-contractile cardiac environment, capturing mechanobiological features that can mimic part of the in vivo wound stabilization and fibrosis response. The contrasting dynamics between CM-only and CM–cFB cultures suggest that injecting cardiac cells in or near the wound, a strategy often proposed for cardiac repair, can affect wound closure depending on their interaction with resident fibroblasts and the surrounding contractile tissue.

How topography governs epidermal stem cell fate: role of curvature, migration and stretch

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Human skin is divided into two parts - the multilayered epidermis, composed of keratinocytes, and the dermis, the underlying connective tissue. The epidermis projects into the dermis to form a network of invaginations known as rete ridges. The undulating ridges serve as niches for undifferentiated keratinocytes called epidermal stem cells (EpdSCs) (1). These ridges eventually flatten out as we age, correlating with reduced stem cell marker expression. Hence, though the rete ridges are an integral component of young healthy skin, the mechanisms that regulate the patterned distribution of EpdSCs between the ridges are not known.

Using an in vitro platform that mimics rete ridge topography, we have previously shown that EpdSCs can pattern on the tips of the undulations, even in the absence of the dermis, suggesting that patterning might be driven by topographical cues provided by the undulations (2). Here, we are investigating the mechanisms by which the undulating topographies regulate EpdSC fate, specifically the contributions of curvature, mechanical stretch and migration. We observe a differential distribution of tension at both cell-cell and cell-ECM contacts on the tips compared to the bases of the undulations. Furthermore, cells on the tips have nuclei with higher lamin A/C expression, higher oblateness, and lower sphericity. Together, these results suggest that keratinocytes at the tips occupy a distinct mechanical niche that may contribute to the patterned distribution of EpdSC, although to elucidate the underlying mechanisms further work is required.

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TRPV1 Mechanosensing drives cytoskeletal and nuclear remodeling in Osteosarcoma cells

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Mechanotransduction and cytoskeletal remodelling are increasingly recognized as key regulators of tumor progression and the metastatic cascade. In osteosarcoma, an aggressive primary bone tumor, the contribution of mechanical cues to cancer cell behaviour remains largely unexplored. In our previous work, we showed that uniaxial cyclic stretching (1 Hz, 0.5% strain for 24 h) induces TRPV1-dependent cellular responses, differentially modulating aggressive traits in two osteosarcoma cell lines U-2 OS and SAOS-2 (Buglione et al., 2025). We further demonstrated that chemical activation of the mechanosensitive Transient Receptor Potential Vanilloid 1 (TRPV1) can mimic the cellular response to mechanical stimulation.
Here we show that by treating cells with sublethal dose of capsaicin, a selective TRPV1 agonist, modulates cytoskeletal organization, nuclear morphology, cell adhesion and migration, mimicking the morpho-functional changes induced by mechanical stimulation. These effects were completely abolished by the TRPV1 inhibitor AMG9810, confirming a channel-dependent mechanism. Immunofluorescence analyses revealed that TRPV1 activation alters focal adhesion organization, accompanied by a redistribution of perinuclear actin structures and Nesprin-2 Giant (N2G), a key component of the Linker of Nucleoskeleton and Cytoskeleton (LINC) complex. Disruption of the LINC complex prevented these structural rearrangements, suggesting that nuclear–cytoskeletal coupling mediates the transmission of TRPV1-dependent mechanical signals. Additionally, inhibition of the RhoA/ROCK pathway altered the cellular responses to capsaicin, supporting a role for ROCK signalling downstream of TRPV1 in regulating cytoskeletal tension and mechanotransduction.
Interestingly, SAOS-2 cells displayed limited responses to the same treatments, consistent with their lower tumorigenic potential and suggesting that TRPV1-mediated mechanotransduction may depend on the genetic background of osteosarcoma cells.
Overall, these findings suggest that both mechanical and chemical TRPV1 activation modulate cytoskeletal and nuclear organization in osteosarcoma cells, potentially influencing mechanosensitive pathways that regulate adhesive and migratory properties.

Buglione et al., 2025. PMID: 41009392

Investigating the principles behind cell coordinated migration as a function of micro-environment space-time warping

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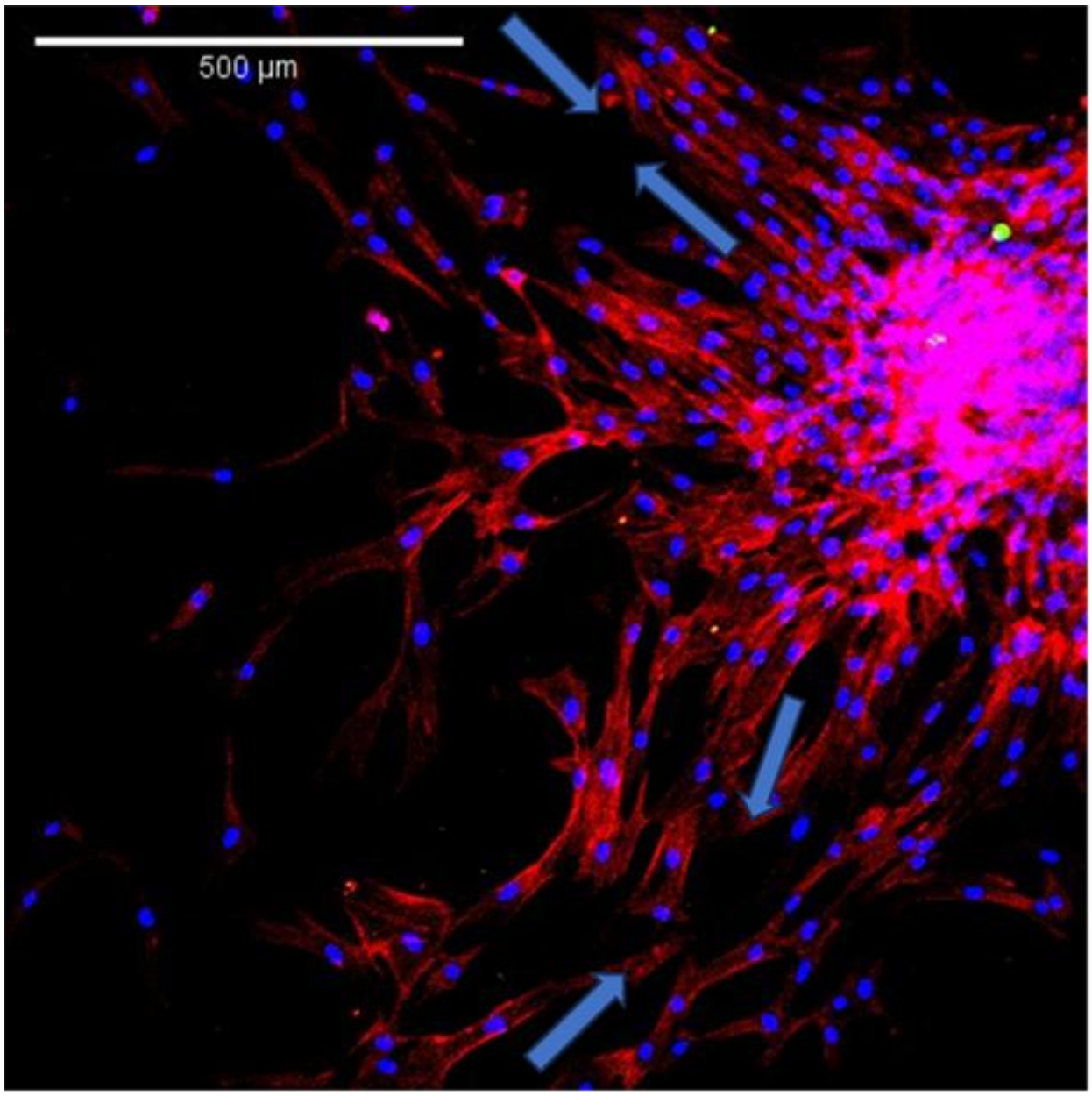
Living organisms rely on cellular coordination, generating intricate motion patterns to fulfil physiological functions such as growth, development and regeneration. Although these patterns are often associated with physical or biochemical signalling, cell motion has never been investigated considering microenvironment space-time warping in the case of soft tissues and substrates. Considering micro-relativity effects, cell time perception may thus vary as a function of this warping affecting cell motility and coordination.

Adipose-derived mesenchymal stem cells were seeded on 5 mg/mL agarose - 20 mg/mL dextran substrates [Cacopardo et al, JMBBM 2019], optimised on the base of an in-silico model to match the mechanical properties of the adipose niche [Guazzelli et al, Materials Today 2025]. The preliminary results suggest that the presence of cell clusters and the resultant substrate warping in space and time may modulate cell migration (fig. attached).

Further studies, in the framework of the INTERCELLAR project (FIS-2023-00416), will focus on a computational setup describing cell-substrate interaction based on motor clutch theories to predict the formation of cell focal adhesions in space and time. Relative cell time will be considered by tuning focal adhesion unbinding rates and lifetimes as a function of substrate. On the base of the in-silico results, culture chamber will be designed to investigate cell migration as a function of: i) different distances between clusters, which may affect the combination of the generated strain fields; ii) different cell numbers in the clusters, resulting in different cluster size/weights; iii) substrate with different viscoelastic properties which affect substrate deformation over time. Cell migration will be then characterized combining atomic force microscopy and advanced imaging techniques.

In the future, this study will pave the way for engineering substrates able to guide cell motion in regenerative medicine and in-vitro applications as well for defining algorithms capable of predicting pathological outcomes.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Visualising mechanoelectrical transduction in cancers

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Mechanotransduction is the conversion of mechanical inputs - cell-generated or externally applied - into a biochemical signal. A key set of molecules that mediate this are mechanically activated (MA) ion channels, which facilitate ionic flux in response to mechanical cues. Cancer cell lines are known for being highly mechanically responsive, and often express multiple different MA ion channels. We have used TIRF microscopy combined with Ca2+ sensitive ligands to visualise these channels activating via cell-generated forces (i.e. mediating cell-intrinsic signalling) in the melanoma WM-266/4 and breast cancer MCF7 cell lines. In WM-266/4 cells which contain functional ELKIN1 and TRPV4, we used a cell wide calcium dye and a strategic combination of channel KOs or inhibitors to visualise the activity of these unique MA channels. Our data indicate that localised ELKIN1 dependent Ca2+ flickers arise in response to acto-myosin contractility, but TRPV4 dependent Ca2+ flickers do not. However, for a complex cell line like MCF7 which contains four potential MA ion channels, modulating the activity of too many channels, either by gene editing or pharmacological manipulation, at the same time runs the risk of triggering compensatory mechanisms which could obscure the native activity of these channels. Thus, a different approach is required to resolve the signalling from individual channels. To address this, we have tagged ELKIN1 and PIEZO1 with HaloTag, a self-labelling protein tag which allows the localisation of a calcium-sensitive dye to our channels of interest. Results from the initial tool validation phase have identified our MA channel-HaloTag constructs as a promising strategy to characterise the cell-intrinsic signalling from multiple channels within complex cellular environments.

Microfluidic Control of Cellular Confinement and Cell Density in Alginate Microgels

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Three dimensional cellular confinement plays a key role in regulating cell morphology, cytoskeletal organisation, and cell–cell interactions. Here, we present a droplet microfluidic strategy for generating size-defined alginate hydrogel microgels that provide controlled microenvironments for three dimensional cell encapsulation. Microgel systems provide a platform for studying mechanobiology in 3D, as their size and cellular occupancy can be precisely tuned to modulate geometric confinement and cell–cell proximity within a defined microenvironment. Using a glass capillary microfluidic device, sodium alginate droplets were produced under controlled flow conditions and ionically crosslinked with calcium chloride to form stable hydrogel microgels. By varying flow rate ratios, three distinct microgel size regimes were generated with high monodispersity and reproducibility across independent experiments. To investigate how confinement and initial cell density influence cellular organisation, NIH 3T3 fibroblasts were encapsulated at defined starting densities within each microgel size condition. Following culture, samples were fixed and stained for filamentous actin (F-actin) using fluorescent imaging alongside nuclear staining to visualise cell morphology and spatial organisation within the three dimensional matrix. Comparative imaging across microgel sizes and cell densities allows investigation of how geometric confinement and cell–cell proximity influence cytoskeletal organisation in three dimensional culture. This work establishes a reproducible microfluidic platform for engineering size-controlled hydrogel microenvironments and provides a tunable system for studying mechanobiological responses to cellular confinement.

Mechanically Defined Microenvironments Regulate Neurovascular Organisation in Blood–Brain Barrier Organoids

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Extracellular matrix (ECM) remodelling contributes to blood–brain barrier (BBB) dysfunction in ageing and vascular dementia, where stiffness elevation and altered viscoelasticity at the neurovascular interface may disrupt endothelial–pericyte–astrocyte crosstalk and compromise tight junction integrity. However, most in vitro BBB models lack defined mechanical microenvironments, limiting mechanistic investigation of disease-associated mechanobiology.

We developed tri-culture BBB organoids within ECM-functionalised sodium alginate hydrogels with tunable mechanical properties modelling compliant brain-like regimes (~0.2–1 kPa) and stiffness-elevated microenvironments (~1–3 kPa) associated with ageing-related ECM remodelling. Alginate formulations (0.5–2% w/v) were ionically crosslinked under controlled calcium conditions to modulate crosslink density and network dynamics. Mechanical properties were characterised using oscillatory rheology and stress relaxation to quantify elastic and viscoelastic behaviour relevant to neurovascular mechanics.

Multicellular spheroids comprising human brain endothelial cells (hCMEC/D3), pericytes, and astrocytes were generated via self-assembly and embedded within laminin- or fibronectin-functionalised matrices to decouple biochemical and mechanical cues. Increased matrix stiffness reduced spheroid compactness and altered F-actin organisation, indicating stiffness-dependent cytoskeletal remodelling. Organoid phenotype was characterised using immunofluorescence staining for endothelial (CD31, claudin-5), pericyte (PDGFR-β), and astrocytic (GFAP) markers, alongside F-actin organisation, DAPI nuclear staining, and Live/Dead viability assays to assess barrier-associated features under defined mechanical conditions.

This work establishes a mechanically defined BBB organoid platform to investigate how ECM stiffness and viscoelasticity regulate neurovascular organisation and contribute to barrier dysfunction in vascular dementia.

UNDER PRESSURE: HOW MECHANICAL LOAD INHIBITS CANCER CELL PROLIFERATION IN THE HEART

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Introduction: The incidence of cardiac cancer is low, as both primary and secondary tumors of the heart are rare. We have recently shown that cardiac mechanical load reduces cancer cell proliferation by inducing heterochromatin reorganization. We identified Nesprin-2 as a key mediator of cardiac mechanical cues in cancer cells. The upstream mechanosensors involved in this process remain unknown, as does the mechanism by which these signals are transduced into chromatin remodeling.
Aims: To identify the mechanosensors responsible for sensing cardiac mechanical load and to characterize the downstream changes in chromatin structure.
Methods: We performed a genetic screen using a custom pooled short-hairpin RNA (shRNA) library targeting 200 mechanosensing genes in GFP-expressing lung cancer cells (LG1233) injected into the heart. Engineered heart tissues (EHTs) were generated to validate candidate genes. LG1233 cells were transduced with lentiviral vectors expressing shRNAs targeting selected enriched mechanosensing genes to generate stable knockdown cell lines.
Results: The pooled screen identified 51 depleted and 43 enriched shRNA sequences targeting mechanosensing genes in the LG1233 population after two weeks of cardiac mechanical loading. Six depleted genes were selected and silenced in cancer cells injected into EHTs, confirming their role in promoting cancer cell proliferation. The selected genes (ARBB2, CASS4, FAM107a, PKHD1, PTRPM and TRIP6) are known to be associated with cancer invasiveness. Furthermore, chromatin analysis by immunostaining of structural proteins such as HP1 and Lamin A/C revealed alterations in heterochromatin organization in response to mechanical loading.
Conclusion: Overall, our results demonstrate a direct role for mechanosensors in regulating the proliferative and invasive phenotype of cancer cells, leading to changes in chromatin organization. Ongoing studies aim to elucidate the signaling cascade that transmits mechanical stimuli from the plasma membrane to the nucleus.

Mechanical Nuclear Integrity as a Regulator of PKA/phosphatase signalling homeostasis

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Compartmentalization is a fundamental feature of cell organization that allows biochemical processes to occur in distinct spatial domains and temporal scales. The nuclear envelope (NE), by acting as a gatekeeper for molecules and reactions between the cytosol and the nucleoplasm, is a key determinant of cell compartmentalization. Among the plethora of functions, the nucleus also spatiotemporally regulates signalling machineries, thanks to the synergistic actions of the nuclear pore complex (NPC), the Lamin scaffold, and the Linker of Nucleoskeleton and Cytoskeleton (LINC) complex. However, nuclear integrity is reported to be altered in pathophysiological conditions, such as ageing and nuclear envelopathies and laminopathies. In this context, despite many studies revealing how NE alterations affect chromatin organization and mechanotransduction, how structural NE defects are translated into dynamic nuclear dysfunction remains unclear.

Here, we propose that nuclear PKA/phosphatase signalling homeostasis represents an additional, underappreciated molecular mechanism in the pathogenesis of disorders related to the alteration of nuclear integrity. By combining biochemical approaches with advanced live-cell imaging performed with novel FRET-based biosensors, we identified a unique nuclear signalling domain in which Protein Kinase A activity is strongly restrained by local phosphatases. Interestingly, we observed that nuclear phosphatase pressure is conserved in electroporated ex vivo mouse skeletal muscle fibers but is lost in aged muscles. An artificial disruption of nuclear PKA/phosphatase equilibrium in favour of the kinase dramatically altered nuclear shape and homeostasis.

Therefore, given the central role of Lamin A/C in nuclear mechanics, we next overexpressed LMNA mutants and observed signalling signatures resembling those of old mouse skeletal muscle, suggesting that the nuclear kinase/phosphatase balance may be an underappreciated disease contributor.

Engineering a zonal Collagen/Chondroitin sulfate scaffold to recapitulate the depth-dependent microarchitecture and mechanics of articular cartilage

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E-Poster Session Tuesday Evening, July 14, 2026, 17:50 - 18:30

Articular cartilage exhibits depth-dependent mechanics and microarchitecture, transitioning from an aligned, surface zone to a randomly organised deep zone, conferring resistance to both shear and compressive forces. To recapitulate this zonal architecture in vitro, we fabricated a fibrillar composite scaffold using Collagen Type-I (Col-I), chondroitin sulfate (CS), and fibronectin (FN), where FN was incorporated to promote cell adhesion via RGD-mediated integrin binding. Utilising a temperature-casting technique with a unidirectional orbital shaker and custom PDMS moulds, we directed surface-zone fibre alignment while preserving random fibre distribution in the bulk, effectively reproducing the native zonal organisation of articular cartilage. Fibre orientation was quantified using the ImageJ plugin FibrilTool; scaffolds cast with CS exhibited significantly higher alignment indices compared to Col-I-only controls, highlighting the role of CS in directing fibre organisation through steric hindrance. Circular dichroism spectroscopy confirmed that the temperature-casting process preserves the native triple-helical conformation of Col-I. Mechanical characterisation by AFM nanoindentation revealed a depth-dependent stiffness gradient across the scaffold, mirroring the zonal mechanical properties of native cartilage. Together, these results establish, for the first time to our knowledge, a multi-component in vitro scaffold that recapitulates both the zonal microarchitecture and depth-dependent mechanical properties of articular cartilage, providing a physiologically relevant platform for cartilage mechanobiology research and regenerative medicine applications.

Cellular topology sensing in the extracellular matrix

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Cell migration is fundamental for many processes such as development, homeostasis and in the context of disease. During migration, cells have to move through a dense network of fibers with different sizes and adhesive properties called the extracellular matrix. While a lot is known about its complex structure, the way cells manage to navigate through this 3D fiber scaffold still remains unclear.

Initial studies on bacterial infections revealed the existence of two modes of interaction between a cell and an adhesive fiber at the nanoscale termed 1D and 2D wetting. We hypothesize that these two modes of interaction are central in dictating how cells will interact with and navigate through the extracellular matrix.

Experimentally, a two-photon polymerization-based system was used to generate in vitro adhesive fibers with controllable parameters. First results showed that HL-60-derived neutrophils actively migrate and adhere to RGD-functionalized thiol-ene fibers of 1µm-diameter. Scanning electron microscopy enables detailed observation of cell protrusion morphology along these adhesive nanofibers. Super-resolution STED imaging allows to resolve actin and membrane remodeling within these protrusions at the nanoscale. These technological tools will then be combined to investigate how single cells interact with fibers of varying sizes and adhesive properties, ultimately uncovering the mechanisms by which cells sense and interpret extracellular matrix cues.

Cellular Interfacial Tension and Tissue Architecture dictate Tissue-Specific Oncogenesis across Epithelia

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E-Poster Session Tuesday lunch, July 14, 2026, 13:00 - 13:50

Why does the same oncogenic mutation initiate tumors in some tissues but fail in others? While driver mutations such as HRasV12 are well characterized, the mechanical determinants of their tissue-specific outcomes remain poorly understood.

Here, we show that mechanical interactions between transformed cells and the surrounding wild-type epithelium dictate oncogenic fate in human mammary and bronchial tissues. In mammary epithelium, isolated HRasV12 cells are apically extruded, whereas small mutant clusters become spatially confined in a kinetically arrested, jammed state marked by a reinforced actin belt at mutant–wild-type interfaces. In contrast, bronchial epithelium permits persistent spreading of oncogenic cells, which extend invasive protrusions irrespective of colony size.

Quantitative analysis reveals distinct biophysical signatures across tissues, including differences in cell shape distributions, intracellular pressure, intercellular tension, and collective motility. Using a cell shape–tension coupled bi-disperse vertex model, we identify interfacial tension at mutant–wild-type boundaries as a critical control parameter that determines whether oncogenic cells are eliminated, mechanically restrained, or expand. Experimental modulation of interfacial tension correspondingly shifts mutant cell fate. Together, these findings establish a mechanical basis for tissue-specific oncogenesis, positioning interfacial tension as a regulator of early tumor initiation.

Extending this framework to curved epithelial architectures, we are currently investigating how tissue geometry reshapes the tension landscape in vivo. Because curvature imposes spatial gradients in cell shape and apical–basal contractility, we test whether geometric constraints reprogram mutant–wild-type force balance. Preliminary results indicate that convex and concave regions differentially bias oncogenic extrusion and expansion, suggesting that epithelial geometry functions as a biomechanical filter of tumor initiation.

Remote control of mechanosensitive ion channels with magnetic nanoconjugates

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E-Poster Session Wednesday Lunch, July 15, 2026, 13:00 - 13:50

Mechanobiology seeks to explain how cells translate physical forces into biochemical signals that regulate development, homeostasis, and disease. Among the key players in this process are mechanoreceptors-membrane proteins such as Piezo1 that convert mechanical tension into calcium signaling, thereby orchestrating different processes such as vascular development, epithelial remodeling, tissue repair or apoptosis. In this work, we propose a dual strategy for the magneto-mechanical stimulation of endogenous mechanoreceptors such as mechanosensitive ion channels (TRPV4 or Piezo1) using magnetic nanoparticles (MNPs) that can generate force upon the application of an external magnetic field. MNP-mediated magnetomechanical actuation enables precise control of the mechanical force delivered, being able to generate a broad range of forces (pN to nN).
Here, we present our preliminary data regarding the remote, spatiotemporally controlled activation of endogenous mechanosensitive ion channels via two different strategies: i) strategy 1, exploring the activation of these receptors via the “force-from-lipids” mechanism, and ii) strategy 2, in which the force is delivered directly to the ion channels.
For strategy 1, the MNPs are anchored through strain-promoted azide–alkyne cycloaddition (SPAAC) to extracellular glycoproteins modified with azide groups or to azide-modified lipids inserted into the plasma membrane. These bioorthogonal chemistry-based methods ensure stable membrane attachment, longer membrane lifetime of the MNPs, and allow control of nanoparticle density on the membrane. Controlled magnetomechanical stimulation produces localized membrane tension or curvature changes to probe direct membrane-mediated activation of mechanosensitive channels. In strategy 2, we use the specific targeting of the mechanosensitive ion channels using MNPs functionalized with antibodies that recognize their extracellular domains.

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Role of epigenetic modifications in the establishment of mechanical memory

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Mechanical memory is defined by the persistent effect of past environment rigidity on cell adaptation to a new environment. Different mechano-sensitive signaling pathways have been implicated in mechanical memory. However, it is currently unknown how past information about substrate stiffness is stored inside the cell. Here, we report that the histone demethylase KDM7a controls mechanical memory of cell division by regulating H3K27 demethylation in a nuclear membrane tension-dependent manner. We observed that KDM7a was overexpressed in cells cultured on a soft substrate and was required to encode memory of a past soft substrate. On soft environments, reduced nuclear membrane tension controlled KDM7a recruitment at the nuclear envelop and H3K27 demethylation. Conversely, KDM7A localized to the nucleoplasm on stiff environments and H3K27 was methylated. These differences of histone methylation was maintained once cells primed on a soft substrate were transferred to a stiff secondary environment. Manipulation of nuclear membrane tension revealed that KDM7A localization was controlled by tension. We propose that information about substrate rigidity is encoded and stored in the epigenome through nuclear membrane tension-regulated H3K27 methylation dynamics.

Antibody-functionalized magnetic nanoparticles for studying mechanosensitive receptor signaling in bone regeneration

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E-Poster Session Tuesday lunch, July 14, 2026, 13:00 - 13:50

Cells constantly sense physical forces through surface proteins to regulate tissue growth, repair, and homeostasis. In bone, mechanical loading is a key driver of regeneration. This project utilises antibody-coated magnetic nanoparticles (MNPs) that bind to a specific mechanosensing receptor. Applying a magnetic field stimulates only that receptor, enabling mechanotransduction to be studied in a precise, remotely controlled manner to potentially guide bone regeneration.

Iron oxide nanoparticles were dextran-coated and functionalised with targeting antibodies. Key properties—including particle size, surface charge, stability, aggregation, antibody binding, cytotoxicity, iron content, and degradation—were characterised using DLS, zeta potential, and ICP-OES. Cell assays then assessed early signalling and subsequent osteogenic responses following magnetic stimulation. For antibody selection, computational docking and molecular dynamics predicted binding stability and receptor accessibility, while immunofluorescence (IF) and Western blotting (WB) confirmed receptor recognition and protein specificity before particle studies.

Two MNP formulations, MM250 and IOC116, were evaluated. MM250 exhibited superior dispersion, with its hydrodynamic diameter increasing from ~270 nm to ~390 nm following TREK1 antibody coating. Conversely, IOC116 remained highly aggregated (~3.8 μm) regardless of coating. Antibody attachment shifted the surface charge of MM250 from ~−7 mV to −4.5 mV, confirming successful functionalisation; thus, MM250 was selected for further studies. ICP analysis revealed greater iron release from coated MM250 than uncoated particles. In Y201 cells, magnetic stimulation increased iron detection, though serum and cellular backgrounds require correction. Computational screening identified stable TREK1-binding candidates. IF highlighted Santa Cruz and Twist Short as top candidates, while WB detected a band near TREK1's expected weight (~47 kDa). As the luciferase assays produced variable data, thallium-ion flux assays were used instead.

Combining nanoparticle optimisation with antibody screening improves the specificity and interpretability of magnetic stimulation. Following candidate validation, the next step will involve antibody humanisation to improve clinical suitability while retaining receptor recognition.

Mechanobiological Modulation of human primary T-Cells by Immunosuppressive Drugs

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In organ transplantation, graft survival depends on a delicate balance between regulatory and effector T-cells accessing the transplanted tissue. While immune signaling guides this process, graft infiltration also requires T-cells to arrest on endothelium and traverse micron-scale tissue barriers. Clinical graft outcomes show marked variability in T-cell infiltration, with distinct subsets differentially accessing the graft despite being present in circulation, pointing to underexplored mechanical determinants of tissue entry. Whether immunosuppressive therapies reprogram the mechanical state of T-cells and thereby influence their access to the graft remains unknown.

Here, we use atomic force microscopy (AFM) to define a multidimensional mechanical fingerprint of primary human $CD4^+$ T-cells and to determine how immunosuppressants reshape this mechanical state. Across healthy donors, we uncover subset-specific heterogeneity in primary T-cell mechanics, revealing intrinsic differences in baseline mechanical fitness. Treatment with frontline immunosuppressants tacrolimus and prednisolone induces a robust stiffening of $CD4^+$ T-cells, whereas changes in cellular fluidity are selectively triggered by tacrolimus.

Upon receptor activation, T-cells follow a characteristic mechanical trajectory, marked by an initial stiffening phase followed by recovery toward a mechanical equilibrium. Tacrolimus overrides this activation-induced mechanical remodeling by accelerating recovery and imposing an early equilibrium, effectively resetting the mechanical setpoint of the cell.

To identify the mechanistic basis of this drug-imposed mechanical state, we combined AFM with confocal microscopy and functional network–guided analysis of cytoskeletal and nuclear components. The most consistent and predictive changes occur at the level of the nucleoskeleton. Lamin B2 intensity and spatial distribution closely mirror drug-induced mechanical adaptations, identifying lamin B2 as a key mediator of T-cell mechanical regulation.

Together, these findings reveal that immunosuppressants do not only suppress signaling but actively reprogram T-cell mechanics with nuclear remodeling emerging as a key mechanistic contributor. This mechanobiological perspective provides new insight into T-cell infiltration in transplantation and immune-mediated disease.

Mechanoregulation of Microvascular Spatial Patterning

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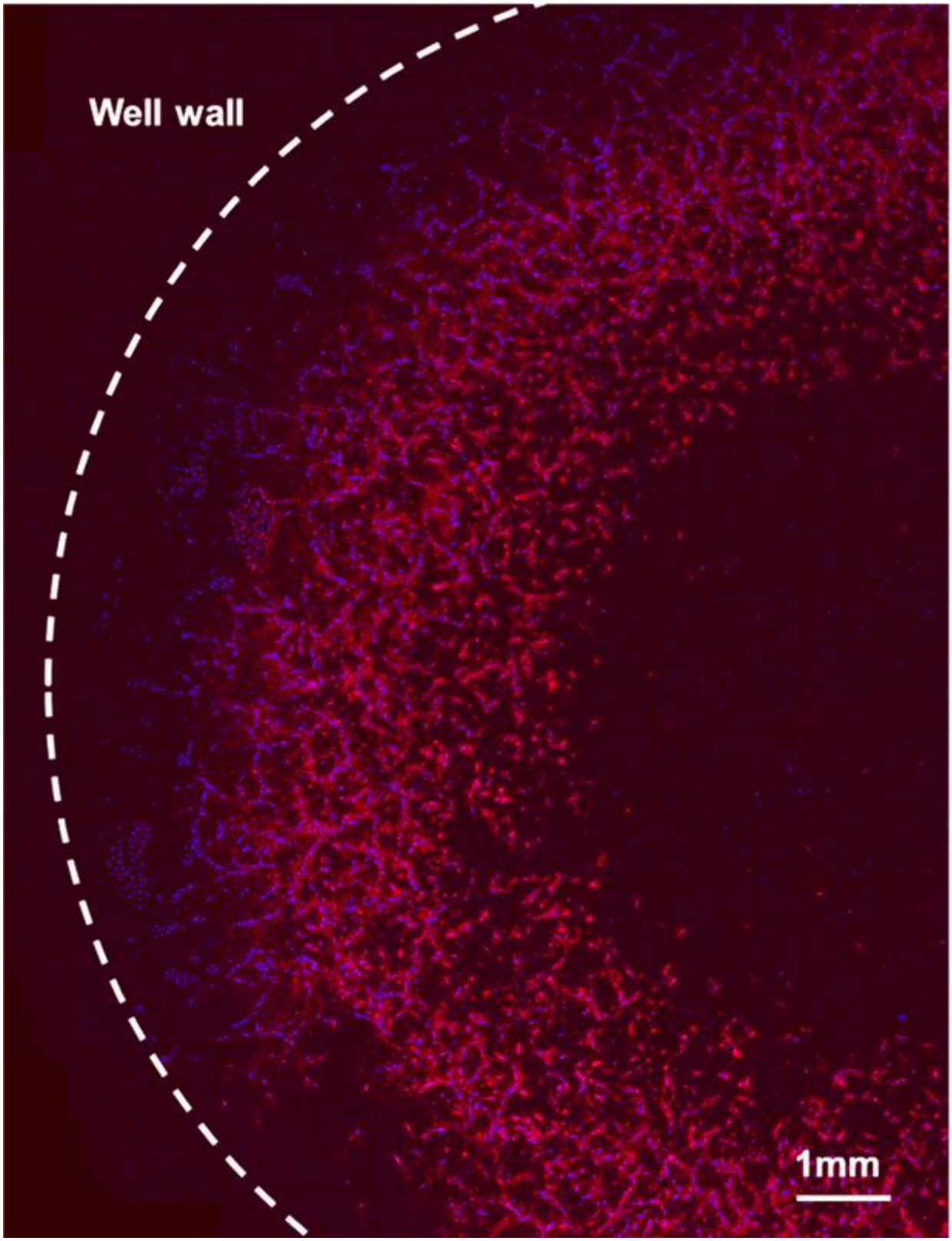
Background: In tissue-engineered human models, vascularisation is critical for model scaling and accurate physiological replication. Achieving this relies on recapitulating tissue-specific vascular patterns, which remains a major challenge in tissue engineering, with neither a clear understanding of the biological mechanisms of microvascular patterning nor wet-lab strategies to control it.

Methods and results: This study reports potential mechanoregulation of microvascular patterning in a 3D vasculogenesis model. HUVECs form a lumenised microvascular network in a 24-well plate, presenting a distinct “doughnut” pattern with a dense vascular network around the well boundary, absent in the centre. It is hypothesised that spontaneous microvascular patterning is driven by collagen fibril organisation and/or mechanical gradients introduced by the well boundary.
Collagen fibre organisation and directionality were imaged using reflectance confocal microscopy, and the mechanical profile of the 3D hydrogel was characterised by rheometry, nanoindentation, and microrheology with optical tweezers. Gene expression at the model’s centre and edge was quantified by qPCR. The region-specific vascular patterns clearly correlate with the divergent hydrogel stiffness and mechanosensing gene expression levels between the centre and the edge.

Summary: This study demonstrates, for the first time, a potential mechanoregulation of microvascular patterning in a 3D bioconstruct. A better understanding of the underlying mechanisms will help to develop strategies to control this behaviour and pave the way towards engineering organ-specific vascularisation.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Viscoelasticity as a key mechanical regulator of breast cancer cell mechanosensing and phenotypic plasticity on tunable polyacrylamide hydrogels.

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E-Poster Session Tuesday Evening, July 14, 2026, 17:50 - 18:30

Introduction: Breast cancer (BC) accounts for approximately 15% of global cancer diagnoses each year, predominantly affecting women. It arises from uncontrolled proliferation of epithelial cells within breast tissue. Increasing evidence highlights the extracellular matrix (ECM), a dynamic structural network surrounding cells, as a key regulator of tumour progression and metastasis. In BC, the ECM undergoes extensive remodelling, including altered fibronectin and collagen expression and increased matrix stiffening relative to healthy stroma. While the influence of ECM stiffness and elasticity on cancer cell behaviour is well established, the role of ECM viscoelasticity, its ability to dissipate mechanical stress over time, remains poorly understood. Here, we investigate how tunable viscoelasticity in a polyacrylamide (PAAm) hydrogel system regulates MCF7 BC cell mechanosensing, morphology, and phenotypic plasticity.

Methodology: PAAm hydrogels with defined stiffness [soft (1.5 kPa) and medium (5 kPa)] and independently tuned viscoelastic properties (loss moduli: 400 and 1000 Pa, respectively) were fabricated. Mechanical properties were characterised by nanoindentation and microrheology. Hydrogels were functionalised with fibronectin to support MCF7 adhesion. Cellular responses, including morphology and Ki67 quantification, were assessed across matrix conditions using fluorescence imaging, ImageJ/QuPath-based quantitative analysis, and RT-qPCR.

Results: Matrix mechanics strongly influenced breast cancer cell behaviour. Soft elastic substrates promoted small, rounded cells with poor actin organisation (spreading area: 152 ± 4 μm^2), whereas increased stiffness and viscoelasticity enhanced cell spreading, elongation, and formation of multicellular clusters. The medium viscoelastic condition produced the most pronounced morphological changes (196 ± 6 μm^2, $p < 0.05$ vs soft elastic). Cell growth increased over time on viscoelastic matrices; however, Ki67 analysis revealed a progressive decline in proliferative cells (Ki67+: 35 ± 3%), suggesting a shift toward a more invasive phenotype. These findings establish viscoelasticity as an independent regulator of breast cancer mechanosensing and phenotypic plasticity, with implications for tumour progression in native ECM.

Modeling the Extracellular Matrix at the Mesoscopic Scale.

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The extracellular matrix (ECM) is a complex three-dimensional network of macromolecules playing a central role in tissue organization, cell adhesion, migration, and signaling. Alterations in the ECM composition and organization are associated with aging and numerous pathologies, including fibrosis, vascular diseases, cancer, and connective tissue disorders. However, due to the size and structural complexity of the ECM, its large-scale dynamics remain difficult to study with conventional atomistic simulations or experimental approaches alone.

This project focuses on the development and application of DURABIN (Developing Utilities for Nanometric Interactions in Biochemistry with augmented Reality), a mesoscopic multi-scale simulation framework developed in our laboratory (MEDyC) to study extracellular matrix organization. DURABIN relies on rigid-body dynamics and simplified geometrical representations of biomolecular domains to reduce computational cost while preserving the large-scale structural behavior of ECM components. This approach provides the simulation and visualization of supramolecular assemblies at an intermediate scale between atomistic molecular dynamics and microscopy. The project will build upon recent improvements introduced in the CHLORAINE extension, including enhanced conformational flexibility and the combination of physicochemical properties such as electrostatic and hydrophobic interactions.

The objectives are to improve conformational sampling, refine collider definitions based on protein structural features, and implement periodic boundary conditions alongside temperature and pressure controls. In the future, we aim to develop new modules that account for biomechanical constraints, such as shear stress, compression, and extension forces, to better reproduce the physical environment experienced by ECM networks. Finally, these developments will be applied to ECM models with varying molecular compositions to understand the structural reorganization associated with aging and pathological remodeling. The lab aims to provide an open-source computational platform for mesoscopic simulation of ECM dynamics and interactions throughout multiple biological conditions.

Neomag: Bridging mechanical actuation with glial mechanotransduction in pathological contexts

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E-Poster Session Tuesday lunch, July 14, 2026, 13:00 - 13:50

This study highlights NeoMag, an innovative technology based on magneto-active substrates and designed to simulate complex and evolving biomechanical environments found in both physiological and disease states. By combination of magnetic-field stimulation with multidomain magneto-responsive polymers, this platform enables the application of precise and reversible mechanical loads to biological samples, facilitating the study of critical processes such as wound repair and traumatic brain injury.

NeoMag offers unprecedented versatility, supporting alternating deformation modes compatible with both upright and inverted microscopy, and adaptable to 2D and 3D culture systems. Furthermore, its integration with nanoindentation allows the real-time measurements of mechanical properties in cultured cells and tissues, under evolving substrate deformations. The potential of this technology is demonstrated here studying the astrocyte response to evolving mechanical environments, to mimic conditions of traumatic brain injury and ischemic stroke. Our observations highlight heterogeneous variations in astrocyte stiffness, primarily driven by the subcellular rearrangement of the cytoskeleton relative to the direction of substrate strain.

Mechanical cues led to significant alterations in astrocyte calcium homeostasis, derived from both extracellular space and intracellular calcium stores. Sustained mechanical loading promoted actin network reorganization and the activation of Piezo1 channels; this led to a sustained calcium influx that suppressed spontaneous calcium oscillations. In contrast, high-speed and dynamic mechanical loading resulted in only transient Piezo1 activation and a collapse of the actin framework, leading to cell softening over 24 hours.

Collectively, these findings highlight the complex interplay between mechanical loading and astrocyte function. They demonstrate the potential of NeoMag as a powerful tool for research in mechanobiology across diverse physiological and pathological contexts.

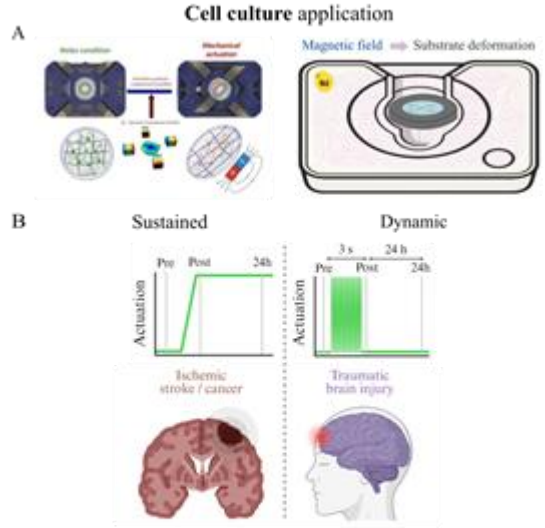

Figure 1. NeoMag for mechanical actuation on cell culture. (A) NeoMag uses multidomain magneto-active materials to actuate on substrates, delivering reversible mechanical cues to biological samples. The system enables diverse deformation modes, compatible with upright and inverted microscopes, and supporting assays in 2D and 3D cultures. (B) Mechanical actuation protocols include slow sustained deformation to model ischemic stroke and cancer, and fast dynamic deformation to model traumatic brain injury.

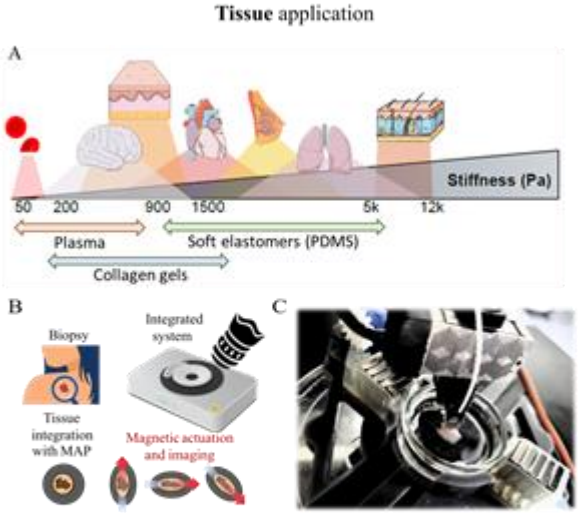

Figure 2. Integration of biological tissue samples on magneto-active substrates. (A) Range of scaffold stiffness compatible with NeoMag, compared with the stiffness of representative tissues. The system allows for (B) imaging tissue deformation under specific forces on the substrate, and (C) for nanoindentation to evaluate mechanical properties under different deformation scenarios.

High-throughput Electrospun and Lithographic Platforms for Advanced Bioimaging of Mechanotransductive-related Events in Glioblastoma

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E-Poster Session Tuesday Evening, July 14, 2026, 17:50 - 18:30

Glioblastoma (GBM) is the most common primary brain tumour in adults and is coupled with a dismal prognosis for patients. Different subpopulations of GBM tumour cells interact with diverse native extracellular microenvironments that possess distinct biophysical features. How mechanobiological aspects of GBM cell/microenvionment affect the pathophysiological properties of GBM subpopulations remains poorly understood. In our approach, we employ electrospinning and e-beam lithography as bioengineering techniques to generate substrates that closely mimic different GBM tumour microenvironments. We optimised the bioengineered substrates for advanced bioimaging approaches and higher experimental throughput, overcoming common limitations. These bioengineered GBM microenvironment-mimicking substrates are then used for the evaluation of the role of mechanotransduction in GBM pathophysiology. In parallel, analyses of open patient glioblastoma datasets (such as 'TCGA-GBM' and the 'IVY Glioblastoma Atlas Project (IVYGAP)') are leveraged to reveal mechanotransduction-related key regulators with particular gene expression patterns in specific anatomic regions of the tumour that we further investigate with the help of the GBM microenvironment-mimicking substrates.

Capillary Micromechanics for Particles and Spheroids

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E-Poster Session Tuesday lunch, July 14, 2026, 13:00 - 13:50

We present a simple method for accessing the elastic properties of microscopic deformable particles, cells and clusters.
This method is based on measuring the pressure-induced deformation of soft objects as they are forced
through a tapered glass microcapillary. It allows us to determine both the compressive and the shear
modulus of a deformable object in one single experiment. Measurements on a model system of polyacrylamide microgel particles exhibit good agreement with measurements on bulk gels of identical composition. Our approach is applicable over a wide range of mechanical properties and is a valuable tool for the characterization of a variety of soft and biological materials including Spheroids or Tissue.

Classification of red blood cells in microflow using machine learning video analysis

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E-Poster Session Wednesday Lunch, July 15, 2026, 13:00 - 13:50

We classify native, chemically modified and diseased red blood cells with an AI based video classifier. Using video analysis enables us to capture not only the morphology of the cell but also the
trajectories of motion of individual red blood cells and their dynamics. We obtain classification accuracies for
all three classes of more than 90% between native and modified cells. Unlike standard cytometers that are based on immunophenotyping our microfluidic cytometer allows to rapidly categorize cells without any fluorescence labels simply by analysing the shape and flow of red blood cells.

When T cells remember: the role of nuclear mechanics in density-induced immunomodulation

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E-Poster Session Tuesday Evening, July 14, 2026, 17:50 - 18:30

The tumour microenvironment presents a major physical barrier to effective immunotherapy: extracellular matrix remodelling increases matrix density and reduces pore size, impeding T-cell infiltration. As T cells typically migrate in an amoeboid manner – squeezing through gaps without degrading the ECM – this stiffened environment severely limits their ability to reach and eliminate cancer cells.

Our lab has shown that primary T cells can overcome this barrier by switching migration modes. In high-density collagen matrices mimicking tumour conditions, T cells adopt a proteolytic, mesenchymal-like migration mode, degrading the ECM to form tunnels. Strikingly, this behaviour is not merely a real-time response: T cells previously primed in dense matrices display enhanced proteolytic activity upon re-exposure to high-density conditions compared to those primed in loose gels, suggesting the acquisition of a mechanical memory. While mechanical memory is known to influence cell migration and invasion in other contexts, its potential role in immunomodulation remains largely unexplored.

To address this knowledge gap, we are characterising several parameters: changes in T cell and nuclear morphology depending on the priming condition, nuclear stiffness, and the expression of nuclear proteins involved in mechanosensing (e.g. lamins, cPLA2). We observe morphological differences and potentially altered nuclear mechanics. Interestingly, while lamin A/C and B expression does not appear to differ between conditions, initial data point toward an effect of mechanical priming on cPLA2 — a phospholipase involved in arachidonic acid release and nuclear tension sensing. Together, these findings suggest that mechanical priming induces nuclear mechanical adaptations and engages cPLA2 signalling, although their precise role in the establishment of mechanical memory remains to be determined.

Understanding how physical cues from the tumour matrix reprogram T cell behaviour could open new avenues for improving adoptive cell therapies to enhance their tumour-infiltrating capacity.

Correlative AFM–Proteomic Mapping Reveals Spatial Mechanobiological Remodeling of Hippocampal ECM in Neuropathic Pain

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E-Poster Session Tuesday Evening, July 14, 2026, 17:50 - 18:30

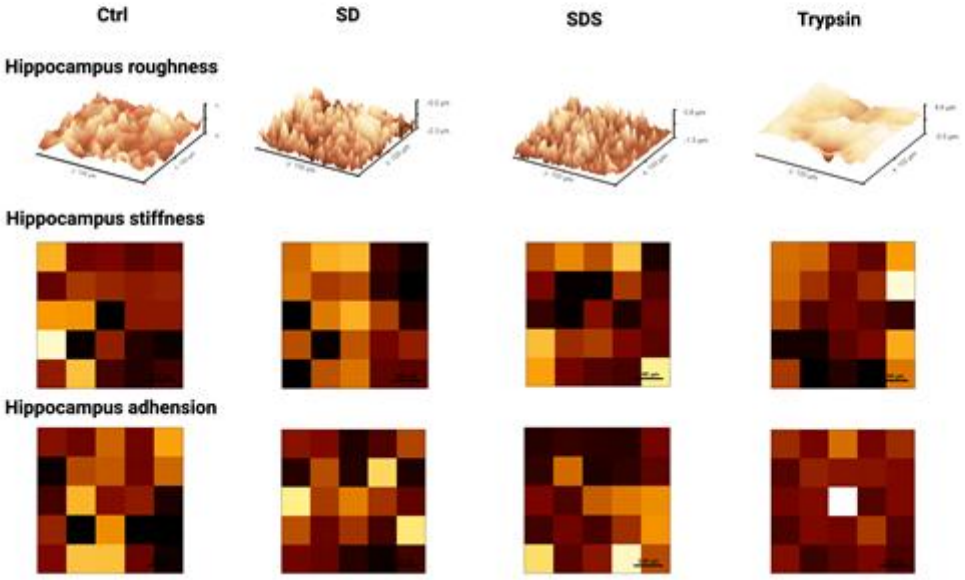
Neuropathic pain following peripheral nerve injury induces persistent central nervous system remodeling that sustains mechanical hypersensitivity. While neuronal plasticity has been widely studied, mechanobiological remodeling of the extracellular microenvironment that may stabilize chronic pain remains poorly defined. The hippocampus, a key structure in affective and cognitive pain processing, constitutes a mechanically specialized brain region in which the extracellular matrix (ECM) forms a biophysical niche regulating synaptic stability and neuro–immune signaling. However, the spatial organization of ECM mechanics and its molecular determinants during pain chronification remain unclear.

Neuropathic pain was induced using the spared nerve injury (SNI) model, and longitudinal behavioral assessments confirmed sustained hypersensitivity. To enable reliable mechanobiological interrogation, we systematically evaluated hippocampal decellularization strategies to preserve ECM ultrastructure and intrinsic mechanical properties while minimizing cellular contamination, establishing an optimized workflow for downstream analyses.

We developed a correlative platform integrating high-resolution atomic force microscopy (AFM)-based stiffness mapping with liquid chromatography–mass spectrometry (LC–MS) and MALDI mass spectrometry imaging on spatially matched hippocampal sections. This approach enabled region-specific coupling analysis between ECM mechanical properties and proteomic and glycosylation signatures. SNI induced progressive, subregion-specific alterations in ECM stiffness accompanied by distinct molecular remodeling. Emerging mechanical heterogeneity spatially corresponded with proteomic and glycosylation changes, indicating coordinated biomechanical–biochemical reorganization.

These findings establish a spatially resolved framework for decoding ECM mechanobiology in the brain and provide insight into extracellular niche remodeling as a contributor to pain persistence.

Method	Type	How decellularization is achieved
Sodium deoxycholate (SD)	Ionic detergent	Disrupts cell membranes and releases cellular contents
Sodium dodecyl sulfate (SDS)	Strong ionic detergent	Solubilizes membranes and denatures proteins for efficient cell removal
Trypsin	Proteolytic enzyme	Cleaves cell-adhesion proteins to detach cells
Triton X-100	Non-ionic detergent	Mildly permeabilizes membranes



Bridging perinuclear actin to the nucleus: new insights into cytoskeletal-nuclear integration

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E-Poster Session Tuesday Evening, July 14, 2026, 17:50 - 18:30

The interaction of actin filaments with the nuclear envelope is essential for diverse cellular processes, including cell migration, nuclear positioning, and transcriptional control. The main studied mechanism that links F-actin to the nucleus is the LINC complex. Recently, the formation of a perinuclear actin rim has been identified in various cell types in response to external force or migration cues. This rim affects transcription and cell motility capabilities, operates independently of the LINC complex, and relies on the activation of the actin nucleator INF2 by calcium influx. However, it is not clear how the rim is coupled with the nuclear envelope.
Here we show that the perinuclear actin rim is sensitive to elevated levels of lamin B1 but not lamin A, suggesting a physical link between the nuclear lamina and the cytosolic perinuclear actin rim. In search of potential coupling factors, we found that the nuclear membrane protein Emerin, which has an actin-binding domain, is not required for the perinuclear actin rim formation. Interestingly, we identified that Ezrin-Radixin-Moesin (ERM) proteins, traditionally known for linking F-actin to the plasma membrane, are also localized to the nuclear envelope. Overexpression of ERM proteins increased the perinuclear actin rim levels, while knockdown of ERM proteins reduced the rim levels. These results suggest that the ERM proteins are part of a lamin B-sensitive mechanism that links F-actin to the nuclear envelope in an alternative mechanism to the LINC complex.

Failed apoptotic extrusion drives an epithelia-intrinsic inflammation program.

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Apical extrusion is an epithelia intrinsic surveillance mechanism that removes unfit or apoptotic cells in an immunologically silent manner whilst preserving barrier integrity. Apoptotic extrusion is a mechanically active process, where neighbour cells generate compressive forces on the apoptotic cell, through cortical contractility and lamellipodial activity. E-cadherin is necessary for this process, and disruption of E-cadherin adhesion and/or mechanotransduction compromises extrusion, with apoptotic cells being retained in the epithelium. Importantly, this led to upregulation of IL-8 expression in neighbour cells to elicit acute inflammatory responses. In this study we used single cell RNA sequencing to further define neighbor cell responses when apoptotic extrusion failed. Apoptosis was induced with etoposide in Caco-2 cells, and extrusion inhibited by E-cadherin RNAi. The analysis of the dataset identified a distinct cluster corresponding to putative immediate neighbours in the failed extrusion model. These cells display significant upregulation of the TNF signalling pathway, which is strongly implicated in the pathogenesis of Crohn's disease and show an increased similarity to scRNA analysis of Crohn's disease patients' biopsies compared to the controls. Together, our transcriptomic and functional validation data support a model in which defective apoptotic extrusion drives pro-inflammatory signalling in epithelial neighbours of apoptotic extrusion. Therefore, impaired extrusion may represent a previously unrecognized epithelia-intrinsic mechanism contributing to chronic inflammation in Crohn's disease. To directly assess clinical relevance, we will perform RNAscope analysis on intestinal biopsies from Crohn's patients to evaluate the spatial expression of candidate inflammatory targets identified in our single-cell dataset. We hypothesize that failed apoptotic extrusion constitutes an epithelial-intrinsic trigger of inflammation, providing a mechanistic bridge between barrier dysfunction and TNF-driven pathology in Crohn's disease.

Mechanical and Transcriptional Responses of Breast Cancer Cells to Microfluidic- Induced Rapid Deformations and Monolayer Stretching

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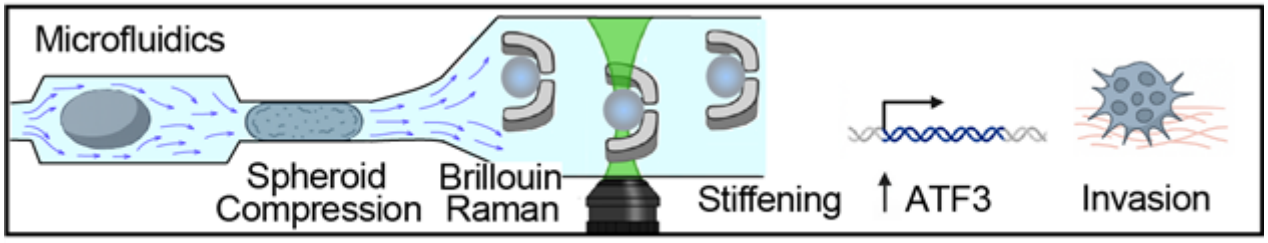
E-Poster Session Tuesday lunch, July 14, 2026, 13:00 - 13:50

Mechanical forces and physical properties play a fundamental role in regulating cellular processes, such as cytoskeletal remodeling, gene expression, and cell behavior, with profound implications for both physiological functions and disease. Despite major advances in the characterization of 3D cell mechanics, significant technical challenges remain in capturing the dynamic coupling between mechanical and biochemical processes. To address these limitations, we developed Brillouin–Raman Microspectroscopy on-a-Chip, which enables high resolution analysis of mechano-chemical responses in complex live 3D biological systems under controlled deformation. This contact-free, optical method combines Brillouin and Raman microscopy within microfluidic devices, providing a unique correlative approach to overcome current limitations in probing cellular mechanics and biochemical responses in live multicellular models.
Applying this platform to breast tumor spheroids, we reveal that rapid, cyclical mechanical deformations, mimicking in vivo stresses, significantly impacts tumor physiology. These responses are accompanied by global spheroid stiffening, as precisely quantified by Brillouin spectroscopy and confirmed by elevated phalloidin levels. Remarkably, repeated deformation imprints a form of mechanical memory in these collective systems, which result in enhanced invasiveness.
The controlled spheroid deformations trigger rapid nuclear shape changes and robust transcriptional reprogramming, marked by a significant upregulation of the early stress response master regulator ATF3. ATF3 is a transcription factor that that is activated rapidly and transiently and can exert either cell-protective or cell-detrimental effects, depending on the nature and duration of the stress. To investigate ATF3 as a mechano-responsive element in breast cancer progression, we employed multiple mechanical perturbation paradigms, including spheroid deformation, hypo- and hypertonic treatments, and monolayer stretching. Consistent with previous reports implicating ATF3 in oncogenic behavior and enhanced invasive potential, our data reveal that prolonged and repeated mechanical stress induces a form of mechanical memory, associated with changes in chromatin remodelling.



Cytoskeleton and focal adhesion organization in a 2.5D sandwich-like model

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Physical properties of microenvironment, including extracellular matrix (ECM) stiffness, substrate topography, confinement and dimensionality, play a crucial role in determining cell behavior and fate. Cells cultured on two-dimensional (2D) substrates exhibit significantly different morphology, migration and focal adhesion distribution compared to cells embedded in three-dimensional (3D) ECM. In the physiological environment, fibroblasts are typically surrounded by ECM within connective tissue, while epithelial cells usually form layers on the basement membrane. During cancer progression, epithelial cells can breach the basement membrane and transition from sheet-like organization to a 3D tissue environment.
In this work, an experimental sandwich-like (2.5D) setup was used to model 2D-to-3D transition in
a controlled setting. Epithelial-type cells and fibroblasts were confined between two surfaces functionalized with either fibronectin or PLL-PEG. This setup allows cells to interact with ECM proteins on both ventral and dorsal surfaces, and has been shown to promote cellular morphology similar to those in 3D environment. Using this system, we characterized cell morphology, focal adhesion organization on dorsal and ventral surfaces, and filopodia dynamics, in dependence on the inter-layer distance and adhesive properties of the upper surface. By targeting Rho-associated protein kinase (ROCK) regulatory pathway, actin polymerization and microtubule dynamics, we studied their role in regulating cellular behavior in sandwich-like environment.
Our results indicate distinct responses to confinement and ECM coating, depending on cell line. Fibroblasts exhibited a protrusion-rich morphology, particularly when the upper surface lacked ECM coating, while epithelial-type cells were less likely to form protrusions or establish adhesion to both surfaces. Those findings may contribute to understanding how cells adapt to changing microenvironment.

Tau-Mediated Cytoskeletal Stabilization Modulates Cell Mechanics and Vulnerability to Mechanical Strain

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Cells experience mechanical loading across a broad range of loading rates, from slow substrate deformations during development and tissue remodeling to rapid, high strain rate events such as medical ventilation-induced lung injury, blast-induced injury, and impact-induced traumatic brain injury. Cell survival under these conditions depends on the ability of the cytoskeleton and plasma membrane to sustain mechanical load without permanent damage. Tau is a microtubule-associated protein best known for its role in neurons and as a marker of neurodegenerative disease, but more generally functions as a regulator of microtubule stability and cytoskeletal organization. How such stabilization influences cellular mechanics during acute deformation remains poorly understood. We investigated how Tau expression, phosphorylation state, and microtubule binding modulates cell viscoelastic behaviour and membrane integrity during high-rate uniaxial stretch. We show that Tau expression and de-phosphorylation stabilize microtubules and cause increases in cell stiffness, suppresses cytoskeletal fluidity, and heightens susceptibility to stretch-induced membrane poration. Interestingly, we also find that these effects cannot be explained by microtubule stabilization alone and that actin architecture also acts as a key determinants of injury vulnerability. Disruption of actin stress fibers reduces poration in Tau-expressing cells, pointing to the importance of cytoskeletal fluidity for rapid force dissipation.

Local axonal translation regulates stretch-induced neuronal growth acceleration

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Mechanical stretch can induce significant acceleration of neuronal growth. Although this process is critical for growth in the maturing nervous system, the underlying molecular mechanisms are largely unknown. We established a system for monitoring stretch-induced neuronal growth in culture and observed marked increases in both growth and axonal protein synthesis rates in response to stretch of mouse sensory neurons. These responses were attenuated in mutants of the retrograde motor dynein, the transport factor importin β1 3'UTR, and the RNA-binding protein nucleolin – all components of a previously described length-sensing mechanism that regulates elongating neuron growth. Stretch-induced growth acceleration required translation, but not transcription, and was specifically dependent on axonal translation of mTOR (mechanistic Target of Rapamycin). Thus, axonal length-sensing and mTOR-controlled local axonal translation regulate stretch-induced neuronal growth.

Pulsed priming with the FAK inhibitor narmafotinib enhances both gemcitabine/Abraxane and FOLFIRINOX chemotherapy response in pancreatic cancer

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E-Poster Session Tuesday lunch, July 14, 2026, 13:00 - 13:50

Objective: Pancreatic ductal adenocarcinoma (PDAC) is a particularly lethal malignancy with few treatment options available. Extensive remodelling of extracellular matrix (ECM) generates a highly fibrotic tumour landscape, which impairs therapeutic response. Focal Adhesion Kinase (FAK) is known to regulate ECM-feedback responses and fibrosis, presenting a compelling drug target to reduce fibrosis and enhance treatment efficacy in PDAC.

Design: Here, we present preclinical data on combining the highly specific FAK inhibitor narmafotinib (AMP945) with gemcitabine/Abraxane and, for the first time, FOLFIRINOX, which are two major standard-of-care chemotherapies for the treatment of PDAC patients. 3D organotypic matrices, intravital imaging, and in vivo syngeneic and patient-derived PDAC models, including orthotopic studies, were used to provide a rationale for an early first-line pulsed priming regimen of narmafotinib prior to chemotherapy.

Results: Neoadjuvant chemotherapy induces early fibrosis in PDAC indicating a need for upfront first-line priming of the ECM to blunt or normalise stromal fibrosis for optimal response to therapy. Narmafotinib is a new potent small molecule FAK inhibitor. Phase I safety data shows excellent safety, tolerability, and pharmacokinetics following oral administration in humans. We reveal that narmafotinib treatment during early ECM remodelling (or 'priming') reduces fibrosis, while limiting subsequent PDAC invasion. Moreover, intravital imaging demonstrates real-time FAK inactivation and cell cycle stalling, leading to improved chemotherapeutic efficacy upon narmafotinib priming in vivo. Long-term assessment in patient-derived models demonstrates that narmafotinib priming prior to gemcitabine/Abraxane or FOLFIRINOX reduces PDAC progression and extends survival in both chemotherapy settings.

Conclusions: Our results using these Phase II-ready drug combinations strongly support the clinical assessment of narmafotinib in PDAC. Narmafotinib is currently in Phase Ib/IIa trials, assessing a pulsed dosing regimen prior to gemcitabine/Abraxane, and warrants further clinical assessment in combination with FOLFIRINOX.

Development of a preclinical model to study the influence of intestinal epithelium-ECM crosstalk

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The extracellular matrix (ECM) is a dynamic structure that, beyond its classical role as a tissue scaffold, actively regulates key biological processes and contributes to pathological contexts. Nevertheless, the specific role of ECM remodelling in intestinal disease progression and its relationship with epithelial barrier dysfunction remains largely unexplored. Here, we investigate how epithelial dysfunction drives ECM remodelling and whether these changes precede or follow immune cell infiltration and represent a mechanism to interfere with pathogenesis in intestinal diseases, such as IBD and cancer.
Methods: To study the influence of epithelial dynamics and alterations in the ECM, we took advantage of a mouse model that carries a deletion in the cytoskeletal protein RhoA in the intestinal epithelium and leads to epithelial barrier impairment and an alteration in the tissue dynamics. Traction force microscopy was used to quantify cellular forces in organoids isolated from these mice. Additionally, we evaluated the collagen-fiber deposition (Sirius red staining), the proximal colon tissue stiffness by Brillouin microscopy (epithelium and ECM) and the level of inflammation (IF and spectral flow cytometry).
Results: RhoA-deficient organoids exerted lower traction forces than wildtype controls. In terms of inflammation, mice showed higher levels of B cells, neutrophils, CD4+ cells and less of CD8+cells, suggesting an activation of the innate and the B and T-cells inflammatory module. Sirius red staining revealed elevated collagen-I and -III deposition. In brillouin microscopy, though significant differences were found in the Brillouin shift when comparing the ECM vs. epithelium of the KO mice, these differences were not found when comparing these compartments with the ones from the control mice.
Conclusion: Collectively, these findings suggest that changes in epithelial integrity due to RhoA deficiency result in altered traction forces, collagen deposition and associated immune infiltration but do not affect the mechanical properties of the ECM.

Mapping the mechanobiology of the developing mammary gland

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E-Poster Session Wednesday Lunch, July 15, 2026, 13:00 - 13:50

The mammary gland is a highly dynamic organ that undergoes three main waves of branching morphogenesis: during embryonic development, puberty and pregnancy. Across these stages, coordinated signalling events establish and maintain the distinct epithelial cell lineages that make up the bi-layered mammary epithelium. Although the role for growth factor and hormone signalling is reasonably well characterised, our understanding of the critical influence of mechanical forces during mammary gland development is growing, and many questions remain regarding its control of mammary stem and progenitor cell behaviour and fate specification.

Our work will further explore how mechanical force transduction shapes both embryonic and postnatal mammary gland development. Using advanced microscopic approaches, we will map the mechanical forces of the epithelium, the surrounding mesenchyme, and determine how altering the stiffness of the microenvironment influences branching morphogenesis and stem cell fate decisions. We will use established culture models, including epithelial organoids, and mammary bud and explant cultures, in combination with hydrogel matrices that will enable precise control of stiffness and viscoelasticity.

Together, these approaches will reveal how mechanical cues integrate with biochemical signalling to guide mammary gland development, providing new insight into the regulation of epithelial lineage specification and tissue architecture.

Spatial confinement regulates primordial germ cell fate in vitro

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Primordial germ cells, direct progenitors of male and female gametes, exhibit evolutionarily conserved single cell migration from their site of specification to the site of gonad formation. This migration occurs through narrow gaps between embryonic cells and tissues , likely imposing confining forces on germ cell nuclei. Mechanosignaling via nuclear deformation, previously known to induce chromatin remodeling and stem cell differentiation, may play a major role in determining germ cell fate. To understand the extent of confinement experienced by primordial germ cells in vertebrates, we quantitatively analyzed interstitial spaces in the migratory path of zebrafish PGCs. We show that PGCs migrate through spaces significantly smaller than typical cell size. Being the largest organelle in the cell, we used nuclear deformation as a measure of degree of confinement. We find that PGC nuclei display highly wrinkled morphologies, consistent with a compliant architecture. Live analysis of nuclear shape also revealed highly dynamic and fast nuclear deformation in migrating PGCs, indicating that soft embryonic tissues impose significant confining forces on germ cell nuclei. To understand the role of nuclear mechanical signaling in fate specification of PGCs, we developed an in vitro model for human PGC trans-epithelial migration based on PDMS microchannels. Introducing pluripotent stem cell-derived primordial germ-like cells to the microchannel device, we show that PGLCs can migrate through highly confining microenvironments and this migration is sufficient to abrogate expression of NANOG, a determinant of pluripotency.

Bioengineered models to investigate lymph node Fibroblastic Reticular Cell (FRC) biomechanics in ageing and disease.

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E-Poster Session Wednesday Lunch, July 15, 2026, 13:00 - 13:50

A hallmark of ageing is decreased functionality of the immune system, or immunosenescence. This increases susceptibility to infection, cancer, and failure to generate long-lasting immunity after vaccination. However, age is not commonly included as an independent variable in pre-clinical testing. Currently, animal models are used to test and study adaptive immune responses despite the lack of human immunity features and immunosenescence. We are developing a 2D hydrogel based immune microenvironment model the recapitulates the key features of a lymph node.

We bioengineer 2D collagen functionalised hydrogels of controlled stiffness - 3kpa (soft), 13kpa (middle) and 33kpa (stiff) and ECM protein presentation - developed in our group – to model healthy and fibrotic lymph node microenvironment and associated biomechanics. Currently, these are cultured with primary human FRCs isolated from tonsil tissue – secondary Lymphoid Organs (SLOs).

We have used a series of immunofluorescent stains to observes changes in cell morphology, mechanosensitivity and immune-associated proteins, such as YAP and podoplanin. When cultured on stiff substrates, FRCs have shown increased nuclear YAP and increased alignment in actin fibres, however, circularity decreases, as does cell area. Microenvironmental stiffness alone does not appear to impact podoplanin, but we will stimulate the cells with CLEC-2, an important biomolecule presented by dendritic cells which binds to podoplanin to trigger the loss of actin-myosin contractility in FRCs during immune response to investigate potential changes.

Techniques such as traction force microscopy will be employed to investigate how age- and disease related changes to the microenvironment impacts mechano-immunological mechanisms. Understanding the underlying biomechanical and immunological mechanisms underlying ageing and disease in the SLO microenvironment is critical to targeting immunosenescence and developing the next generation of therapies effective in older people.

Reconfigurable Microenvironments Uncover Mechanosensing Timescales and Direct Cell Polarity

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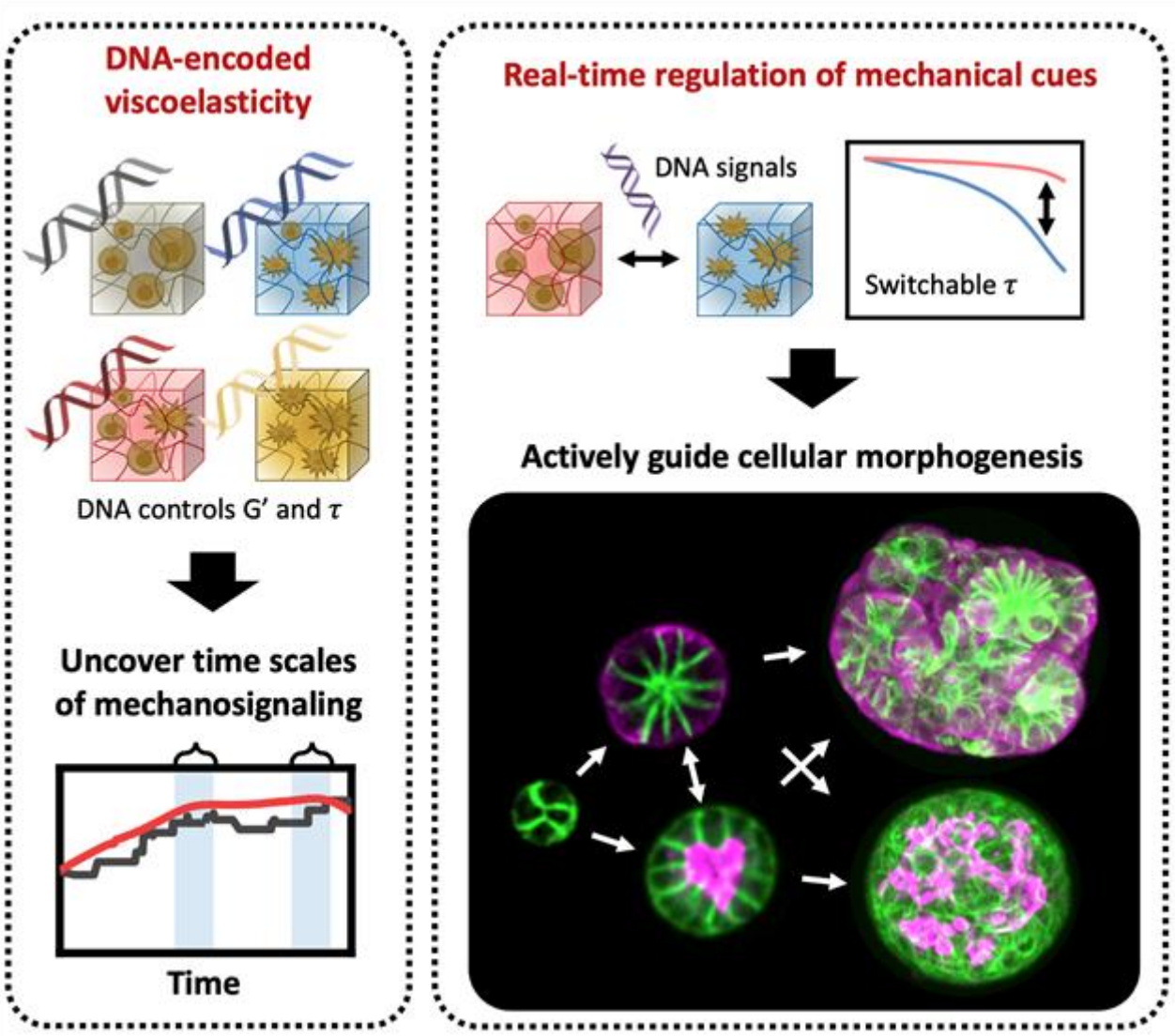
E-Poster Session Tuesday lunch, July 14, 2026, 13:00 - 13:50

Mechanical interactions between cells and their 3D environment govern fundamental processes in tissue development, cancer, and regeneration. Yet, it is challenging to modulate the mechanical cues that cells experience, thus limiting the ability to study these processes in vitro. Natural tissue microenvironments display complex viscoelastic behaviors and undergo continuous remodeling—properties not easily reproduced in synthetic cell culture matrices. Here, principles of DNA nanotechnology are leveraged to introduce programmable mechanical cues into a hydrogel that guides and interrogates the development of embedded cells. By systematically modulating stiffness and stress relaxation, two distinct timescales of mechano-sensitive processes controlling polarity in epithelial cells are uncovered. Our analysis highlights that the commonly reported matrix “stiffness” value, often measured at ≈ 1 Hz frequency, has limited physiological relevance. These findings prompted us to develop novel switchable DNA modules that enable dynamic viscoelasticity changes during ongoing cell culture. The controlled matrix reconfiguration induces reversible cell polarity inversions and guides the morphogenesis of complex multicellular structures. The material platform offers unprecedented control over the mechanical microenvironment, opening new avenues for advanced applications in biophysics, tissue engineering, and disease modeling.


DNA-encoded viscoelasticity
DNA controls G' and τ
Uncover time scales of mechanosignaling
Time
Real-time regulation of mechanical cues
DNA signals
Switchable τ
Actively guide cellular morphogenesis

Redirecting Glioblastoma Infiltration Using Mechanotactic Biomaterials

Claudia Huesa Carballo[1,2], Aroa Cernadas Pazos[3], Alba Ferreirós[1,3], Francesco Baschieri[4], Cristóbal Fernández Santiago[2,5], Nicolás Costa Fraga[2], Rafael López-López[1,2,3,5,6], Miguel Abal[1,2,3,5], Jorge Barbazán[2,3]

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Glioblastomas (GB) are highly aggressive tumors with a strong infiltrative pattern that renders the disease nearly uncontrollable with surgery. Residual GB cells invade along topographical and mechanical cues within the tumor microenvironment, including vessels and nerves, and typically migrate toward stiffer tissue regions through durotaxis, a migration mode driven by substrate mechanosensing via focal adhesions and actomyosin contractility. In this work, we sought to therapeutically exploit this intrinsic cellular behavior to redirect GB infiltration toward a controlled location using mechanotactic biomaterials, designed to guide tumor cells into a mechanically-controlled structure, with the goal of limiting invasion into healthy brain tissue. For this, we engineered macroporous polycarbonate-polyurethane (PCPU) collagen-coated scaffolds, significantly stiffer than brain tissue (140 vs 2 kPa). Using 2D and 3D culture systems, softer porous materials as well as genetic perturbations of durotaxis-associated genes in cancer cells, we first demonstrated that durotaxis is the main driver of scaffold-infiltration. These results were then validated in orthotopic syngeneic GB in vivo models, in which we observed a 70% reduction of invasive tumor foci compared to controls. We also characterized the intra-scaffold tumor ecosystem, which is composed primarily of tumor cells (60%), along with microglia, monocyte-derived macrophages, T cells, and endothelial cells that created neo-vasculature. Finally, we showed that, in combination with radiation therapy, the implant of mechanotactic scaffolds increased the tumor ablative effects of radiation. Importantly, these effects were not observed when implanting materials matching brain stiffness, reinforcing the relevance of the material's mechanics.

Altogether, our findings support the idea of taking advantage of inherent cellular biophysical properties like durotaxis as a strategy to prevent tumor invasion, introducing the concept of mechanotherapeutics as a novel tool in cancer therapy.

Biophysical profiling of YAP/TAZ dependent mechanical responses

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E-Poster Session Wednesday Lunch, July 15, 2026, 13:00 - 13:50

Ageing manifests as architectural alterations at the tissue level and a decline in function. Biochemical and mechanical changes in the extracellular matrix during ageing result in decreased cellular mechanotransduction. These changes negatively affect intra- and inter-cellular communication, homeostasis, and regeneration. Remarkably, modifying the aged systemic environment can sometimes reverse aged phenotypes, offering valuable insights into therapeutic interventions for tissue repair and regeneration.

Numerous studies have shown that the Hippo pathway, a well-recognized mechanotransductive cellular pathway, and its downstream transcriptional co-activators, YAP and TAZ, play prominent roles in proliferation, regeneration, and wound healing. Interestingly, these are often found to be dysregulated in aged tissue. Yet, the precise mechanisms of YAP/TAZ regulation on cellular responses in an ageing niche remain incompletely understood.

In this study, I investigate the role of the Hippo pathway in coordinating cellular responses to mechanical stimuli by utilizing different cellular models. These include an isogenic HEK293A cell library with knockouts of core Hippo pathway components, as well as fibroblasts derived from spiny mice and mice. Cell morphological responses to mechanical cues resembling the ageing environment, including stiffness, hydrostatic pressure, and ECM composition, were assessed using digital holographic microscopy, a label-free quantitative imaging approach. The findings suggest that ECM composition modulates mechanosensitive signalling in a context-dependent manner, with certain collagen substrates influencing YAP/TAZ activity and downstream transcriptional responses. Additionally, cellular adaptation to mechanical cues appears to vary across ECM conditions and cell types, with distinct differences observed between regenerative and non-regenerative fibroblast models.

This work enhances our understanding of how mechanical and biochemical cues converge to regulate cellular behaviour during ageing, highlighting the potential of targeting YAP/TAZ activity to harness regenerative capacity and ultimately promote healthy ageing.

Remodelling the bone marrow niche: A 2.5D in vitro platform for discovery

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E-Poster Session Tuesday Evening, July 14, 2026, 17:50 - 18:30

The bone marrow (BM) niche integrates biochemical and mechanical cues that regulate hematopoietic stem cell (HSC) maintenance, yet recreating these interactions in vitro remains difficult because HSCs rapidly differentiate under standard culture conditions. There is a clear need for simple, mechanically relevant systems that preserve stromal function while allowing controlled interrogation of niche-driven regulation in both healthy and malignant haematopoiesis.
Here, we establish a 2.5D BM niche model based on soft, fibronectin-functionalised, degradable poly(ethylene glycol) (PEG) maleimide hydrogels (~700 Pa) overlaid onto mesenchymal stromal cells (MSCs). This configuration introduces defined mechanical confinement while retaining the advantages of a 2D interface: easy imaging access and intact MSC paracrine signalling. Using confocal imaging, we quantified canonical niche-associated stromal markers (NESTIN, SCF, CXCL12, ALCAM, LepR), YAP1 localisation, Ki67 expression, VINCULIN organisation, and extracted projected cell area. Functional readouts included primary HSC maintenance by flow cytometry, MOLM13 proliferation quantified by AlamarBlue, and MSC-mediated support of MOLM13 determined by flow cytometry.
MSCs overlaid with the FN PEG hydrogel consistently upregulated niche-associated markers and remained LepR positive. They were smaller in size, consistent with mechanical confinement, and displayed reinforced focal adhesions with increased VINCULIN density and an increased adhesion footprint. Notably, MSCs maintained total YAP1 even under ROCK inhibition, suggesting a stabilised cytoskeletal state not solely dependent on tension-regulated YAP dynamics. They remained largely quiescent in 2% FBS and re-entered the cell cycle only upon exposure to proliferation media. Mechanically primed MSCs supported a higher proportion of primitive HSCs compared with 2D controls and enhanced MOLM13 proliferation. These findings show that a simple hydrogel overlay is sufficient to drive MSCs toward a niche-like stromal phenotype through confinement, strengthened adhesion architecture, stabilised YAP signalling and controlled proliferation. This accessible, tunable 2.5D system provides a mechanistically relevant platform for studying stromal mechanobiology and improving human-relevant haematopoietic culture models.

Assessing the differential impact of RAS mutations on tissue mechanics and tumour formation

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Human RAS genes encode three isoforms: KRAS, NRAS, and HRAS. In cancer, RAS proteins are often mutated at hotspot codons G12, G13, and Q61. Studies have shown that different RAS isoforms and point mutations exhibit distinct mutation frequencies across cancer types, which may be attributed to their unique signalling and functional properties.

However, these differences have not yet been fully examined from a mechanobiological perspective. Hyperactivated RAS has been shown to increase cell contractility, which is linked to multiple tumorigenic processes, including dysregulated cell division, live-cell extrusion, and metastasis. The extent to which different RAS mutations alter the physical properties of cells during early tumorigenesis, however, remains to be elucidated.

We adopted a targeted microinjection system that delivers RAS-mutant RNA to a fate-restricted cell in developing Xenopus laevis embryos. This injected single cell generates a clonal tumour cell cluster in the epithelium of early gastrula stage embryos, allowing live imaging and laser ablation to study the mechanical properties of cancerous cells and their surrounding wild-type cells. Furthermore, we then grow the embryos to early tadpoles where the clonal clusters become induced tumour-like structures (ITLS), enabling the study of early tumorigenesis in complex tissue environments. This study focuses on four RAS variants: KRAS^G12V, KRAS^G12D, NRAS^G12V, and NRAS^Q61K. Preliminary data show that different RAS variants generate ITLS with distinct sizes, compositions, and intracellular RAS localisation patterns.

Laser ablation and western blot experiments indicate that KRAS^G12V and KRAS^G12D significantly increase junctional tension in tissues and are associated with elevated MAPK and PI3K/AKT pathway activity, whereas NRAS^Q61K does not increase junctional tension and is associated only with MAPK hyperactivation.

These results suggest that distinct RAS mutations exert differential tumorigenic and mechanical effects during early tumorigenesis, potentially explained by their variant-specific signalling profiles.

Investigating the Mechanical Properties of the Intestinal Stem Cell Microenvironment

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The intestinal epithelium is subject to sustained mechanical and biological insult, requiring dynamic intestinal stem cell (ISC) activity to replenish damaged enterocytes. Investigating the role of the ISC microenvironment in regulating intestinal regeneration is key to advancing our understanding of diseases such as inflammatory bowel disease and colorectal cancer, in which aberrant ISC proliferation is observed. Research from our lab and others has highlighted reciprocal crosstalk between the midgut epithelium and its associated vascular-like tracheal system (Perochon et al., 2021; Tamamouna et al., 2021). Whilst biochemical tracheal-gut crosstalk has begun to be appreciated, the biomechanical consequences of gut remodelling and its implications for tracheal remodelling remain poorly understood. Dynamic remodelling of the trachea is required for ISC proliferation; remodelling implies motion, and motion requires the exertion and perception of forces (Charras & Sahai, 2014). Data from our lab indicate that subsets of tracheal cells express the mechanosensitive protein Piezo. Piezo expression is upregulated in the trachea in regenerating midguts, whilst tracheal Piezo knockdown significantly reduces tracheal remodelling and ISC proliferation (Phillips & Perochon et al, 2025 pre-print). During development, apoptosis and cellular extrusion have been shown to alter tissue tension (Arnould et al., 2025). Using cell segmentation tools and force inference models to analyse the adult intestinal epithelium, our lab has uncovered an increase in pressure following damage-induced cell death, a change in force within the regenerating midgut, which we've validated using atomic force microscopy (AFM). As well as characterising the downstream signalling pathways following Piezo-mediated mechanosensation in the trachea, we've begun translating these findings into murine models of post-irradiation intestinal regeneration, with promising parallels between models.

Optogenetic construction of de novo integrin-adhesion complexes reveals role for biocondensation in adhesion nucleation

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Integrin-adhesion complexes (IACs) form in cells at sites of attachment to extracellular matrix substrates, allowing them to sense matrix composition and transduce force. However, IACs often do not form uniformly across a cell, which begs the question: What is required to nucleate an adhesion, and what factors enable the stabilization of an IAC once it has formed? Many factors have been suggested to promote formation and the subsequent stabilization of IACs. It is difficult to explicitly test these factors in vivo as IACs undergo constant remodeling. Here, we employ optogenetics to explicitly test the ability of talin in states which promote phase separation to nucleate and stabilize IACs in regions where none are present. We find that fusion of intrinsically disordered regions directly to talin enhances its adhesion nucleation potential and allows new adhesions to be produced in response to optogenetic talin clustering. Similarly, expression of factors previously shown to enhance biocondensation in vitro, such as paxillin, the paxillin N-terminus, or removal of talin autoinhibition, allows for adhesion nucleation and biocondensation of talin. We show that these biocondensates of talin can cluster and activate integrins even in the absence of extracellular matrix. By applying optogenetic activation to regions of the cell with or without ventral actomyosin, we demonstrate actomyosin engagement promotes the formation and stability of adhesions. These results are corroborated by theoretical modelling which shows that phase separation of talin in adhesion complexes is enhanced by differential clutch formation in the presence of actomyosin thus enabling peripheral adhesion formation and stability. This work establishes a model in which increased cooperativity of talin enables IAC nucleation through talin biocondensation, which clusters and activates integrins. In addition to these findings, we generate multiple optogenetic tools that enable local nucleation or enhancement of IACs.

CapG is a mechanoresponsive transcriptional co-regulator of cancer cell invasion programs.

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Mechanical forces are increasingly recognized as central regulators of cancer behavior, promoting invasion and therapy resistance through the induction of force-responsive molecular pathways. These effects are particularly relevant in solid tumors that experience elevated mechanical stress, such as pancreatic ductal adenocarcinoma (PDAC) and glioblastoma (GBM). Although morphologically and mechanistically different, both develop within physically challenging microenvironments, where elevated intratumoral pressures and tissue stiffness can impact signaling pathways that promote invasion, including epithelial-to-mesenchymal transition (EMT). Identifying force-responsive elements driving these processes across highly invasive epithelial and non-epithelial tumors will thus provide valuable insight into potential therapy targets.

Using comparative proteomics studies of invasive and non-invasive GBM cell lines, we identified significantly elevated levels of actin-capping protein CapG in the nuclei of highly invasive cells. We find that CapG subcellular localization changes in response to cell density and to mechanical stimuli, increasing in its nuclear localization upon higher force loads, similar to the behavior of prototypical mechanosensitive regulator YAP. Furthermore, we find that Lamin A/C acts as a retention factor for this protein's nuclear localization. Importantly, we find that nuclear CapG interacts with EMT-associated transcription factors and regulates expression of hallmark EMT genes. Finally, we confirm in patient samples that elevated expression and nuclear localization of CapG correlate with PDAC progression and Lamin A levels, and are associated with -nuclear- biomechanical properties, EMT and TGFβ signaling gene upregulation in infiltrating tumor regions.

Taken together, our findings implicate CapG in a novel mechanosensitive pathway that drives invasive behavior in PDAC and GBM, highlighting a potential new therapeutic avenue for these malignancies.

Polymer–ECM Substrates Regulate Mesenchymal Stromal Cell Phenotype via Stiffness Modulation

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INTRODUCTION: Mesenchymal stromal cells (MSCs) are important in research because a wide array of therapies can be developed by focusing on the immunomodulatory and differentiation capabilities that they possess. Therapeutic approaches based on obtaining large numbers of high-quality MSCs that are expanded ex vivo, struggle to maintain the stemness and differentiation potential of these cells. To ameliorate this issue, we are employing the synergistic effects of the polymer poly(ethyl acrylate) (PEA) and the extracellular matrix (ECM) protein laminin (LM). This specific biomaterial allows LM to self-assemble on its surface and form nanonetworks. Importantly, this reveals the growth factor binding and integrin binding domains of the protein, causing enhanced cell-ECM signalling when compared to the control tissue culture plastic (TCP) surface that is routinely used in research. The synergy between PEA and LM (hereon PEA+LM) has also been shown to decrease the intracellular tension that MSCs experience in culture, consistent with a more naïve and stem-like phenotype.
METHODS: MSCs were cultured on well plates coated with PEA and treated with LM. Immunofluorescence, In-cell Western and qRT-PCR were used to assess markers associated with proliferation and cellular homeostasis. In addition, cell stiffness was assessed using nanoindentation and real-time deformability cytometry. Fluorescence microscopy was used to assess the organisation of the actin cytoskeleton, intermediate filaments, and focal adhesions as indicators of cellular mechanics
RESULTS: Data obtained conveys that cells grown on PEA+LM are softer compared to the conventionally used TCP surface. The biomaterial-ECM protein synergy also increases cell proliferation and decreases the relative levels of markers indicative of cellular stress and dysfunction.

DISCUSSION & CONCLUSIONS: The results demonstrate that MSCs are less stiff when grown on PEA+LM, consistent with a more naïve phenotype. There is also an improved cellular homeostasis and higher proliferation when grown on PEA+LM as opposed to the control conditions.

Measuring the pushing force exerted by cytoskeleton proteins using optical tweezers.

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A cell's ability to interact with its environment through membrane protrusions is fundamental to interpretation and navigation of complex 3D environments of extracellular matrices (ECM). Membrane protrusions can take various forms (filopodia, lamellipodia, blebs) with actin machinery engaging with the cell membrane, pushing it forward and retracting it when required. During migration, protrusions can interpret various signals, matrix stiffness, pore sizes or chemokine gradient, allowing the cell to travel the path of least resistance. Assuming that these protrusions can exert not only pulling but pushing forces to probe/deform/displace the ECM, the global aim of the project is to measure these pushing forces and identify the mechanisms producing them.
Using beads trapped by an optical tweezers, membrane tethers are pulled from adherent cells and the dynamics of the cytoskeleton components can be studied. Additionally, the forces applied by the cell to the bead during this process can be measured and the presence of pushing forces can be identified.
Furthermore, in an aim to understand the mechanisms leading to the growth of Actin into the tethers we investigate if coating the beads with different proteins plays a role. Interestingly, our preliminary results indicate that, actin grows into the pulled tether when fibronectin or concanavalin A coated beads are used. However, length of the tether potentially dictates the type of growth, continuous from the base or patchy throughout the tube, and the forces exerted on the bead. Finally, we observe that microtubules polymerize into the membrane tethers only when Actin is depolymerized using Latrunculin B, this also allows us to measure the force that MTs can exert on their environment inside a cell and their dynamics in protrusions

Giant cytoplasmic vacuoles reshape membrane and nuclear mechanics to orchestrate YAP/TAZ-dependent cell survival

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Cellular morphology is closely coupled with the mechanical properties that regulate cellular behavior, function, and fate. While cytoskeletal organization and external mechanical forces are recognized as primary determinants of cellular mechanics, how internal organelles contribute to such physical properties remains unclear. Here, we report that the formation of giant vacuoles profoundly alters both the mechanical and transcriptional states of mammalian cells, promoting their survival and immune evasion. Mechanistically, vacuolized cells exhibit high plasma membrane tension and nuclear envelope stretching independent of the actin cytoskeleton, thereby facilitating YAP/TAZ nuclear translocation. This promotes phosphorylation of Akt and surface accumulation of CD24 to increase cell survival and potentiate the antiphagocytic role. Notably, vacuole-mediated mechanotransduction is recapitulated in human signet ring cell carcinoma cells, a tumor type histologically diagnosed by mucin-filled vacuoles. Together, these findings suggest a previously unrecognized role of large cytoplasmic vacuoles as mechanical regulators that activate YAP/TAZ, providing a physical mechanism underlying anoikis resistance and immune escape.

3D traction force microscopy reveals activation and contractility dynamics of healthy and profibrotic hepatic stellate cells at single cell resolution

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Hepatic stellate cells (HSCs) are central drivers of liver fibrosis and act as malicious vasoconstrictors in portal hypertension. While the increase in contractility of activated HSCs is well-documented, current approaches largely rely on bulk measurements and on cells passaged on non-physiologically stiff tissue culture plastic, potentially masking relevant nuances of early activation and cell-ECM interactions.
In this study, we employed 3D traction force microscopy to quantify force exertion by single HSCs embedded within soft (shear modulus of ~10 Pa at 1% strain), biomimetic fibrillar collagen hydrogels. This approach allows for the high-resolution tracking of extracellular matrix interactions independent of mechanical cell-cell crosstalk. We monitored quiescent HSCs isolated from BALB/c mice up to seven days post isolation. Cytoskeletal organization of desmin, actin and α-SMA, cell morphology and lipid droplet depletion were used as additional markers of phenotypic transition.
Our findings demonstrate that quiescent murine HSCs undergo fibrogenic activation—characterized by increased contractility, α-SMA expression, and loss of lipid droplets—even when cultured in soft 3D environments. This suggests that high stiffness is not a strict prerequisite for the initiation of the fibrogenic phenotype. Furthermore, we applied the model to patient-derived HSCs and LX-2 cells (immortalized activated HSCs), and observed a significant increase in contractility when exposing those cell types to TGF-ß stimulation, while the myosin II inhibitor blebbistatin and ROCK inhibitor fasudil effectively reduced contractility. PDE5 inhibitor vardenafil and the collagen receptor DDR2 inhibitor WRG-28 failed to bring down contractility in our setup.
In conclusion, our data confirms the usefulness of our 3D model for studying HSC activation and contractility at single cell resolution, and for screening therapeutics to counter fibrosis and portal hypertension, complementary to animal models.

Missing LINC: The role of nuclear mechanotransduction in corticogenesis

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Biological materials exhibit huge mechanical diversity, with the elastic moduli of mammalian tissues spanning over seven orders of magnitude. Nowhere is this range more apparent than during development, where the formation, growth and morphogenesis of diverse tissues create a highly dynamic mechanical environment. Such heterogeneity is not merely a passive effect of establishing tissue architecture, but has the potential to encode information vital to cell fate decision-making. In the brain, changes in tissue mechanics have been implicated in processes ranging from the maintenance of neural progenitors to long-range axon guidance. However, the precise mechanisms by which cortical mechanics influence the differentiation and organisation of cells in a such a complex tissue environment remain elusive. Here, we leverage a 3D organoid model of human cortical development in which we selectively disrupt a key component of nuclear mechanosensing, the LINC complex, rendering cells insensitive to their mechanical environment. LINC-decoupling alters nuclear morphology in a compartment-specific manner, driving preferential exclusion from the germinal zone and concomitant premature differentiation. Excluded cells exhibit a biased spatial distribution and altered fate allocation, with loss of intermediate progenitors and upper-layer neuron populations. Transcriptomic profiling reveals a signature of impaired maturation and density sensing in LINC-decoupled cells, contributing to widespread disruption of histone mark deposition during differentiation. Taken together, these data illustrate how the dynamic mechanical environment of a complex tissue such as the cerebral cortex can dictate cell fate and function in development.

Chemo-mechanical characterisation of engineered bone marrow niches using correlative Brillouin and Raman spectroscopy

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The bone marrow (BM) niche is a dynamic mechano-chemical environment that regulates haematopoietic stem cell maintenance, cancer evolution and dormancy. Capturing these processes in human-relevant models requires non-invasive technologies capable of resolving both mechanical and biochemical changes over time. Here, we develop a correlative Brillouin–Raman micro-spectroscopy platform for label-free chemo-mechanical characterisation of engineered BM niches.
Both techniques rely on inelastic light scattering but probe distinct regimes: Brillouin scattering detects GHz frequency shifts arising from interactions with acoustic phonons, reporting on viscoelastic properties, while Raman scattering measures THz vibrational modes linked to molecular composition. The large spectral separation of these signals enables their collection within a shared optical pathway, providing complementary, high-content information beyond conventional endpoint assays.
We apply Brillouin micro-spectroscopy to a 2.5D BM niche model consisting of mesenchymal stromal cells interfaced with synthetic PEG-fibronectin hydrogels with controlled degradability rate and implemented in miniaturised PDMS devices. Focusing on microenvironmental mechanics provides an effective strategy to monitor niche evolution, capturing subtle, time-dependent changes driven by coordinated cell-mediated remodelling. Brillouin mapping confirms spatial mechanical homogeneity within developed niche-on-chip models and detects time-dependent changes driven by cell-extracellular matrix interactions. Degradable and non-degradable matrices show distinct mechanical evolution over one week, highlighting the sensitivity of our system to progressive remodelling of the cellular environment. These results illustrate the strength of Brillouin spectroscopy as a robust mechanical readout for optimisation of niche-on-chip systems.
Ongoing work focuses on integrating Raman spectroscopy to complement mechanical measurements with biochemical information, enabling correlative tracking of dynamic processes within engineered BM niches. Future developments will include automated acquisition to improve throughput. Together, this platform provides a scalable, non-invasive framework for studying mechanobiological processes in human-relevant models.

From organ-on-chip to organs-on-a-plate: scalable mechanobiology for drug discovery

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Conventional drug screening relies on static cell cultures in multiwell plates, which inadequately capture the dynamic physical microenvironment that governs cellular function in vivo. While organ-on-a-chip technologies have advanced physiological relevance, their complexity, cost, and limited scalability have hindered adoption in high-throughput screening (HTS) and high-content screening (HCS).
Here we introduce a minimalistic yet scalable platform that integrates controlled mechanical stimulation into standard multiwell plate formats, enabling physiologically relevant screening at scale. This “organs-on-a-plate” approach recapitulates key biomechanical cues present across diverse tissues, including heart, lung, muscle, bone, skin, and tumor microenvironments, while maintaining full compatibility with robotic workflows.
The system is designed for simplicity, manufacturability, and throughput, supporting both 2D cultures and 3D models such as spheroids and organoids, and accommodating cell numbers sufficient for downstream molecular analyses. By embedding mechanical cues into a high-throughput format, this platform overcomes a central limitation of current in vitro models: the absence of dynamic physical regulation.
This strategy bridges the gap between physiological relevance and scalability, providing a practical route to incorporate mechanobiology into drug discovery pipelines. Its broad applicability across disease models—including cardiovascular, fibrotic, musculoskeletal, oncological, and neurodegenerative contexts—positions it as a transformative tool for next-generation in vitro screening.

Mechanical stress and cell fate acquisition during zebrafish trunk neural crest cell migration

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During development, cells migrate throughout the body along morphogenesis, often encountering mechanical stress that deforms their nuclei, potentially influencing gene expression. In zebrafish embryos, trunk neural crest cells (TNCs) are an embryonic cell type that serves as an ideal model for studying in vivo cell squeezing. They originate from a progenitor region with large interstitial spaces (10–12 μm) and migrate into a channel narrower than 3 μm between surrounding tissues. TNCs acquire different fates depending on their position in the migratory chain, with leader cells preferentially becoming neurons and followers acquiring glial or pigment cells.

In this study, using live imaging of transgenic zebrafish and immunostaining, I observed that leader cells deform their nucleus more often and for longer than follower cells. Leaders gradually lower the expression levels of H3K9me3 constitutive heterochromatin as they migrate, possibly in response to confinement, and undergo adaptive softening of the nucleus. Conversely, in zebrafish spadetail mutant embryos, where somite tissue is reduced, the H3K9me3 remains highly expressed. Thus, I hypothesise that mechanical deformation of the nucleus experienced by TNCs might influence cell fate choices by affecting chromatin compaction and, in turn, its accessibility to transcription factors.

Next, I performed single-molecule imaging of neural crest–specific H2B dynamics and live tracking of CBX1 (heterochromatin formation) puncta to compare histone mobility between pre-migratory and migrating TNCs. Furthermore, using neural crest–specific transgenic H2B-Dendra2 zebrafish, I can track the specific photoconverted cells to observe whether nuclear deformation correlates with their neuronal, glial, or pigment cell fates by HCR of fate-specific markers (i.e., Phox2bb for sympathetic neurons, Sox10 for glia, and mitfa for pigment).

Together, this ongoing work integrates nuclear squeezing, chromatin reorganisation, and fate specification, aiming to uncover how mechanical forces regulate gene expression programs during in vivo confined cell migration.

Nanopillar Arrays Reveal Senescence-Associated Subnuclear Deformability in Skin Cells

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Cellular senescence is a key driver of skin aging, one of the earliest and most visible manifestations of organismal aging. Senescence can arise from diverse insults, including replicative stress, ultraviolet irradiation, oxidative damage, and genetic mutations such as progerin-associated premature aging. Despite their distinct origins, senescent skin cells commonly exhibit abnormal nuclear morphology, including wrinkles, invaginations, and grooves across the nuclear envelope. However, these subnuclear features are distributed randomly in three dimensions, making them difficult to quantify and mechanistically investigate. Here, we leveraged vertically aligned nanopillar arrays to impose controllable subnuclear deformations and establish a quantitative platform for evaluating skin cell senescence. By guiding nuclear deformation into defined and analysable patterns, nanopillars enabled robust differentiation of young and senescent skin cells across multiple senescence models, including progerin- and P16-INK4A-induced senescence. Quantitative single-cell analysis further revealed strong correlations between nanopillar-guided subnuclear deformation patterns and canonical senescence markers, including DNA methylation and SA-β-Gal activity, demonstrating that nuclear deformability progressively changes during senescence. To further dissect the molecular determinants governing subnuclear deformability, we employed progerin-induced senescence as a mechanistic model and systematically characterized Lamin mutations associated with altered nuclear architecture. Distinct Lamin variants displayed markedly different deformation responses on nanopillars, revealing differential contributions of Lamin processing and nuclear lamina organization to senescence-associated nuclear mechanics. Together, this work establishes nanopillar-guided nuclear deformation as a quantitative mechanobiological readout for skin cell senescence and provides new insights into how Lamin-associated nuclear mechanics contribute to skin aging and accelerated aging disorders.

Nuclear mechanical collapse of Purkinje neurons in Ataxia-telangiectasia

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The ATM kinase regulates the DNA damage response and the mechanical properties of the cells. ATM mutations cause Ataxia-telangiectasia (A-T), a disorder characterised by progressive loss of Purkinje neurons. The mechanisms behind Purkinje cell death remain unclear. We characterised Purkinje neuron degeneration in cerebella, hiPS cells and cerebellar organoids derived from A-T patients by integrating functional analyses, imaging and Brillouin microscopy. Human Purkinje cells are mechanically soft and exhibit low viscosity, but in A-T they develop hyperstiffness, accompanied by nuclear envelope deformation and chromatin hypermethylation. Quantitative proteomics using laser microdissection revealed a depletion of ITPR1 and ITPR3 calcium channels, dysregulated mechano-transduction and epigenetic pathways, and an accumulation of KAP1 and PRMT5 chromatin remodellers. Remarkably, pharmacological inhibition of heterochromatin rescued these nuclear shape defects, restored ITPR1 and ITPR3 expression, and alleviated sensitivity to glycolytic stress in A-T Purkinje neurons. Our findings identify Ataxia-telangiectasia as a ‘mechano-disease’, revealing that the intrinsic visco-elastic properties and euchromatic epigenetic landscape of human Purkinje neurons make them particularly vulnerable to the mechanical stress generated by loss of ATM. Our findings pave the way for potential therapeutic interventions aimed at correcting nuclear mechano-dysfunction in Purkinje cells of A-T.

Deconstructing Cell-Extracellular Matrix Co-Adaptive Mechanisms by Mechano-Actuating Hydrogels in Pathological Microenvironments

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The interactions between cells and the extracellular matrix (ECM) are far from static; they exert forces and signals that are crucial for the organisation, maintenance, and repair of tissues, as well as in the progression of various diseases such as fibrosis. However, most of our disease mechanism knowledge comes largely from studying cells under static conditions. This approach has led to inconsistencies, such as the discrepancy observed between in vitro models that associate increased stiffness with fibrosis and clinical findings in pulmonary fibrosis that suggest a more complex relationship. Such contrasts not only challenge our current understanding of these diseases but also underscore a significant gap in translating laboratory findings into practical, real-world applications.

Our work aims to address these challenges by recreating and deconstructing the dynamic interactions between cells and the ECM within both healthy and pathological microenvironments. Our particular focus is to deepen our understanding of mechanotransduction—the process by which cells translate mechanical stimuli into biochemical signals—particularly as it pertains to disease progression. To achieve this, we engineer mechano-actuating hydrogels based on stimuli-responsive poly(N-isopropylacrylamide) (pNIPAM) to reproduce key features of fibrotic disease, including evolving mechanical properties that will facilitate the establishment of a predictive in vitro model to recapitulates key stages of fibrosis progression. This innovative strategy will advance current platforms for drug discovery, enhance early diagnosis, and develop new tools for monitoring fibrosis and similar conditions. Our work represents a paradigm shift in treating mechano-diseases, aligning with urgent healthcare needs and offering hope for more targeted and effective solutions.

Activation of the Metalloproteinase ADAM17 by the Mechanosensitive Ion Channel Piezo1

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We here demonstrate that mechanical activation of the ion channel Piezo1 can enforce the activity of the metalloproteinase ADAM17 in various cell types leading to increased shedding of surface molecules. In endothelial cells this process controls shedding of junctional adhesion molecule (JAM) A and cell migration and proliferation. In osteoclast precursors limited differentiation is obseved due to increased shedding of osteogenic receptors. In keratinocytes the Piezo1/ADAM17 axis promotes inflammatory mediator release via the shedding of growth factors and activation of epidermal growth factor receptor (EGFR). Since ADAM17 is well known to be regulated though the adapter molecule iRhom2, we questioned how Piezo1 mediated signalling can tune this regulation. Cell stimulation with the Piezo1 agonist Yoda1 or the PKC agonist PMA can activate several kinases including ERK1/2. In coprecipitation studies with transfected HEK293 cells we found that ERK1/2 associates with tagged iRhom2 and that bound ERK1/2 is phosphorylated when cells are stimulated with Yoda1 or PMA. Notably, this cell stimulation is also associated with increased binding of iRhom2 to 14-3-3 protein which is known to strongly depend on phosphorylation of the target proteins. Removal of potential phosphorylation sites in the iRhom2 N-terminus abrogates 14-3-3 binding but does not affect ERK1/2 binding. Moreover, inhibition of ERK1/2 kinase was found to abrogate 14-3-3 protein binding. Finally, we studied the effect of ERK1/2 inhibition on ADAM17 in endothelial cells. Yoda1 treatment induced ERK1/ 2 phosphorylation and ADAM17 activation which was measured in terms of JAM-A or TNFR shedding. This response could be suppressed in part by the ERK1/2 inhibitor indicating that the ERK1/2 pathway is involved but not sufficient to explain ADAM17 regulation by Piezo1 signaling.

Biomechanical Vulnerability of Oral Cancer Cells Enables Low-Frequency Ultrasound Treatment

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E-Poster Session Tuesday Evening, July 14, 2026, 17:50 - 18:30

India accounts for more than a quarter of the total oral cancer burden globally. Despite advances in current treatment therapies, the survival rates over the last five decades have remained unchanged. The severe side effects associated with conventional radio- and chemotherapy are attributed to the nonselective targeting that damages both cancer cells and adjacent normal tissues. Here, we describe an alternative low-frequency (39kHz) pulsed ultrasound (US) approach that leverages the distinct mechanical vulnerability of cancer cells. We show that ultrasound applied at optimised parameters induces selective apoptosis of patient-derived oral cancer cells without significantly damaging healthy normal epithelial cells. Molecular studies reveal that US treatment enables the disruption of focal adhesions (FAs) and cytoskeletons (F-actin and myosin IIA fibers) in oral cancer cells, which correlates with the decrease in contractility. The mechanical vulnerability of oral cancer cells to US-mediated mechanical forces is due to reduced expression of Tpm2.1, a cytoskeletal mechanosensory protein. Furthermore, ultrasound treatment reduces proliferation in oral cancer cells. The findings of this study indicate that US treatment not only triggers selective apoptosis but also reduces the invasive and proliferative properties of patient-derived oral cancer cells. Overall, this work suggests that it will be possible to lay the foundation for developing potentially safer, personalized, and non-invasive ultrasound-based mechano-treatment against oral cancer.

Novel Light Scattering Technique to Detect Neuronal Activity

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E-Poster Session Tuesday lunch, July 14, 2026, 13:00 - 13:50

Neurons are known to undergo mechanical contraction during the propagation of action potentials. This has been attributed to both – the physical opening and closing of ion channels, as well as the transport of neurotransmitters. However, these contractions are difficult to observe and have mostly been reported in large squid axons and individual, isolated mammalian neurons, subsequently hindering real world applications such as the use of mechanical neuronal contraction as a diagnostic tool in the whole brain.
Here, we present a novel label free technique to detect mechanical contractions as a measure of neuronal activity. We demonstrate proof of concept in ex vivo brain slices i.e. at the tissue level and is expected to operate also at the organ level. Our approach relies on the measurement of light that undergoes multiple scattering by a cluster of active neurons. A laser beam illuminates an electrically stimulated acute brain slice. The light is scattered and reflected back from the brain slice and exhibits a complex, random interference pattern – a speckle – collected on a CMOS camera running at 1kHz framerate. This speckle pattern is sensitive to sub-nanometre changes in the neuronal membrane. Fluctuations in the speckle pattern are shown to be directly related to neuronal activity as also seen in the correlated calcium imaging in the same tissue regions.
These optical changes due to neuronal activity can be leveraged to develop novel neurotechnologies that are non-invasive, label free, and offer better spatiotemporal resolution for practical biomedical applications.

investigating cell-material interaction for the study of cell migration induced by substrate space-time warping

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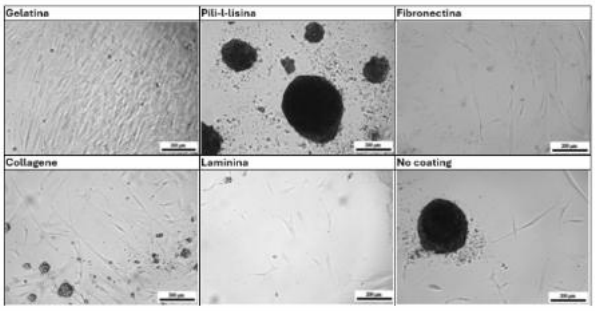
Cell–material interactions regulate adhesion, migration, and tissue organization, yet the influence of substrate biochemical functionalization remains poorly standardized, particularly in soft systems. Current studies compare only a few coatings, using heterogeneous metrics, preventing quantitative cross-study comparisons. This gap is especially relevant for adipose-derived mesenchymal stem cells (ADSCs), a clinically promising and mechanoresponsive cell population, widely used in regenerative medicine and organ-mimetic models. We, systematically, investigate ADSC adhesion dynamics (as monolayers and spheroids) on soft substrates functionalized with five coatings, with the long-term goal of enabling controlled cell migration through cell-induced substrate warping as a contactless guidance strategy. ADSCs were seeded (31250 cells/cm2) on 5 mg/mL agarose-20 mg/mL dextran gels coated with gelatine (50 mg/mL), collagen (100 µg/mL), fibronectin (10 µg/mL), laminin (100 µg/mL), poli-l-lysine (100 µg/mL) and on culture plates as control. Cells were monitored through live bright-field images taken every two minutes for one hour, starting two hours after seeding and every two hours for three days. To determine the optimal cell number allowing for spheroid formation, different cell numbers (5,000-200,000 cells) were cultured for 48 hours on low-adhesion wells to promote aggregation and then transferred to non-coated substrates. Imaging was performed to assess morphology at 10x magnification, using a bright field microscope. Spheroid diameter and roundness were quantified analysing images with ImageJ. The results demonstrate coating-dependent differences in cell morphology and adhesion behaviour (Fig.1) and a cell number-dependent increase in spheroid size, sphericity, and cohesion (Fig. 2). These preliminary findings, show that substrate coating significantly modulates cell adhesion. Ongoing quantitative analyses of shape descriptors, migration velocity, and adhesion kinetics will provide standardized metrics linking substrate chemistry to cell dynamics. This unified dataset will support computational modelling and the development of advanced in vitro systems for the study of cell migration as a function of substrate space-time warping.

a)



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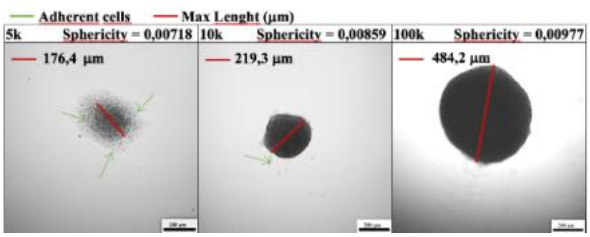

Revealing label-free, multiplexed molecular information for mechanobiology through Raman spectroscopy and advanced data science

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E-Poster Session Tuesday lunch, July 14, 2026, 13:00 - 13:50

Mechanobiology has developed sophisticated approaches to apply and quantify mechanical forces in living systems. However, methods capable of simultaneously revealing the molecular response of cells to mechanical perturbation without exogenous labels remain scarce. We envision that the combination of Raman spectroscopy (RS) with advanced chemometric and data science approaches can bridge this gap by transforming complex vibrational spectra into biologically meaningful molecular information.
Here, we present the evolution of a research line aimed at establishing RS as a label-free and multiplexed molecular readout for mechanobiology. This work began with the integration of RS and optical tweezers to simultaneously manipulate and probe biological samples, demonstrating the feasibility of monitoring force-induced molecular changes in DNA molecules and red blood cells. In parallel, we developed advanced chemometric and data science methods to identify molecular signatures associated with mechanically-induced cellular responses from complex Raman datasets.
Building on this foundation, we applied this approach to investigate the molecular response of living cells under mechanical confinement, revealing that cPLA2 activity at the inner nuclear membrane produces arachidonic acid, which is a metabolite regulating cortical contractility in confinement (in collaboration with V. Ruprecht, S. Wieser and V. Venturini; Science 2020). Importantly, these findings demonstrated that label-free Raman spectroscopy can identify biochemical pathways activated by mechanical stress in living cells.
We are currently extending this framework to cancer mechanobiology by developing label-free Raman imaging strategies to study cancer cells migrating through highly confined microfluidic channels and cancer organoids. By integrating molecular imaging with advanced computational analysis, we aim to uncover molecular programs associated with confinement, invasion and mechanotransduction in physiologically relevant models.
These studies lay the foundations for a next-generation mechanobiology platform that integrates mechanical perturbation, label-free RS and advanced data science methods to decode mechanotransduction across biological systems, from single biomolecules to cancer organoids.

Mechanosensitive gene regulation that coordinates epiboly cell movements in zebrafish gastrulation

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E-Poster Session Wednesday Lunch, July 15, 2026, 13:00 - 13:50

During vertebrate embryogenesis, mechanical and geometric inputs have to integrate with gene regulatory networks to guide differentiation and organ formation. However, how these physical cues influence the epigenetic landscape of developing tissues remains poorly understood. Recent studies have revealed direct links between cellular mechanotransduction and epigenomic regulation, but the underlying genetic programs and their developmental relevance are still emerging. We propose to investigate this interplay in the Enveloping Layer (EVL) of the zebrafish embryo during epiboly, the first global morphogenetic movement dependent on the capacity of EVL cells to undergo drastic morphological flattening and to regulate mechanical tension driven by the actomyosin ring near the yolk.

To identify mechanosensitive genomic response regions (mGRRs) triggered by these geometric changes, we modulate cell geometry and tension by (i) changing the dimensions of the yolk (remove yolk vs increase yolk volume by injecting big oil droplets), (ii) altering actin-cytoskeletal intracellular tension using drug treatments (Rockout vs. Calyculin A) or (iii) applying geometrical constrictions to the embryo with capillaries of different stiffness. Furthermore, we are optimizing additional strategies to induce controlled mechanical stress in the developing embryo by using magnetic beads. Following these different mechanical perturbations, we have analyzed changes in gene expression and chromatin accessibility. We aim also to perform integrative multiomic analysis using 10X Chromium Single Cell Multiome (scATAC-seq + scRNA-seq) and Whole Genome Bisulfite Sequencing (WGBS).

By mapping mechanosensitive genes and correlating them with chromatin accessibility and DNA methylation patterns, our integrative analysis will reveal how mechanical and geometric cues are encoded into stable epigenetic and gene regulatory states. Ultimately, this study aims to elucidate how cells interpret and “remember” physical inputs, providing insights into the fundamental principles governing cell fate decisions and tissue architecture in developing tissues.

Single-molecule magnetic tweezers to probe mechanosensitive proteins in focal adhesions

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E-Poster Session Wednesday Lunch, July 15, 2026, 13:00 - 13:50

Focal adhesions (FAs) are integrin-mediated mechanosensitive protein complexes that link the extracellular matrix (ECM) to the cytoskeleton, enabling cells to sense and respond to mechanical cues from their environment. Mechanical forces transmitted through FAs induce conformational changes in constituent proteins, exposing cryptic binding sites or residues targeted by post-translational modifications (PTMs), thus converting mechanical stimuli into biochemical signals that regulate key cellular processes such as migration, proliferation, and differentiation. However, characterising these mechanosensitive molecular mechanisms remains experimentally challenging: conventional biochemical techniques fail to account for the effect of mechanical forces, while traditional single-molecule force spectroscopy tools often lack the resolution or stability needed to probe the low-force and long-timescale relevant to the physiological function of FA proteins. To overcome these limitations, here we developed an ultra-stable single-molecule magnetic tweezers setup capable of measuring the conformational dynamics of single proteins under low forces (0-60 pN) with exceptional precision (<0.1 pN resolution) and over extended periods (from several hours to days), closely mimicking the conditions experienced by proteins in FA. Using this approach, we have been able to characterise the nanomechanics of key FA proteins including talin, and focal adhesion kinase, revealing distinct, finely tuned force-response behaviours. In addition, we have investigated how force-dependent conformational dynamics are modulated by physiologically relevant protein interactors and PTMs, uncovering specific regulatory mechanisms of their mechanosensing properties. Overall, our results establish a versatile and precise technique for probing mechanosensing and mechanotransduction at the single-molecule level, opening new avenues for studying the molecular mechanisms underpinning mechanotransduction.

Epithelia can fluidise despite crowding due to curvature changes and osmotic imbalance

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Hemicysts, or fluid-filled domes, arise in crowded epithelial monolayers and rely on apicobasal fluid flow to achieve curved architecture in 2D epithelia. However, the role of tissue dynamics that accompanies this transition from epithelial sheets to dome structures remains understudied. Here, we compared the dynamics of overcrowded monolayers in the presence and absence of hemicysts. Initially, overcrowded monolayers were jammed. As hemicysts emerged, cell velocities increased dramatically, marking a transition to a more fluid-like, unjammed state - contrary to the conventional association between crowding and jamming. To investigate this, we studied cytoskeletal changes and tissue movement patterns during hemicyst formation upon overcrowding and altered osmotic balance by treatment with sodium acetate. Actin and E-cadherin increased with overcrowding and sodium acetate treatment, thereby enabling the forces required for tissue curvature changes. Furthermore, low levels of tight junctions were observed in overcrowded conditions, indicative of paracellular pathway activation whereas increased levels of the same upon administration of sodium acetate - suggesting transcellular pathway for fluid transport. Since hemicyst formation at overcrowding and fluidisation was associated with both curvature changes and apicobasal fluid flow, to delineate the role of curvature and fluid flux in modulating tissue dynamics, we induced domes with sodium acetate at low and high densities. At high density, hemicysts formed and the tissue fluidised. When sodium acetate was added at low density, hemicysts did not form; however, the tissue still presented fluidisation even without curvature. Taken together, we report essential links between curvature, fluid flux and cell density in driving fluid-like dynamics in epithelial tissue, whereby both curvature and fluid flow are required for fluidisation in overcrowded conditions whereas either one is sufficient to drive fluidisation at homeostatic densities. These findings on active phase transitions in epithelia have broad implications for diseases including cystic kidney disease, cancer metastasis, and asthma.

Nucleoli are mechanosensitive structures regulating cell migration

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E-Poster Session Tuesday Evening, July 14, 2026, 17:50 - 18:30

Metastases are the leading cause of cancer-related mortality and are influenced by the tumor microenvironment, whose stiffness plays a key role. This microenvironment becomes stiffer due to increased secretion of extracellular matrix by cancer-associated fibroblasts, promoting the emergence of an aggressive tumor phenotype, particularly by stimulating cell migration. Indeed, mechanosensitive cancer cells migrate more slowly on soft substrates than on stiff ones. This phenotypic adaptation may be regulated by the nucleus through mechanotransduction. However, the role of nuclear organization in response to physical changes in the environment remains poorly understood. Transcriptomic analysis revealed that nucleophosmin 1 (NPM1), a nucleolar protein, is overexpressed on stiff substrates.
Our work shows that healthy RPE cells and cancerous HS578T cells exhibit fewer nucleoli on soft substrates compared to stiff substrates, along with reduced expression of the NPM1 protein on soft substrates. Moreover, inhibition of NPM1 on stiff substrates leads to decreased cell migration.
Our research therefore aims to understand how nucleoli, and particularly the protein NPM1, regulate cell migration. As nucleoli are nuclear condensates involved in ribosome synthesis and in the retention of heterochromatin—thereby maintaining genes in a transcriptionally inactive state—our hypothesis is that NPM1 may control cell migration by anchoring heterochromatin to nucleoli and by regulating ribosome biogenesis.

Nematic order as a fundamental force of biological organisation

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[1]University of Strathclyde, United Kingdom

E-Poster Session Wednesday Lunch, July 15, 2026, 13:00 - 13:50

The long-range orientational alignment in nematic order is increasingly recognised as a fundamental driver of organisation across biological systems, from cytoskeletal filaments to epithelial cell monolayers. Yet its role in early developmental contexts, specifically outside of mammalian contexts, remains underexplored. Here, we investigate the emergence of nematic order in a minimal system: rod-shaped ascospores of the lichen Xanthoria parietina. During development, spores are confined within the ascus, creating a mechanically constrained environment analogous to crowded cellular systems. We hypothesise that such confinement drives the emergence of orientational order, and informs the next stage of development. Ascospores were obtained via discharge and imaged using high-resolution time-lapse microscopy throughout the transition from confinement to hyphal formation. Nematic analysis was applied over time to quantify the evolution of orientational domains. By varying temperature, we probe how growth rate and activity modulate the dynamics of ordering. This work establishes lichen ascospores as a minimal biological model for studying mechanically driven self-organisation, providing a bridge between well-studied active nematic systems, such as cell monolayers, and less explored developmental contexts. This suggests that orientational order may act as a precursor to morphological organisation across living systems, linking physical alignment to biological function.

Characterisation of Tumour Cell Biomechanics using High-Throughput Microfluidic Devices

Orlaith McSweeney[1], María José Gómez-Benito[2], Irish Senthilkumar[1], Bart Smeets[3], Eoin McEvoy[1]
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INTRODUCTION
Personalised treatment requires mechanistic insight into heterogeneous tumour cell behaviour, such as identifying biomarkers for chemoresistance. This study presents a microfluidic aspiration platform, integrated with computational modelling, to characterise heterogeneity in tumour cell biomechanics.

METHODS
We developed a high-throughput system for cell membrane aspiration within microfluidic devices, by controlling pressure gradients (ΔP) across microchannels. We developed computational fluid dynamics (CFD) models to predict how geometry and boundary conditions govern ΔP (Fig. 1A, COMSOL). PDMS chips were fabricated and interfaced with pressure controllers to impose ΔP (0.6-1 kPa). We seeded T47D cells ($1x10^6$ cells/ml) within the device, monitoring aspiration into microchannels over time (Fig. 1B). ImageJ was used to measure cell diameters pre-aspiration and aspiration lengths. Finite element (FE) models incorporating active cortical, cytoplasmic and nuclear regions (Fig. 1B, Abaqus) captured viscoelastic behaviour, and were calibrated to experimental timescales (Fig. 1E). Finally, models were extended to multicellular models (Fig. 1F, MPacts) to parse heterogeneity across larger scales.

RESULTS & DISCUSSION
CFD modelling revealed experimental conditions to ensure gradual ΔPs across microchannels (Fig. 1A). Optimal cell aspiration occurred in 6-9μm channels, with aspiration length increasing with channel width and ΔP (Fig. 1D). Result variability reflected heterogeneity in cell size and stiffness. Modelling uncovered the time-dependent interplay between non-linear cortex and nucleus stiffness in governing aspiration length arising from biomechanical heterogeneity (Fig. 1C). While stiff cells are more readily aspirated when smaller, softer cells exhibit greater aspiration lengths when larger due to a transition from an elasticity-limited to a volume-limited response.

This platform enables quantitative characterisation of tumour cell biomechanics and can be extended to investigate chemoresistance, multicellular spheroids, and patient-derived tissue.

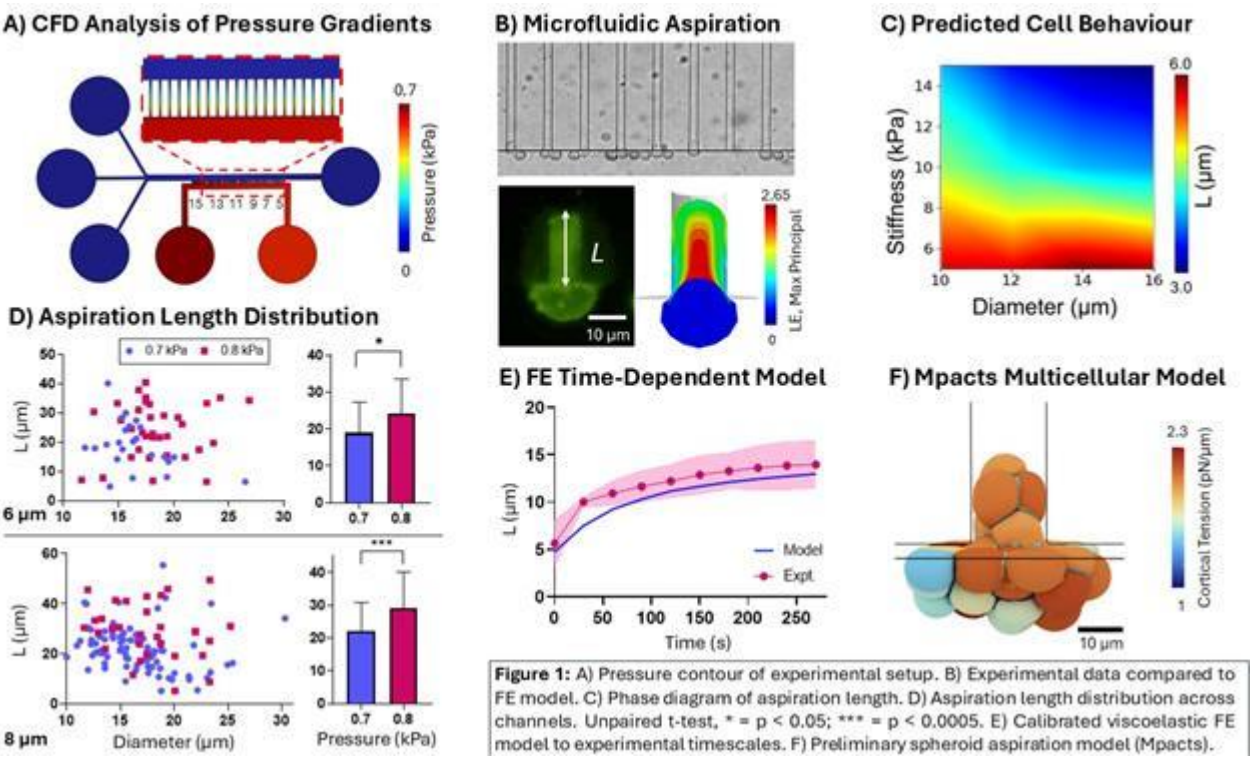

Figure 1: A) Pressure contour of experimental setup. B) Experimental data compared to FE model. C) Phase diagram of aspiration length. D) Aspiration length distribution across channels. Unpaired t-test, * = $p < 0.05$; *** = $p < 0.0005$. E) Calibrated viscoelastic FE model to experimental timescales. F) Preliminary spheroid aspiration model (Mpacts).

Fingerprints as frozen nematic fields

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[1]University Of Strathclyde, United Kingdom

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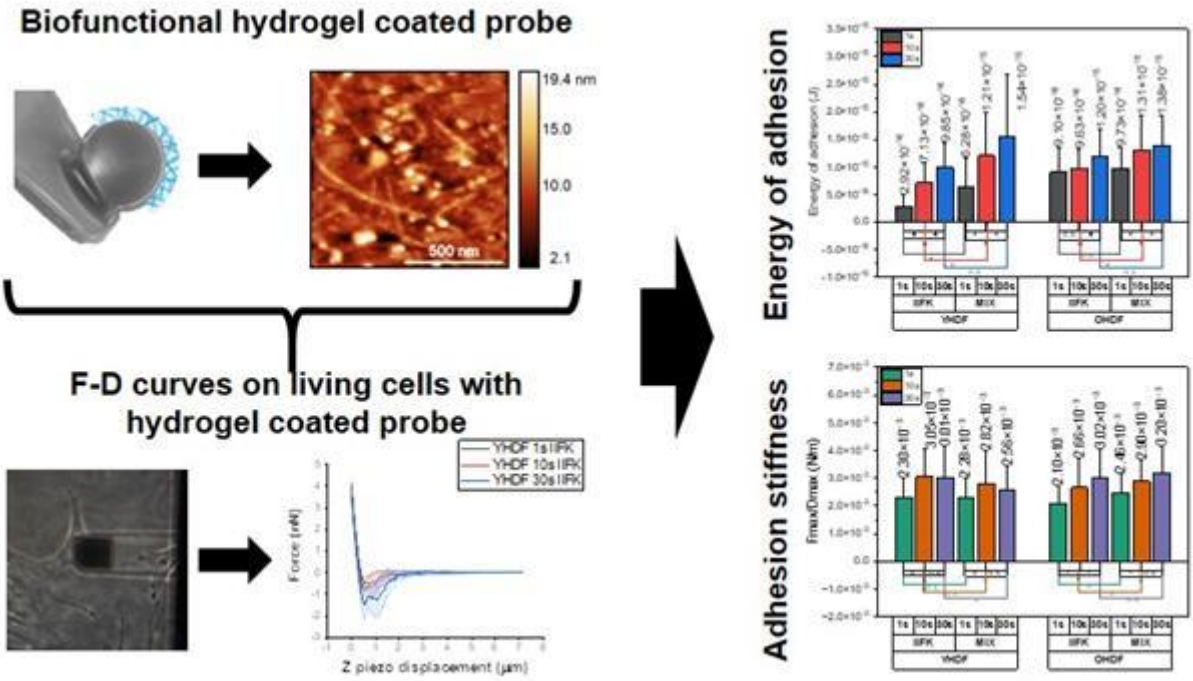
Biological pattern formation is often defined in terms of biochemical signalling and local growth rules, yet the range of permissible patterns is fundamentally constrained by underlying physical principles. Here we demonstrate that ridge patterns in human fingerprints are shaped by topological constraints characteristic of a nematic field on a bounded surface. Treating ridge orientation as a two dimensional nematic director field reveals a global restriction on pattern configurations linking boundary geometry to internal singularities. Within a nematic framework, triradii, loops, and whorls correspond to −1/2, +1/2, and +1 topological defects whose total charge balances the Euler characteristic of the fingerprint domain together with boundary winding through a generalised Poincaré–Hopf theorem. Across 133 fingerprints from open access databases, 95.5% satisfy the predicted charge neutrality despite substantial variability in local ridge patterning. Measured boundary winding values deviate from those of an idealised fingerprint and reveal a threshold above which charge neutrality is maintained and below which geometric frustration emerges. These results identify a mathematical limit on fingerprint configurations and position fingerprints as a macroscopic, passive biological record of nematic order during development.

Single-Cell Mechanoprofiling of Aging and Cancer by AFM Force Spectroscopy Using Probes Coated With Biofunctional Ultrashort Peptide Hydrogels

Manola Moretti[1], Vanesa Gamez Baez[1], Dana Alhattab[1], Sherin Abdelrahman[2], Rosario Montserrat Perez-Pedroza[1], Panayiotis Bilalis[1], Malak AbedAlthagafi[3], Christian Baumgartner[4], Charlotte A. E. Hauser[4]
[1]King Abdullah University of Science and Technology, Saudi Arabia, [2]Max Planck Institute, Germany, [3]Tufts University, United States, [4]Graz University of Technology, Austria

E-Poster Session Tuesday lunch, July 14, 2026, 13:00 - 13:50

Cell–extracellular matrix interactions are central to both aging and cancer, yet tools capable of probing these processes at the single-cell level in physiological conditions remain limited. Here, we present a label-free mechanoprofiling platform that combines atomic force microscopy (AFM) force spectroscopy with AFM probes coated with self-assembling ultrashort peptide nanofibers functionalized with and without extracellular matrix adhesion motifs. In particular, we investigated the effect of an RGD-containing peptide hydrogel coating on single-cell adhesion behavior across biologically distinct models: young versus senescent human dermal fibroblasts, healthy versus acute myeloid leukemia-associated mesenchymal stromal cells, and human neuroblastoma cells. Peptide nanofiber formation and secondary structure were confirmed by AFM imaging and Raman spectroscopy. Force–distance measurements revealed that the RGD functionalized coating elicited cell-type specific adhesion responses that could not be captured by the parent peptide alone. Young fibroblasts showed a marked increase in adhesion energy, consistent with more dynamic and persistent receptor-mediated interactions, whereas healthy mesenchymal stromal cells displayed increased adhesion stiffness, suggesting mechanically reinforced anchoring. In contrast, senescent fibroblasts and leukemia-associated stromal cells showed weaker sensitivity to the RGD cue and appeared to rely more strongly on non-specific adhesion mechanisms. Neuroblastoma cells exhibited a more heterogeneous response, indicating the presence of subpopulations with distinct adhesion states. Overall, this study demonstrates, to our knowledge for the first time, the use of hydrogel biofunctional ultrashort peptides as AFM probe coatings for live-cell adhesion analysis. The approach provides a versatile and physiologically relevant strategy to distinguish healthy, aging, and cancer-associated cell states through their mechanoadhesive fingerprints, with potential applications in mechanobiology, biomaterials design, diagnostics, and personalized therapeutic screening.


Biofunctional hydrogel coated probe
19.4 nm
15.0
10.0
2.1
500 nm
F-D curves on living cells with hydrogel coated probe
YHDF 1s IFK
YHDF 10s IFK
YHDF 30s IFK
Force (nN)
Z piezo displacement (µm)
Energy of adhesion
Adhesion stiffness
IFK
MIX
YHDF
OHDF

Maturation-Dependent Mechanobiology of hiPSC-Derived Cardiomyocytes: Toward Enhanced Mechanical Integration in Cardiac Cell Therapy

Dylan Mostert[1,2], Chiara Mameli[1], Leon de Windt[1]
[1]Maastricht University, Netherlands, [2]DWI-Leibniz Institute for Interactive Materials, Germany
E-Poster Session Tuesday lunch, July 14, 2026, 13:00 - 13:50

Heart failure (HF) remains a global pandemic, affecting over 64 million people worldwide and projected to rise 46% by 2030. Following a heart attack, the irreversible loss of cardiomyocytes (CMs) drives progressive cardiac dysfunction, highlighting an urgent need for regenerative strategies. Human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs) represent a promising cell source for cardiac repair; however, their therapeutic potential is constrained by poor electromechanical coupling with host myocardium, largely attributed to impaired cell-cell interactions and insufficient alignment with the host extracellular matrix.

We hypothesize that the mechanobiological profile of hiPSC-CMs is governed by their maturation stage, and that selecting the appropriate maturation state can enhance mechanical integration and functionalization within injured myocardial environments. To test this, we employ a two-part experimental framework. First, we characterize the mechanobiological signatures of hiPSC-CMs across four maturation stages — from CM progenitors to late-stage hiPSC-CMs — using immunohistochemistry and high-resolution confocal imaging. Cells are subjected to microfabricated protein patterns, cyclic mechanical deformations, and tunable hydrogel substrates to assess their mechanosensing capacity. Second, we evaluate the integration of selected hiPSC-CM populations into engineered disease models of the myocardial wall, using both 2D monolayer systems and 3D engineered heart tissues as the gold-standard platform. Functional readouts include contraction strength, frequency, and synchronization.

This work challenges the prevailing paradigm of using late-stage hiPSC-CMs in regenerative strategies, instead proposing that less mature, mechanobiologically active cells may achieve superior host tissue coupling. Ultimately, these findings may guide the rational selection of hiPSC-CM maturation states for cardiac cell therapy, advancing treatment outcomes for heart failure patients.

Chromatin Reorganization Overrides the Substrate Rigidity-mediated Mechanoresponse and Lineage Specification in Human Mesenchymal Stem Cells

Mr. Sourav Mukherjee[1], Rohit Joshi[1], Pooja Dharmambal Muralidharan[1], Tejas Suryawanshi[1], Pushpendra Yadav[1], Vedanshi Dharnidharka[1], Abhijit Majumder[1]
[1]Indian Institute Of Technology Bombay, India

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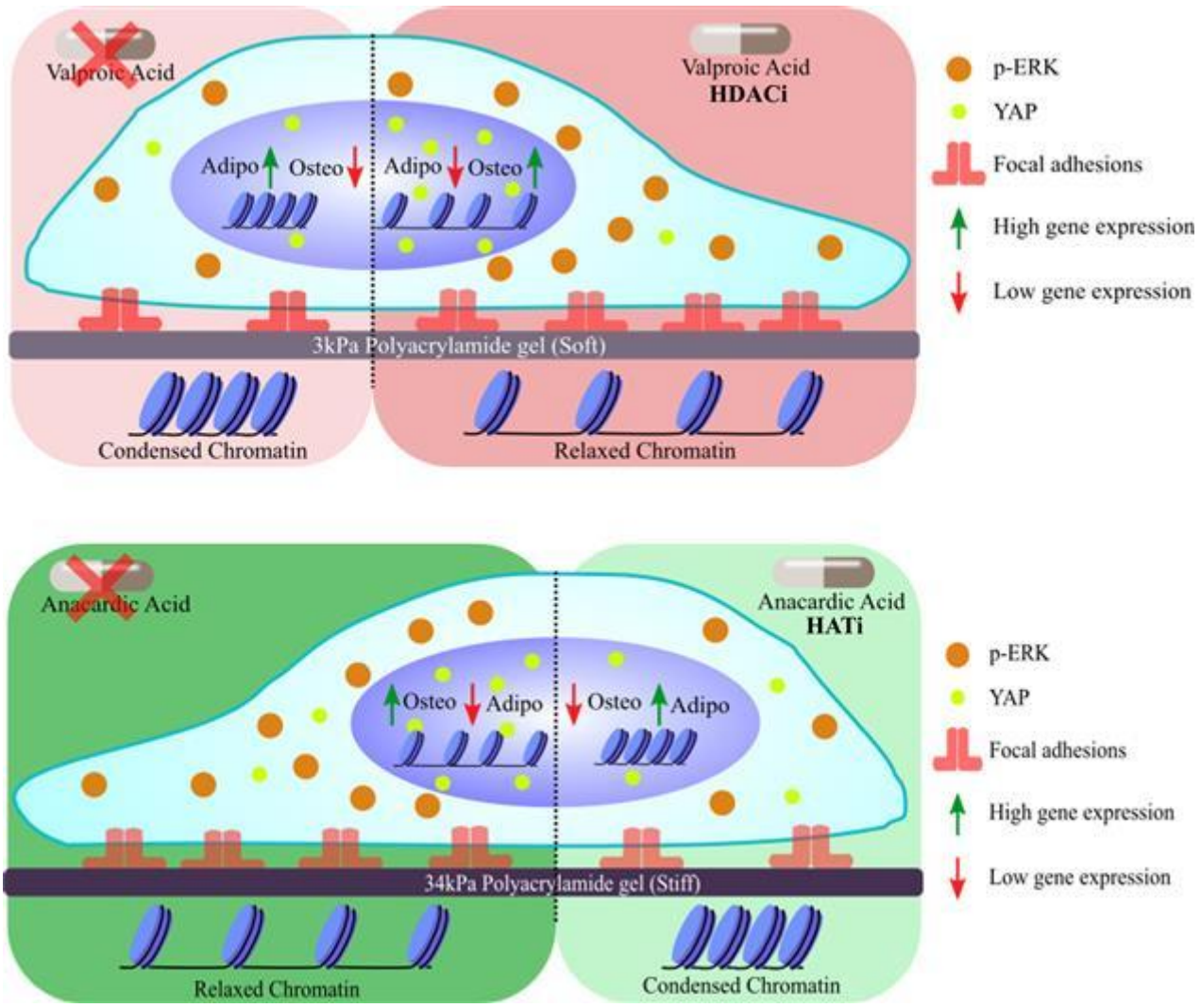
Substrate rigidity is a well-established regulator of cellular phenotype and lineage specification in human mesenchymal stem cells (hMSCs). Adipogenic differentiation is favored on soft substrates and osteogenic differentiation promoted on stiff substrates. These outcomes are accompanied by distinct changes in cell area, traction forces, focal adhesion, and actomyosin cytoskeletal organization. This outside-in mechanotransduction pathway, through which the extracellular mechanical signals are transduced to the nucleus and remodel the chromatin landscape, has been extensively studied.

While soft substrates promote chromatin condensation, chromatin remains decondensed in hMSCs on stiff substrates. However, whether chromatin packaging alone is sufficient to override rigidity-dependent cellular responses through an inside-out pathway remains poorly understood. To address this, chromatin decondensation was induced in hMSCs cultured on soft polyacrylamide substrates (3 kPa) using a histone deacetylase inhibitor (HDACi), while chromatin condensation was induced in hMSCs on stiff substrates using a histone acetyltransferase inhibitor (HATi). Chromatin decondensation in hMSCs on soft substrates induced a stiff-like phenotype, characterized by increased cell spreading, traction forces, focal adhesion formation, actin stress fiber formation, and osteogenic differentiation. Conversely, chromatin condensation in hMSCs on stiff substrates promoted a soft-like phenotype with reduced cellular spreading, actin expression, focal adhesion formation and adipogenic differentiation.

To investigate the downstream mechanism, localization of the mechanosensitive transcriptional regulator Yes-associated protein (YAP) was examined. Chromatin decondensation on soft substrates increased YAP nuclear localization, whereas condensing chromatin on stiff substrates resulted in cytoplasmic retention of YAP. Since p-ERK acts downstream of YAP and regulates hMSC differentiation, chromatin decondensation on soft substrates and chromatin condensation on stiff substrates altered p-ERK expression, which correlated with the corresponding lineage specification. Collectively, these findings demonstrate that global chromatin compaction can override the mechanoresponse of hMSCs, providing a mechanistic basis for understanding mechanosignalling and controlling hMSC differentiation in tissue engineering and regenerative medicine.


Valproic Acid
Valproic Acid
HDACi
Adipo
Osteo
Adipo
Osteo
3kPa Polyacrylamide gel (Soft)
Condensed Chromatin
Relaxed Chromatin
p-ERK
YAP
Focal adhesions
High gene expression
Low gene expression
Anacardic Acid
Anacardic Acid
HATi
Osteo
Adipo
Osteo
Adipo
34kPa Polyacrylamide gel (Stiff)
Relaxed Chromatin
Condensed Chromatin
p-ERK
YAP
Focal adhesions
High gene expression
Low gene expression

Force Sensing via Ion Channels in Pancreatic Cancer

Mr Riley Mumberson[1]
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The tumour microenvironment (TME) of pancreatic cancer is comparatively denser and more dynamic than other cancerous TME's. The progression of pancreatic cancer has been associated with significant changes in the mechanics of its tumour microenvironment, requiring cells to sense and distinguish the physical forces they are exposed too. Force sensors such as mechanically activated (MA) ion channels can regulate cancer cell behaviour in response to changes within the TME. We found that there are multiple force sensing MA ion channels linked with migratory, invasive and/or poor prognostic outcomes in other cancers that are expressed in several pancreatic cancer cell lines. These were then shown to exhibit strong mechanically evoked currents in response to membrane stretch, cellular indentation and pillar deflection at the cell-substrate interface.

It was found that when either ELKIN1 or PIEZO1 were knocked-down (KD), cells displayed alterations in their mechanically driven behaviours depending upon the force imposed, rather than an ablation of their response. ELKIN1-KD's for example, increased currents in response to cellular indentation and membrane tension, however currents were reduced when deflected at the cell-substrate interface.

To understand these effects and investigate the influence multiple channel expression has on cellular force sensing, a series of inducible heterologous cell lines were created that express either one or two MA ion channels at similar concentrations. The distinct combination of channels produced diverging impacts on the magnitude of mechanically evoked currents, aligning with and expanding upon what was observed in the pancreatic cancer cell lines. This suggests a complex crosstalk between these force sensors when different MA ion channels are co-expressed in cells that can lead to changes in cellular mechanosensitivity. The data implies that it is essential to understand the molecular interconnectivity between these molecules to predict changes in cell mechanosensitivity of disease states such as pancreatic cancer.

Glassy dynamics in active epithelia emerge from an interplay of mechanochemical feedback and crowding.

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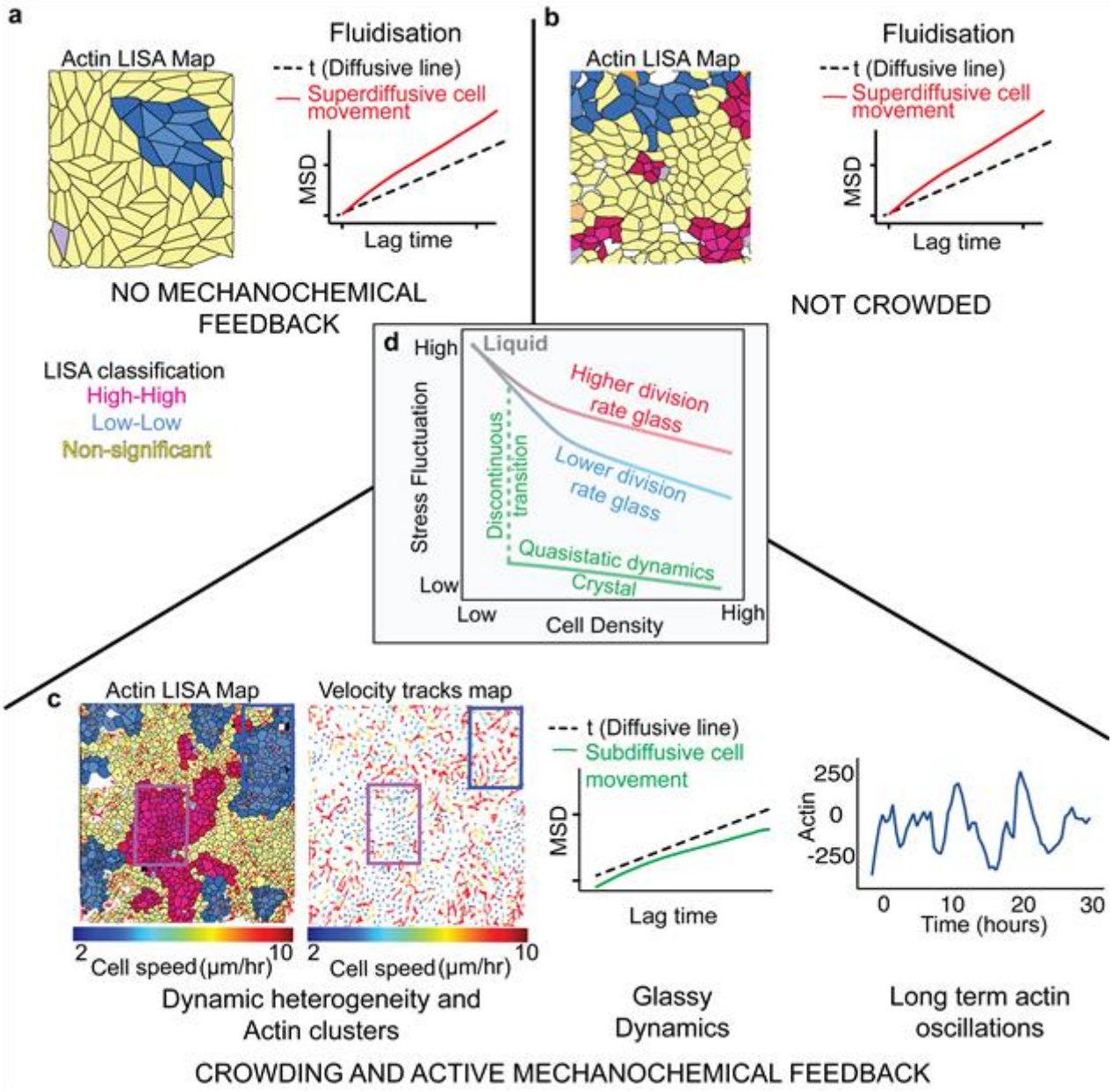
Glassy dynamics in active biological cells remain a subject of debate, as cellular activity rarely slows enough for true glassy features to emerge. In this study, we address this paradox of glassy dynamics in epithelial cells by integrating experimental observations with an active vertex model. We demonstrate that while crowding is essential, it is not sufficient for glassy dynamics to emerge. A mechanochemical feedback loop (MCFL), mediated by cell shape changes through the contractile actomyosin network, is required to drive glass transition in dense epithelial tissues, as revealed via a crosstalk between actin-based cell clustering and dynamic heterogeneity in experiments. Incorporating MCFL into the vertex model reveals contrasting results from those previously predicted by theories- that glassy dynamics can emerge even at high cellular activity if the strength of the MCFL remains high. We show that the MCFL can counteract cell division-induced fluidisation and enable glassy dynamics to emerge through active cell-to-cell communication. Furthermore, our analysis reveals, for the first time, the existence of novel collective mechanochemical oscillations that arise from the crosstalk of two MCFLs. Together, we demonstrate that an interplay between crowding and active mechanochemical feedback enables the emergence of glass-like traits and collective biochemical oscillations in epithelial tissues with active cell-cell contacts.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Time (hours)
Long term actin oscillations
CROWDING AND ACTIVE MECHANOCHEMICAL FEEDBACK

PIEZO2 LOSS PROMOTES COLORECTAL TUMORIGENESIS BY ENHANCING WNT ACTIVITY

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Piezo channels are increasingly recognized as key regulators of epithelial physiology; however, their roles in intestinal epithelial cells (IECs) and gastrointestinal disease remain unclear. Here, we investigated the function of epithelial Piezo2 in gut homeostasis and its contribution to pathology.
Methods: Mice with IEC-specific Piezo2 deletion using the Villin-Cre recombination system were generated and characterized. Models of Inflammatory Bowel Disease (IBD) and Colorectal Cancer (CRC) were assessed, and public RNA-sequencing datasets from CRC patients were analyzed.
Results: Piezo2 was detected in a subset of colonic epithelial cells in mice. Piezo2 deficiency and subsequent reduced expression of Itpr3, did not affect intestinal architecture or barrier integrity, demonstrated by normal histology, preserved epithelial structure, and intact barrier function. Piezo2-deficient mice exhibited a similar disease course compared to controls in dextran sodium sulfate (DSS)-induced colitis (IBD model), with no significant differences in weight loss, endoscopic scores, and histopathological scores. Notably, Piezo2-deficient mice showed increased susceptibility to intestinal tumorigenesis in both colitis-independent CRC (azoxymethane (AOM) model) and colitis-associated CRC (AOM-DSS model), with a higher number and larger size of tumors compared to controls. RNA sequencing analysis revealed activation of Wnt signaling pathway as potential underlying mechanisms in Piezo2-deficient intestine. Consistently, increased levels of non-phosphorylated β-catenin, together with upregulation of Wnt target genes (Sox4, Myc), were observed in Piezo2-deficient tumors. In vitro, intestinal organoids derived from knockout mice exhibited reduced dependence on exogenous Wnt3a-conditioned medium. In humans, PIEZO2 expression was found to be reduced in colon adenocarcinoma and rectal adenocarcinoma compared to normal tissue.
Conclusion: Piezo2 is dispensable for intestinal epithelial integrity under homeostatic and acute inflammatory conditions, but acts as a tumor suppressor in the colon by modulating Wnt/β-catenin signaling. These results identify a novel function of Piezo2 as a mechanosensitive regulator of intestinal tumorigenesis and a potential therapeutic target in CRC.

Inhibiting mechanotransduction as a novel approach for cancer therapy

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Increased tissue stiffness is a hallmark of many solid tumours, driving tumour progression. This occurs through mechanotransduction, the process by which cells sense and respond to mechanical signals. Our lab has identified a key interaction between two proteins, essential for mechanotransduction. This interaction is triggered by force-induced unfolding of a target protein, which occurs only in stiff tissues. Hence, we propose a novel therapeutic approach that targets mechanotransduction by inhibiting the stiffness-induced unfolding of the target protein. This innovative approach provides a new angle to cancer therapy and novel insights into the role of mechanical signals in disease progression. With this aim, we have identified peptide hits that can increase the mechanical stability of the target protein upon binding to it. This in turn inhibits target protein unfolding and subsequent mechanotransduction events important for cancer progression. The peptide hits have been thoroughly validated in various in vitro assays. In cellulo, transient expression of peptide hits in fibroblast decreased focal adhesions (FAs), cell spreading and the nuclear to cytoplasmic ratio (N/C) of the mechanosensitive transcription factor YAP on stiff substrates. Peptide hits had no effect on soft substrates, indicating a specific inhibition of mechanotransduction. Currently, we are expanding the functional characterisation of the biological activity of the peptide hits in fibroblasts and pancreatic cancer cells and in vivo.
Overall, our goal is to demonstrate a clear mode of action of the peptide hits on cancer cells, fibroblasts, and in a pancreatic cancer mouse model. This study will lead to a first-in-class mechanoinhibitor drug like candidate, with potential applications in cancer (with a focus on pancreatic cancer) and other conditions characterized by mechanical stress, such as fibrosis.

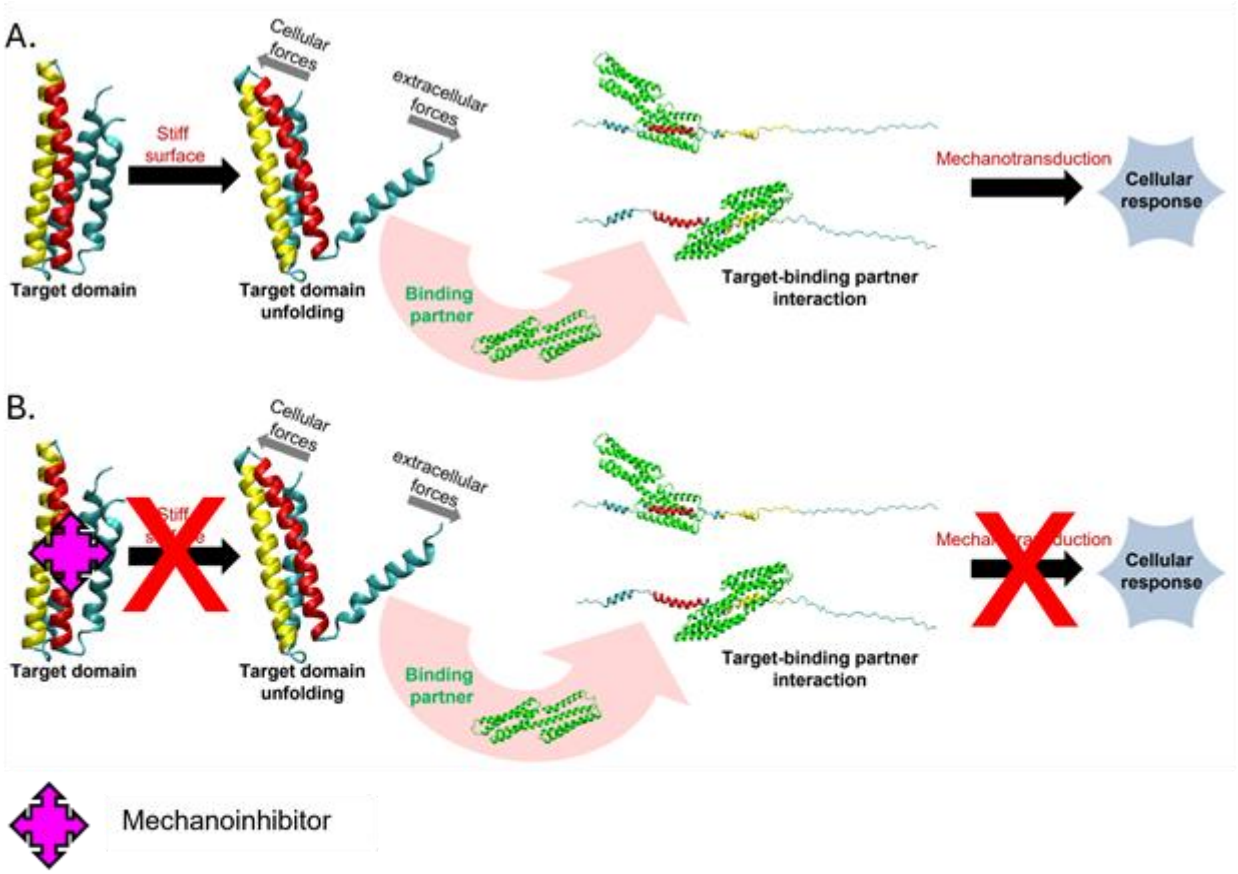

Fig. 1: Schematic of the project concept. **A.** In stiff environment, cells and tissues exert forces that lead to unfolding of the target protein Talin R3 and opening of cryptic binding sites. Binding of Talin to its partner Vinculin leads to a cascade of events in the process called mechanotransduction. Finally, the mechanical cues are transduced into biochemical signals, results in cellular responses that promote tumor progression. **B.** The mechanoinhibitor (magenta inset) bind to the surface of our target, mechanically reinforcing and increases its stability. Subsequently hinders the unfolding of the target blocking mechanotransduction events.

Strain Rate Impacts Biological Properties and Membrane Tension of Cells in Xenopus laevis Epithelia

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Cells within our tissues are constantly subjected to internal and external mechanical forces and must detect and respond to these forces appropriately through the process of mechanotransduction. These mechano-responses play a key role in maintaining tissue homeostasis, morphogenesis, and the prognosis of many common diseases, such as cancer. The exact method by which cells can detect forces is not yet fully understood. Direct detection of changes in the membrane tension has provided one potential mechanism for sensing forces applied to a tissue. Moreover, membrane tension shown to be involved in regulating processes such as cell fate determination and cell migration. In this work, we demonstrated that the downstream responses of cells to a force of the same magnitude can be influenced by the rate at which that force has been applied. For instance, fast stretches are associated with the promotion of mitotic entry and the alignment of the mitotic spindle with the axis of stretch. Interestingly, we found that following a slow stretch, there was no increase in the proportion of cells entering mitosis, whereas the mitotic spindles still aligned with the axis of stretch. A vertex model-based analysis pipeline was used to quantify differences in the physical and geometric properties of cells and tissues following different strain rates. To test the possibility that directly detecting changes in membrane tension may regulate the mechanoresponse of tissues under different strain rates, we developed a protocol using the fluorescent membrane tension probe, Flipper-TR, to quantify membrane tension in tissues subjected to different rates of stretch. This has revealed differences in the ways membrane tension adapts in response to the application of fast or slow stretch. Flipper-TR was also used to detect increase in membrane tension of cells in tissues after treatment with MβCD and the induced expression of constitutively active ezrin.

Subcellular viscoelasticity and dynamic force generation quantified with optical tweezers

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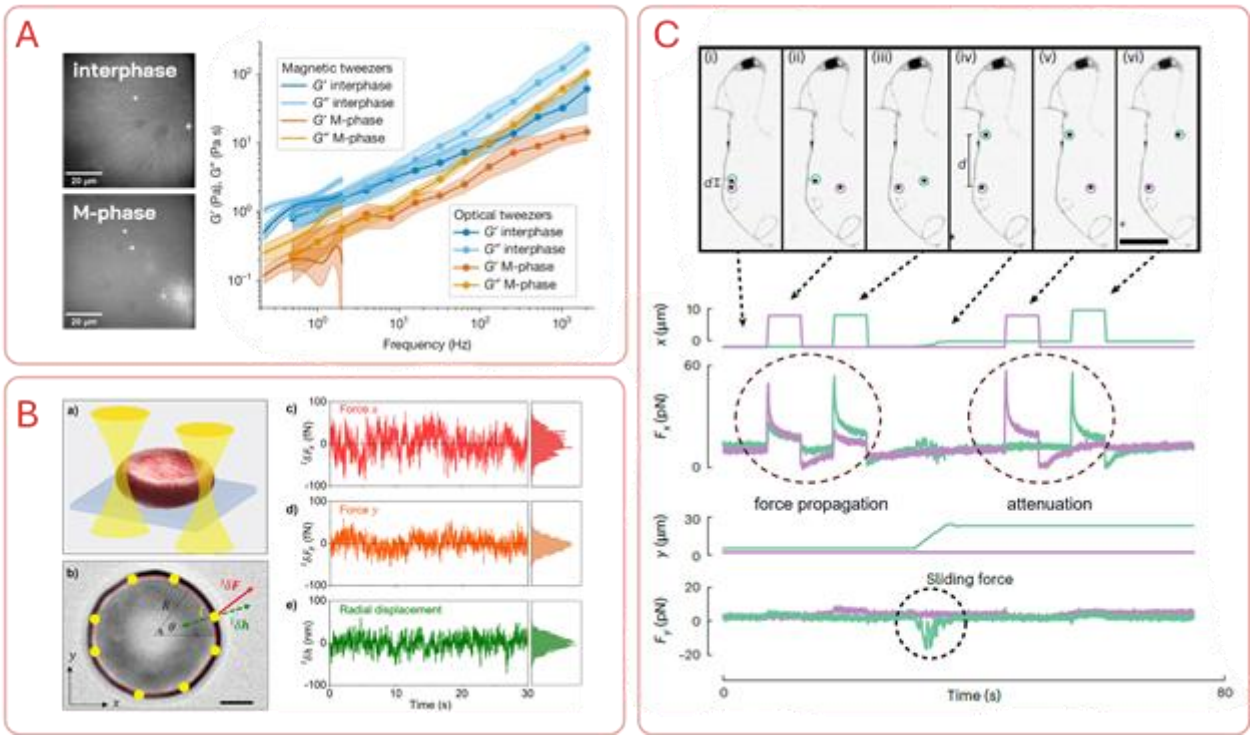
Mechanical forces sculpt cells and tissues, regulate migration and intracellular transport, organize subcellular architecture, and provide cues for mechanoresponsive and behavioral processes. Different parts of the cell therefore display distinct mechanical signatures that are dynamically modulated across space and time during cell physiological processes. For example, cytoplasmic viscoelasticity is mechanically coupled to cytoskeletal scaffolding for cell and nucleus integrity, but is downregulated during the mitotic phase to allow chromosome segregation (Fig. 1A, Brugués Lab, DOI:10.1038/s41586-025-09915-x). While the membranecortex shapes the outer scaffold of the cell, membrane flickering enables active remodeling of red blood cells,allowing them to adapt to extreme confinement (Fig. 1B,Monroy Lab, DOI: 10.1002/advs.202514778). Similarly, the actin–spectrin cortex underlying axonal membranesprecisely tunes the range of membrane tension propagation, supporting the function of neuronalproprioceptors and mechanosensors. (Fig. 1C, Krieg Lab,DOI: 10.1038/s41567-025-03037-x). Together, these examples illustrate how subcellular materials —plasmamembrane, cortex, filament networks, and chromatin—respond to mechanical stress through regulated viscoelasticity, active force generation, and energy dissipation. In this talk, we will review how optical force spectroscopy can reveal the physics behind these examples using SENSOCELL, our multi-trap optical tweezers platform.



Actin crosslinking regulates cortical mechanics and cell polarity in a length-dependent manner

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The dynamic regulation of both the mechanics and structure of actin networks is critical to drive cellular shape changes during migration, division, or differentiation. Actin crosslinking is essential to this interplay as it controls actin network architecture and thus the transmission of contractile forces. In vitro and in silico studies have shown that crosslinker length and concentration endow actin networks with diverse mechanical properties. However, how cells employ crosslinkers in a physiological context remains unclear.
To address this fundamental gap in knowledge, we have designed optogenetic actin crosslinkers of three different lengths similar to physiological crosslinkers - 4nm (fascin), 8nm (fimbrin), and 28nm (alpha-actinin) - and assessed their impact on cell mechanics and polarity. We observed that fast, global activation of short and mid-length crosslinkers at high density triggers frequent cortical actin delamination. To investigate the mechanical effects of actin crosslinking with high spatio-temporal resolution, we used magnetic pincher experiments to measure cortical rheology and thickness. We found that fast, global activation of short and mid-length crosslinkers increases cortical linearity, stiffness, and thickness in a density and myosin-dependent manner. Moreover, short crosslinkers promote actin recruitment while mid-length crosslinkers strongly increase phospho-myosin.
Next, we explored longer timescales of cell motility and uncovered that low-frequency, global activation of long crosslinkers triggers cortical actin polarization. This effect is observed at low and high densities and depends on myosin activity. On the other hand, short and mid-length crosslinkers lead to actin delamination only at high density. Notably, low doses of Latrunculin B favour cortical polarization instead of actin delamination for mid-length crosslinkers, suggesting that actin connectivity regulates the length threshold for polarization. Finally, we observed that cortical polarization driven by long crosslinkers can direct cell spreading. Overall, crosslinker length and density act synergistically to regulate surface mechanics and promote symmetry breaking over different timescales.

Active tissue rupture of Epithelia is governed by nanoscale regulation of Cell-ECM interaction

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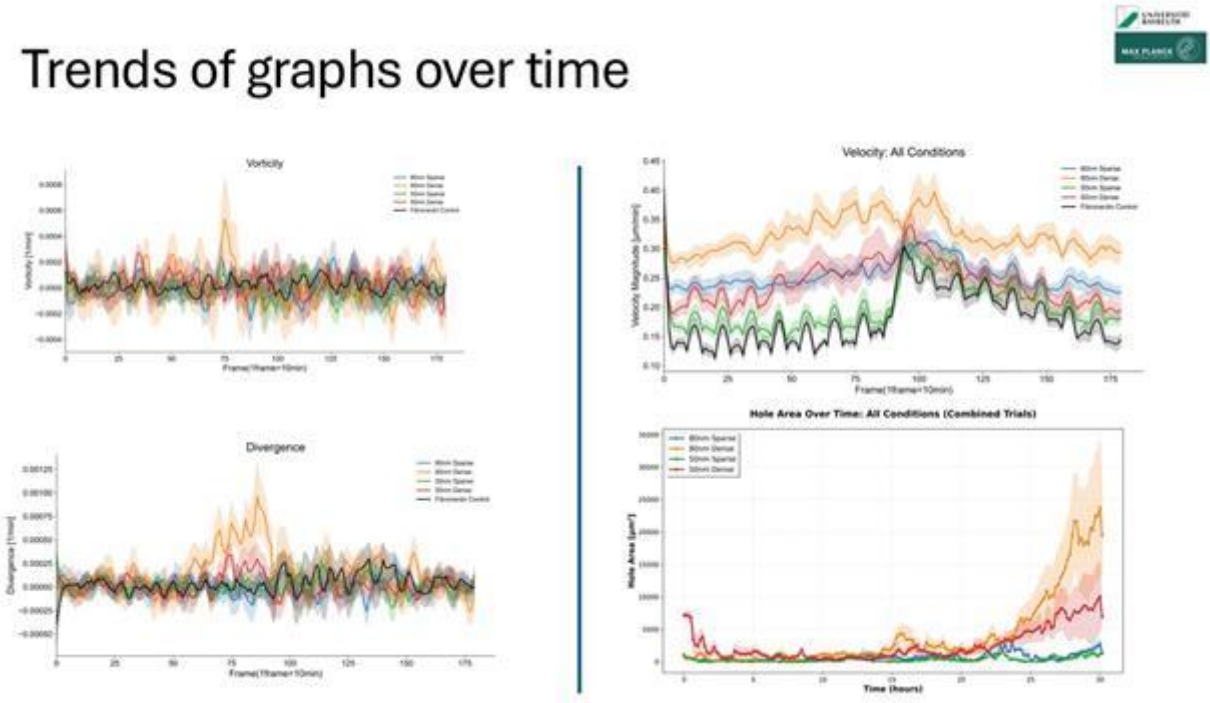
Epithelial monolayers serve as barriers to many organs against everyday environmental stress. The molecular and mechanical properties that regulate the integrity of monolayers are not well understood. The environment surrounding epithelia is one of the key contributors to the properties of the monolayer. Extracellular matrix (ECM) varies dramatically during normal physiological and pathological conditions such as ECM- Remodelling, morphogenesis, cancer progression, fibrosis and aging. To mimic these variabilities in the ECM, we use Nano-Patterned surfaces with lateral integral spacing varying from 50nm, close to normal physiological condition to 80nm, 100nm and 150 nm which pushes it beyond its normal regime. With increase in the spacing, the migration velocity of the monolayer is higher. This is consistent with the actin clutch engagement between the cell and the substrate. Extrapolating the velocity data to derive divergence and vorticity we observe sharp peaks in monolayer before the ruptures. The peaks reflect collective increase in turbulent motion and accumulation of tensile stress. After decrease in the peak, we observe rapid and consistent formation and propagation of holes through the monolayer. Blebbistatin which inhibits actomyosin contractility strongly suppresses the formation of holes indicating that it is driven by cell contractility rather than passive failure in mechanical properties of monolayers. We further observe pronounced focal adhesions few hours after the formation of a hole supporting active cytoskeleton in these areas. Hole formation is not observed in fibronectin control which provides abundant adhesion protein. These findings show that active tissue rupture of epithelia is governed by nanoscale regulation of cell-ECM interactions.



Matrix Stiffness-Dependent Drug Target Engagement in 3D Colorectal Cancer Models

Karim Osouli[1], Hammed A. Badmos[1], Ross Cagan[1], Massimo Vassalli[2]
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Extracellular matrix (ECM) stiffness is a key regulator of tumor behavior, yet its impact on drug–target interactions in three-dimensional (3D) cancer models remains insufficiently understood. In this study, we investigate how ECM stiffness modulates drug binding and therapeutic response in 3D colorectal cancer (CRC) systems.

We engineered a series of tunable 3D matrices using defined combinations of gelatin and sodium alginate to recapitulate a physiologically relevant range of ECM stiffness. These bioengineered platforms enable systematic control of mechanical properties while maintaining a supportive environment for tumor spheroid formation. Preliminary data demonstrate that variations in matrix stiffness significantly influence the morphology, growth dynamics, and structural organization of SW620-derived 3D spheroids.

To quantitatively map the mechanical landscape of these models, we'll employ Brillouin microscopy for non-invasive, high-resolution assessment of stiffness and viscoelastic heterogeneity in both cell-free and cell-laden constructs. Drug target engagement is evaluated using luminescent reporter systems (SW620-BRAF-Nluc and SW620-MEK1-Nluc), enabling direct correlation between ECM mechanics and drug binding efficiency.

By integrating mechanical characterization with biological readouts, including cell viability, spheroid architecture, and mechanotransduction signaling, we aim to elucidate how stiffness-driven changes in the tumor microenvironment influence drug accessibility and efficacy. Ongoing work extends these findings to patient-derived organoids to enhance translational relevance.

This study will establish a mechanistically grounded platform to dissect the role of ECM stiffness in regulating drug–target interactions, providing insights that may improve the predictive power of 3D cancer models and inform more effective therapeutic strategies.

Harnessing Geometry to Drive Scaffold Cellularisation

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Introduction

Cells respond to the complex shapes of their surroundings, transducing physical stimuli into biochemical responses (1). In vitro, designed, cell-scale 2.5D concave curvatures have been shown to drive curvotaxis, a cell migration response to shape (2), but this phenomenon has not been translated into 3D biomaterial design. Here, we screen a range of cell-scale, 3D porous shapes in vitro for ability to stimulate mesenchymal stromal cell (MSC) curvotaxis. The optimal design is then tessellated into a 3D scaffold for further in vitro analysis before implantation subcutaneously to validate in vivo.

Methods

Using multi-photon polymerisation (MPP), arrays of 100 µm diameter, wireframe mathematical solids with defined 3D geometries were fabricated. Quantitative confocal microscopy identified designs that promoted cell infiltration. The optimum candidate (DesignX) was tessellated into scaffolds, assessing cell ingrowth in larger constructs. Subcutaneous implantation in rats allowed histological assessment (days 7, 28).

Results

Across different synthetic polymers, DesignX demonstrated significantly greater MSC infiltration. When tessellated into scaffolds, influence on cell infiltration was conserved, with DesignX demonstrating greater cellularisation across the full thickness of the scaffold than control architectures. When implanted subcutaneously, it demonstrated superior cell infiltration to MEDPOR membranes at day 7, with new blood vessel formation within and around the implant evident by day 28.

Discussion

The latest additive manufacturing technologies can precisely control the geometry of a cells 3D environment, mediating cell's mechanobiological responses both in vitro and in vivo. This paves the way to using bioinstructive shapes to achieve other desirable cell responses in tissue engineering, reducing reliance on biochemical factors to achieve efficacy.

Acknowledgements

We acknowledge funding from the MRC (MR/R015651/1) and EPSRC (EP/X525765/1). RO thanks the University of Nottingham for the award of his Nottingham Research Fellowship.

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Biomimetic lung tumor model reveals ligand-dependent opposing effects of stiffness in disease progression

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Lung cancer is the leading cause of cancer mortality with poor prognosis, drug resistance and high risk of relapse. The tumor microenvironment including tumor-specific extracellular matrix (ECM) and a heterogenous cast of different cell types interacting with tumor cells constitutes a vital regulator of disease progression. There is a high need for human in vitro models which biomimic the complexity of tumor ECM for a better understanding of disease-governing phenomena and development of effective therapeutic strategies. ECM stiffening has been an established hallmark for tumors with roles in tumorigenesis, epithelial-mesenchymal transition (EMT), metastasis and drug responses. Tissue stiffness has been proposed as a risk factor for tumorigenesis. In this work, we investigated the role of ECM composition on the effect of tissue stiffening on tumor cells. We decellularized native lung tissues to obtain reconstituted organotypic ECM hydrogels. We then fabricated mechanically tunable double-network hydrogels of alginate with either decellularized native lung ECM (dLung) or tumor-derived reconstituted basement membrane (rBM). Mechanical characterizations were performed with shear rheology to obtain soft (G': 0.5 kPa) and stiff (G': 5 kPa) hydrogels. We encapsulated lung tumor cells in the hydrogels and assessed proliferation, morphology, invasiveness and therapeutic responses. Within tumorigenic ECM composition, increase in stiffness promptly induced tumor cell growth, EMT, and invasion. Conversely, within organotypic, healthy ECM composition, stiffness alone suppressed tumorigenic growth, EMT and invasive phenotype. We then performed comprehensive analyses such as small molecule inhibitor screens, gain-of-function/loss-of-function validations to dissect the underlying signaling mechanisms involved in the observed phenomena. We performed phospho-proteome screening, RNA sequencing and integrative network construction to reveal key intermediates in the relevant signaling routes and predict context-specific therapeutic targets. Our work demonstrates that stiffening synergizes with tumorigenic ECM composition in order to regulate tumor growth and progression whereas stiffening in a healthy microenvironment acts in complete opposition.

Oil Droplets as Tunable Nanoindenters for FluidFM-based Cell Mechanics

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Atomic force microscopy (AFM) indentation techniques have advanced the mechanical characterization of living cells. However, classical AFM indentation presents limitations, including difficulty in rapidly changing indenters and limited flexibility in adjusting indenter geometry. FluidFM, an AFM technique based on hollow cantilevers, partially addressed these issues by enabling reversible capture of spherical beads for indentation. Nevertheless, bead capture remains tedious and time-consuming.

In this study, we propose and characterize an approach leveraging FluidFM's existing capability to generate spherical oil droplets, employing them for the first time as mechanical indenters and removing the necessity for manual bead handling.

For indentation-based mechanical assessments, precise knowledge of indenter geometry is essential, alongside understanding interactions between the indenter and the cell during contact. To accurately control and characterize oil droplet geometry and size in real time, we implement a self-excited cantilever strategy. The cantilever is maintained in resonance via a feedback loop that tracks frequency variations induced by changes in droplet size. The self-excitation and control architecture is implemented on a Red Pitaya FPGA-based system, which applies amplitude correction and signal saturation to ensure stable oscillation. In parallel, a PID controller regulates overpressure in the cantilever channel using resonance frequency as feedback. By adjusting the applied pressure to maintain a predefined frequency shift relative to baseline, the system dynamically stabilizes droplet size during experiments.

Using oil droplets as dynamic indenters offers multiple advantages: automatic droplet creation, rapid size tuning for adjustable measurement resolution, and soft, deformable probes that more closely mimic biological materials' properties, providing gentler, more physiologically relevant indentations similar to biomembrane force probes.

By comparing our experimental data with established contact mechanics models, we aim to develop a robust, versatile platform to advance cellular mechanics studies.

BAF mobility tunes nuclear mechanics to enable confined invasion in glioblastoma

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Glioblastoma (GBM) is the most common and aggressive primary brain tumours in adults, characterized by extensive invasion, high cell heterogeneity and pronounced cellular plasticity. Invasive GBM cells are exposed to substantial mechanical forces, as they need traverse a biomechanically challenging microenvironment, shaped by elevated intracranial and intratumoural pressures, and spatial confinement through a dense extracellular microenvironment. How these biomechanical stresses influence invasion, how cells adapt to such constraints, and whether these adaptations ultimately drive tumour aggressiveness remain unclear. To investigate this, we first showed that GBM nuclei experience pervasive biomechanical stress in patient tissue and GBM cell lines, manifested by nuclear dysmorphia and frequent loss of nuclear envelope (NE) integrity. Using a panel of GBM cell lines, we showed a link between nuclear morphology, nuclear fragility and mechano-resilience. The ability of cancer cells to withstand mechanical force strongly correlated with their invasive capacity in a 3D collagen matrix, connecting mechanical resilience to tumour aggressiveness. Through proximity proteomics, we identified an NE-associated mechano-regulatory hub selectively enriched in invasive GBM cells, consisting of lamin A/C, Leucine-Rich Repeat-Containing protein 59 (LRRC59), and the BAF-targeting Vaccinia-Related Kinase 2 (VRK2). This mechano-adaptative module converged on barrier-to-autointegration factor (BAF), a critical chromatin-NE tether and first responder to NE rupture. Consistent with this, perturbation of these regulators or complementary disruption of BAF function altered BAF mobility, increased nuclear stiffness, and abolished 3D invasion of GBM cells. Collectively, these findings demonstrate that precise control of BAF dynamics at the NE-chromatin interface is essential for the transient nuclear deformations required for confined migration. Our work uncovers an NE-centric mechano-adaptive protein hub that is required for GBM invasion and reveals a selective vulnerability that could be exploited to curb GBM invasiveness.

Physiological and Spatiotemporal Imaging of Mechanically Induced Calcium Signaling in Epithelial Monolayers

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Mechanotransduction, the process where mechanical signals are transduced into biochemical activity, is fundamental to cellular function. Accordingly, altered mechanosignaling has been shown to be involved in the development various diseases, including cancer. A range of methods have been developed to study cellular responses to mechanical stimuli, e.g., micropillars, stretching devices, or deformable hydrogels. However, achieving physiologically relevant, precise mechanical manipulation together with near-simultaneous high-resolution live imaging remains challenging.
Here, we present an approach that integrates light-responsive azobenzene-based Disperse-Red 1 -glass (DR1-glass) with a polyacrylamide (PAA) hydrogel with tunable mechanical properties. DR1-glass can be spin-coated as thin films on glass coverslips. Upon illumination with 488 nm laser, photoisomerization of the azo molecules is transduced into material movement. This material movement is regulated by the polarization and intensity of stimulation light, the number of light stimulation repetitions, and angle of the laser beam.
We found that polymerizing a thin (~10 µm) PAA hydrogel on top of the DR1 layer leads to strong adhesion between the hydrogel and the DR1 surface. Using gel-embedded fluorescent beads (Ø0.2 µm), we demonstrate that photoinduced movement of DR1 propagates through the hydrogel to adherent epithelial cells, producing micrometer-scale deformations (up to ~2 µm) at the basal cell interface. When combined with genetically encoded calcium indicators, this platform enables near real-time imaging of cellular responses to localized, non-invasive, and controlled mechanical stimulation. This platform thus provides a unique tool for studying mechanotransduction in physiologically relevant environments while remaining compatible with live cell imaging.

High Throughput Mechanical Phenotyping of Nanovibrated Mesenchymal Stem Cells

Rui Pedro Pereira Sousa[1], Stuart Reid[1], Matthew J. Dalby[2], Melanie Jimenez[1], Peter G. Childs[1]
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Vibrational stimulation is being increasing explored for cell and tissue engineering, as a method of initiating mechanotransduction. Some studies focus on nanovibration, characterised as sinusoidal, kilohertz frequency, 30 nm amplitude motion. This parameter combination has shown the potential to osteogenically drive the differentiation of mesenchymal stem cells (MSCs). The mechanical stimulation of these cells raises the question of how their mechanical phenotype changes when stimulated. So far attempts to answer this question have employed low throughput techniques such as atomic force microscopy. Here, Real-Time Deformability Cytometry (RT-DC) was employed to understand the population shifts of mechanically stimulated MSCs and the changes associated with their differentiation commitment. Initial RT-DC optimisation was performed using the MG63 osteoblastic model, demonstrating a shift in the mechanical phenotype of the cells. MSCs from three different donors were cultured and testing following the previously established protocols. RNA sequencing was performed to confirm cell lineage commitment in tandem with RT-DC to establish correlations in trends between the two. Results presented a change in mechanical properties of the MSCs between days 7-28. Significantly a progressive correlation between cell deformability and time in culture was established. RNA sequencing results demonstrated that nanovibrated cells presented a weaker osteogenic transcript profile than the positive control, osteogenic media. However, the regular osteogenic media showed less specificity in commitment with upregulation of both osteogenic markers and chondrogenic markers such as SOX5/6 and COMP. Furthermore, less explored molecules such as MALAT1 have shown a significant increase across all mechanically stimulated donors. These findings importantly show the mechanical differences between control, nanovibrated and chemically differentiated cells with RT-DC detecting shifts as early as day 3. Consistent upregulation of MALAT1 across vibrationally stimulated donors also highlights a potential which could bypass issues around variable expression of traditional osteogenic markers between donors.

Self-organized mechanical gradients coordinate tumor cell-state patterning

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Tumor heterogeneity - the coexistence of multiple phenotypic cell states within a single tumor - cooperatively drives growth, metastasis, therapy resistance, and relapse. This heterogeneity is commonly attributed to genetic mutations or microenvironmental cues. In contrast, the role of intrinsic mechanical interactions between cancer cells remains poorly understood. Here, we show that cancer cells follow self-organized programs that are sufficient to coordinate the spatiotemporal patterning of tumor cell states. By combining quantitative measurements in tumors and organoids with theoretical modeling, we identify emergent mechanical gradients that orchestrate state transitions during tumor growth. Compression at the tumor center induces a transition from a fetal-like state into a cancer stem cell (CSC) state. The CSC compartment exhibits a characteristic size determined by tumor rheological properties. Once this size is surpassed, a translationally arrested apoptotic core emerges, triggering a shift from homogeneous proliferation to a hierarchical cell turnover. These findings establish mechanochemical self-organization as a novel principle coordinating tumor heterogeneity and plasticity.

Mechanosensation regulates myeloid cell function

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E-Poster Session Tuesday lunch, July 14, 2026, 13:00 - 13:50

Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system characterized by increases in tissue stiffness. To model this mechanical change in vitro, we established a tunable 3D-collagen hydrogel system and investigated its effects on myeloid cell polarization. Specifically, we differentiated HoxB8FL cells, a hematopoietic progenitor cell line into pro-inflammatory and anti-inflammatory macrophages within the 3D culture system. We found that increasing stiffness promotes pro-inflammatory myeloid phenotypes, indicating that mechanical cues contribute to myeloid polarization fate.
To further characterize the stiffness-dependent transcriptional response, we performed bulk RNA sequencing across multiple stiffness conditions. Transcriptomic analysis identified genes previously described in macrophage mechanosensing and transduction, validating our experimental setup. We additionally curated gene sets reflecting either gradual stiffness-dependent changes or threshold responses to specific stiffness conditions. Preliminary pathway analysis revealed key signaling networks influenced by tissue stiffness. These gene signatures, together with literature review candidates, will inform an upcoming pooled CRISPR/Cas9 knockout screen using HoxB8FL cells to determine key regulators of mechanosensing and stiffness-response in myeloid cells. To contextualize our findings within neuroinflammation, we will leverage human and murine datasets to determine their translational relevance.

Effect of Strain Rate on Nuclear Mechanics and Cell Division in Epithelial Tissues

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E-Poster Session Tuesday Evening, July 14, 2026, 17:50 - 18:30

Cells can sense and respond to mechanical forces in their environment, regulating various cell behaviours such as cell division, adhesion and migration. Mechanical forces are known to upregulate cell division by promoting cell cycle progression and mitotic entry. Recent works revealed that this could occur through force-induced nuclear deformation. However, majority of these studies predispose the cells to relatively fast strain rates that do not reflect the slower mechanical deformations typically experienced by tissues in vivo. Here, we investigate how strain rates affect nuclear deformation and cell division. By stretching Xenopus laevis animal cap epithelial tissues at defined strain rates, we find that fast strain promotes nuclear deformation and upregulate mitotic entry, whereas slow strain does not induce nuclear deformation nor increase mitotic entry. To further examine how strain rate influences cell cycle progression, we used fluorescence ubiquitination-based cell cycle (FUCCI) reporter to monitor cell cycle dynamics in living tissues. To probe the mechanotransduction pathway underlying this response, we performed a knockdown of Nesprin-2, a component of the LINC complex that mechanically couples the cytoskeleton to the nucleus. Knockdown of Nesprin-2 disrupts the ability of nuclei to deform accordingly to mechanical stretch and reduces the mitotic response to strain. Together, these findings highlight strain rate as an important parameter in the mechanoregulation of cell division and support a role for nuclear deformation as a mechanosensitive event. Additionally, we developed a scalable, cost-effective mechanical stretcher using LEGO components to apply stretch to cells and tissues at varying strain rates, offering tunability and broad applicability across diverse biological systems.

Ultrasound-augmented osteochondral regeneration in spatially graded porous scaffolds

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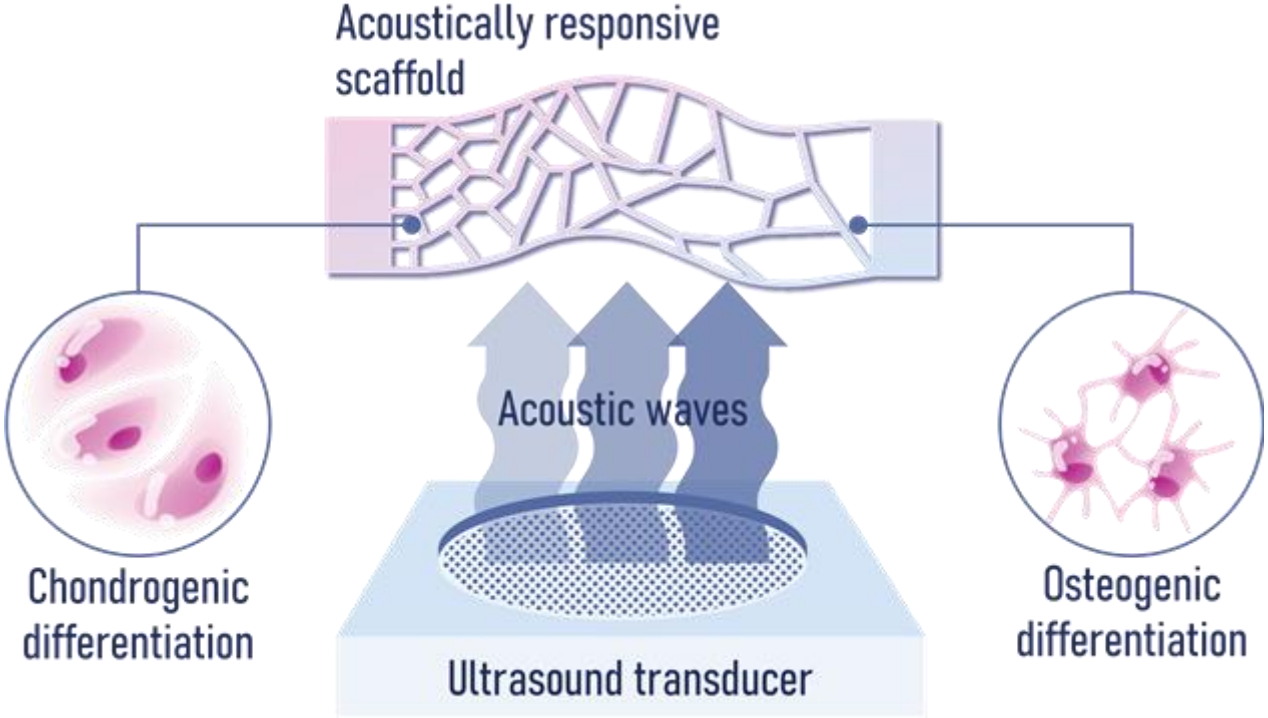
E-Poster Session Wednesday Lunch, July 15, 2026, 13:00 - 13:50

Three-dimensional scaffolds are commonly used to support cell growth and trigger differentiation for tissue engineering and regeneration. Varying the size and shape of pores in cell-seeded scaffolds, it is possible to influence the expression of markers typically associated with osteogenic or chondrogenic differentiation. However, structural cues alone are often not sufficient to induce clear and prominent cell lineage commitment. Ultrasound (US)-based systems may serve as external stimuli influencing cell behaviour and differentiation on the scaffolds and offering tuneable input with potential biological effects adjusted through frequency, intensity, duty cycle and other relevant parameters. However, acoustic stimulation, widely used in clinics for musculoskeletal regeneration and healing, is rarely investigated in the context of 3D scaffolds mediating ultrasound effects on cells in vitro.
In our study we aim to subject cell-seeded polymer scaffolds with pore size gradients to ultrasound stimulation. Scaffolds were designed to maximize potential mechanical stimulation arising from the ultrasound application by covering most of the transducers' effective area and, at the same time, maintaining a minimal thickness. Experimental setups with different acoustic parameters, namely 40kHz custom-built US setup and 1.5 MHz US clinical device, were used to stimulate designed scaffolds. By accessing the main differentiation markers expression at relevant time points we can assume the effect of pore size and US stimulation modality on human mesenchymal stem cells. Investigation of proliferation, which is reported to be influenced by clinically used 1.5 MHz pulsed ultrasound, is relevant in the context of differentiation and overall cellular activity. Moreover, to get a more informative overview and make assumptions on the origin of the effects observed, more in-depth methods including kinases profiling has been applied. Overall, our study aims to observe if mechanical and morphological cues can act together to enhance lineage specific differentiation.



Seeing Forces in Flow: Label-Free 3D TFM of Endothelial Remodeling in Perfused Microvessels

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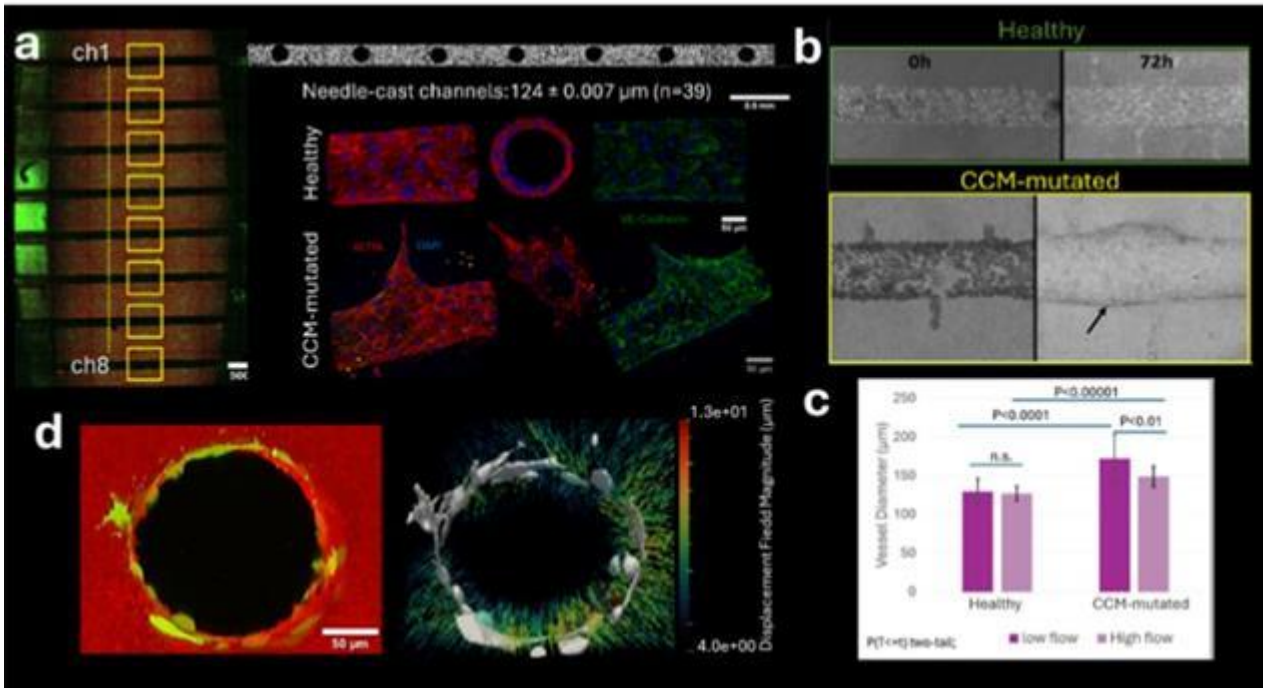
Hemodynamic forces and extracellular matrix (ECM) interactions play essential roles in regulating endothelial behavior and maintaining vascular stability during remodeling. Although endothelial responses to wall shear stress (WSS) are well characterized, how endothelial cells actively transmit forces into a three-dimensional ECM under continuous perfusion remains poorly understood, particularly in the context of vascular remodeling and disease.

Here, we introduce a novel three-dimensional traction force microscopy-integrated vessel-on-chip (3DTFM-VOC) platform that enables direct, label-free quantification of endothelial force transmission in perfused microvessels. The system consists of parallel, perfusable cylindrical microchannels (120 µm diameter) embedded within collagen hydrogels and lined with human brain microvascular endothelial cells, including CCM2-silenced cells, to model cerebral cavernous malformations (CCM)-on-a-chip. ECM deformations were visualized using confocal reflectance microscopy, allowing direct measurement of collagen fiber displacement without embedded tracer particles. Continuous perfusion at low and high WSS (0.1–1 Pa) was maintained for up to 72 hours to recapitulate physiological flow conditions. Stable flow distribution across channels was confirmed using confocal µPIV, and matrix stability analysis throughout perfusion verified that displacement measurements were not influenced by bulk hydrogel motion.

Using this approach, we mapped three-dimensional matrix displacements generated by endothelial cells over time. Endothelial forces produced stable, radially inward displacement fields surrounding the vessel lumen that decayed with distance from the wall. In contrast, CCM2-deficient vessels displayed enhanced angiogenic sprouting and vessel dilation, accompanied by localized amplification of collagen displacements at sprout tips, indicating spatially heterogeneous force transmission during pathological remodeling.

Overall, this work establishes the 3DTFM-VOC platform as a robust tool for quantifying endothelial mechanobiology under physiologically relevant flow conditions. These findings provide new insight into how endothelial force transmission contributes to vascular remodeling in both healthy and diseased states and highlight the relevance of this approach for studying cerebrovascular pathologies such as CCM.


a
ch1
ch8
Needle-cast channels:124 ± 0.007 µm (n=39)
Healthy
CCM-mutated
b
Healthy
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72h
CCM-mutated
c
P<0.00001
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Vessel Diameter (µm)
250
200
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Healthy
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P(T<=t) two-tail
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Displacement Fiedd Magnitude (µm)

Investigating the Interplay of Cell and Extracellular Matrix Mechanics in driving the Pathology in Hypermobile Ehlers-Danlos Syndrome

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Hypermobile Ehlers-Danlos Syndrome (hEDS) is characterized by generalized joint hypermobility with extensive multisystem involvement including chronic pain. Unlike classical EDS subtypes with primary collagen biosynthetic defects, hEDS exhibits pro-inflammatory myofibroblast activation and matrix degradation, yet lacks clearly defined genetic markers. A critical unresolved question is whether altered cellular mechanosensing drives pathogenesis or results from extracellular matrix (ECM) disruption. Fibroblasts interact with ECM through integrin-mediated focal adhesions where force generation and mechanosensing occur. In hEDS, loss of α2β1 integrin and compensatory upregulation of αvβ3 integrin fundamentally alters mechanosignalling and force generation at cell-matrix adhesions, driving differential ECM remodelling and myofibroblast differentiation through the αvβ3-ILK-Snail1 signalling. We employed two-dimensional traction force microscopy on collagen I-coated polyacrylamide gels to generate spatiotemporal force maps of fibroblasts. Preliminary findings reveal that hEDS fibroblasts generate significantly elevated traction forces compared to control cells, suggesting compensatory hypercontractility in response to impaired α2β1-mediated adhesion. Collagen gel contraction assays confirm this enhanced contractility is maintained in bulk. Future reciprocal ECM-swapping experiments (control cells on hEDS-derived ECM; hEDS cells on control-derived ECM) will reveal whether elevated traction represents cell-intrinsic defects or adaptive responses to pathological matrix composition. In connection with these experiments, we perform computational phase field modelling to predict emergent behaviours from cellular interactions. The model couples force-dependent integrin binding kinetics with actin polymerization, myosin contractility, and spatial-temporal focal adhesion dynamics. By integrating ILK-Snail1 signalling, MMP secretion-diffusion, and ECM degradation feedback loops, the phase field approach captures how local traction forces and matrix mechanics co-evolve. Parameter fitting to experimental traction data will reveal which molecular processes are rate-limiting, guiding targeted experimental perturbations through in silico screening. Future atomic force microscopy will quantify temporal matrix stiffness evolution as cells remodel substrates, determining whether hEDS fibroblasts progressively stiffen or soften their pericellular matrix, validating model predictions of mechanical feedback driving pathology.

Mechanotransduction-driven neural differentiation on elastic and auxetic 4D microenvironments fabricated via multiphoton lithography

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E-Poster Session Wednesday Lunch, July 15, 2026, 13:00 - 13:50

Mechanical cues critically regulate neural stem cell (NSC) fate through mechanotransduction pathways. However, elucidating the individual contributions of scaffold elasticity and auxeticity remains challenging due to their frequent coupling with architectural variations. Here, we present precisely engineered three-dimensional microstructured platforms fabricated via multiphoton lithography (MPL) that decouple mechanical parameters while preserving identical geometry and porosity. These microenvironments function as mechanically responsive 4D systems.

Three scaffold types were fabricated: auxetic elastic, non-auxetic elastic, and stiff controls. Mouse neuroectodermal stem cells (NE-4C) were cultured for up to 20 days under proliferation conditions, starvation-induced differentiation, and retinoic acid (RA)-driven differentiation. Elastic microenvironments exhibited pronounced cell-driven deformation, with auxetic scaffolds contracting inward and non-auxetic elastic scaffolds expanding outward, consistent with their intrinsic Poisson's ratio. Scanning electron microscopy revealed that deformation modes under cell-generated forces closely matched those identified through conventional compression testing, linking mechanical characterization with biologically relevant loading conditions. Neuronal differentiation, assessed by Tuj-1 expression, was significantly enhanced on elastic scaffolds compared to stiff controls, revealing elasticity-dependent differentiation trends with an auxetic-specific enhancement. Increased Tuj-1 expression was also observed under proliferation conditions without differentiation medium, indicating mechanically driven spontaneous neuronal differentiation. Under starvation-induced differentiation, elastic scaffolds maintained enhanced neuronal commitment, whereas RA treatment induced robust differentiation across all scaffold types, masking elasticity-dependent mechanotransduction effects. YAP-associated responses appear to correlate with these differentiation trends. Together, these findings demonstrate that scaffold elasticity is a dominant regulator of neuronal fate, with auxeticity providing an additional mechanotransductive advantage. MPL-fabricated elastic and auxetic 4D microenvironments offer a powerful platform to dissect mechanically driven neurogenesis independent of biochemical cues. In injury contexts where soluble differentiation signals are limited, early substrate-derived mechanical cues may play a decisive role, highlighting the potential of auxetic microarchitectures for neural repair strategies.

Nanovibrational stimulation for mesenchymal stromal cell osteogenesis: investigating the relationship between osteogenesis and inflammation

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Bone anomalies pose a global burden, emphasizing the need for improved understanding of bone biomechanics, pathophysiology, and regenerative strategies. Conventional bone tissue engineering relies on exogenous agents, such as growth factors (BMP2) and corticosteroids (dexamethasone), to promote osteogenesis, but these have limitations, including poor differentiation specificity and side effects. We developed a nanovibrational bioreactor capable of inducing mesenchymal stem cell (MSC) osteogenesis using 30 nm amplitude, 1 kHz stimulation (NK30) without chemical supplementation. Therefore, we investigate the effects of high-amplitude nanovibration (100 nm, NK100, 1 kHz) compared with NK30 on MSC osteogenesis, redox balance, and inflammatory pathways. To address this, human bone marrow-derived primary MSCs (hBMSCs) were cultured at NK30 and NK100 with osteogenic media (OGM), basal control, and stress conditions (10 μM TBHP, 0.1 μM Doxorubicin) for 4 and 6 weeks. In-cell western was performed to quantify phospho-p38/p38 ratio, osteopontin (OPN), and osteocalcin (OCN) protein expression. Late-stage matrix mineralization was determined by Von Kossa staining. Flow cytometry was used to analyse total ROS production, while in-cell western assessed protein expression of glutathione reductase (GSR), superoxide dismutase 1 (SOD1), and catalase. DNA damage was determined based on ϒH2AX-foci count using immunostaining. Secretory profiling of inflammatory cytokines (IL-6, TNF-α, IL-8 and TGF-β1) was performed using ELISA. Our findings suggest that high-amplitude nanovibrational stimulation may promote enhanced MSC osteogenesis, likely under eustress or mild physiological stress and optimal inflammatory conditions. This is supported by an increased phospho-p38/p38 ratio, osteopontin (OPN), and osteocalcin (OCN) protein expression, considerable late-stage matrix mineralisation, optimal total ROS production, and lower expression level of glutathione reductase (GSR), superoxide dismutase 1 (SOD1), and catalase. This was further reflected in fewer ϒH2AX-foci count and non-significant secretion of pro-inflammatory cytokines, IL-6, TNF-α, IL-8, and moderate anti-inflammatory cytokine, TGF-β1.

Bioengineered human leukaemia model on chip for drug development

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The bone marrow (BM) microenvironment is a specialised niche that supports the maintenance of haematopoietic stem cells and progenitor cells. Most leukaemias originate in the BM which later infiltrate secondary lymphoid organs. The lack of complexity from current in vitro models leads to a lack of understanding of the disease, and drugs that fail at later stages of clinical trials. Here, we develop a 3D human BM model using hydrogels, to mimic it in health and disease and later connect it to a secondary lymphoid organ using an organ-on-chip device.
We bioengineer hydrogels of similar stiffness to the BM using polyethylene glycol (PEG) functionalised with full length extracellular matrix protein fibronectin (FN), and 25% protease-degradable peptide VPM (GCRDVPMSMRGGDRCG). Spheroids made from human primary mesenchymal stromal cells (MSCs) were embedded into the hydrogels and co-cultured with acute myeloid leukaemia (AML) cell line MOLM13.
We added leukaemic cells to our model to study leukaemic remodelling and saw an increase in nestin expression in MSCs, but a decrease in stem cell factor (SCF) expression, suggesting AML-induced changes to MSC phenotype. To understand if survival and proliferation of the leukaemic cells was affected by the niche, we looked at AML proliferation in 2D, 3D, monoculture, and co-culture with MSCs. We found that proliferation was affected by MSCs both in 2D and 3D, but that the niche was more protective of leukaemic cells when cultured in 3D and treated with cytarabine than in 2D.
Our model shows leukaemic remodelling of the niche as well as protection of the AML cells in 3D, that is not recreated in 2D. Next, we will incorporate this model onto chip to monitor leukaemic infiltration into the secondary site and target it pharmacologically. This will provide a platform to assess leukaemic infiltration, monitor chemotoxicity and haematotoxicity in health and disease.

The Role of Extracellular Matrix Stiffness on Protein Folding Machinery

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E-Poster Session Tuesday Evening, July 14, 2026, 17:50 - 18:30

Adherent cells within the extracellular matrix respond to mechanical cues which regulate, cell signalling and functions. These cues are transmitted through the cytoskeleton and converted into biochemical signals via mechanotransduction. While mechanotransduction is known to influence cell behaviour and fate, its role in protein folding remains largely unexplored. Within the endoplasmic reticulum (ER), molecular chaperones such as Protein disulfide isomerase (PDI), Heat Shock Protein 47 (HSP47), Binding Immunoglobulin Protein (BiP), and Glucose Regulated Protein 94 (GRP94) facilitate protein folding, ensuring its proper structure and function. PDI introduces and rearranges disulfide bonds, helping proteins achieve their native functional conformations, which is especially crucial for proteins with disulfide bridges that do not form spontaneously in the ER. Additionally, HSP47 specializes in collagen I folding and secretion, while BiP and GRP94 have broader roles in protein folding, calcium homeostasis, and ER stress regulation. Our work investigates the relationship between mechanotransduction and chaperones that governs protein folding capacity within the ER. To investigate the link between mechanotransduction and ER chaperones, we engineered polyacrylamide hydrogels with varying stiffness levels to provide mechanical cues to immortalised mesenchymal stem cells and brain endothelial cells. Western blot analysis shows increased expression of HSP47, BiP, GRP94 and PDI in cells on rigid gels compared to soft, implying their sensitivity to mechanical cues. Overall, we provide insights into mechanistic pathways linking stiffness and chaperone regulation which could enhance our deeper understanding of how mechanical cues drive cellular adaptation and remodelling in the context of disease and regeneration.

Chromatin-dependent regulation of nuclear size, shape, and mechanics

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Mechanical stress is a constant in the cellular environment. External forces are rapidly propagated to the nucleus, causing it to deform. The ability of nuclei to deform under force is determined by their mechanical properties, including their shape, size and stiffness. These properties can be tuned in response to physical cues from the environment. As the primary structural component of the nuclear interior, chromatin contributes to both genome organization and nuclear architecture. Increasing evidence suggests that chromatin also directly influences the mechanical properties of the nucleus. However, how chromatin composition and compaction regulate nuclear size, and how these features relate to the mechanical properties of the nucleus, remains incompletely understood. To address this gap, we developed a method to apply piconewton-range forces to isolated nuclei using optically-trapped beads. Using a force-feedback system, we apply a constant, precisely controlled force and record nuclear deformation over time, enabling robust quantification of mechanical and material properties of the nucleus. Using this approach, we demonstrate how changes in chromatin composition regulate nuclear size and mechanics. We show that chromatin compaction determines the size of an isolated nucleus, and that these changes in size are linked to mechanical properties. We contextualize these findings in different ionic environments, and propose that chromatin (de)compaction forces and osmotic pressure together determine the size and mechanics of the nucleus. Extending our findings to the cellular context, we further investigate how mechanical constraint of the cytoskeleton limits the effect of chromatin (de)condensation on nuclear size and shape in intact cells. Together, our findings establish a quantitative relationship between chromatin compaction state, nuclear size, and nuclear mechanics.

Directional effects on pigment cell precursors in uniaxially stretched mouse embryonic skin

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E-Poster Session Wednesday Lunch, July 15, 2026, 13:00 - 13:50

In embryonic morphogenesis of the mammalian skin, mechanical forces help coordinate epidermal cell behaviours. For example, tensile forces, caused by rapid embryonic growth, promote basal cell proliferation and tissue expansion. Later, local cell crowding and contractile flows influence basal cell fate as stratified layers and hair follicles are formed. However, it is less clear if these forces affect other embryonic skin cells, such as melanoblasts – the precursors to mammalian pigment cells.

Melanoblasts are highly motile melanocyte progenitors, originating from the multipotent neural crest. As they populate the developing skin, melanoblasts migrate through the epidermis, proliferate to increase their numbers and segregate fates to become melanocytes or melanocytic stem cells. We hypothesise these dynamic behaviours are cued by mechanical changes in surrounding tissue. In addition, we ask if melanocytic cells respond to mechanical regulation and dysregulation in wider contexts of health and disease.

To reproducibly manipulate global and local forces in the native tissue environment, we have built bespoke stretch systems to culture and image mouse embryonic skin ex-vivo on deformable PDMS membranes. We use fluorescent reporter mouse models to identify the melanocytic lineage by targeting the Dct promoter – a melanocyte specification and pigmentation gene – and track changes in melanoblast behaviour and epidermal tissue organisation.

In E14.5 skin explants, we have followed melanoblasts before and after application of 5 mm uniaxial stretch across the dorsoventral axis. This stretch was chosen to modulate the asymmetric elongation of epidermal cells – which at earlier developmental stages naturally occurs in the dorsoventral direction. We observe stretch impacts the directionality of melanoblast movement and orientation of melanoblast nuclei. In future work, we aim to identify patterns of strain responsible for this effect, characterise the pathways responsible and understand its significance to melanocyte biology – in embryogenesis and beyond.

Bioengineered models to study leukemic bone marrow remodelling

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E-Poster Session Wednesday Lunch, July 15, 2026, 13:00 - 13:50

Haematopoietic malignancies like leukaemia conform a group of disorders caused by abnormal or uncontrolled proliferation of haematological precursors, leading to depleted or inadequate pools of set mature blood cell types. In health, the haematopoietic stem cells (HSCs) population resident in the bone marrow (BM) exists balanced between quiescence and proliferation ensuring a steady, self-sustaining replenishment of blood cells throughout an individuals' lifetime. This equilibrium is tightly regulated by a complex network of interactions between HSCs, other BM cells like mesenchymal stem cells (MSCs), and their chemical and physical environment.

The identification and characterization of these interactions have enabled a better understanding of the pathophysiology of leukemic disorders. For example, understanding the mechanisms by which leukemic stem cells (LSCs) recruit their environment to aid immune and pharmacological evasion explains the high relapse rates behind a 10-year survival rate of 50% following a leukaemia diagnosis. However, progress is still slow in identifying, testing, and validating potential targets for clinical use, with up to 95% of test compounds failing at pre-clinical testing stages. This bottleneck highlights a need for tools that accurately study the interactions between potential therapies and the human BM environment.

Research in our group has produced an in vitro model that recapitulates the main characteristics of the human haematopoietic niche using human BM-sourced MSCs and HSCs cultured in a substrate + hydrogel system. The use of biodegradable hydrogels with tuneable stiffness allows HSCs to engage mechanotransducive pathways and facilitates the dynamic organisation of extracellular matrix components and growth factors. This humanised model is the basis for this PhD project, which aims to characterize tumour- and pharmacologically-induced remodelling of the BM to study the effects of chemotherapies on select elements of the leukemic haematopoietic niche, highlighting potential therapeutic targets.

Mechanical Modulation of Macrophage Phenotype and Function

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Macrophages are highly plastic immune sentinels found across various mammalian tissues, where they confer protection against infections, clear cellular debris, and maintain local homeostasis. These tissue-resident populations derive from yolk sac, foetal liver, or bone marrow precursors and colonise developing organs to occupy specific tissular “niches”. The microenvironmental cues found in the niche drive specification during development via a process referred to as “niche imprinting”, giving rise to several tissue resident macrophage (TRM) subsets. While several prior studies highlight the role of biochemical and cellular cues present within the niche on macrophage phenotype, the role of tissue biomechanics on niche imprinting and TRM specification is an underexplored axis. Macrophages are highly mechanosensitive and constantly integrate mechanical cues such as matrix stiffness, viscoelasticity, and cyclic strain into their effector functions. Perturbations in tissue mechanics, as observed in physiological processes like aging as well as in pathological conditions, can have profound effects on macrophage specification and disease phenotypes.

In the present study, we aim to elucidate the role of tissue stiffness in conferring macrophage phenotypes. Rather than focusing on the development of transient polarised activation states (M1/M2) on biomechanical substrates, we seek to understand if changes in matrix stiffness coaxes human peripheral blood monocyte-derived macrophages towards adopting TRM-like identities. We employ a two-dimensional polyacrylamide gel system with tuneable Young’s moduli to mimic the mechanical diversity observed across the various tissue niches. By characterising the transcriptional and functional shifts induced by these physical environments, we expect to identify mechanosensitive pathways that govern macrophage specification. This work would potentially offer new strategies for directing immune cell identity via engineering physical microenvironments, advancing immune disease modelling.

Selective Killing of Cancer-Associated Fibroblasts by Ultrasound-Mediated Mechanical Forces

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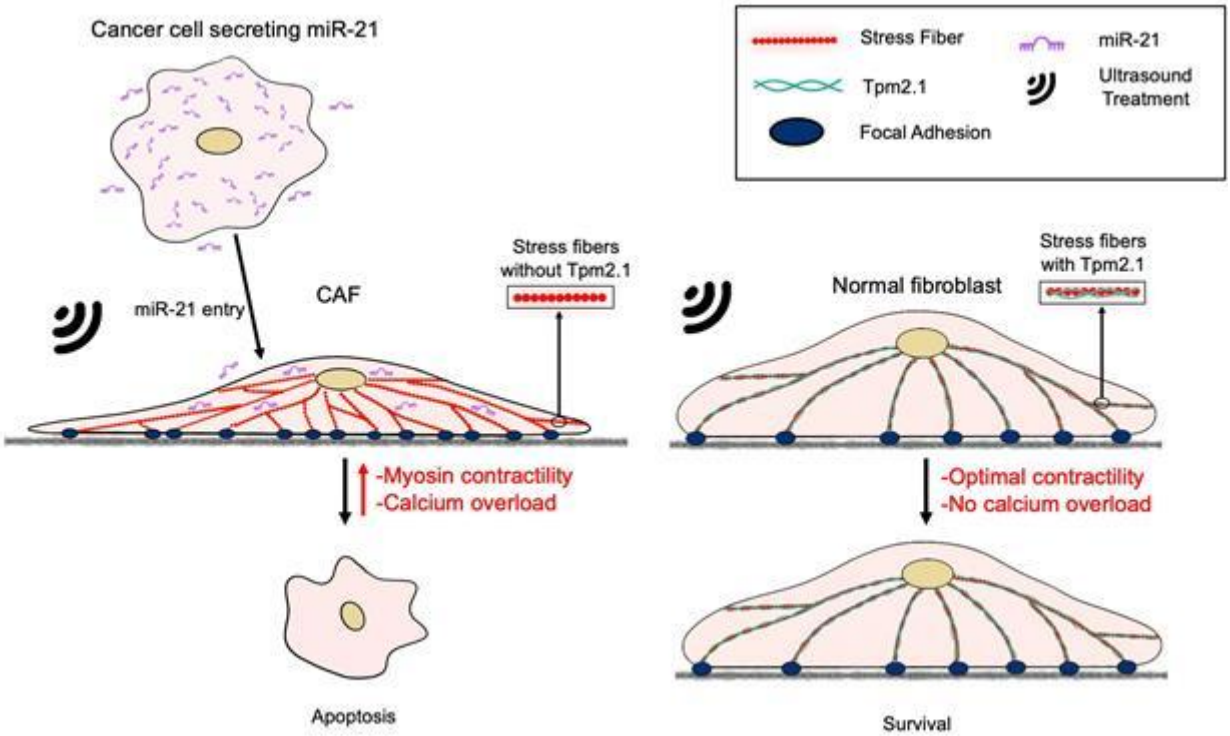
Recent studies show that stretch/ultrasound (US)-generated mechanical forces cause selective apoptosis in several cancer cells, tumor organoids and animal models without damaging normal cells. Cancer-associated fibroblasts (CAFs) are an integral tumor microenvironment (TME) constituent. They display altered biomechanical properties similar to cancer cells, such as matrix secretion and its remodeling, chemokine secretion, and high contractile force generation. We thus test the effect of US-mediated mechanical forces on patient-derived CAF survival. Surprisingly, US treatment causes CAF apoptosis (mechanoptosis) through a calcium-activated apoptotic pathway but not in normal fibroblasts. MicroRNA-21 (miR-21) secreted by primary cancer cells suppresses the mechanosensory cytoskeletal protein tropomyosin 2.1 (Tpm2.1) in CAFs. This Tpm2.1 depletion in CAFs is responsible for mechanoptosis. Interestingly, normal fibroblasts behave similarly when Tpm2.1 was depleted. Further, 3D gel contractility and migration assay confirm that a prolonged US treatment disrupts myosin IIA-mediated contractility, which CAFs primarily use to support cancer invasion. Since US treatment causes mechanoptosis and reduces contractility, this approach could be used to develop ultrasound-based CAF-targeting therapy to augment cancer treatment.



Biomechanical characterisation of chemoresistant and chemosensitive breast cancer cell lines

Alessia Saponara[1], Valeria Cassina[1], Maria Grazia Cerrito[1], Elisabetta Valeri[1], Riccardo Campanile[1], Francesco Mantegazza[1], Marina Elena Cazzaniga[1,2]
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E-Poster Session Tuesday lunch, July 14, 2026, 13:00 - 13:50

Understanding how mechanical properties differ between chemosensitive and chemoresistant cancer cell lines may provide valuable insights into the mechanisms underlying chemoresistance. In this study, Atomic Force Microscopy (AFM) was employed to investigate cellular mechanical properties such as stiffness, adhesion and viscoelastic properties, including stress relaxation and cell mechanical memory. The study included MCF-7 and T47D human breast cancer cell lines, both sensitive and resistant to palbociclib and MCF-10A normal epithelial cells as a control. We observed that cancer cells exhibit different mechanical parameters compared to wild-type cells. Notably, palbociclib-resistant cells showed mechanical differences compared with their chemosensitive counterparts, suggesting that the acquisition of resistance is associated with substantial mechanical remodeling. Cell morphology was further analyzed using AFM quantitative imaging (AFM-QI) measurements, providing label-free markers, alongside confocal microscopy with specific fluorescent markers. Resistant cells showed increased cell size, both in height and length. Moreover, cytoskeletal organization and nuclear structure differed between sensitive and resistant phenotypes. Overall, these results indicate that cellular mechanics can provide quantitative markers of drug resistance and therapeutic response.

Spatial localization of chromosome territories are altered in cells cultured on softer matrices

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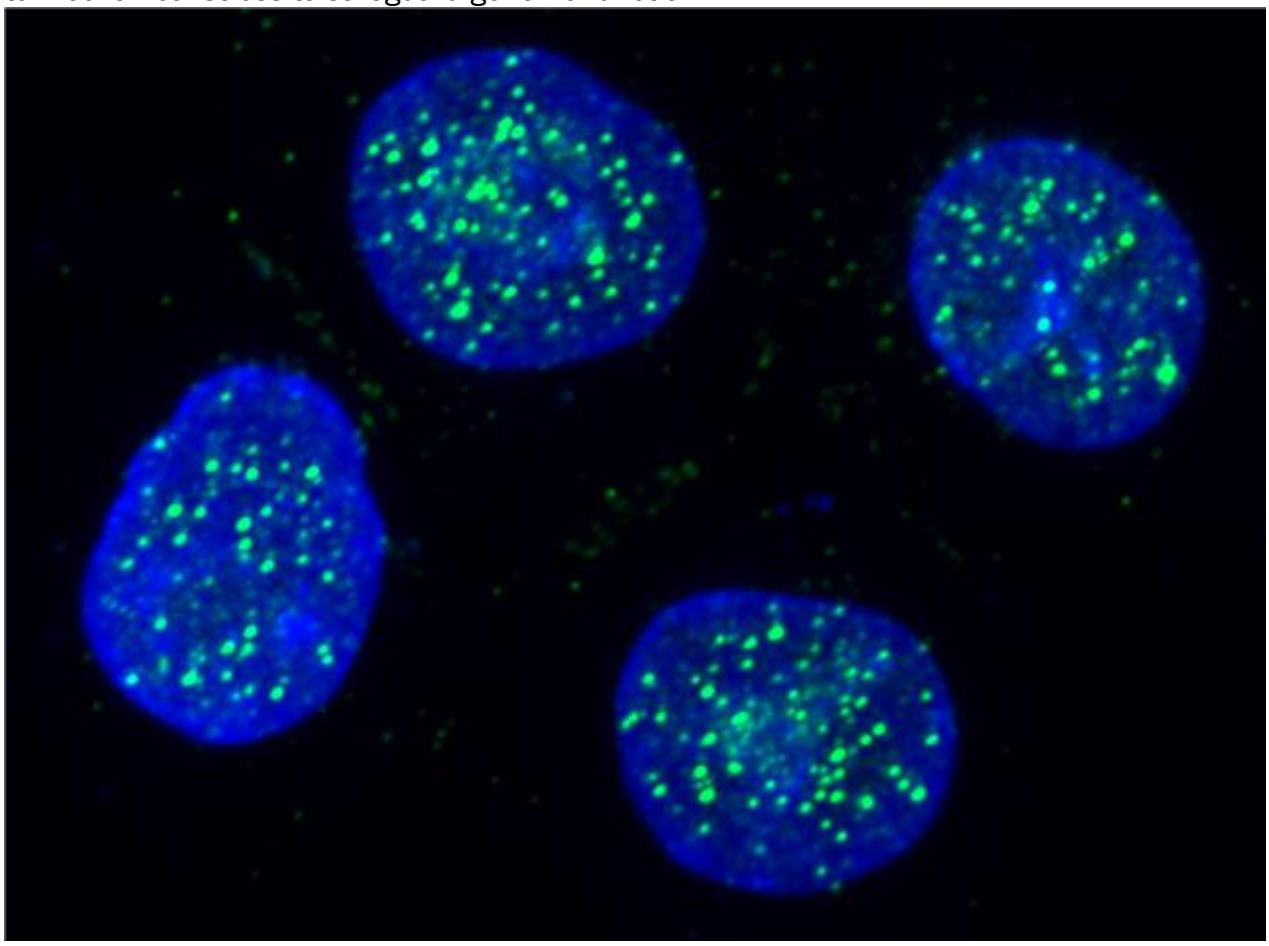
E-Poster Session Tuesday lunch, July 14, 2026, 13:00 - 13:50

Chromosomes are non-randomly organized within the interphase nucleus into specific sub-volumes known as Chromosome Territories (CTs). Generally, gene-rich chromosome territories reside in the nuclear center while gene-poor territories occupy the periphery. To determine the molecular mechanisms driving this organization, we exposed cells to softer hydrogel substrates (2–55 kPa) and compared them to rigid glass controls (~1 GPa). On softer substrates, cells showed increased surface area and a significantly altered transcriptome. Crucially, the invariant positioning of CTs was disrupted. This reorganization was linked to the mislocalization of the LINC complex and lamins into the nuclear interior, as well as changes in the distribution of histone marks. We identified Emerin phosphorylation as the critical relay for these mechanochemical signals; inhibiting this phosphorylation prevented CT movement. Our recent studies reveal an altered organization of telomeres in cells cultured on softer matrices. Collectively, these results highlight the inherent plasticity of the nucleus and its ability to adapt to mechanical stress to safeguard genome function.



Origin-Specific Mechanical Signatures Define Endothelial Cell Behavior in 2D and 3D Microenvironments

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E-Poster Session Tuesday Evening, July 14, 2026, 17:50 - 18:30

Endothelial cells (ECs) exhibit structural and transcriptomic diversity based on the organ or vascular bed of origin, yet their mechanical heterogeneity and its impact on vascular behavior remains poorly defined. Because mechanosensing, force generation, and matrix interactions regulate angiogenesis, barrier function, and tissue repair, understanding origin-dependent mechanobiology is essential. We integrated RNA sequencing with 2D (single-cell and monolayer) and 3D (sprouting) mechanobiology assays to define mechanical signatures—cytoskeletal organization, adhesion, degradation, and force generation—of HUVECs and microvascular ECs from the brain, lungs, and dermis. We identified distinct mechanical strategies employed by each EC type. HUVECs and brain ECs invaded 3D matrices through filopodia-guided exploration and moderate matrix degradation, with HUVECs additionally showing coordinated pMLC activation and β1-integrin–rich adhesions. Lung ECs were minimally degradative, thereby limiting invasiveness. Dermal blood ECs displayed a hyper-mechanical phenotype with strong matrix degradation, abundant filopodia, robust actin fibers, and high cell–ECM forces—traits likely reflecting adaptation to their stiff native microenvironment. In contrast, dermal lymphatic ECs were highly contractile but showed little degradation or filopodia formation, resulting in poor invasion, consistent with the lower mechanical demands of basement membrane-lacking lymphatic vessels. RNA-seq analysis further revealed that cell-type-specific differences in β1-integrin and MMP expression recapitulate the observed variation in adhesion and matrix degradation, linking the functional heterogeneity identified in the 3D sprouting assay in underlying gene expression programs. We show that EC mechanical phenotypes are strongly origin-specific and shaped by native microenvironments. Selecting appropriate ECs is critical for physiologically relevant mechanobiology and for improving the design, interpretation and translation of vascular studies.

Role of PEZO-1 in Maintenance of the Germline Stem Cell Population in Caenorhabditis elegans

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E-Poster Session Wednesday Lunch, July 15, 2026, 13:00 - 13:50

Stem cells are essential for the development and maintenance of tissues. Germline stem cells (GSCs), in particular, sustain the reproductive capacity as well as modulate systemic aging of an organism. The population of germline stem/progenitor cells in Caenorhabditis elegans is maintained by their single-cell niche, known as the Distal Tip Cell (DTC), and their numbers gradually decline as the worms age. PEZO-1, the homolog of the mammalian mechanosensitive ion channel Piezo in C. elegans, is extensively expressed throughout the gonad and in all stages of germ cells within the organism. Additionally, PEZO-1 is necessary for proper ovulation and fertilization in the proximal gonad of worms. However, its potential role in the distal gonad, where the stem cells reside, remains unclear.
I am investigating the role of PEZO-1 in maintaining the germline stem/progenitor cells in the distal part of the gonad in C. elegans. While perturbing the levels of PEZO-1 did not demonstrate any measurable effect on the morphological attributes of the niche, I observed that the loss of PEZO-1 directly impacted the germline stem cell population as worms aged. We are currently exploring the possible pathway through which PEZO-1 regulates the stem cell dynamics. This study will enhance our understanding of the mechanical regulation of stem cells broadly, with a specific focus on GSCs, and will provide valuable insights into the role of mechanics in aging phenotypes.

Excessive cortical contractility triggers early oocyte polarization and aberrant cytoplasmic flows in mammals

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Female meiosis produces oocytes. In mammals, this process ends with two successive asymmetric divisions in size (meiosis I and II), resulting in a large haploid oocyte containing the maternal stores required for early embryonic development after fertilization. The geometry of these divisions is controlled in part by cortical tension, which decreases in a spatiotemporal manner after meiosis I entry due to actomyosin cortex reorganization, allowing the spindle to migrate along its long axis towards the closest cortex via a Myosin-II dependent pulling mechanism, permitting an asymmetric division in size. Mechanical defects are frequent in mammalian oocytes, mirroring the variability in cortical tension and Myosin-II cortical enrichment. Particularly, mouse and human oocytes with a too high cortical tension produce embryos that stop developing after fertilization. To elucidate the consequences of excessive cortical tension on oocyte development, we engineered mouse oocytes with excessive cortical contractility by forcing active Myosin-II to their cortex through cortical targeting of the RhoA/ROCK pathway. We observe that these oocytes progress through meiosis I as successfully as control ones, with comparable timing and geometry of division. However, their actomyosin cortex spontaneously polarizes upon meiosis I entry, forming a flattened zone opposite as to where division will occur. Directional cytoplasmic flows originate from this polarized zone, pushing the spindle away, towards the opposite cortex, resulting in faster spindle migration and random spindle orientation. These directional flows disrupt organelle distribution, reducing mitochondrial and Golgi content by half after meiosis I, potentially depriving the future embryo of energy reserves and vital organelles. Furthermore, CD9 and Juno, essential for oocyte fertilization, accumulate precociously and in a restricted manner in the polarized zone, potentially altering fertilization efficiency, still to be tested. Finally, we have shown that the phenotypes observed in these engineered mouse oocytes exist in natural populations of mouse and human oocytes.

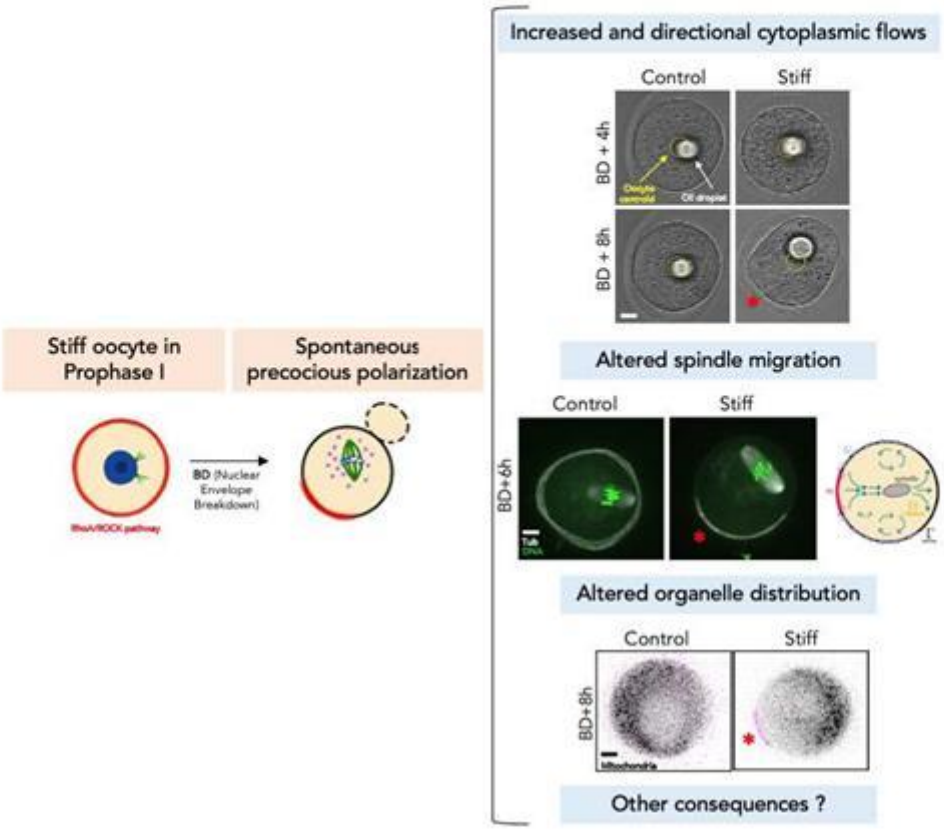

Figure: Stiff oocytes in Prophase I, due to cortical targeting of the RhoA/ROCK pathway (red) spontaneously polarize after meiosis I entry, marked by nuclear envelope breakdown (BD; DNA in blue, microtubules in green, organelles in pink). From this polarized zone (pink asterisks) emerge strong and directional cytoplasmic flows, able to displace an oil droplet away from the oocyte center. These aberrant flows alter spindle migration, with different outcomes depending on the initial conditions, as assessed by mathematical modelling. They also alter organelle distribution in meiosis I.

Development of 3D Organotypic Models for Fibrotic Lung Epithelia to Study Cancer Initiation

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E-Poster Session Tuesday Evening, July 14, 2026, 17:50 - 18:30

Fibrosis is a condition that leads to drastic changes in the composition, crosslinking, and stiffness of the extracellular matrix (ECM). It is a pro-tumorigenic state and constitutes a significant risk factor for cancer development. Patients with idiopathic pulmonary fibrosis (IPF) i.e. fibrosis of the airway ECM, have a higher risk of lung cancer and a poor prognosis.
In this study, we hypothesise that dysregulated ECM and modified cellular mechanics upon fibrosis impair the inherent defence mechanism against cancer, thus leading to cancer initiation. Therefore, we developed a one-of-a-kind 3-Dimensional organotypic model that allows us to capture the immediate mechanical, biophysical and biochemical shifts occurring at the very onset of tumorigenesis in a spatiotemporal manner. This approach provides an unprecedented window into how the fibrotic landscape dictates the earliest stages of tumorigenesis.
Using an air-liquid interface culture, we established a 3-dimensional organotypic lung model consisting of fibroblasts, collagen-based connective tissue, and a pseudostratified epithelium. Furthermore, we modulate collagen density and induce fibrotic markers by activating the TGF-β/Smad signalling pathway to recapitulate fibrosis in the organotypic models. To study changes in cellular mechanics upon tumorigenesis, we used lentiviral-mediated oncogene transfection in organotypic models. Oncogene transfection of the organotypic models reveals a distinct spatial organisation of oncogenic cells under the fibrotic conditions, resulting in a dense cellular cluster of elongated cells.
While most current models focus on established tumours, our platform uniquely enables the study of cancer initiation within a controlled microenvironment.

Could molecular extensibility determine the fate of disseminated cancer cells?

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E-Poster Session Tuesday Evening, July 14, 2026, 17:50 - 18:30

The mechanical properties of the microenvironment and associated biochemical signaling play important roles in tumor progression and metastasis. Still, it is unclear to what extent they regulate the fate of disseminated cancer cells–their survival, dormancy, or reawakening. The study aims to investigate the role of the biophysical properties of the environment on metastatic cancer cells by examining the influence of the extracellular matrix's molecular extensibility on cellular responses. We prepared and characterized surface coatings with the highly elastic biomolecule, tropoelastin, and its synthetic analog, based on the extendable polymer poly(hydroxyethyl methacrylate) (pHEMA). The latter was also optimized to enable high-throughput for cell biological experiments by immobilizing pHEMA block copolymers (PHEMA-b-BPMA) on polystyrene, offering varying molecular extensibilities depending on the molecular weight of PHEMA-b-BPMA. Different morphologies and cell-matrix adhesion responses of metastatic cells were observed on highly extensible tropoelastin compared with cross-linked tropoelastin, with reduced extensibility. Metastatic cancer cells seeded on surfaces coated with varying molecular weight PHEMA-b-BPMA exhibited different morphologies depending on molecular extensibility, with cells adhering more strongly to surfaces with lower extensibility. With both tropoelastin and PHEMA-b-BPMA-coated surfaces, we observed that molecular extensibility influenced the mechanosensitive FHL2-p21 signaling axis. Cell-cycle progression was monitored via live-cell imaging of cell-cycle indicator cells, and it was observed that the duration cells spent in a particular phase varied depending on the molecular extensibility of the substrate. Cells spent more time in G0 (cell-cycle arrest) on high-extensibility substrates. The obtained results indicate the potential influence of molecular extensibilities on tumor cell cycling, proliferation, and dormancy. Thereby helping us establish model systems for mechanosensitivity studies in metastatic cancer cells and enhance our understanding of the role of molecular extensibility as a biophysical cue in regulating the fate of disseminated tumor cells.

A photoablation-based Vessel-on-a-chip system to elucidate human perivascular macrophages differentiation and functions

Pauline Smilovici[2], Jérôme Ng-Wong[1], Samy Gobaa[1], Pierre Guermonprez[1], Guillaume Duménil[1]
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E-Poster Session Tuesday Evening, July 14, 2026, 17:50 - 18:30

Tissue-resident macrophages are a heterogeneous immune cell population with tissue-specific phenotypes and functions. Perivascular macrophages (PVMs) are a LYVE1+ FOLR2+ TIMD4+ subset of interstitial macrophages residing alongside blood vessels in multiple organs. PVMs have been shown to sample blood content and to be involved in various pathological contexts such as infection and cancer. Yet, the environmental signals required for the establishment of their phenotype and the precise blood sampling mechanisms remain poorly understood. To address these questions, we aim to design an in vitro system in which PVMs can differentiate and exert their functions. We take advantage of a recently developed human microfluidic Vessel-on-chip system where endothelial cells organize in laser-carved channels under flow within an extracellular collagen I matrix with controlled size and barrier's permeabilities similar to in vivo conditions (Pinon et al, eLife 2025). This system allows to perfuse human monocytes purified from fresh blood into the artificial lumen, observe their extravasation and follow their differentiation into PVMs in the surrounding matrix. Expression of different macrophage modulating chemokines are ensured by the introduction of genetically modified fibroblasts in the extravascular compartment. This approach will allow us to elucidate essential signals that drive PVM's identity using immunofluorescence, flow cytometry and live imaging under controlled conditions, as well as to study their sampling and immune signalling functions in various pathological settings.

Adenocarcinoma cell mechanobiology is altered by the loss modulus of the surrounding extracellular matrix

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E-Poster Session Tuesday lunch, July 14, 2026, 13:00 - 13:50

Elastic and viscoelastic properties of extracellular matrices (ECM) are known to regulate cellular behavior and mechanosensation differently, with implications for morphogenesis, wound healing, and pathophysiology. Most in vitro cellular processes, including cell migration, are studied on linear-elastic substrates to mimic extracellular matrices. However, tissues are viscoelastic and display a loss modulus (G´´) that may be 10-20% of their storage modulus (G´). Recent research has shown that cells can distinguish between elastic and viscoelastic ECM, leading to alterations in their cellular morphology, migration rates, and contractility. Here, we present a protocol for creating PAH-based model ECMs that enables the fabrication of viscoelastic substrates with storage moduli similar to those of their elastic counterparts. To explore how G´´ influences epithelial cell mechanobiology, we fabricated tunable viscoelastic model ECMs with G´ of 3 kPa, 8 kPa, and 12 kPa, and for each, independently tuned G´´ values to approximately 300Pa, 500 Pa, and 700 Pa, respectively. We found that A549 cells cultured on stiff elastic model ECMs migrated ~30% slower and formed larger focal adhesions compared to their viscoelastic counterparts. Conversely, A549 cells on intermediate viscoelastic model ECMs exhibited a ~54% reduction in migration speed, with no significant difference in focal adhesion size relative to their elastic counterparts. These findings highlight the complex interplay between substrate (ECM) elastic and viscoelastic properties in regulating epithelial cell mechanobiology and emphasize the importance of time-dependent matrix mechanics in governing epithelial responses.

Continuous Low-Intensity Ultrasound Reprograms Fibronectin Fragment–Activated Macrophages Toward a Reparative Phenotype:

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[1]Universiy of Alabama-Huntsville, United States

E-Poster Session Tuesday lunch, July 14, 2026, 13:00 - 13:50

Macrophages are key regulators of inflammation, capable of adopting pro-inflammatory (M1) or anti-inflammatory (M2) phenotypes in response to environmental cues. In chronic conditions such as post-traumatic osteoarthritis (PTOA), persistent M1 activation contributes to tissue damage and impaired healing. Traditional models using lipopolysaccharide (LPS) to induce inflammation may not fully capture the complex microenvironment of joint injury. This study employs fibronectin fragments (Fnfs), which are associated with matrix degradation, to establish a physiologically relevant inflammatory model and to apply transcriptomic analysis to investigate how continuous low-intensity ultrasound (cLIUS), a non-pharmacological biophysical stimulus, modulates macrophage responses under Fnfs-induced conditions. Beyond identifying differentially expressed genes (DEGs), we introduced network-level differential clustering (DC) to capture transcriptional remodeling, revealing context-specific regulators and coordinated co-expression shifts overlooked by gene-level analyses. cLIUS reprogrammed Fnfs-induced macrophages toward an M2-like reparative phenotype, marked by downregulation of pro-inflammatory and upregulation of tissue repair and immune-regulatory genes. DC identified significant genes not detected by DEG analysis, with only partial overlap between ranked gene lists, as quantified by concordance indices of 0.52 for SD genes and 0.42 for DS genes (scale 0–1). These findings highlight that coordinated shifts in expression captured by DC complement standard differential expression, providing a perspective on how biophysical treatments such as cLIUS modulate immune cell behavior

Biophysical mechanisms behind cancer initiation in 3D mammary breast acini

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[1]Indian Institute Of Science, India

E-Poster Session Tuesday lunch, July 14, 2026, 13:00 - 13:50

Breast cancer is one of the most common cancers found in women worldwide. It initially starts in mammary ducts, where transformed cells proliferate into a mass of tumor. This tumor mass eventually gains the ability to escape confinement of the ducts by breaching the basement membrane and invading the surrounding tissue, thus becoming a metastatic cancer. While a volume of research focuses on metastasis in breast cancer, how cancer initiates remains largely elusive. To this end, studies in the past decade have shown that tumor cells actively compete with host tissue cells, and the outcome of this competition dictates the fate of cancer. Such competition allows epithelial cells to recognize and remove misfit transformed cells- a phenomenon called Epithelial Defense Against Cancer (EDAC). While studies suggest the roles of the tissue microenvironment and extracellular matrix mechanics in EDAC, these studies have been conducted on model epithelial cell lines in 2D monolayers and often with transformed cells harboring only one oncogenic pathway. Furthermore, a mechanistic understanding of how EDAC fails to give rise to cancer remains missing. In this project, we aim to mimic breast cancer initiation in 3D mammary acini and study the biophysical mechanisms involved in EDAC. We aim to initiate cancer via the accumulation of mutations, which deregulate both cell polarity and the Akt signaling pathway by overexpressing ERBB2 (a receptor tyrosine kinase). ERBB2 is found to be overexpressed in many breast cancer patients, and when overexpressed in breast acini, it induces translocation of cells into the lumen. Furthermore, polarity dysregulation via Scribble downregulation is shown to allow cancer growth in cells with ERBB2 overexpression. By sporadically accumulating mutations in mammary breast acini using lentiviral vectors, we explain how tissue architecture, ECM mechanics, cell-generated forces, and mechanotransductive signaling pathways influence EDAC outcomes in 3D epithelial systems.

Mechanics of spinal cord regeneration in Xenopus laevis.

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E-Poster Session Tuesday Evening, July 14, 2026, 17:50 - 18:30

The African clawed frog (Xenopus laevis) can regenerate central nervous system (CNS) neurons during its early life stages, pre-metamorphosis, while in its larval form. However, this ability is lost post-metamorphosis, after the frog transitions into its adult form. Biochemical differences between pre and post metamorphosis frog spinal cord tissue identified so far cannot fully explain the differences in their regenerative capacity, suggesting that other signals may contribute to regulating wound healing and neuronal regeneration. Following spinal cord injury (SCI), the composition of the extracellular matrix changes, and scar tissue forms. In mammals, this scar tissue, which is softer than healthy tissue, inhibits axon regeneration. In contrast, in zebrafish, whose CNS neurons regenerate after SCI, tissue stiffens after injury. Mechanical properties of frog spinal cord tissue have not been measured yet. Because mechanosensing of tissue stiffness is critical for axon growth, we here test the hypothesis that tissue stiffness is a critical factor facilitating or impeding axon regeneration after SCI. We investigate the mechanical differences in the spinal cord lesion environment in pre- and post-metamorphosis Xenopus laevis. By examining factors such as tissue stiffness and molecular changes, we will illuminate the relationship between these factors and the regenerative capabilities.

Cagging of membrane-to-cortex attachment can trigger cellular symmetry breaking

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E-Poster Session Tuesday Evening, July 14, 2026, 17:50 - 18:30

Cell surface mechanics are the main functional driver of cell migration, differentiation and proliferation. The link between membrane fluidity and membrane to cortex attachment affecting cytoskeleton architecture has been poorly explored in vitro and in vivo. Recent data from the laboratory has shown the importance of membrane fluidity and the effect of membrane-to-cortex attachment protein size on actin network dynamics in vitro, supporting a direct crosstalk between linker size, membrane fluidity and actin network dynamics. Here we explore the effect of linker length in the actin cortex and plasma membrane in vivo.
To that end, we engineered membrane to cortex linkers with diverse predicted lengths (25 and 50nm, corresponding to those of endogenous proteins and their dimers) and explored their behavior in cells. The expression of linkers of ≥25nm in length leads to symmetry breaking, whereby a patch rich in both the linkers and actin is formed. Longer versions in addition generate cell-scale protrusions resembling uropods in migrating immune cells. All these phenotypes can be recapitulated with endogenous overexpression of membrane-to-cortex attachment proteins, suggesting, the mechanics of both synthetic and endogenous linkers are similar. The polarization and the formation of uropod-like structure is lost upon actin polymerization inhibition, suggesting that a feedback mechanism exists between linker polarity and the actomyosin cortex. Furthermore, we see that mechanical polarization of the cortex leads to directional cell spreading in a linker length dependent manner. Altogether our data shows that linker length can effectively increase its Kon, by caging molecules within the underlaying actin cortical mesh. This work showcases how the coupling of membrane mechanics to polymer physics can lead to unexpected cellular morphogenesis and aid migration.

Extracellular Matrix-Based Patient Stratification and Network Modeling for Mapping Therapeutic Vulnerabilities in Lung Cancer

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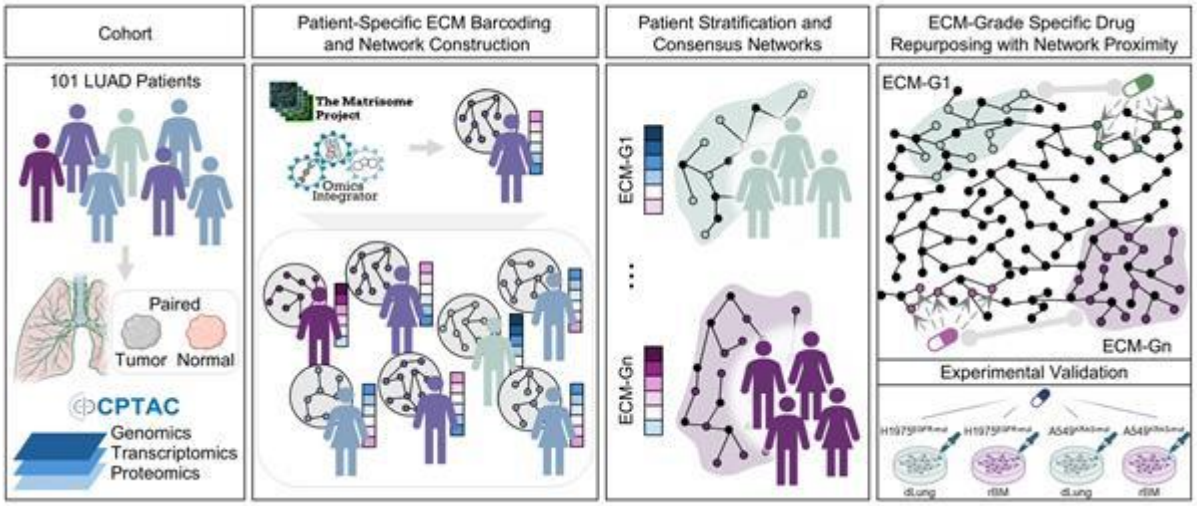
E-Poster Session Wednesday Lunch, July 15, 2026, 13:00 - 13:50

The extracellular matrix (ECM) is a critical determinant of tumor progression and therapeutic response, yet its profound heterogeneity has limited its use in clinical stratification. In this study, we developed an ECM-guided patient stratification framework for lung adenocarcinoma (LUAD) by integrating multi-omic data, patient-specific network modeling, and experimental validation. We obtained four patient groups, representing ECM-grades (composite molecular signatures abstracting the matrix composition) that showed distinct clinical features, mutation profiles, and cellular heterogeneity.

Our findings reveal that higher ECM grades, characterized by increased matrix density and complexity, correlate with significantly worse overall survival, elevated recurrence rates, and enhanced cellular heterogeneity. Higher ECM grades correlate with increased stromal cell abundance, particularly cancer-associated fibroblasts and endothelial cells, leading to a more aggressive, high-risk tumor microenvironment. We found that moderate-to-high ECM enrichment is essential for efficient ECM-integrin interactions, as evidenced by significantly lower interaction scores in ECM-poor tumors. Additionally, we identified a striking association between ECM profiles and oncogenic drivers: KRAS mutations are enriched in ECM-rich environments, whereas EGFR mutations dominate ECM-poor tumors.

At the systems level, patient-specific network modeling demonstrated that higher ECM grades converge on pathways governing angiogenesis, PI3K-Akt signaling, and EMT, driven by regulators such as TWIST and SNAI2. Crucially, we show that the ECM modulates drug efficacy. By integrating in silico drug proximity analysis with ECM-specific networks, we identified Olaparib as an ECM-dependent therapeutic, while Erlotinib remained ECM-insensitive. These computational predictions were experimentally validated on lung tumor cells with distinct mutational profiles in response to differing ECM microenvironments, confirming that matrix context directly alters pharmacological sensitivity.

Overall, our ECM-mediated stratification provides a robust, high-resolution system for capturing microenvironmental diversity. By linking matrix signatures to specific molecular vulnerabilities, this framework offers a powerful tool for personalizing therapeutic strategies in lung cancer.



SMALL MOLECULE THERAPIES TO RESCUE GAP JUNCTIONAL INTRACELLULAR COMMUNICATION AND OVERCOME STIFFNESS-INDUCED CHEMORESISTANCE

Charlotte Turner[1], Raja Vadivelu[1], Brian Harkin[1], Eóin McEvoy[1]
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E-Poster Session Tuesday Evening, July 14, 2026, 17:50 - 18:30

INTRODUCTION
Breast cancer (BC) is the leading cause of cancer death in women globally. Matrix stiffening, reduced cell proliferation, and a loss of functional gap junction (GJ) expression are associated with BC progression. Here we investigate how these factors could influence chemosensitivity in BC and identify pathways to mitigate such chemoresistance.
METHODS
T47D cells were cultured in supplemented RPMI. Low passage (LP) and high passage (HP) cells fall between P1-10 and P11-20 respectively. Single cells seeded into gelatin-mTG hydrogels spontaneously formed spheroids over 12 days. Samples received 24-hour treatment with GJ-modulators ATRA, dipyridamole, or resveratrol in DMSO prior to chemotherapeutic doxorubicin (DOX). Calcein diffusion was tracked between connected cells to characterise GJ functionality.
RESULTS
Spheroids exhibited stress-dependent growth, with those encapsulated in stiff hydrogels (sfH) significantly smaller and compact than spheroids in soft hydrogels (stH) (Figure1.A-B). stH-spheroids reduced in size following treatment with doxorubicin, while no significant differences were observed for sfH-spheroids (Figure1.C), suggesting mechanosensitive resistance.
Cx43 expression and function was significantly higher in LP compared to HP T47D cells, largely diffuse in the cytoplasm in both cases. Following HP treatment with GJ-modulators, Cx43 was significantly increased. ATRA and dipyridamole pushed Cx43 expression to the membrane, specifically increasing concentrations at the cell-cell interfaces (Figure1.D-E).
DOX treated sfH-spheroids decreased in size when treated in combination with ATRA, dipyridamole, or resveratrol, compared to chemotherapy alone (Figure1.F).
DISCUSSION
T47D cells cultured under higher mechanical stress developed smaller, more compact spheroids, regulated via mechanosensitive pathways. Increased cell density and lower proliferation interfere with chemotherapy diffusion and sensitivity. As T47D cells mature through passages, they appear to lose GJ expression which may compound chemoresistance, but GJ assembly was overcome through treatment with small molecule drugs. Overall, we utilised combinational therapy to enhance gap junctional intercellular communication, promoting chemotherapy diffusion and sensitivity in BC spheroids.

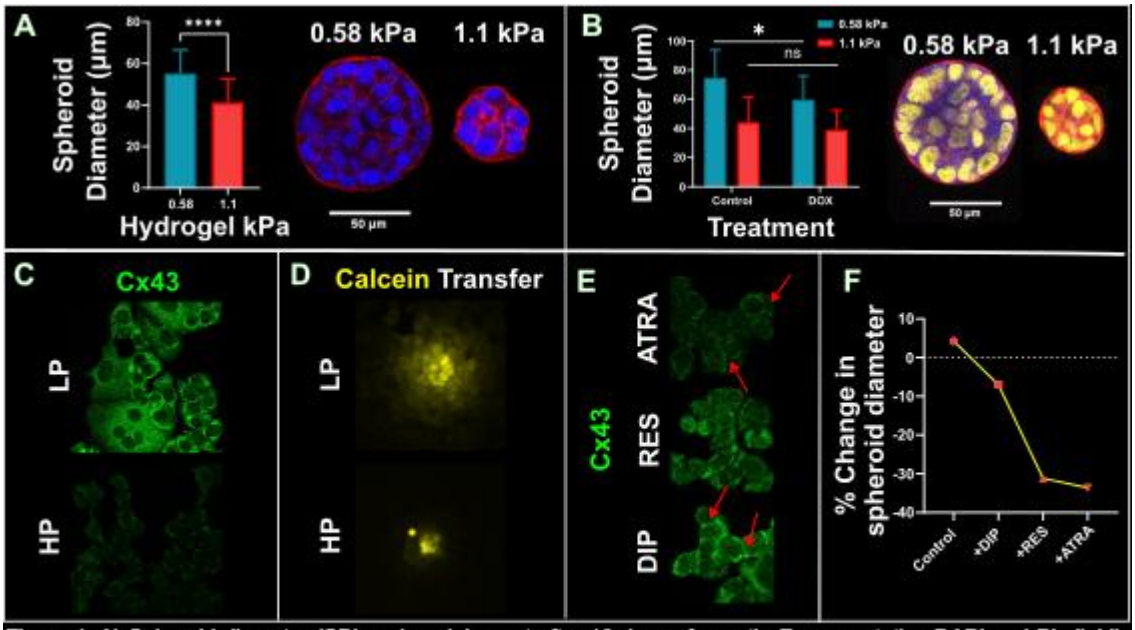

Figure 1. A) Spheroid diameter (SD) and nuclei count after 10 days of growth. Representative DAPI and Phalloidin images. B) Change in SD following 10µM DOX treatment. Representative DAPI, Phalloidin, and DOX (yellow) images.C) Cx43 IF. D) Parachute Assay. E) Cx43 IF of HP 24hr treatment with ATRA (20µM), RES (20µM), or DIP (60µM). F) % Change in SD following 10µM DOX treatment in combination with ATRA, RES, or DIP.

Tissue-engineered outer retina model to study the influence of extracellular matrix on retinal cell interactions

Vasudha Turuvekere Krishnamurthy[1,2], Laura Klasen[2,3], Ramin Nasehi[2,3], Lisa Jungbluth[1], Eva Miriam Buhl[5], Alice Podesta[6], S-Ting Wu[1], Björn Kampa[6], Laura De Laporte[2,3,4], Jacopo Di Russo[1,2]

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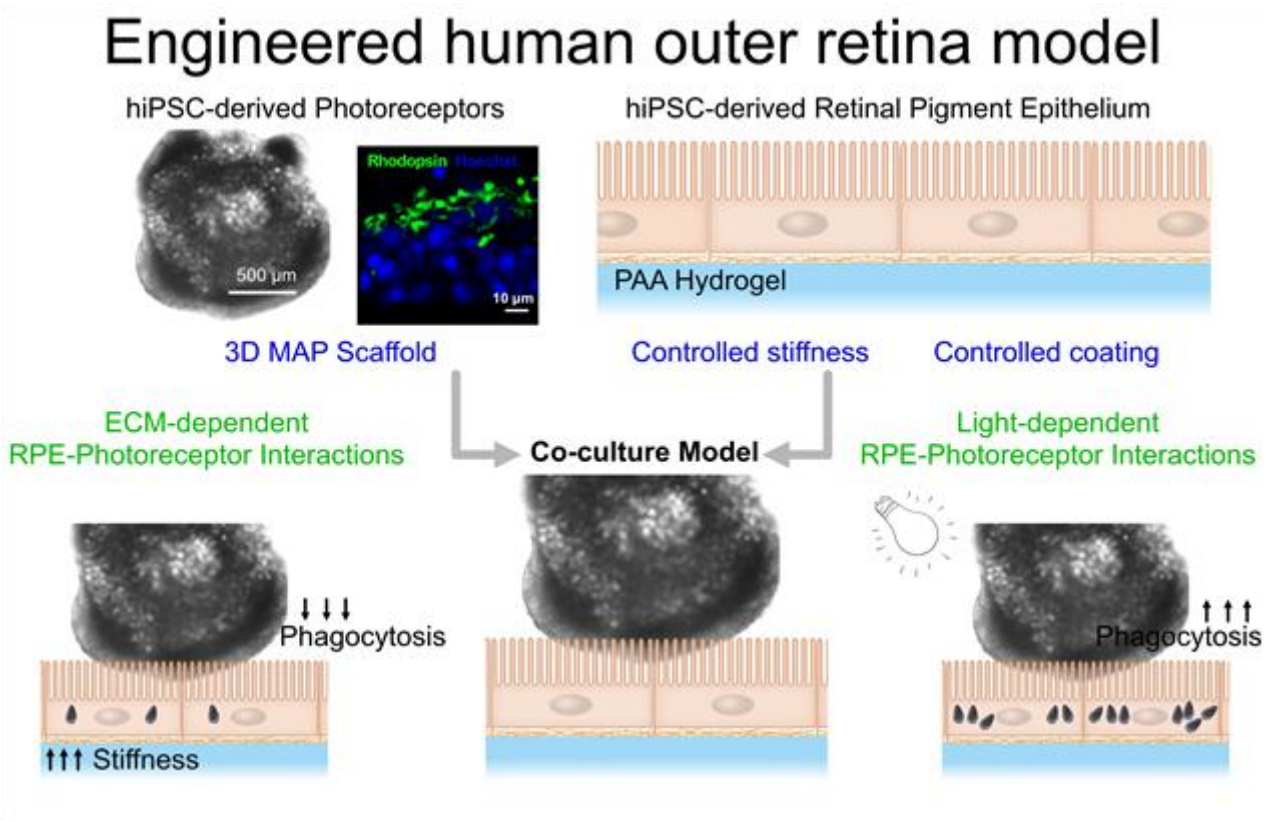
E-Poster Session Tuesday Evening, July 14, 2026, 17:50 - 18:30

Outer retinal degeneration is a leading cause of vision loss and is strongly influenced by age- and disease-associated changes in the extracellular matrix (ECM). The outer retina represents a mechanically and biochemically specialised niche in which ECM properties regulate photoreceptor (PR)-retinal pigment epithelium (RPE) interactions. However, current human retinal organoid models fail to reproduce this microenvironment and lack a mature, functional outer retina.

To address this gap, we developed a human-relevant co-culture system that recapitulates ECM-RPE-PR interactions and enables controlled perturbation of ECM biochemical and mechanical cues. Human induced pluripotent stem cells (hiPSCs) were differentiated into mature PRs within three months, significantly faster than conventional retinal organoid protocols, by assembling cells into a 3D microporous annealed particle (MAP) scaffold composed of spherical poly (ethylene glycol) microgels. The PR MAP scaffolds were co-cultured with stem cell-derived RPE on ECM-mimicking hydrogels.

PRs formed light-responsive outer segments displaying the “eat-me” signal, phosphatidylserine, confirmed by pSIVA staining. When co-cultured with hiPSC-derived RPE on tunable hydrogels, PR outer segment fragments were efficiently phagocytosed and localised to endosomes. Phagocytosis was reduced by MERTK receptor inhibition, confirming specificity. Following dark-to-light transition, phagocytosis increased, consistent with in vivo behaviour. Finally, increasing ECM stiffness to mimic age- and disease-associated tissue stiffening reduced phagocytic efficiency, consistent with earlier findings obtained using porcine outer segment fragments. Collectively, this human-based in vitro model enables mechanistic studies of how ECM changes associated with ageing and disease regulate RPE-photoreceptor interactions, providing a new platform for investigating outer retinal mechanobiology.


Engineered human outer retina model
hiPSC-derived Photoreceptors
hiPSC-derived Retinal Pigment Epithelium
500 µm
Rhodopsin
10 µm
PAA Hydrogel
3D MAP Scaffold
Controlled stiffness
Controlled coating
ECM-dependent
RPE-Photoreceptor Interactions
Co-culture Model
Light-dependent
RPE-Photoreceptor Interactions
Phagocytosis
↑↑↑ Stiffness
Phagocytosis

STOML3 forms ring-like membrane clusters that organize mechanosensitive ion channels

Angela Tzu-Lun Huang[1], Clement Verkest[2], Stefan G. Lechner[2], Gary R Lewin[1]
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Stomatin-like protein 3 (STOML3) potentiates mechanosensitive channels including PIEZO1, PIEZO2, and ELKIN1, yet its structural organization remains poorly understood. Using multi-scale super-resolution imaging — Airyscan, STED, and MINFLUX — we show that STOML3 assembles into heterogeneous ring-like structures (0.1–1.6 µm diameter) on the plasma membrane. Ring formation depends on a conserved proline residue; the P40S mutation abolishes ring architecture without eliminating membrane targeting, instead redistributing STOML3 into dispersed puncta with significantly reduced cluster size and increased cluster number. STOML3 colocalizes and physically associates with the mechanosensitive ion channels PIEZO1, PIEZO2, and ELKIN1, as demonstrated by co-localization imaging and affinity purification. The P40S mutation reduces interaction with these channels, and pharmacological inhibition of STOML3 oligomerization with the small molecule OB-1 similarly disrupts STOML3 association with mechanosensitive ion channels. Cholesterol depletion by MβCD produces a comparable reduction in channel interaction. These findings establish STOML3 ring structures as supramolecular membrane platforms that organize mechanosensitive ion channels and identify ring integrity as a potential therapeutic target for mechanical allodynia.

Morphogenesis across scales: the role of cell surface mechanics in regulating tissue fluidity during gastruloid development

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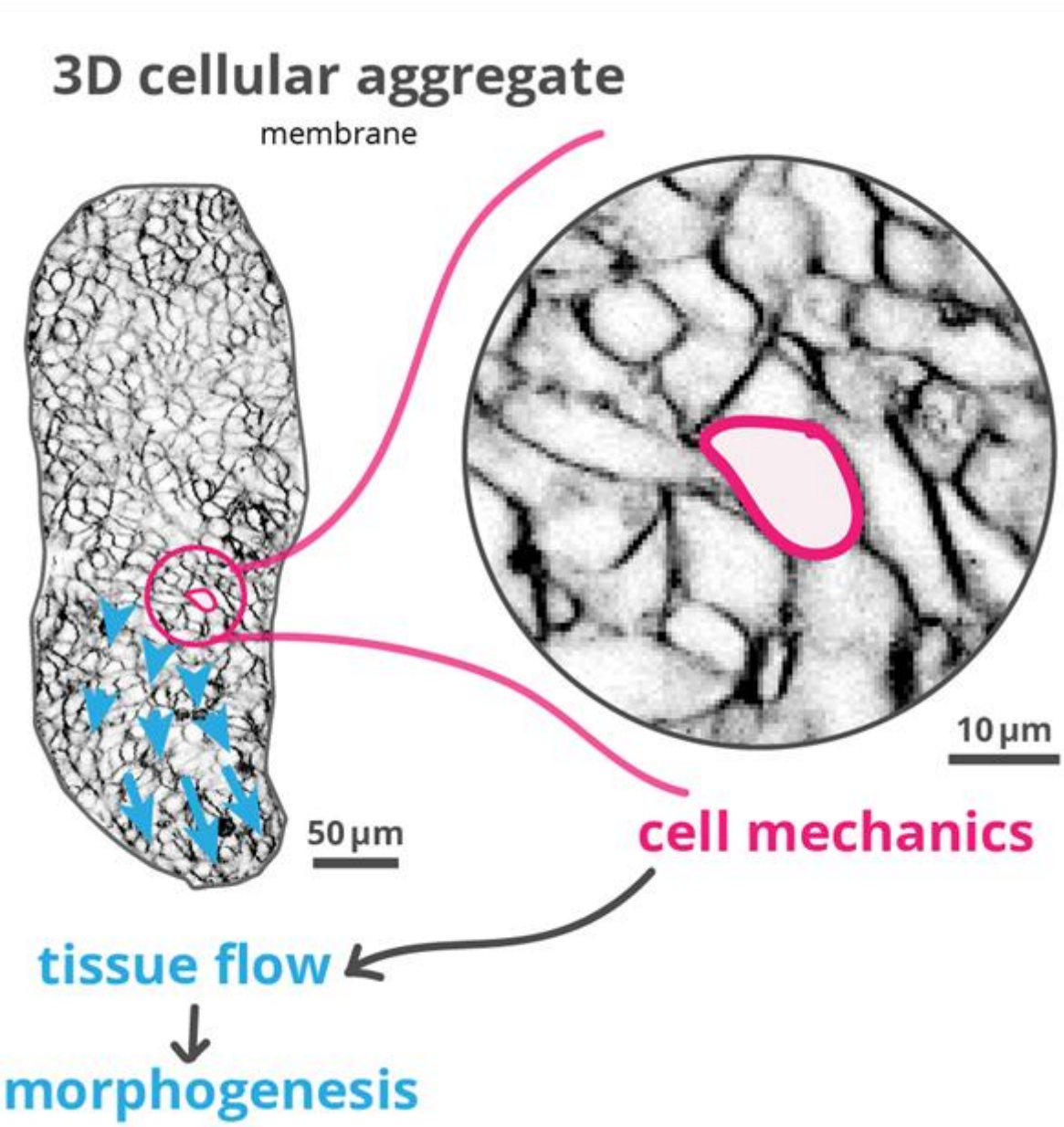
E-Poster Session Tuesday Evening, July 14, 2026, 17:50 - 18:30

During early embryonic development, pluripotent cells differentiate, change shape, and rearrange spatially to form the blueprint of the adult body. While the molecular pathways controlling developmental morphogenesis have been studied extensively, the role of physical properties of cells and tissues in this inherently mechanical process has only recently been brought into focus. Gastruloids—three-dimensional aggregates of mouse embryonic stem cells—have emerged as a robust model system that recapitulates key features of early post-implantation mouse development, including anterior-posterior patterning and body axis elongation. To address the mechanisms underlying gastruloid elongation, we investigate the role of cell surface mechanics in this process. We have shown that gastruloid elongation is inhibited by maintaining high cellular plasma membrane tension through expression of constitutively active ezrin (ezrinCA), an actin-membrane linker protein. We further show that ezrinCA expression does not abolish mesodermal lineage commitment, indicating that the morphogenetic defect is not primarily a result of arrested developmental progression. Using gastruloid fusion as an assay to probe tissue-level mechanics, we find that ezrinCA expression impairs the fusion dynamics of the spherical aggregates at the onset of elongation. This strongly suggests that maintaining high membrane tension leads to decreased tissue fluidity. We are currently investigating how changes in cell surface mechanics control tissue-level viscoelastic properties and drive gastruloid elongation. Our work sheds light on the interplay between cell surface mechanics and morphogenetic movements in developing gastruloids, and more broadly on how mechanical properties of single cells influence tissue fluidity.


3D cellular aggregate
membrane
10 µm
50 µm
cell mechanics
tissue flow
morphogenesis

3D degradable hydrogels unlock enhanced contractility of osteoarthritic chondrocytes

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E-Poster Session Tuesday Evening, July 14, 2026, 17:50 - 18:30

Osteoarthritis (OA) drives phenotypic changes in chondrocytes and disrupts extracellular matrix composition and mechanics. While the importance of mechanical loading in OA etiology is generally accepted, the impact of OA on active cell-generated forces, central to cell-matrix interaction, remains insufficiently understood. Here, we systematically compared the force generation capacity of human OA and non-OA articular chondrocytes and examined how cell culture dimensionality (2D versus 3D) and matrix degradability shape the force generation capacity. Through traction force microscopy (TFM) and high-resolution immunostaining, we found that OA modifies the expression and organization of key proteins involved in force exertion and transmission in both 2D and 3D cultures. Strikingly, only in a 3D degradable hydrogel environment, did these changes translate into increased contractile activity. This elevated contractility by OA chondrocytes is accompanied by enhanced protrusive activity, increased F actin and myosin levels and augmented actomyosin engagement. Additionally, F-actin, β1 integrin and fibronectin redistributed towards the protrusions. Altogether, these alterations may underlie the increased cell-matrix interactions observed in OA chondrocytes. Contrary to this, OA chondrocytes did not exhibit increased contractility when cultured on 2D hydrogel substrates. These findings show that the ability to identify OA-driven mechanobiological changes depends strongly on both the degradability and dimensionality of the culture environment. In conclusion, our findings underscore the importance of 3D degradable environments for revealing disease-associated shifts in chondrocyte force generation and emphasize the importance of selecting appropriate model systems for OA mechanobiology research.

Inferring cell-generated forces through a multisystem generalized 2.5D TFM method

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E-Poster Session Tuesday lunch, July 14, 2026, 13:00 - 13:50

Cell-generated forces play a central role in driving key biological processes, such as angiogenesis and wound healing and their dysregulation has been linked to the onset and progression of numerous diseases. Traction force microscopy (TFM) is the most widely used technique to quantify cell-generated forces. By tracking fiducial markers incorporated into a deformable hydrogel, cell-induced displacements can be measured and, combined with the hydrogel's mechanical properties, used to recover tractions. Conventional 2.5D TFM approaches typically rely on Tikhonov-regularized analytical solutions using Green's functions and the Boussinesq solution, assuming a flat elastic half-space. However, this assumption is frequently violated in practice, because of non-zero displacements at the boundary (e.g. induced by neighboring cells outside the imaged region) and/or non-planar substrates as a hydrogel tilt is often observed in experiments. To overcome these limitations, we propose a multisystem generalized 2.5D TFM method. Our approach implements a physics-based inverse method within a finite element framework, using balance of forces as regularization. The hydrogel surface is automatically detected, meshed and given as input to the finite element framework. To validate the multisystem generalized 2.5D TFM method, we developed an advanced in silico validation framework and compared our method against conventional 2.5D TFM based on Green's function and the Boussinesq solution. Preliminary GT simulations without added noise demonstrate that, under zero hydrogel surface tilt, both the multisystem and conventional 2.5D TFM methods result in minimal traction errors (<1%). In contrast, when substantial hydrogel tilt is introduced, traction errors from the conventional method increase markedly (up to 85%), while the multisystem method maintains consistently low errors (<1%). Overall, our multisystem generalized 2.5D TFM method eliminates the elastic half space assumption, which is experimentally often unfeasible, thereby making 2.5D TFM more accurate and compatible with diverse in vitro experimental setups.

Investigating Heart-Generated Mechanical Stimuli as an innovative Cancer Therapy

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E-Poster Session Tuesday lunch, July 14, 2026, 13:00 - 13:50

Cancer is the second leading cause of death worldwide, accounting for approximately 1500 cancer-related deaths every day. Despite significant therapeutic advances, current treatments are often associated with severe side effects and rely predominantly on systemic approaches for metastatic disease. There are no effective technologies to control local cancer recurrence.

While most organs are frequently affected by cancer, primary cardiac malignancies are sporadic. This observation is intuitive for cardiomyocyte-derived tumors, given cardiomyocyte limited proliferative capacity, but remains unexplained for other cardiac cell types that retain replicative potential. Moreover, cardiac metastases are uncommon, despite constant exposure of the heart to circulating tumor cells.

We hypothesize that the unique mechanical forces generated by the beating heart act as a natural barrier to cell proliferation, including that of cancer cells. Building on this concept, we aim to develop an innovative technology capable of mimicking cardiac contraction and applying physiologically relevant mechanical forces to cancer cells.

By recreating heart-like mechanical stimulation in vitro, we investigated how dynamic mechanical cues regulate cancer cell proliferation and survival in a mouse model of cutaneous melanoma. We found that a specific combination of pressure intensity and frequency significantly reduced cancer cell proliferation and tumor growth. No metastatic spread was detected upon mechanical stimulation.

These data introduce a new paradigm in cancer research, leveraging mechanical systems to control tumor growth, and pave the way to a mechanical therapy for human cancer.

Spontaneous morphogenesis of fibrous micro-tissue

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E-Poster Session Wednesday Lunch, July 15, 2026, 13:00 - 13:50

The extra-cellular matrix (ECM) is a mesh-like network that provides structural support and mechanical cues for cells, directly regulating behaviors such as differentiation, migration, and proliferation (Rozario & DeSimone, Dev Biol, 2010). Stromal cells can chemically change the ECM through secretion and enzymatic digestion of the matrix, but they can also mechanically remodel the ECM through the traction forces they exert onto it via focal adhesions (Hall et al., PNAS, 2016). Due to the fibrous micro-structure of the ECM, these forces can propagate and potentially be sensed by neighboring cells over large distances. This raises the question of whether and how stromal cells can collectively self-organize by inter-cellular communication through the ECM.

To answer this question, I developed a micro-tissue assay composed of mesenchymal stem cells embedded in a 3D gel of type I collagen. By monitoring 3D tissue shape changes with cell-scale resolution over days, I observed the formation of localized regions of negative curvature at the micro-tissue surface (Fig 1A), corresponding to tissue invaginations. These regions progressively deepen over time and organize at the tissue scale into polyhedral patterns (Fig. 1B). By performing targeted pharmacological perturbations of the acto-myosin cytoskeleton and integrin-mediated adhesions, I could demonstrate the role of cell-generated forces and integrin dynamics in these morphogenetic events. I am currently investigating whether these invagination regions correspond to heterogeneities in cell phenotypes and/or ECM mechanical properties.

Altogether, this newly identified surface instability of active origin should help to uncover mechanistic principles governing cell-ECM interplay and tissue self-organization, with potential implications for ECM-associated pathologies and future strategies in tissue engineering and regenerative therapies.

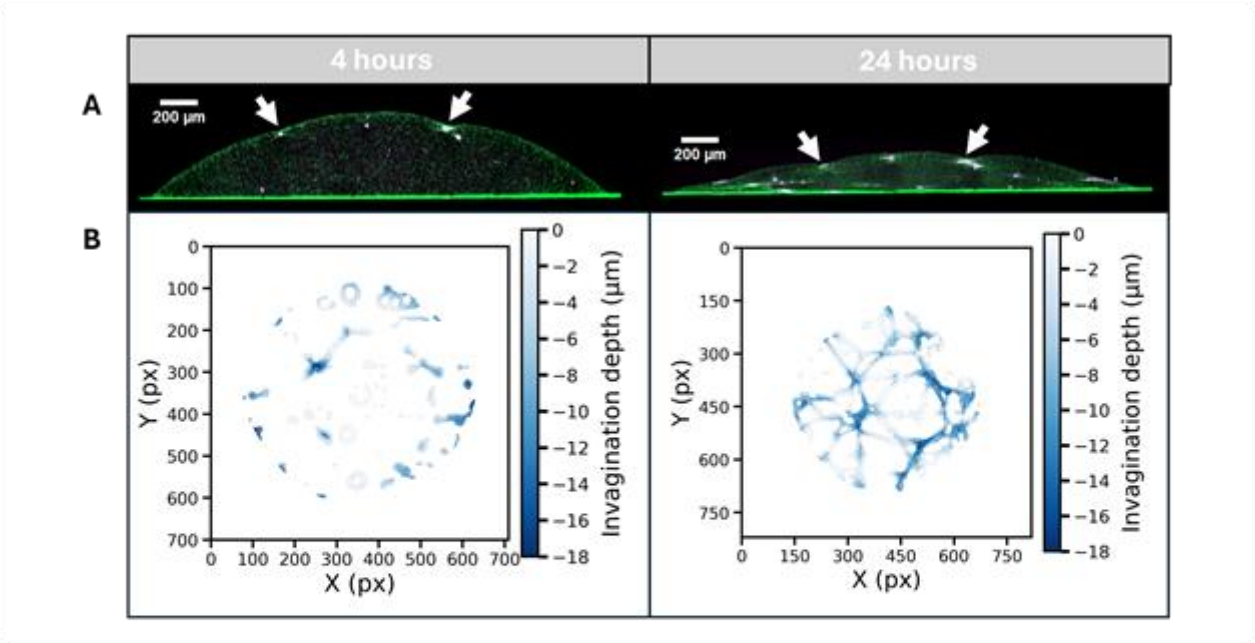

Figure 1. Emergence of micro-tissue invaginations. (A) Confocal microscopy central micro-tissue reslice in XZ plane, after 4 and 24 hours of culture. Collagen fibers are visualized by reflectance (green), C3H 10T 1/2 cell membranes labeled with cell mask (magenta). **(B)** Visualization and quantification of micro-tissue invaginations at 4 and 24 hours of culture, obtained from confocal microscopy data and image-analysis pipeline. See scale of invagination depth on the right.

Exploring how extracellular matrix stiffness influences breast cancer cell sensitivity to cell cycle inhibitors

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E-Poster Session Wednesday Lunch, July 15, 2026, 13:00 - 13:50

Metastatic breast cancer cells colonise secondary organs of varying extracellular matrix (ECM) stiffness, ranging from soft brain niches to rigid bone microenvironments. Matrix stiffness is a key regulator of mechanotransduction pathways and has been implicated in regulating tumour progression and therapeutic responses. In HR+/HER2- breast cancer, increased ECM stiffness activates YAP/TAZ signalling, promoting epithelial-mesenchymal transition (EMT) and stem-like phenotypes with reduced proliferation. Conversely, downregulation of FAT1 in increased stiff conditions has also been linked to induce proliferation, promoting cell cycle progression and potentially reduce sensitivity to CDK4/6 inhibitors.

How these opposing mechanotransduction pathways are integrated to determine cell cycle fate and response to CDK4/6 inhibitors remains unclear. Consequently, this project aims to elucidate how matrix-dependent mechanotransduction regulates breast cancer cell cycle progression and sensitivity to CDK4/6 inhibitors.

To investigate this, we are culturing (HR+/HER2-) breast cancer cell lines on hydrogels of varying stiffness across a physiologically relevant range (0.1kPa–100kPa) and determining sensitivity to CDK4/6 inhibitors using quantitative, single-cell, high-throughput imaging. EMT is assessed in parallel by analysing cell morphology and the expression of epithelial and mesenchymal proteins. Additionally, we are using an MCF-7 fluorescent reporter cell line to track the cell response to CDK4/6 inhibitors in 3D spheroids over time. These reporter cells express mCherry-Geminin to track cell cycle phase, p21-GFP to monitor senescence and TagBFP2-H2B to track individual nuclei. We identified significant changes in how cells respond to CDK4/6 inhibitor treatment in 2D versus 3D that we are now investigating further.

Our findings suggest that matrix stiffness modulates the proliferative response of MCF-7 cells to CDK4/6 inhibitors, indicating that ECM mechanical properties could contribute to CDK4/6 inhibitor tolerance, independently of genetic resistance mechanisms. Thus, identifying specific mechanotransduction pathways underlying the different cell responses across matrix stiffness could aid in restoring cell sensitivity to these drugs across all metastatic niches.

Bioengineering breast cancer dormancy in the bone marrow niche

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E-Poster Session Tuesday lunch, July 14, 2026, 13:00 - 13:50

Breast cancer recurrence is frequently driven by dormant disseminated tumour cells that persist within the bone marrow niche and later reactivate. To address this challenge, we are developing a bioengineered platform that models and detects dormancy using bioactive metabolites delivered via lipid nanoparticles.

In 2D studies with MCF-7 breast cancer cells, treatment with bioactive metabolites reduced expression of the proliferation marker Ki-67 and increased expression of dormancy-associated markers p27 and COUP-TFI, confirming induction of a quiescent phenotype. We further demonstrate that lipid nanoparticles can be efficiently loaded with these metabolites and are readily internalised by MCF-7 cells, enabling controlled delivery.

Building on this, we are engineering a 3D bone marrow–mimetic niche in which breast cancer micrometastases are embedded within a highly compliant hydrogel matrix (<1 kPa), recapitulating the soft mechanical environment of marrow. The model incorporates haematopoietic and mesenchymal stem cells to support long-term maintenance of dormancy and stemness, capturing key cellular and mechanobiological interactions.

Importantly, these systems are designed as technologies to detect and study recurrence by identifying cues that trigger reactivation, such as infection-induced inflammation. By integrating the model into microwell-based chip platforms, we enable high-throughput screening of microenvironmental and inflammatory stimuli. This approach provides a powerful tool to uncover mechanisms of dormancy escape and supports the development of improved diagnostic strategies and personalised therapies aimed at preventing fatal breast cancer recurrence.

Design of mechano-protective drugs to tackle solid cancers

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E-Poster Session Tuesday lunch, July 14, 2026, 13:00 - 13:50

Micropatterns with pre-designed shape, stiffness, topology, and wettability will affect the adhesion, migration, proliferation, apoptosis, ECM production, differentiation, and transformation of cells. The main aim of project is to develop high-throughput methods to study the impact of the geometry and tensional state of cells on cellular adhesion, cellular mechanics, and mechanosensitivity and explore mechanoprotection strategies.

Alveole photopatterning device is utilized to make micropatterns. C2C12 cells are used for the preliminary experiments and then fixed and stained with phalloidin and checked under the LSM980 confocal microscope. Quantification pipelines of micropatterns and cells are custom-built with Python. Cellular deformation model is built based on paper Torres et al., 2012 to compare the experimental result. Chiaro nanoindenter from Optics 11 Life is utilized to measure the elasticity of cells adhered to micropatterns.

Micropatterns have great effects on the cytoskeleton and cellular mechanics and adhesion. The cell membranes shows arc-shape and are under high tension. Micropatterns affect the arrangement of actin. Actins form stress fibers which aligns with the boundary of the micropatterns, but not many actins form meshwork in the center of the cell compared with cells not on the pattern. The cell nucleus is elongated under high strain. The distribution of deformed cellular area may come from the effects of shape, size and spacing of micropattern. The timescale of cellular adhesion may also affect the mechanical properties of the cell and the relevant signaling pathway.
The stiffness of the cell on the pattern is smaller than the stiffness of the cell not on the pattern. Although the micropattern regulates the cytoskeleton of the cell, the micropattern has a softening effect. There is a high heterogeneity of the measured stiffness of cells on the pattern and not on the pattern, the viscoelastic mechanical property cannot be neglected for adhered cells.

Engineered viscoelastic hydrogels to maintain mesenchymal stem cell phenotype and limit senescence via mechanotransduction

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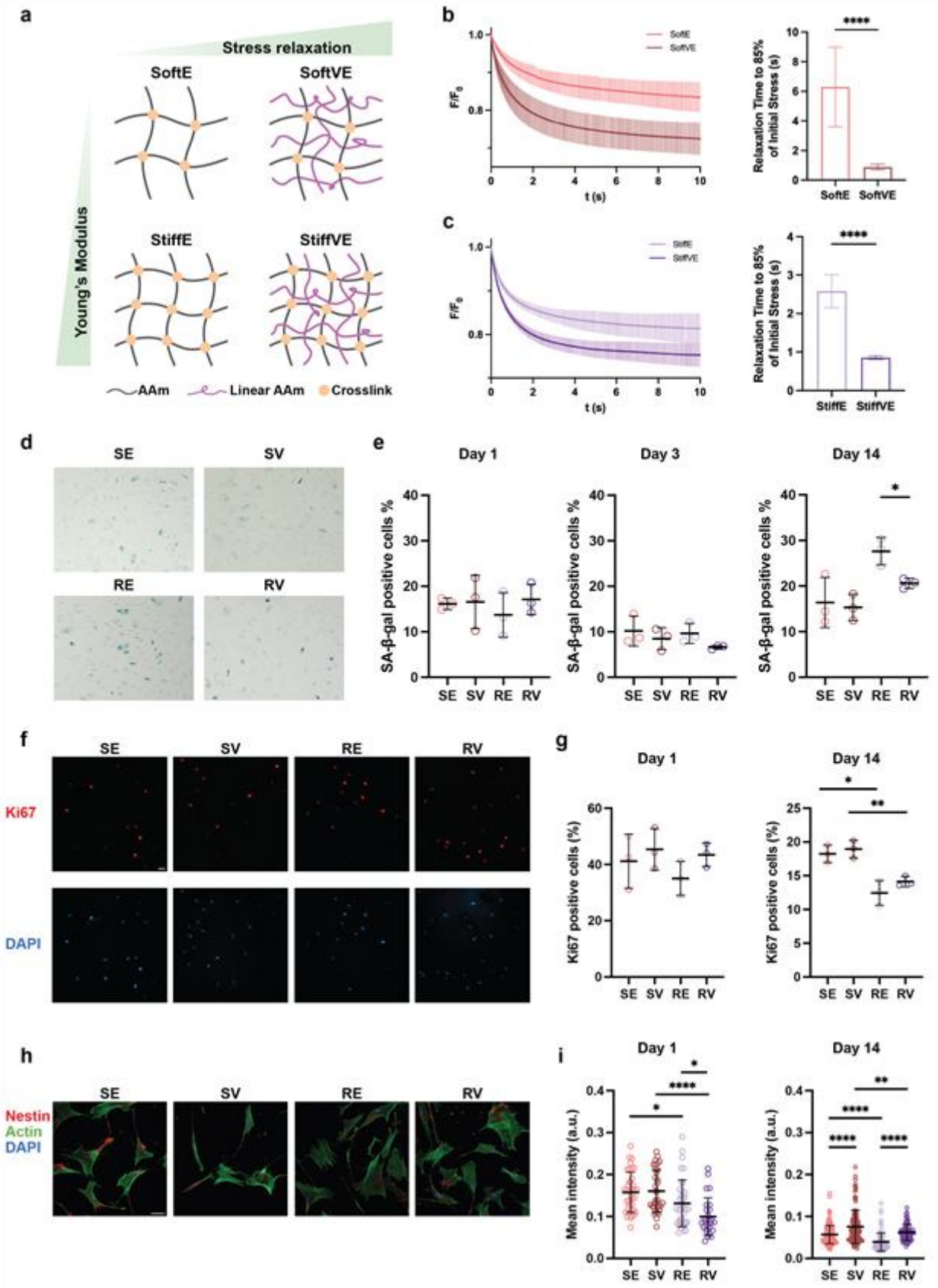
E-Poster Session Wednesday Lunch, July 15, 2026, 13:00 - 13:50

Mesenchymal stem cell (MSC) phenotype is governed by cell-material interactions via extracellular matrix (ECM), where mechanical properties and biochemical cues synergise to regulate proliferation and differentiation. While substrate stiffness is a well-established mechanobiological regulator, matrix viscoelasticity has emerged as a governing mechanical property capable of directing stem cell fate. However, the potential of viscoelasticity to maintain MSC stemness while controlling their proliferation and limiting senescence remains unexplored.

Here, we engineered polyacrylamide (PAAm) hydrogels with low (~5 kPa) and high (~15 kPa) stiffness, each with controlled dissipative components using linear acrylamide, modulating stress relaxation. The developed hydrogels were functionalised with collagen type I. The results showed that MSCs respond to stiffness and viscoelasticity, with reduced cell area on softer and viscoelastic substrates. After 14 days of culture, both viscoelastic substrates decreased the proportion of senescence-associated β-galactosidases (SA-β-gal)-positive cells. While stiff viscoelastic substrates decreased expression of the cellular senescence marker P21. Viscoelasticity also increased the proportion of Ki67-positive cells for both early and later culture periods, suggesting improved proliferative activity. In addition, MSCs on viscoelastic substrates showed higher Nestin expression, indicating improved maintenance of a stem-like phenotype and bone marrow niche-associated characteristics.

To investigate the mechanism of these responses, we examined molecular clutch-related mechanotransduction. MSCs on viscoelastic hydrogels exhibited an increased phosphorylated myosin light chain 2 (pMLC)/MLC ratio, indicating enhanced actomyosin contractility. Interestingly, nuclear YAP localisation was higher on elastic hydrogels, with the greatest nuclear translocation observed on soft elastic substrates. These findings suggest that sustained elastic resistance, rather than contractility alone, may preferentially promote YAP nuclear localisation. We further hypothesise that viscoelasticity modulates force loading within the molecular clutch, thereby altering focal adhesion maturation and downstream senescence-associated mechanotransduction. Ongoing experiments will study how focal adhesions contribute to the ability of engineered viscoelastic matrices to preserve MSC phenotype.


a
Stress relaxation
SoftE
SoftVE
StiffE
StiffVE
Young's Modulus
AAm
Linear AAm
Crosslink
b
SoftE
SoftVE
F/F0
t (s)
Relaxation Time to 85% of Initial Stress (s)
****
c
StiffE
StiffVE
F/F0
t (s)
Relaxation Time to 85% of Initial Stress (s)
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d
SE
SV
RE
RV
e
Day 1
Day 3
Day 14
SA-β-gal positive cells %
SE SV RE RV
*
f
SE
SV
RE
RV
Ki67
DAPI
g
Day 1
Day 14
Ki67 positive cells (%)
SE SV RE RV
*
**
h
SE
SV
RE
RV
Nestin
Actin
DAPI
i
Day 1
Day 14
Mean intensity (a.u.)
SE SV RE RV
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A Light-tunable Phantom Cell to Study Epithelial Mechanical Equilibrium

Felix Reul[1,2], Tanishka Watts[1,2], Cédric Bergerbit[2,3,4], Vasudha Turuvekere Krishnamurthy[1,2], Alexandra Raab[1,2], Yuxin Ji[1,2], Laura De Laporte[2,3,4], Jacopo Di Russo[1,2]
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E-Poster Session Wednesday Lunch, July 15, 2026, 13:00 - 13:50

Epithelial monolayers maintain their function through a finely tuned mechanical equilibrium between cell–extracellular matrix (cell–ECM) and cell–cell adhesion. Age-related changes in ECM remodelling or cell density can disrupt this balance, yet how such perturbations propagate across tissues remains poorly understood. While tools exist to perturb and measure cell–ECM mechanics, precise control over cell–cell adhesion forces remains challenging and often relies on genetic perturbations (e.g., optogenetics) or disruptive approaches such as laser ablation. To address this need, we developed a poly(ethylene glycol)-based microgel that acts as a “phantom cell”, integrating into epithelial monolayers via cadherin-based adhesion. Incorporation of a light-cleavable crosslinker enables spatiotemporal control of the microgel’s mechanical properties using brief UV illumination. This local modulation of stiffness alters the microgel’s mechanical contribution to the surrounding tissue, enabling controlled investigation of epithelial force balance by selectively engaging the actin or keratin network of the surrounding monolayer depending on the microgel protein coating: E-cadherin to couple to the actin cytoskeleton, or desmoglein to interface with the keratin network. To quantify the resulting mechanical responses at a multicellular level, we optimised thin hydrogel substrates embedded with fluorescent beads, enabling traction force microscopy. This versatile platform is readily adaptable to other epithelial systems, providing a powerful tool to probe force propagation and mechanical homeostasis in tissue mechanobiology.

Mechanochemical feedback couples cranial neural crest migration and neural tube morphogenesis via mechanosensitive fibronectin remodelling

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E-Poster Session Tuesday Evening, July 14, 2026, 17:50 - 18:30

Cranial neurulation and collective migration of cranial neural crest cells are two major processes during embryonic morphogenesis. Although often considered distinct and functionally independent, spatiotemporal overlap exists between both to a various degree across many species. Using Xenopus laevis as a model, we show that collective cranial neural crest migration is a prerequisite for cranial neural tube closure. Neural crest delamination and invasion into extracellular matrix, secreted by the cranial mesoderm, leads to fibronectin remodelling along the neural crest-neural plate border. The emerging fibronectin sheet not only segregates neural crest and neural plate but is also necessary for neural tube morphogenesis. Mechanistically, neural crest cells express the membrane-bound matrix metalloproteinase MMP14, which is necessary and sufficient for this fibronectin remodelling. Thus, the mechanism depends on spatially localised MMP14 activity, facilitated by collective neural crest cell movement, rather than diffusion. Finally, our data reveal that the neural crest-specific expression of MMP14 is mechanosensitive and amplified by compressive forces. Strikingly, such forces arise in vivo due to neurulation itself, as the bending motion of the neural folds spatially confines neural crest cells between the underlying mesoderm and the superficial ectoderm.

3D ECM Stiffness Modulates Energy Metabolism to Drive Stem Cell Osteogenic Differentiation

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Matrix stiffness is a critical regulator of stem cell behavior. Nevertheless, the mechanisms by which stem cells perceive and respond to matrix stiffness during the early stages of bone remodeling remain unclear. This study aimed to investigate how extracellular matrix (ECM) stiffness influences osteogenic differentiation in human mesenchymal stem cells (hMSCs) within a three-dimensional (3D) GelMA hydrogel system and to reveal the underlying mechano-mechanisms.
A 3D culture platform with varying matrix stiffness was established using GelMA hydrogels. A soft 3D matrix (~5 kPa) significantly enhanced osteogenic differentiation compared to a stiff matrix (~20 kPa), as evidenced by upregulated osteogenic gene expression and increased alkaline phosphatase (ALP) activity in vitro. MSCs within the soft matrix exhibited accelerated spreading and a larger cell volume. Notably, these cells displayed a higher proportion of elongated, filamentous mitochondria and sustained elevated metabolic activity, including increased ATP production, oxygen consumption rate, and extracellular acidification rate. Further investigation into the cytoskeletal mechanoresponse revealed that soft matrix conditions upregulated the expression of the microtubule acetyltransferase αTAT1 and enhanced α-tubulin acetylation, indicating modified microtubule stability. Disruption of microtubule dynamics with Taxol or knockdown of αTAT1 via siRNA attenuated mitochondrial networking, suppressed metabolic activity, and inhibited ALP activity in the soft matrix group. In summary, this study demonstrates that a soft 3D matrix promotes hMSC spreading, microtubule reorganization, mitochondrial networking, and bioenergetic activation, collectively driving osteogenic commitment. These findings establish a mechanotransductive axis wherein microtubule integrity facilitates mitochondrial adaptation and metabolic reprogramming to meet the bioenergetic demands of osteogenesis. This study demonstrated the important role of soft ECM in the design of tissue engineering materials for bone repair and revealed the necessary effects of soft tissues in promoting the osteogenic differentiation of cells at the early stage of bone reformation.