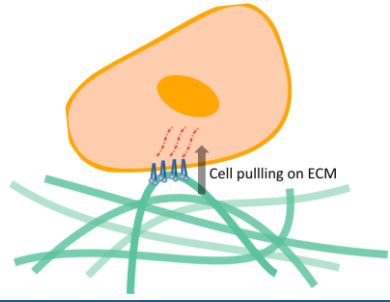


Could molecular extensibility determine the fate of disseminated cancer cells?

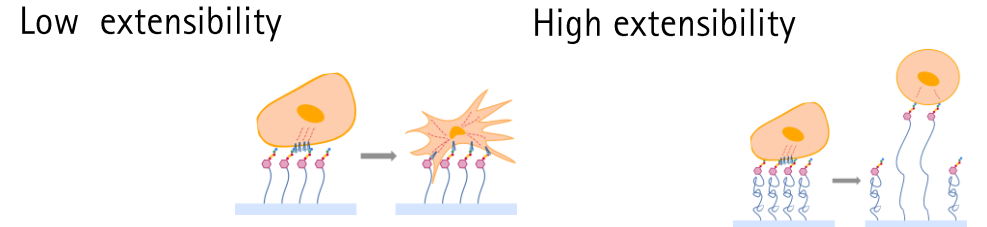


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Molecular extensibility: A mechanical cue cells can pull on...

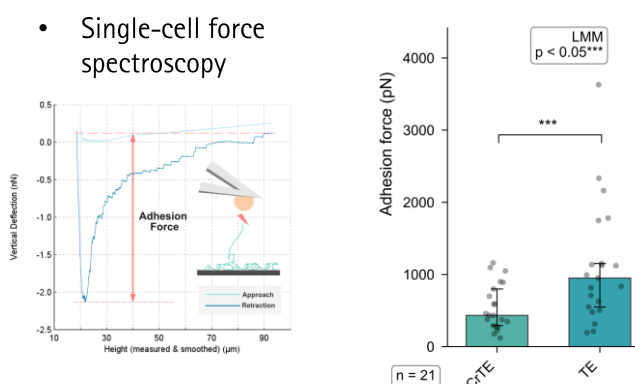
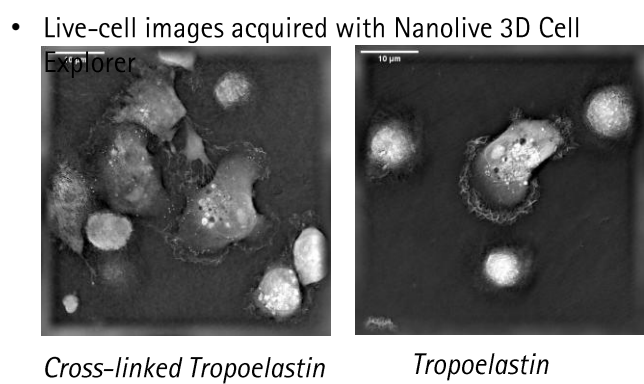
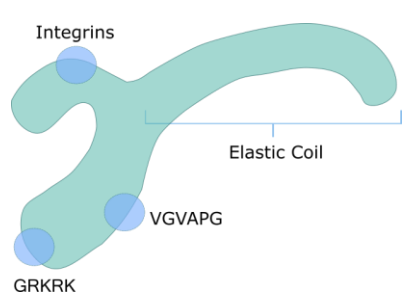
How do the mechanical properties of the microenvironment influence disseminated cancer cells?

Cells behave differently on substrates with varying extensibilities. They feel a lower resistance on substrates with high extensibility, and vice versa



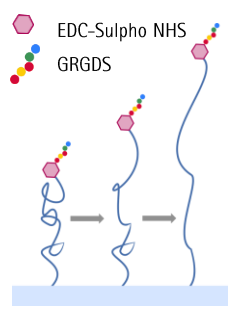
Model systems to study the influence of molecular extensibility on cells

Tropoelastin: a highly extendable biomolecule



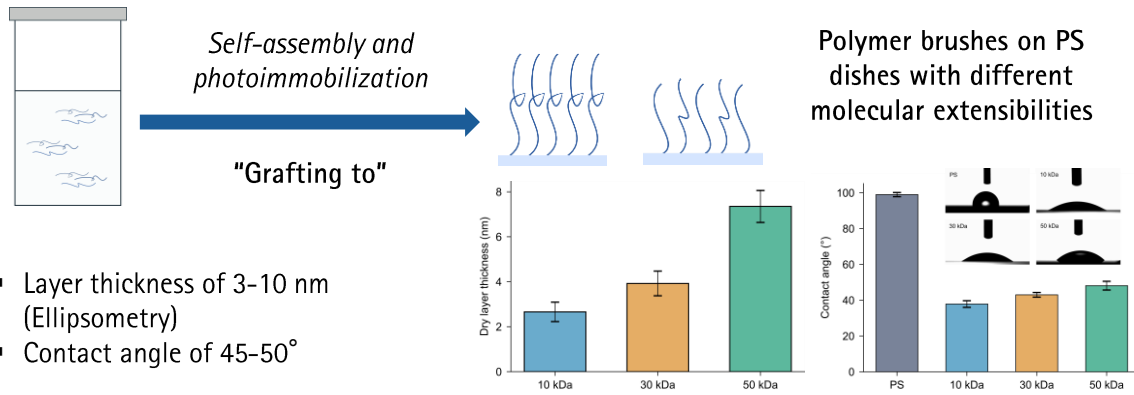
MDA-MB-231 cells (metastatic breast cancer cell line) exhibited different morphological behaviors and cell-matrix adhesion responses on tropoelastin (TE), compared to cross-linked tropoelastin (CrTE) with reduced extensibility

PHEMA-b-BPMA: a synthetic analog for extendible biomolecules

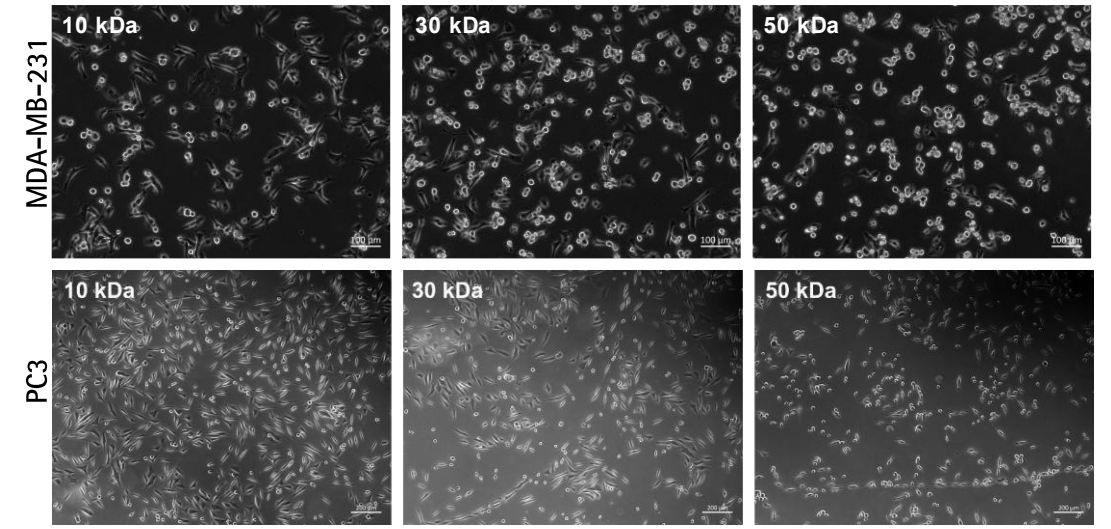


Synthetic, bioinspired, extendable, biofunctionalized polymers with mechanical properties decoupled from biochemical cues with a high throughput for cell-biological experiments

- Different molecular weight poly (hydroxyethyl methacrylate-block-4-hydroxybenzophenone methacrylate) (PHEMA-b-BPMA) with tunable contour lengths were coated on polystyrene (PS) surfaces



MDA-MB-231 and PC3 (metastatic prostate cancer cell line) cells were cultivated on biofunctionalized 10, 30 and 50 kDa PHEMA-b-BPMA in a serum-deprived state and imaged with phase contrast microscopy

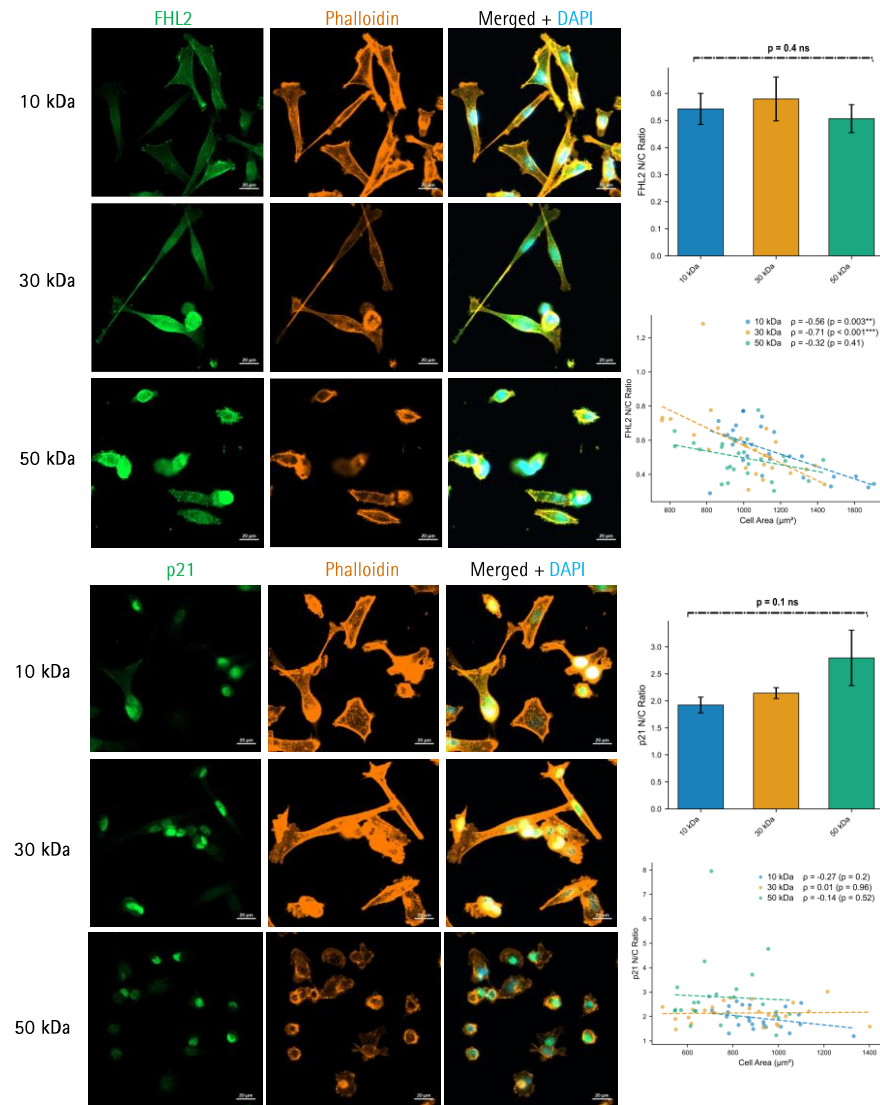


Substrates with low extensibility offers higher resistance to pulling forces of cells, therefore, a stronger adhesion was observed on lower molecular weight PHEMA-b-BPMA

Mechanotransduction, and cell-cycle progression dependent on molecular extensibility

FHL2 and p21 localization dependent on molecular extensibility

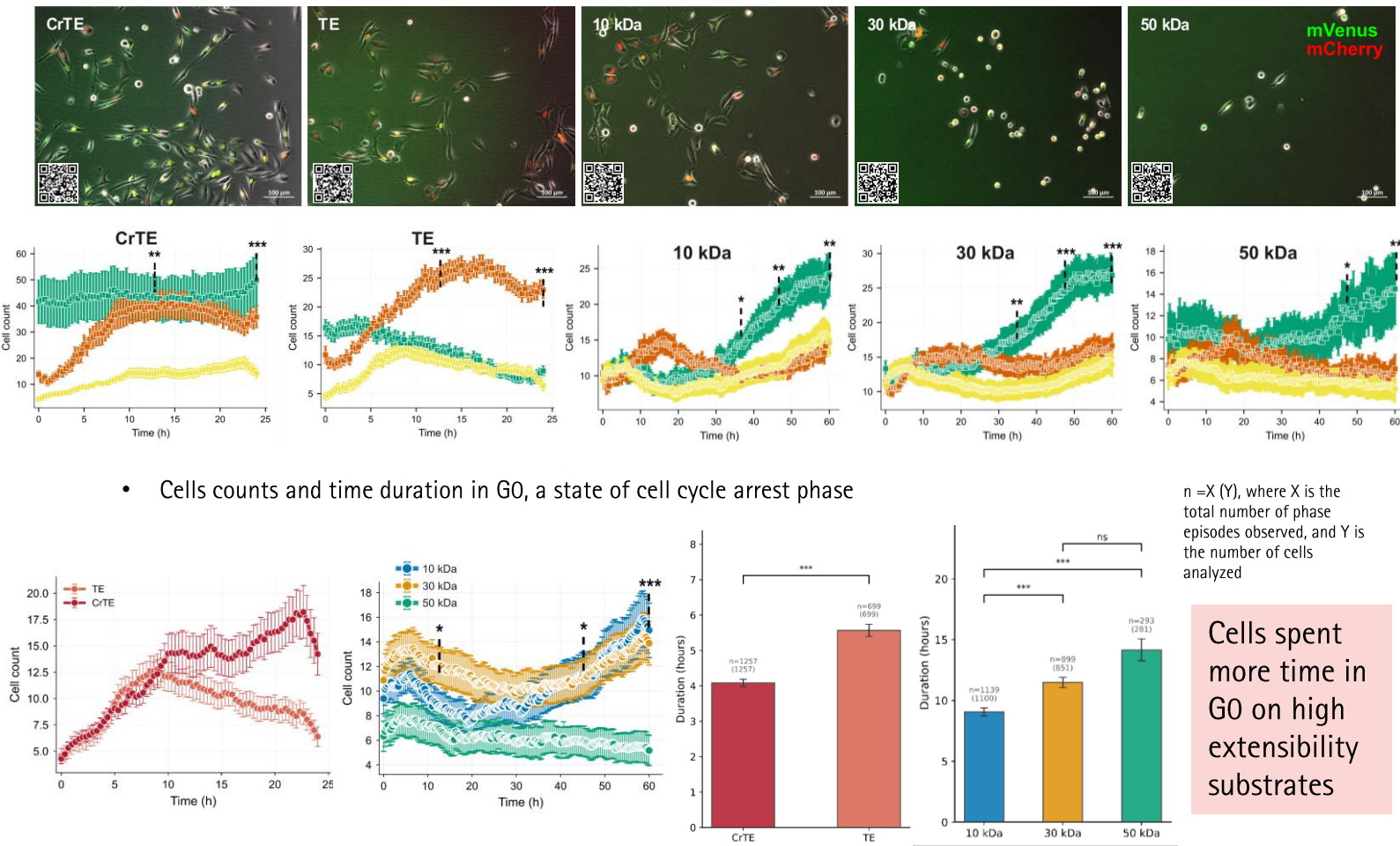
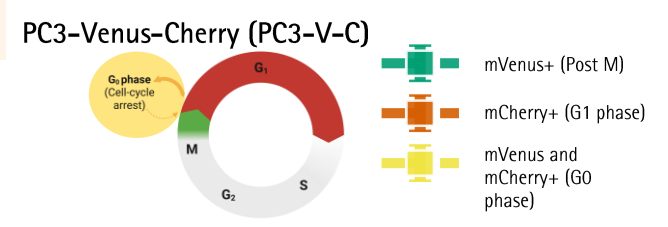
MDA-MB-231 cells were cultivated on PHEMA-b-BPMA coated dishes in a serum-deprived state for 3 days; then fixed, stained and imaged with a confocal microscope, followed by quantification of nuclear/ cytoplasmic (N/C) ratios



p21 levels increase for high extensibility substrates

Live cell imaging with cell-cycle indicator cell lines

Cells were cultivated on both tropoelastin and PHEMA-b-BPMA model systems, and the cell-cycle progression was monitored with time-lapse live cell imaging; followed with quantitative analysis using ConfluentFUCCI framework



Cells spent more time in G0 on high extensibility substrates

→ The results indicate the potential influence of molecular extensibility on tumor cell cycling, proliferation, and dormancy and enhance our understanding of the role of molecular extensibility as a biophysical cue in regulating the fate of disseminated tumor cells.