Engineering Mechano-actuating Hydrogels to Deconstruct Cell-Extracellular Matrix Co-Adaptive Mechanisms

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Challenges

Fibrosis is characterised by progressive extracellular matrix (ECM) stiffening and dysregulated mechanosensitive signalling, particularly involving FAK activation and YAP nuclear localisation. However, current models are limited by static conditions that fail to reflect the dynamic cell mechanics in vivo environment.

Objectives

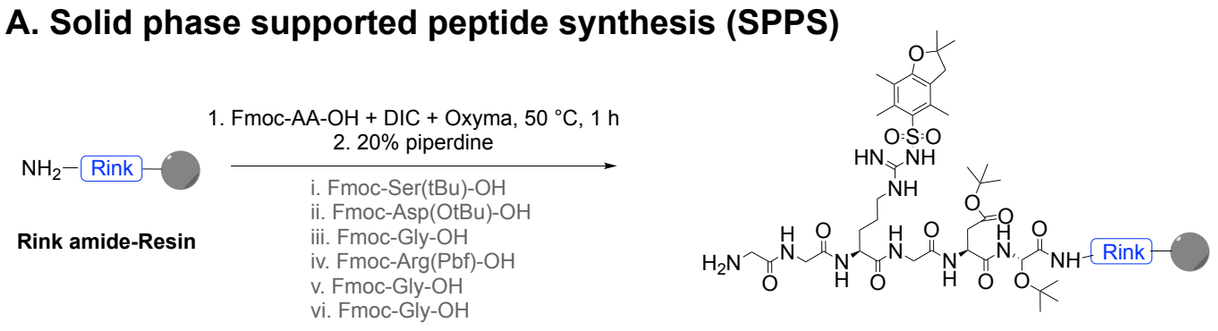
- Engineering mechano-actuating hydrogels based on PNIPAm to recapitulates the evolving mechanical environments in cell mechanics.
- Decoupling force from the bulk stiffness of hydrogels by creation of time-varying and localised forces.

Design of AuNR-PNIPAm-GGRGDS Actuator

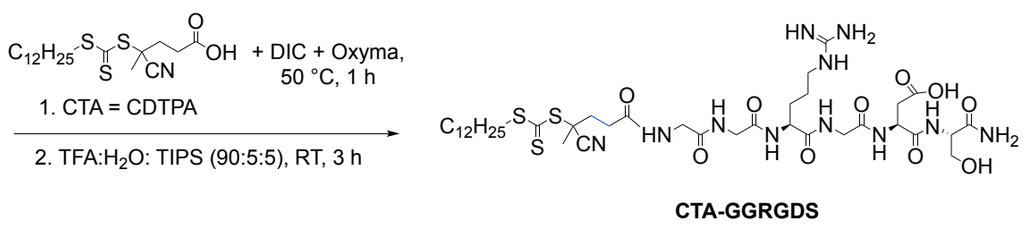
- **PNIPAm incorporated with gold nanorods (AuNR):** enabling rapid photothermal conversion of **near-infrared (NIR) light** into heat and facilitate force localisation under cytocompatible conditions.
- Force control: Molecular weight of PNIPAm.
- **Introduction of integrin-binding peptide (RGD) into the system:** promoting force transmission from ECM and regulate intracellular mechanotransduction.

Synthesis route

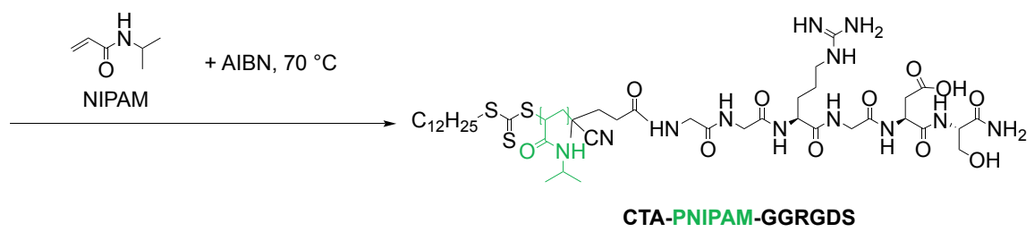
A. Solid phase supported peptide synthesis (SPPS)



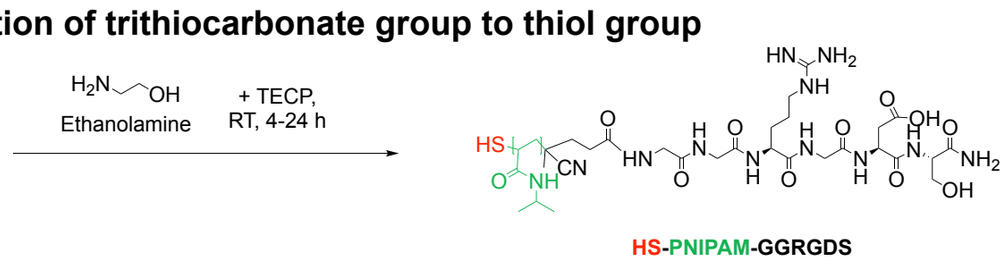
B. Introduction of the chain trasfer agent (CTA) and cleavage from the support



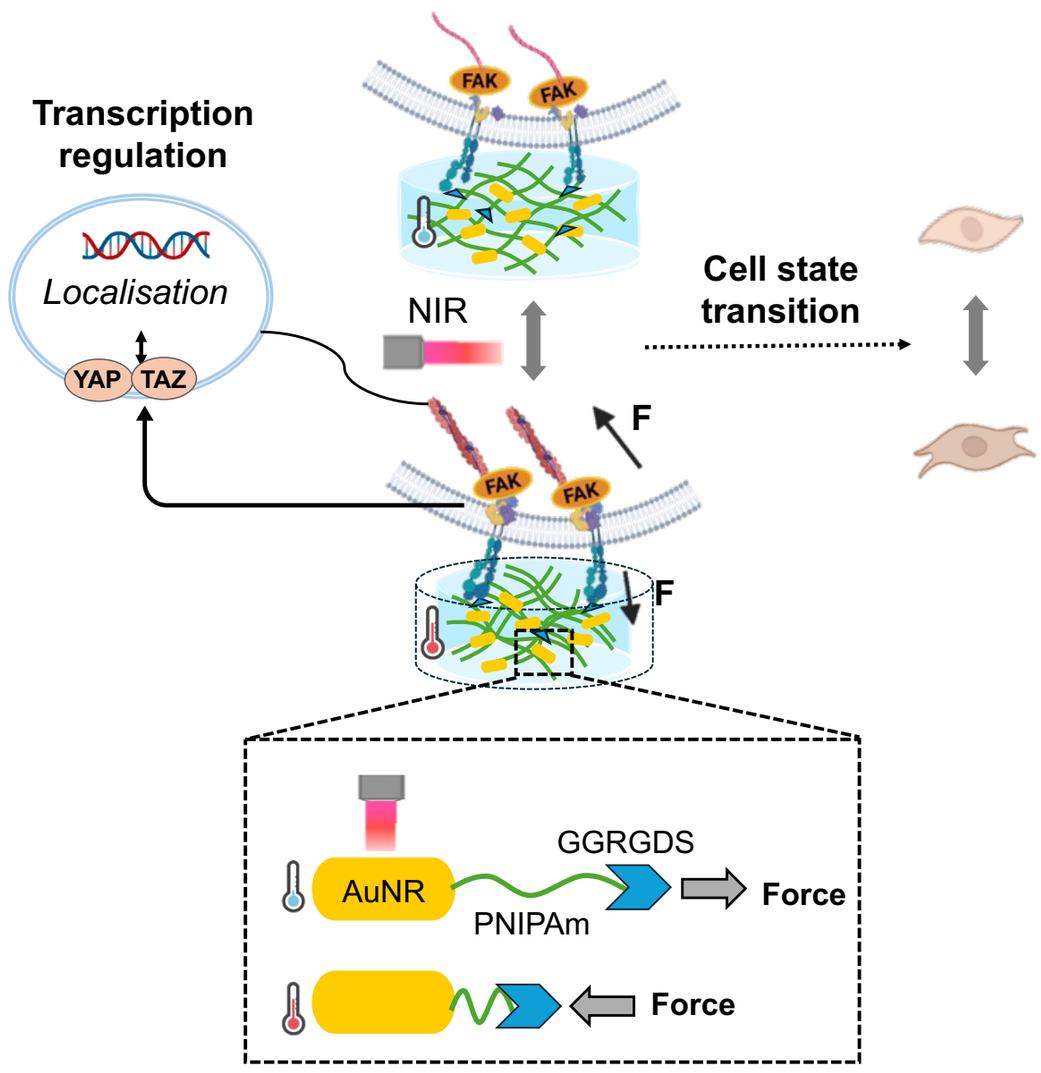
C. RAFT polymerisation of NIPAm on the peptide



D. Transformation of trithiocarbonate group to thiol group

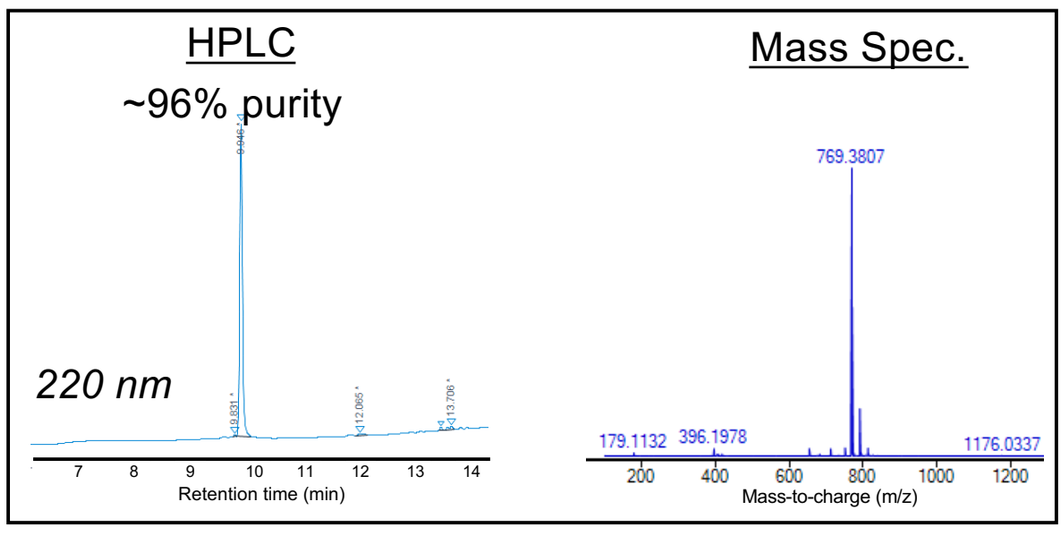


Mechanical modulation on mechanotransduction and cell state

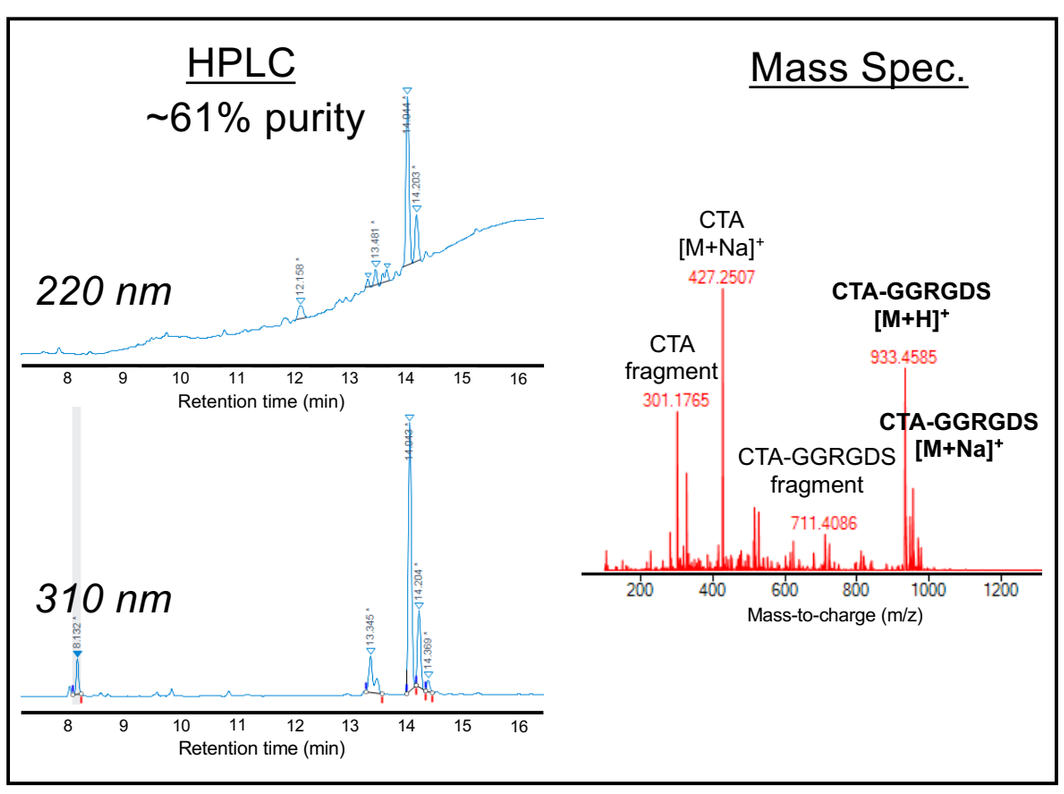


AuNR-PNIPAm-GGRGDS Actuator

Fmoc-GGRGDS



CTA-GGRGDS



Discussions & Outlook

- SPPS approach facilitates peptide synthesis with high purity ~ 96%. However, attaching hydrophobic CTA to peptides reduces the overall purity, suggesting that the purification strategy requires further optimisation.
- The next step is to syntehsyse different molecular weight of PNIPAm-GGRGDS via RAFT polymerisation, and attach RGD-PNIPAm-GGRGDS conjugates on AuNR for further investigations of force magnitudes, application rates, and relaxation dynamics under NIR light that will affect cellular force transmission.

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European Commission