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MECHANOBIOLOGY & SOFT MATTER *group*

Role of molecular and supramolecular chirality of the protein matrix on epithelial cell migration

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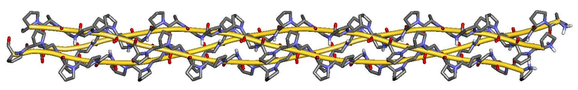
Chirality is ubiquitous in Nature, from living organisms to biomolecules, and influences fundamental processes that involve intermolecular interactions. Interestingly, many of these biological processes are based on cell proliferation and migration, that both rely on interactions with proteins of the extracellular matrix (ECM). While various physico-chemical cues of the cell microenvironment have been studied extensively, the influence of the ECM chirality on cell migration has been overlooked. To explore this issue, we propose to use multi-hierarchical self-assemblies of (oligo)peptides to design well-defined in vitro migration assays. By using this multidisciplinary approach, we will investigate the effect of chirality, from the molecular to the supramolecular level, on the migration of epithelial cells in 2D and 3D microenvironments.

We aim at understanding how molecular and supramolecular chirality can modulate integrin-based mechanotransduction mechanisms involved in cell migration

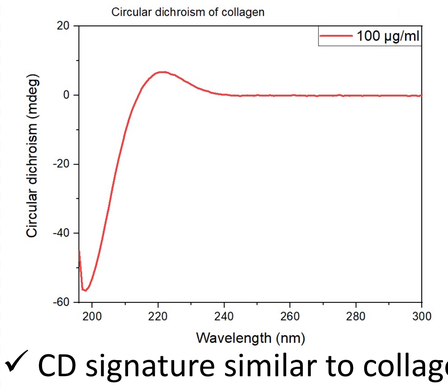
Structures of L and D peptides

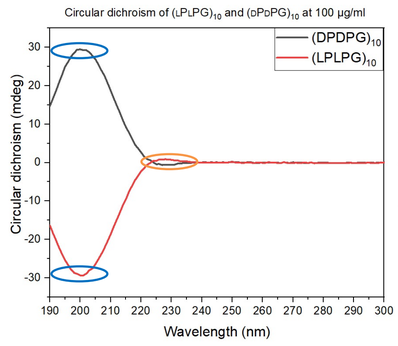
$(LPLPG)_{10}$: LPLPGLPLPGLPLPGLPLPGLPLPGLPLPGLPLPGLPLPGLPLPGLPLPG

$(DPDPG)_{10}$: DPDPGDPDPGDPDPGDPDPGDPDPGDPDPGDPDPGDPDPGDPDPGDPDPG

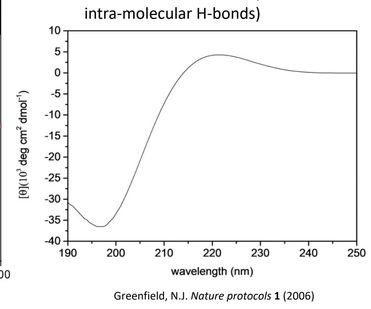


Representation of the collagen triple helix from the intertwining of 3 (PPG)10 peptidic chains, as obtained from a crystal structure available on the Protein Data Bank (PDB ID: 1K6F).





Polyproline P_{II} helix (left-handed extended helix, NO intra-molecular H-bonds)



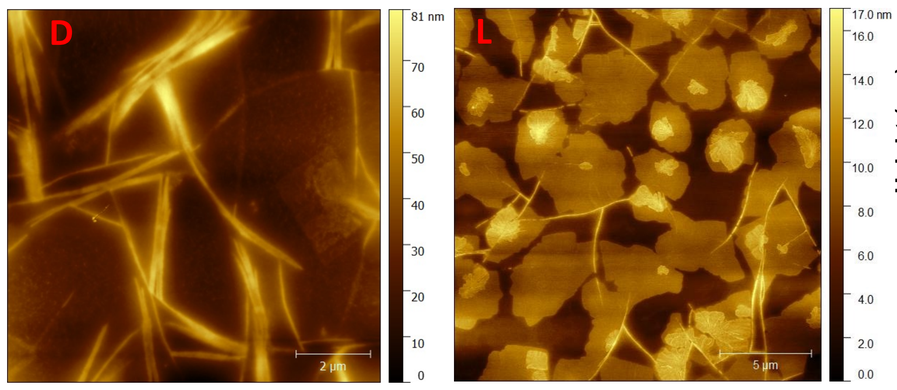
Greenfield, N.J. *Nature protocols* **1** (2006)

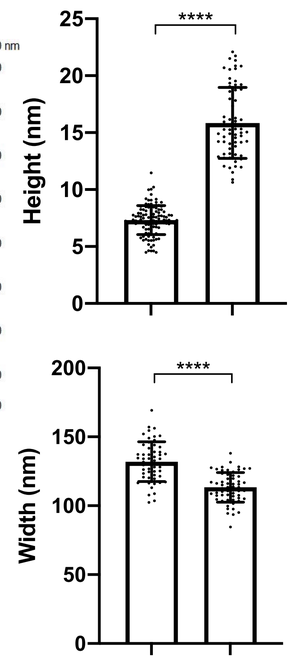
✓ CD signature similar to collagen

✓ **Positive/negative peak** (L/D) at 225 nm and **negative/positive peak** (L/D) at 200 nm

✓ Self-assembly of the chains in triple helix with PPII conformation

Morphological analysis (AFM)

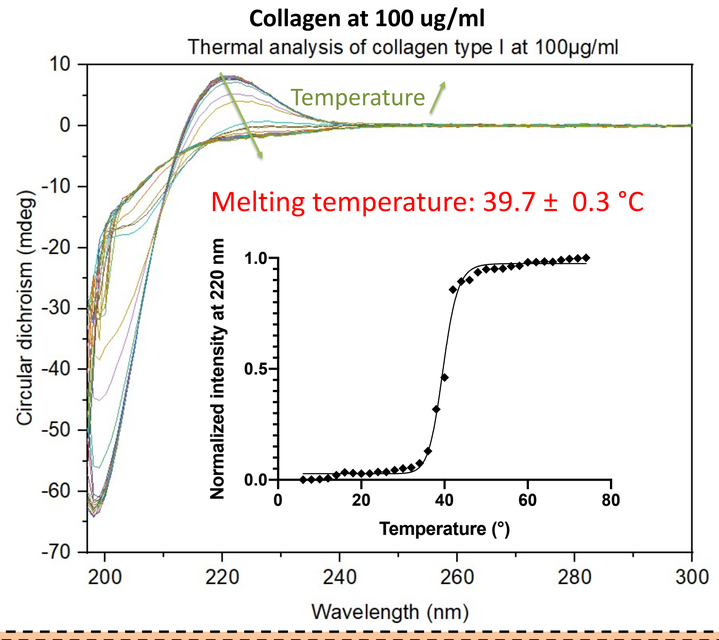




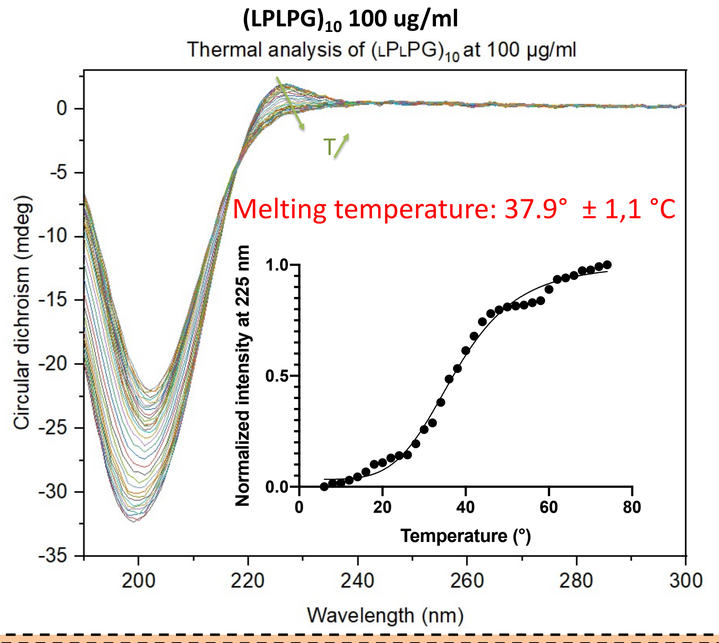
	D peptide	L peptide
Heigth (nm)	15.9 ± 3.1	7.3 ± 1.3
Width (nm)	115 ± 11	132 ± 15
Length (µm)	0.5-6.5	0.5-4.6

Thermal fusion of chiral peptides

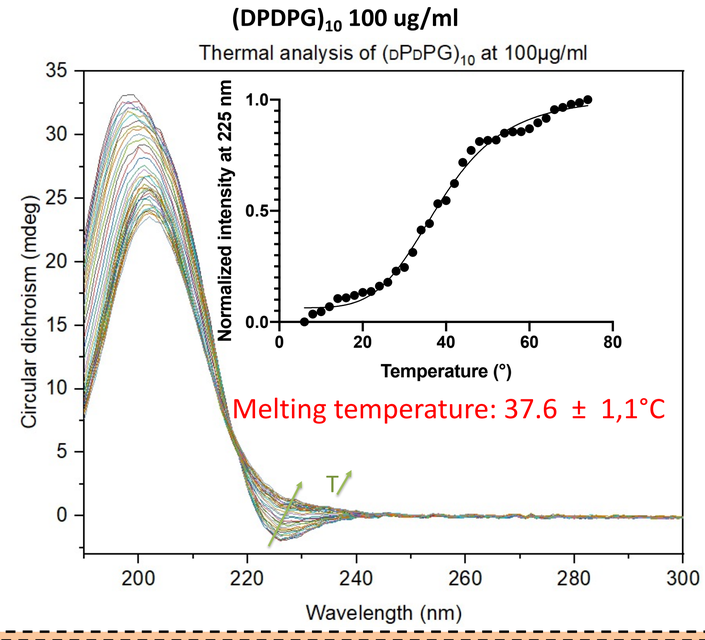
Collagen at 100 ug/ml



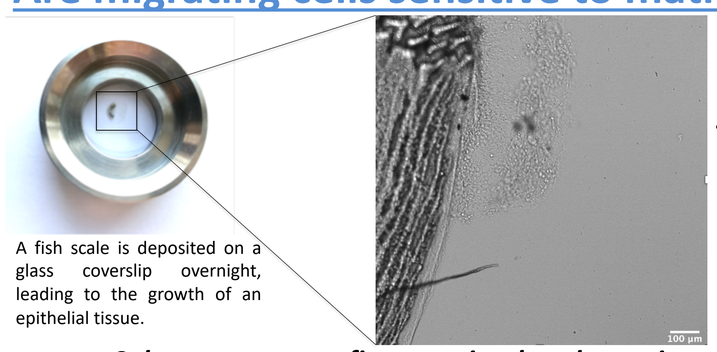
$(LPLPG)_{10}$ 100 ug/ml



$(DPDPG)_{10}$ 100 ug/ml



Are migrating cells sensitive to matrix chirality ?



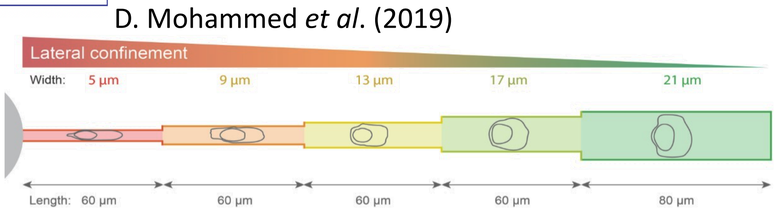
- A fish scale is deposited on a glass coverslip overnight, leading to the growth of an epithelial tissue.

- DIC image of epithelial tissue formation after 2 hours deposition on glass coverslip

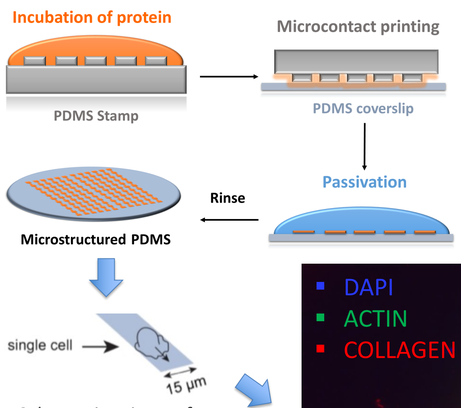
nature physics

Substrate area confinement is a key determinant of cell velocity in collective migration.

D. Mohammed *et al*. (2019)



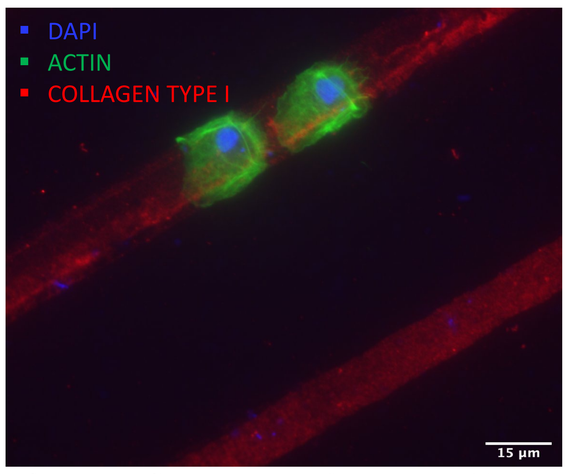
✓ The lateral confinement modulates the migration speed through significant changes of cell morphologies



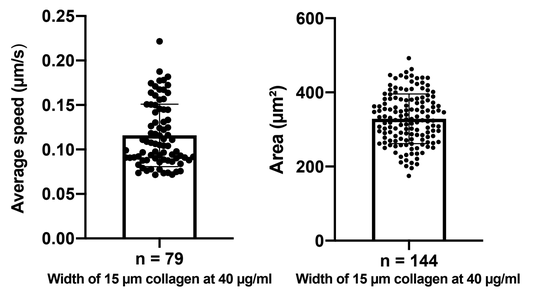
Schematic view of a cell on microstripe

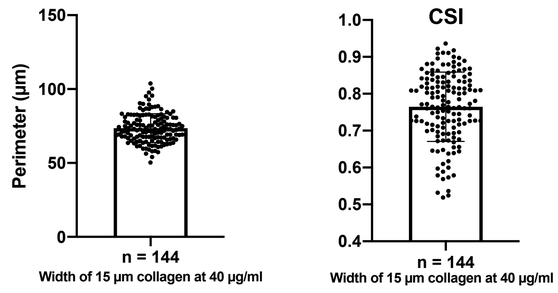
✓ Microcontact printing allows to create patern with micrometric resolution

✓ Preliminary results on collagen Type I



Epifluorescent image of keratocytes migrating on collagen microstripes. Scale bar: 15 µm.





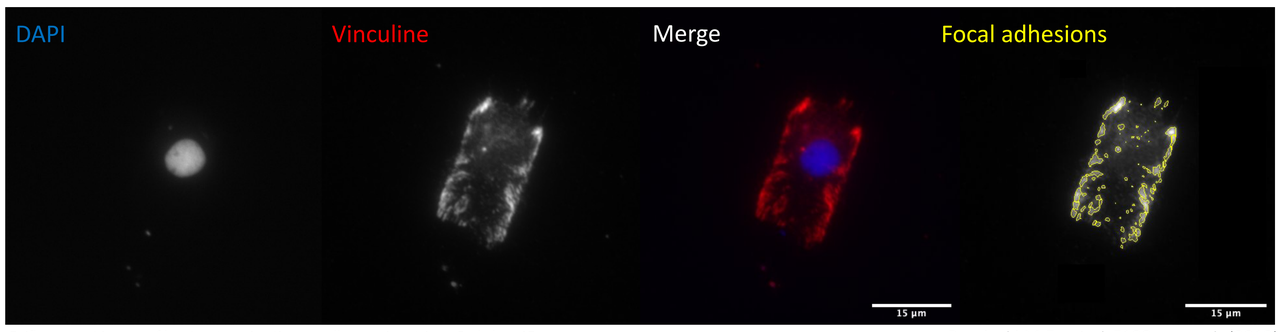
✓ Average speed: 0.12 ± 0.04 µm/s

✓ Average area: 330 ± 67 µm²

✓ Average perimeter: 74 ± 10 µm

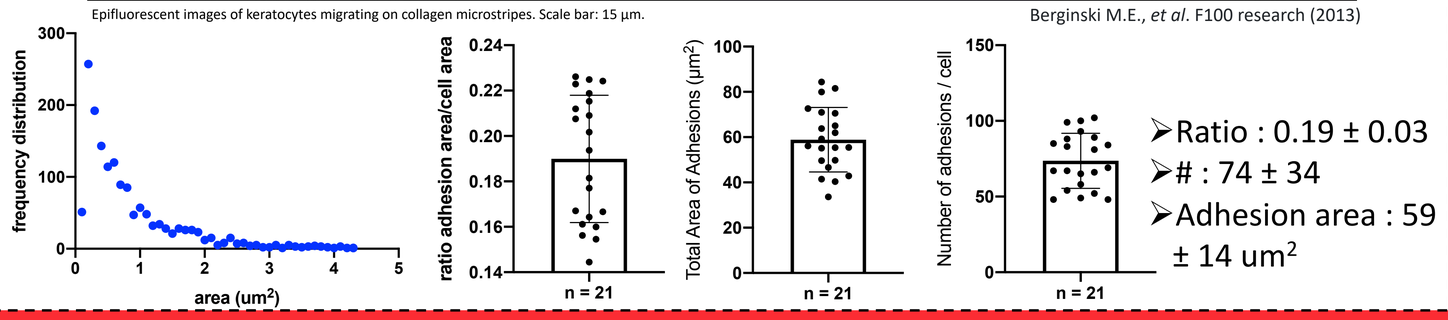
✓ CSI: 0.77 ± 0.09

Cell-matrix interactions ?



Epifluorescent images of keratocytes migrating on collagen microstripes. Scale bar: 15 µm.

Berginski M.E., *et al*. F100 research (2013)



➢Ratio : 0.19 ± 0.03

➢# : 74 ± 34

➢Adhesion area : 59 ± 14 um²

Conclusion and prospect

- Peptides mimic the collagen structure
- More cooperativity leads to higher melting temperature
- AFM experiments showed that peptides mainly formed fibers
- Specific interactions between collagen and cells via integrin recruitments

Taken together, these results point the way towards original strategies to study the cell migration with enantiospecific surfaces

Interactions between cells and chiral surfaces?

Building 3D chiral hydrogels to mimic the ECM?

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