Control of cell morphodynamic and displacement orientation by precise tuning between substrate nanopatterning and rigidity

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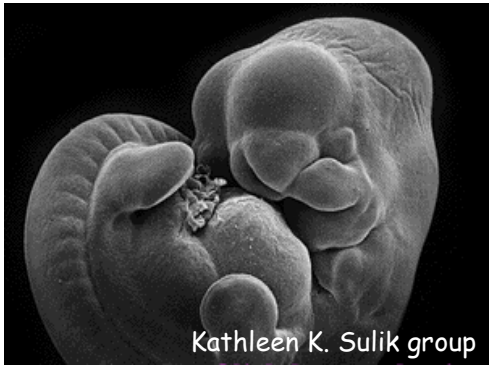
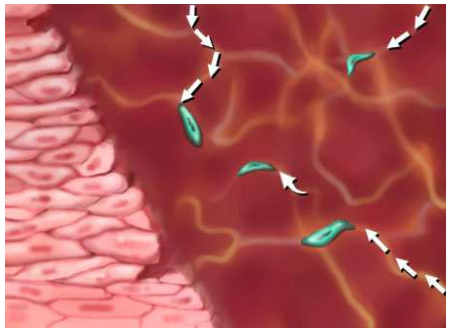
Why is it important to control cell morphodynamic and displacement orientation?

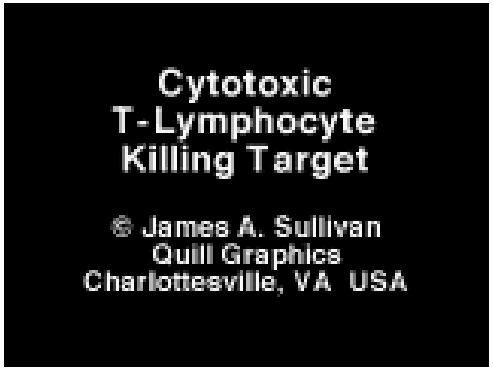
Morphogenesis (tissues remodeling)



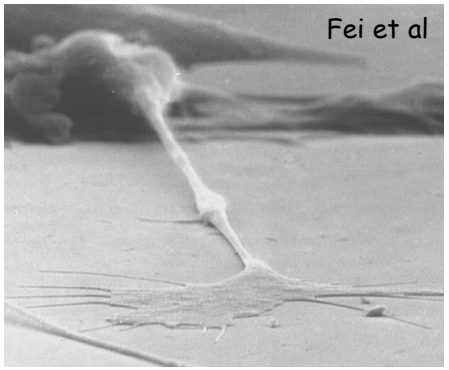
Wound healing



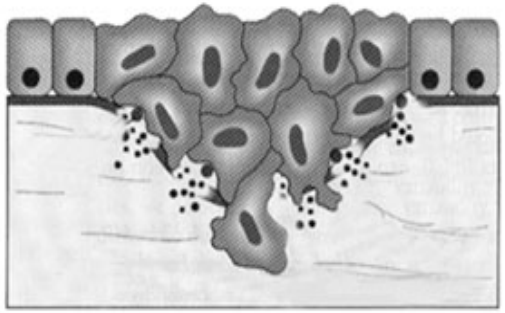
Lymphocyte migration and phagocytosis

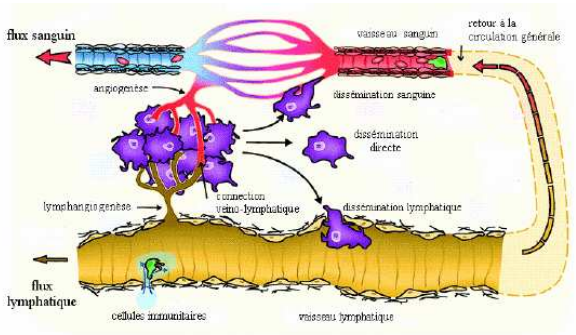


Neural development

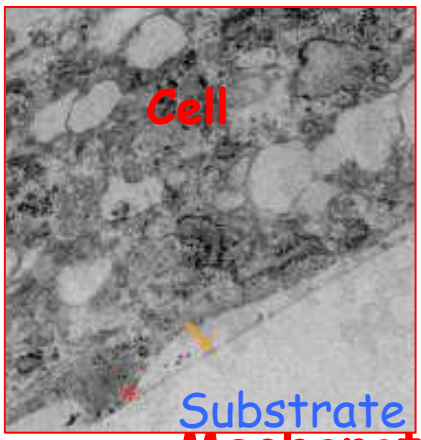


Tumor invasion and metastasis





Cells can respond and adapt to changing environment



Mechanotaxis

Contact guidances

Force equilibrium

- Substrate Rigidity

Chemotaxis

- Equilibration point

Mechanotaxis & contact guidance are resulting from cell-substrate interaction at the Focal adhesion sites*

☞Cell morphodynamic & displacement on a substrate= Force equilibrium

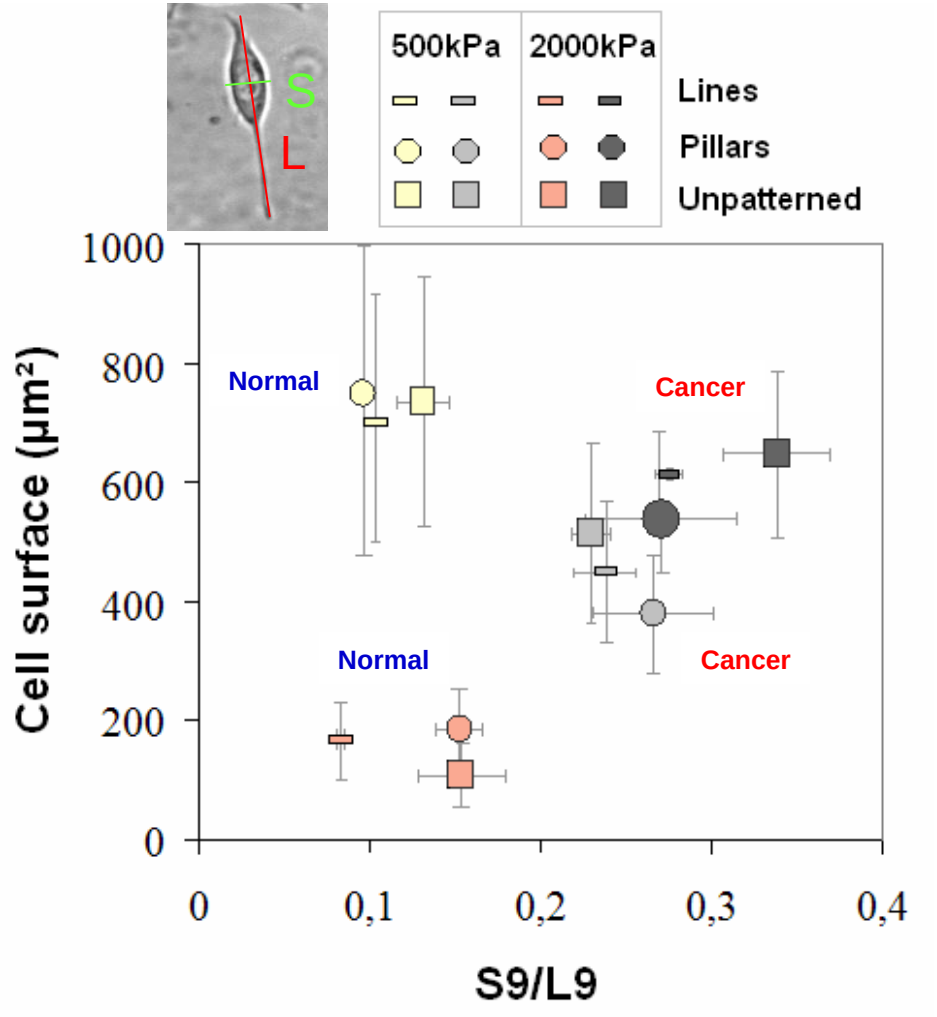
Objectives

1. How cells sense combinations of physical signals such as substrate rigidity and topography ?

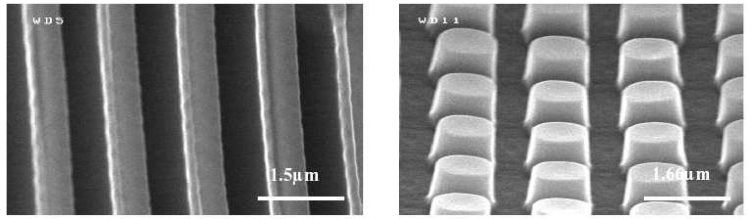
2. Which of those factors predominantly governs cell responses?

3. Do cancer and normal cells behave differently with mechanical changes in the environment?

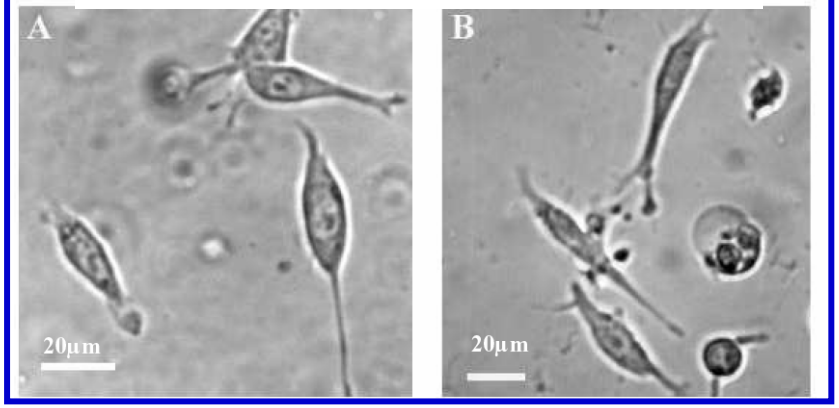
Cell morphology



PDMS substrates (500& 2000kPa)

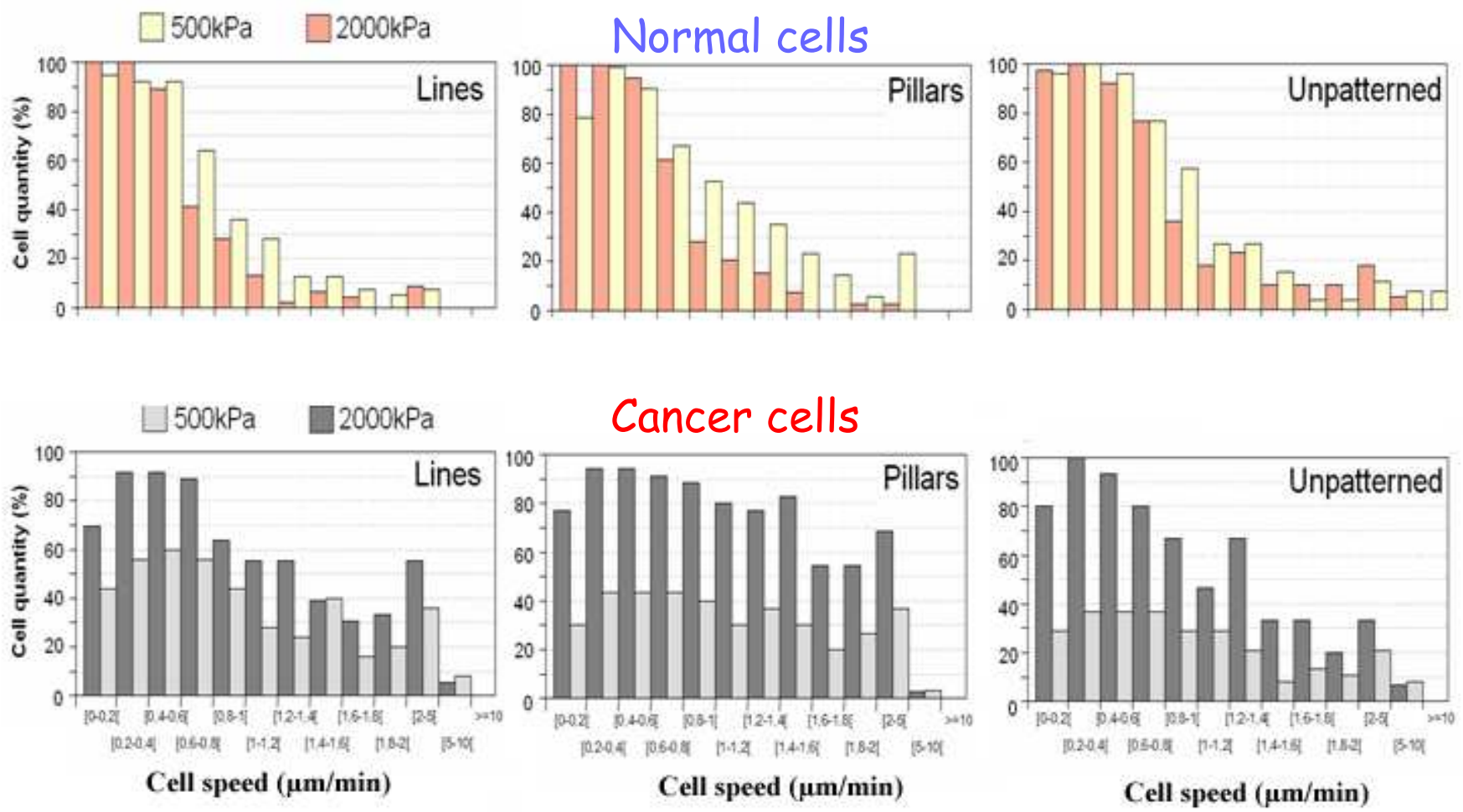


Normal 3T3 Cancer SaI/N



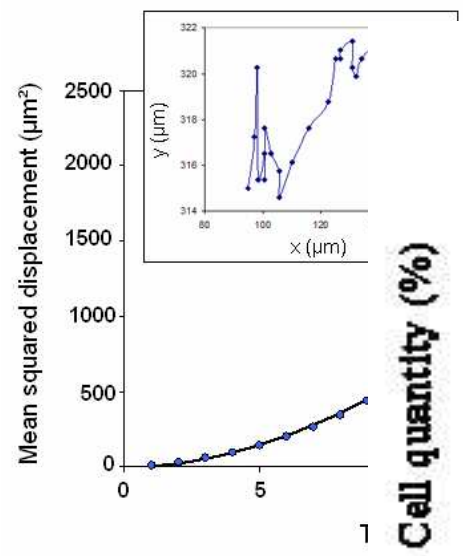
☞ Normal cells morphology is more sensitive to structural and mechanical changes than the cancer cells

Cell migration

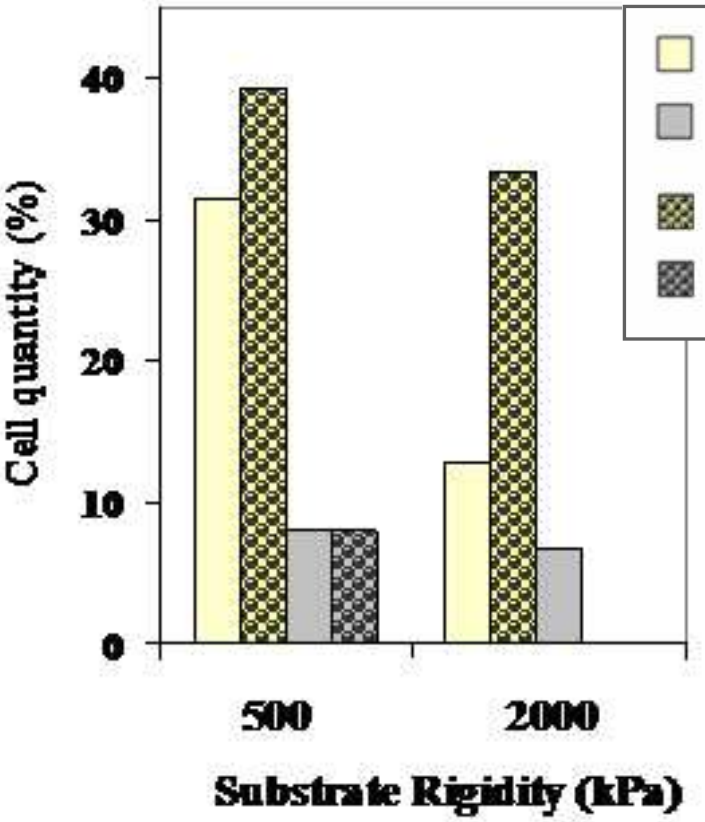


- Normal cells speeds are not (or probably very slightly) controlled by the structural & mechanical changes in the substrates
- Cancer cell speeds are controlled by the substrate rigidity

Quantitative characterization of the cell motility by a Persistence random walk model



Cells with persistent time larger than 80 min



placement

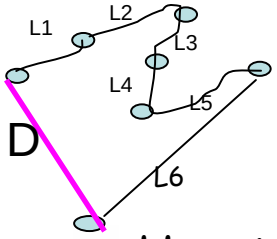
time

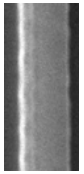
ervation

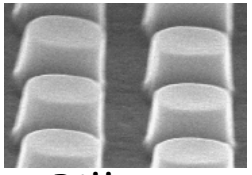
$$>= 2V^2P\left[t - P(1 - e^{-t/P})\right]$$

- Normal cells trajectories are more persistent than the cancer cells
- We can control normal cell persistence time by modification of the cell rigidity and topography (for tissue engineering)

Impact of the topographic anisotropy on cell displacement orientation



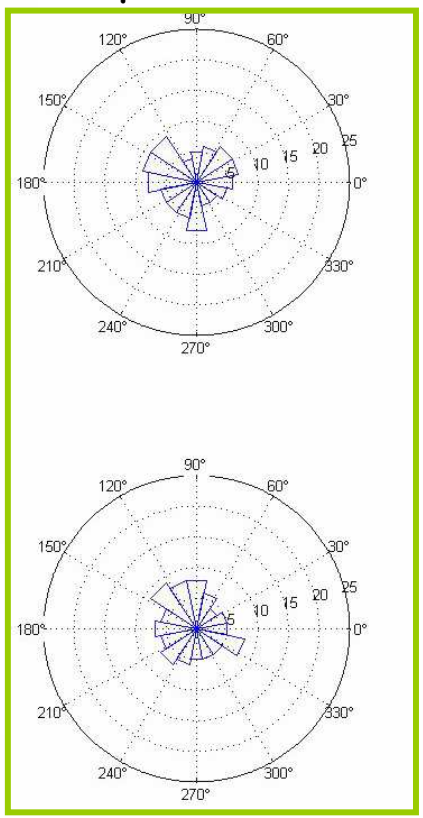


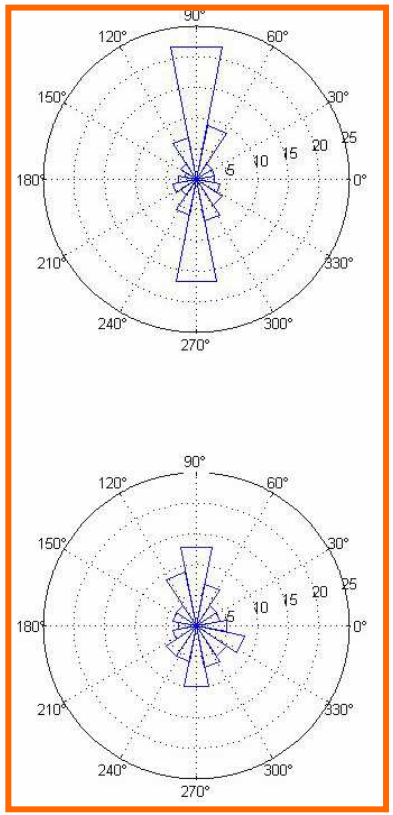


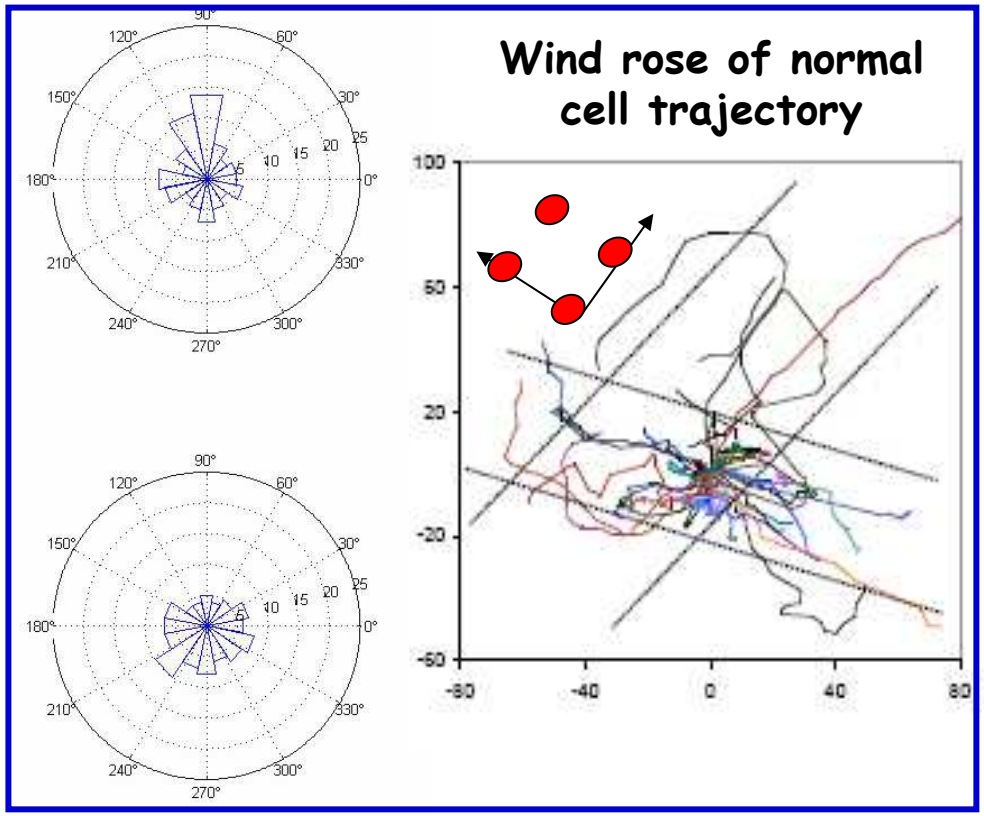
Unpatterned Lines Pillars

Normal

Cancer







Wind rose of normal cell trajectory

- Line topography induces oriented cell displacement along the lines
- Pillar topography induces oriented cell displacement along the 0° and 90° for normal cells but cancer cells escape from this topographic control

Conclusions

•Precise tuning between substrate patterning and rigidity would allow for the control of cell morphodynamic and displacement

*Topography (cell orientation)

*Rigidity (cell surface, polarization & persistence)

•Cancer cells escape from the topographic control

•Nanotechnology based approaches

a) Cancer cell phenotypes screening

b) Cancer progression restriction

Thank you very much for your attention