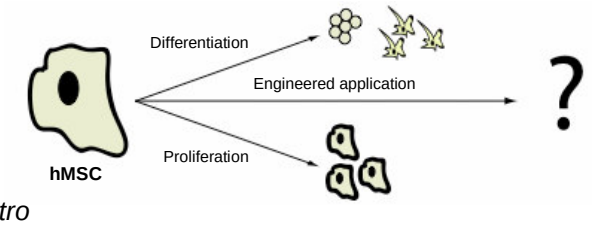
Understanding and engineering the mesenchymal stem cell niche

OVERVIEW: Human mesenchymal stem cells (hMSCs) offer a unique cellular approach to the modeling and treatment of human disease. Easily harvested from human bone marrow, these cells are progenitor cells for a variety of human tissues including bone, muscle, connective tissue, and vascular endothelium [1]. In addition, these cells have been shown to exhibit pluripotent properties that make them amenable to research intended to treat a broad diversity of diseases. The purpose of this project is to investigate the role of mechanical microenvironment or niche in the determination of cell fate among hMSCs. The ultimate goal is to enable and demonstrate novel techniques towards the development of *in vitro* and *in vivo* platforms to study and to treat disease states such as cancer metastasis and vascular inflammation / scarring.



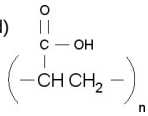
OBJECTIVES:

- Develop a model material system to modulate the mechanical microenvironment of hMSCs
- Determine the parameters necessary for maintaining plasticity among hMSCs cultured *in vitro*
- Investigate specific disease states that may be induced by modulated microenvironmental cues
- Refine current techniques for isolating, expanding, and differentiating hMSCs

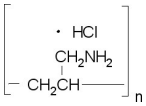
APPROACH:

- Use polyelectrolyte multilayers (PEMs) as a synthetic material system: elastic modulus depends upon assembly pH [2,3]

Poly(acrylic acid) **(PAA)**

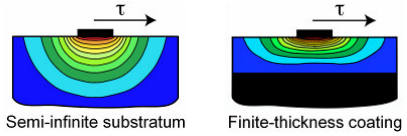


Poly(allylamine hydrochloride) **(PAH)**



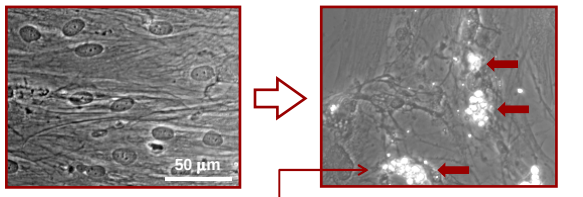
Chemical formulae courtesy Sigma Aldrich - www.sigmaaldrich.com

- Investigate traction-induced displacements in semi-infinite and finite substrata



RESULTS:

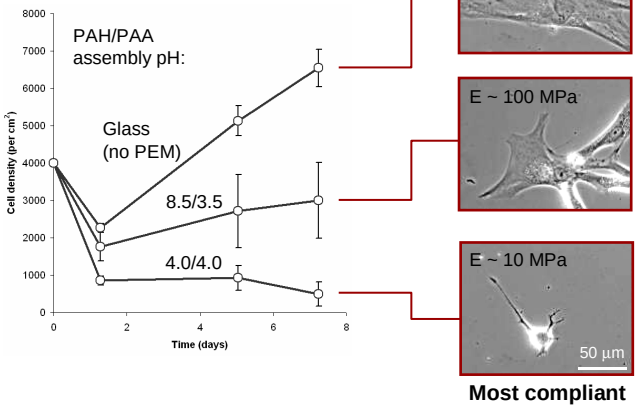
- Chemically induced hMSC differentiation



hMSCs → **Adipocytes**

Lipid droplets are a characteristic of the adipocyte phenotype

- Compared cell spreading and proliferation on PEM substrates of different stiffness



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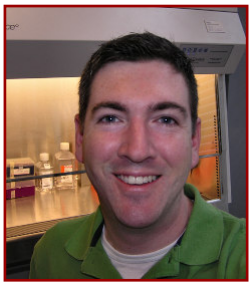

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Interesting fact about me:
My father (Notre Dame '59), grandfather (USNA '22), and great-grandfather (Cooper Union '88) were all engineers.

References and acknowledgments:

1. Pittenger M F et al 1999 Multilineage potential of adult human mesenchymal stem cells *Science* **284** 143–147
2. Thompson M T et al 2005 Tuning compliance of nanoscale polyelectrolyte multilayers to modulate cell adhesion *Biomaterials* **26** 6836–6845
3. Milwid J M 2006 *Mechanical Characterization and Application of Hydrated Nanoscale Films as Tunable Cell Culture Substrates* MS thesis MIT

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