RUTGERS
THE STATE UNIVERSITY OF NEW JERSEY

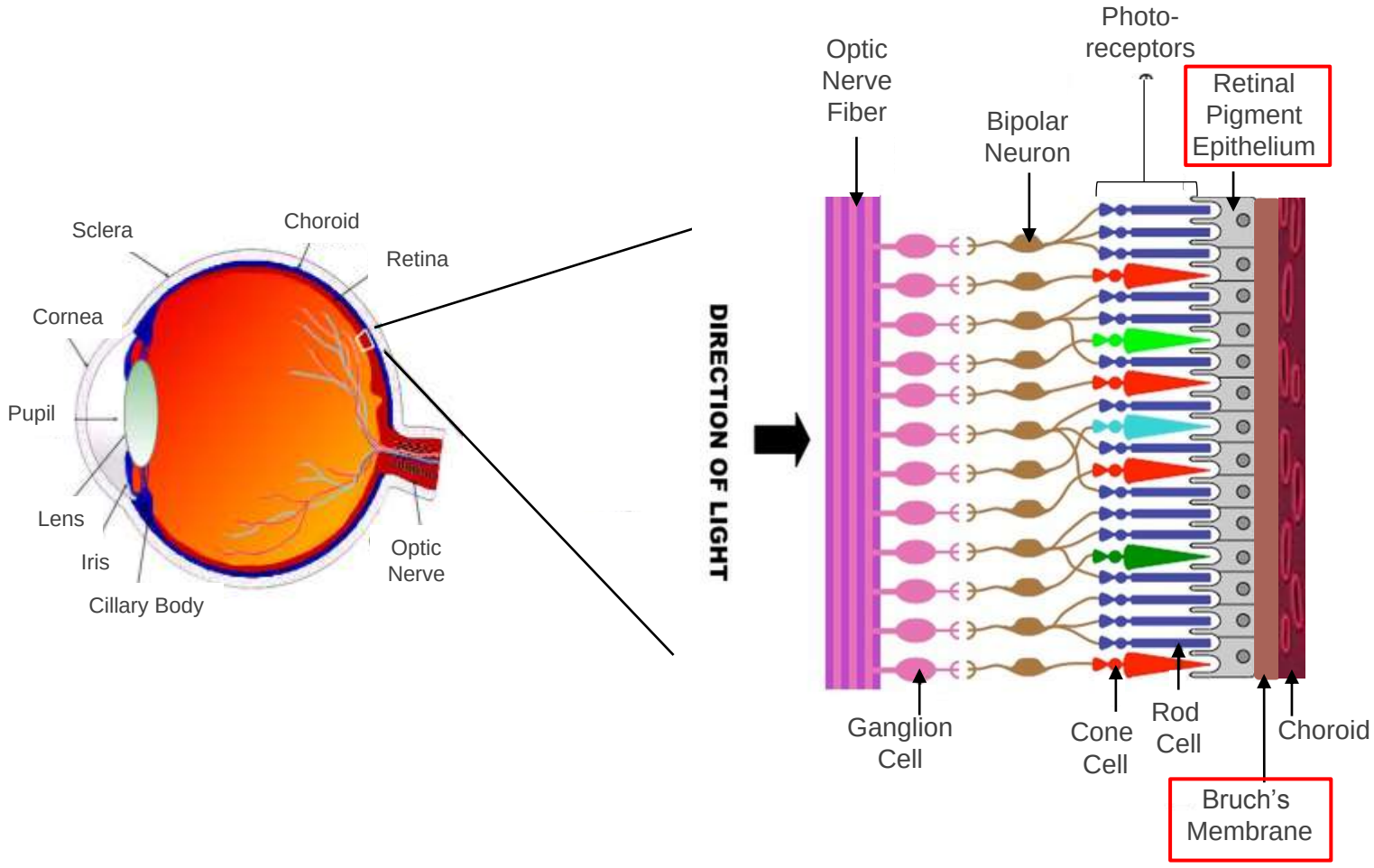
The Effects of Scaffold Rigidity on Retinal Pigment Epithelial Cells

Corina White

Symposium on Biomaterials Science

24 October 2016

The retina is the light-responsive tissue layer at the back of the eye where the transduction of light signals to vision begins.

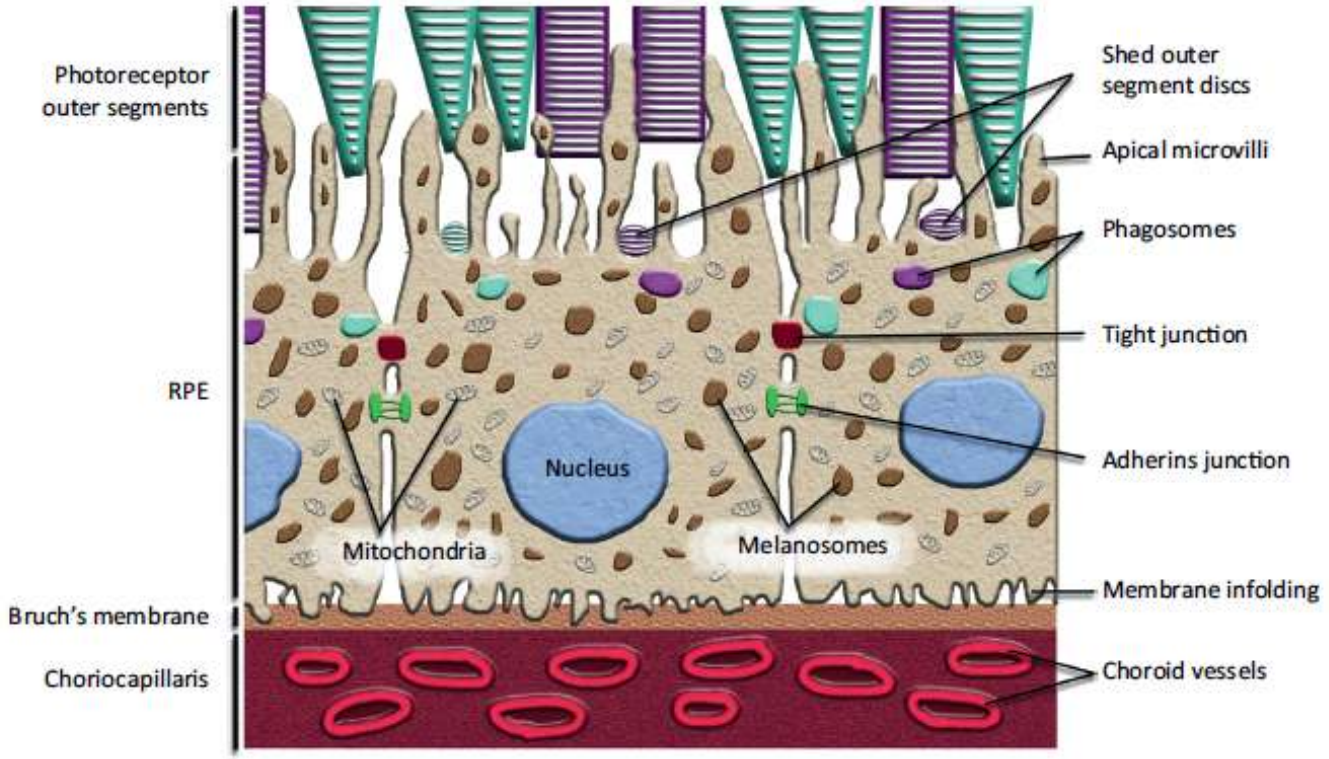


Modified from: http://webvision.med.utah.edu/book/part-i-foundations/simple-anatomy-of-the-retina/

The Bruch's Membrane (BM) and Retinal Pigment Epithelium (RPE) are crucial in maintaining a viable and functional neural retina.

KEY FUNCTIONS OF BM & RPE

- Provide Physical Support
- Phagocytosis of Retinal Waste
- Regulate Transport
- Secrete Proteins
- Absorb Excess Light

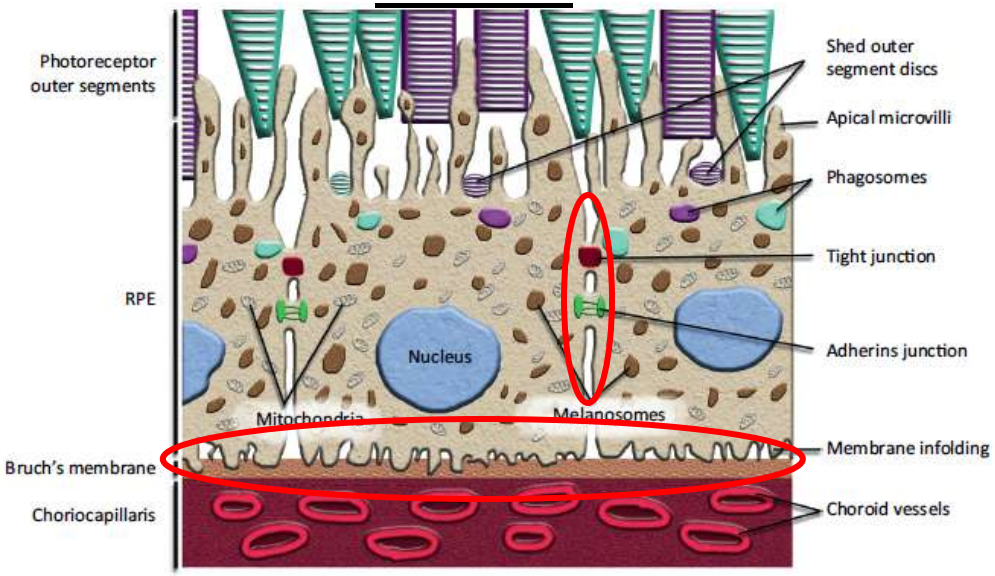


http://www.sens.org/sites/srf.org/files/Anuj_Fig_2jpg.jpg

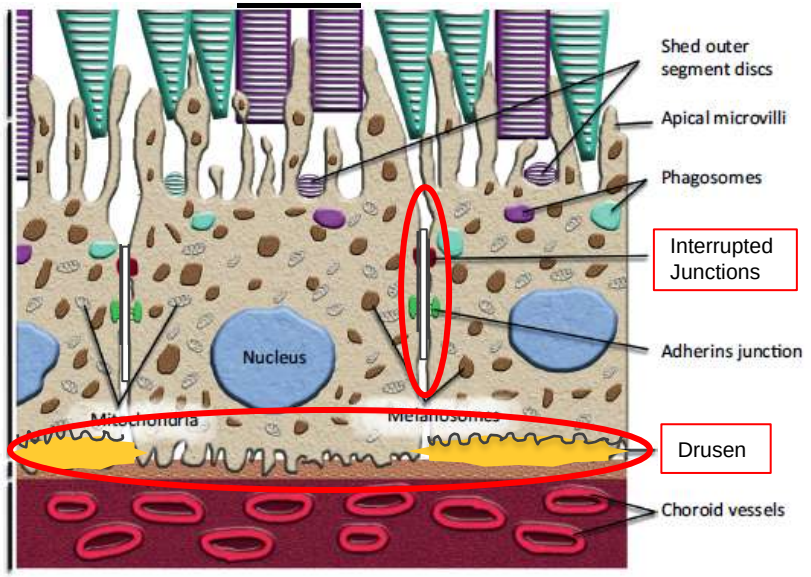
Several changes to the retina occur naturally with aging and are characteristically present during age-related macular degeneration.

NUMBER OF CASES EXPECTED TO DOUBLE BY 2050

HEALTHY

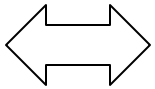


AGED



Changes of BM

- Thickness of membrane increases
- Higher level of collagen cross-linking
- Increased presence of lipids
  - Appearance of drusen



Aged/Diseased Phenotype

- Decreased phagocytic activity
- Altered regulation of transport
- Altered protein expression

There are several hurdles that must be overcome in order for current approaches to be translational.

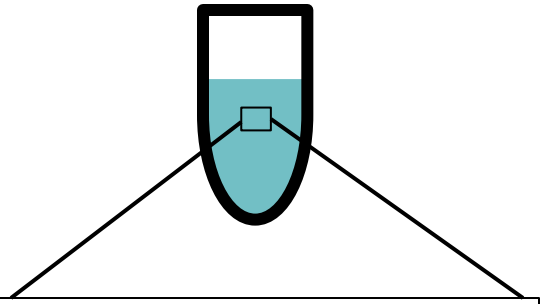
APPROACH	CHALLENGES
Bolus Free Cell Injection	• **Monolayer does not form** • **Long term efficacy still under investigation** • **Does not address altered transport and mechanical properties** • ***In vitro* cell studies on aged BM indicate poor attachment, morphology, and viability** [1,2]
Cell-Scaffold Implants	• **Inflammatory response *in vivo*** • **"De-differentiation" of transplanted RPE cells** [3,4]

[1] Lu, B., et al. Stem Cells, 2009. **27**(9): p. 2126-35.
[2] Sun, K., et al. Mol Vis, 2007. **13**: p. 2310-9. PMID: 18199972
[3] Diniz, B., et al. Invest Ophthalmol Vis Sci, 2013. **54**(7): p. 5087-96. PMC3726243
[4] Christiansen, A.T., et al. Stem Cells Int, 2012. **2012**: p. 454295. PMC3328168

Synthetic polymer scaffolds with varying moduli were fabricated.

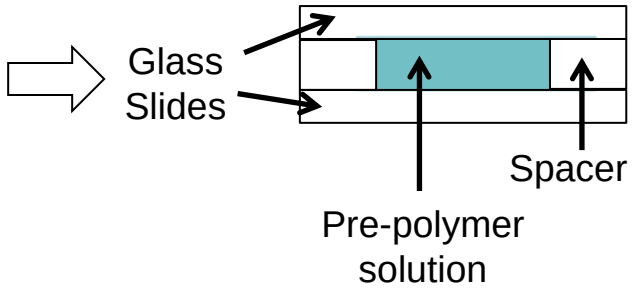
Fabricate and characterize scaffolds of various elastic moduli → **Culture RPE cells on scaffolds to investigate effects of modulus**

Pre-polymer solution

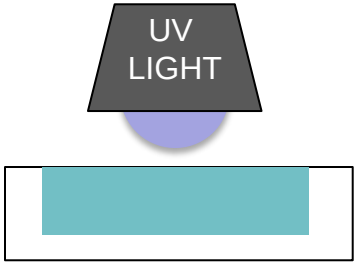


- Poly(ethylene glycol) diacrylate (PEGDA)
- Argenine-Glycine-Aspartic Acid-PEG-Acrylate
- Photoinitiator
- Buffer

Glass Mold

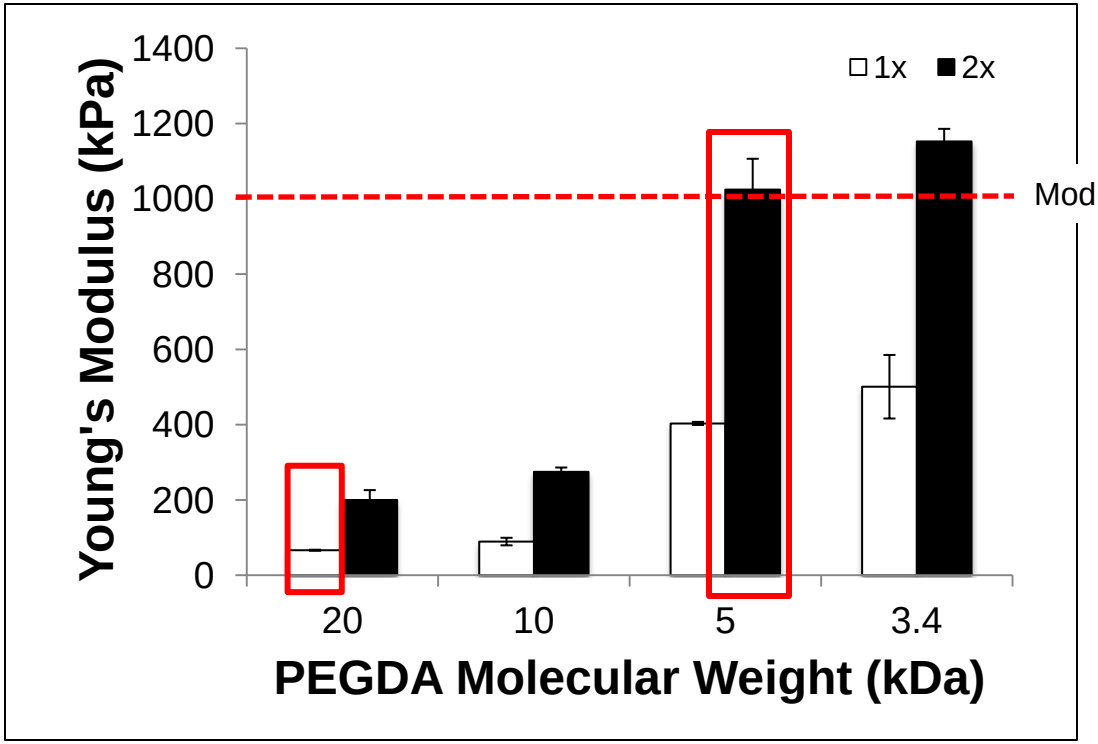


UV Polymerization



Scaffold modulus is tunable through polymer molecular weight and concentration.

Molecular Weight	1x Concentration	2x Concentration
kDa	%w/v	%w/v
3.4	20	40
5	20	40
10	10	20
20	10	20

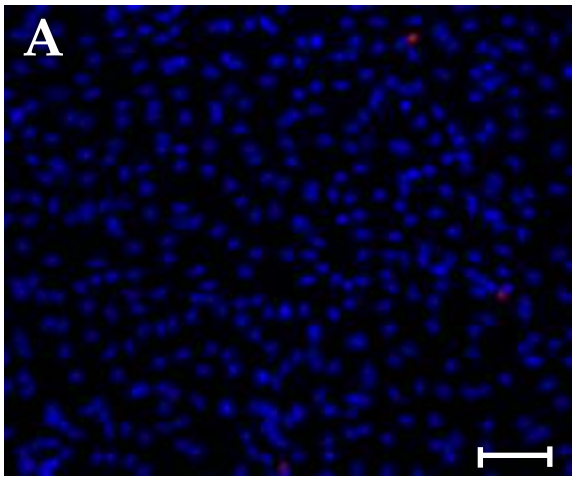


[5] Candiello, Joseph.
FEBS Journal 274.11 (2007): 2897-908.

RPE cells qualitatively show different adhesion patterns on different moduli scaffolds.

Day 7

CONTROL
Tissue Culture Polystyrene (TCPS)

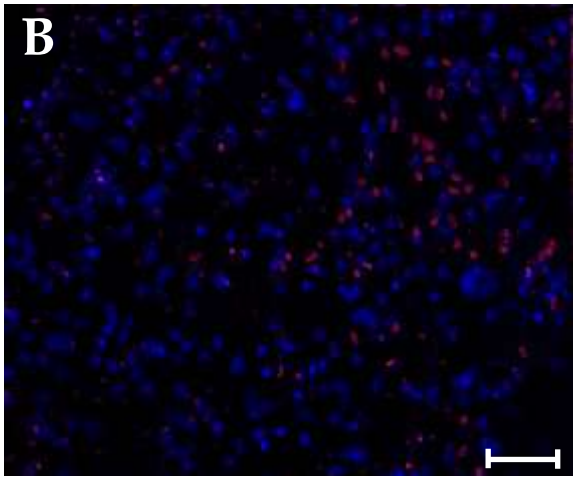


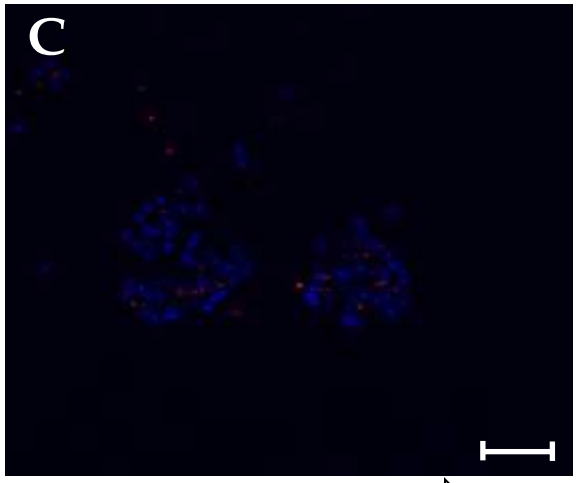
DEAD
(Ethidium Homodimer-1)

DAPI

B – High Modulus
C – Low Modulus

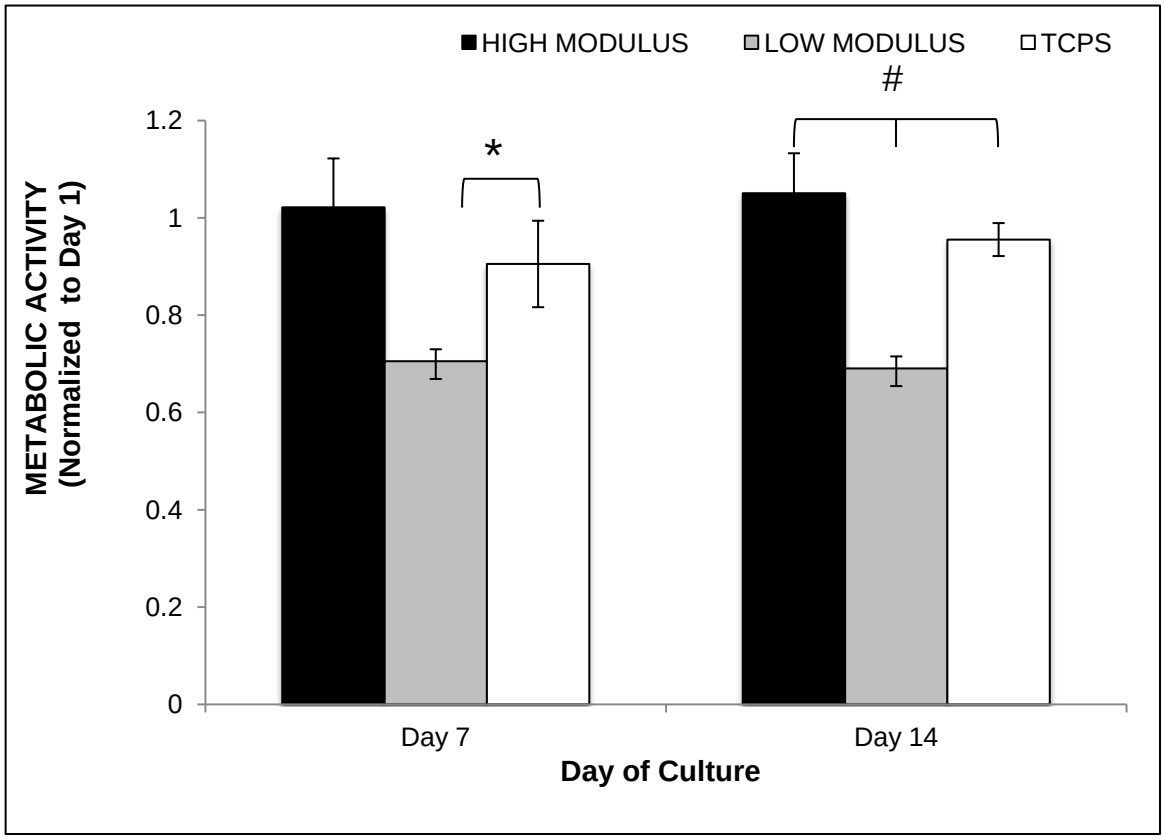
SCAFFOLDS



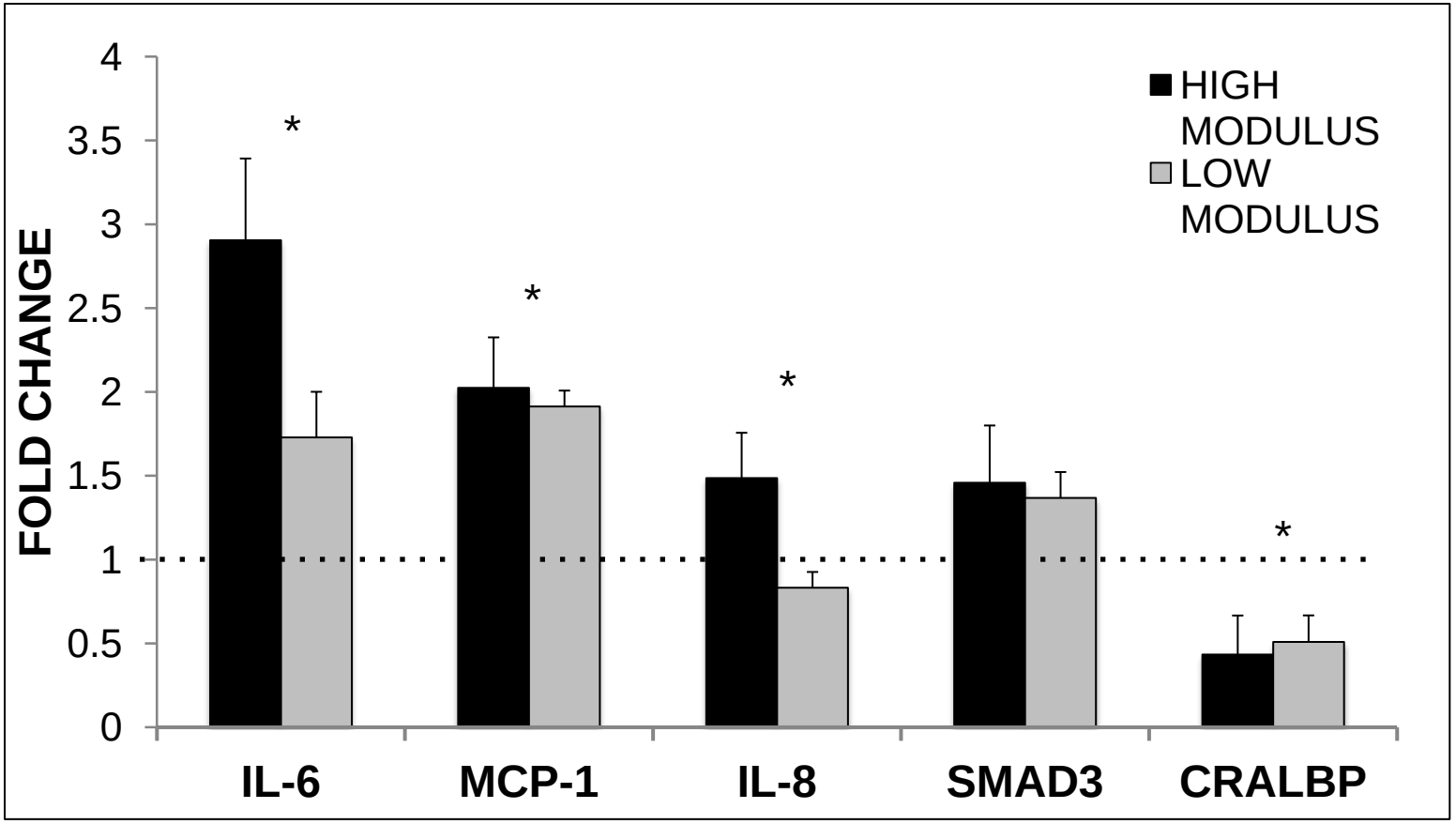


DECREASING STIFFNESS

The metabolic activity of RPE cells significantly decreases on a low modulus scaffold during 14 day culture.



Cells cultured on substrates with different moduli exhibited significant differences in gene expression compared to control.



Scaffold modulus affects cell adhesion, metabolic activity, and expression and can be tuned to optimize post-transplantation survival and function.

Growing cells on a viscoelastic surface compared to TCPS affects the cells.

Scaffolds with a modulus that mimics native BM stiffness demonstrate:

- More homogenous cell attachment
- Higher RPE metabolic activity

CONCLUSIONS

- Scaffold modulus can be tuned to control cell behavior and, with a deeper understanding of the effects, it can be optimized to increase post-transplantation survival and function

RUTGERS
THE STATE UNIVERSITY OF NEW JERSEY

The Effects of Scaffold Rigidity on Retinal Pigment Epithelial Cells

Corina White

Symposium on Biomaterials Science

24 October 2016