IOWA STATE UNIVERSITY
Chemical and Biological Engineering

Honors Poster Session
April 26, 2017

Catherine Le Denmat[1], Dr. Kaitlin Bratlie[1,2,3]

1. Department of Chemical and Biological Engineering, Iowa State University
2. Department of Materials Science and Engineering, Iowa State University
3. Ames National Lab, Ames, Iowa

Fibroblast to myofibroblast differentiation on modified poly-L-lysine surfaces

Background

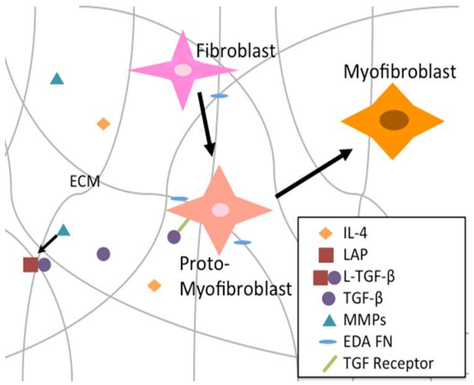
The **foreign body response** to implanted devices is responsible for encapsulation of the device[1], often hindering its function for patients.

- **Transforming growth factor β (TGF-β**) is involved in fibrous capsule formation[2,3]
- **TGF-β leads to the differentiation of fibroblasts into myofibroblasts.**[2,3] Myofibroblasts secrete large amounts of collagen and express α-smooth muscle actin, a cytoskeletal protein that enables myofibroblasts to contract collagen to form a dense, acellular, fibrous capsule[1]
- **TGF-β must be activated from its latent form (L-TGF-β) by MMPs**

Goal

R**educe the thickness of the fibrous capsule** formed in response to implanted devices.

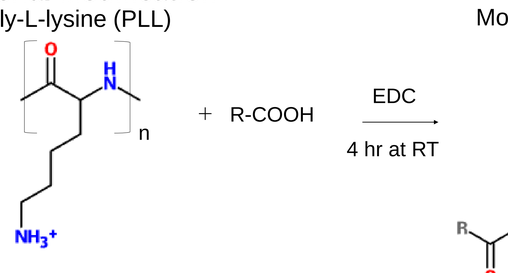
- **Use MMP-inhibiting materials** to impede cleavage of L-TGF-β to TGF-β in order to prevent fibroblast to myofibroblast differentiation
- Evaluate material characteristics to determine which factors influence this differentiation process

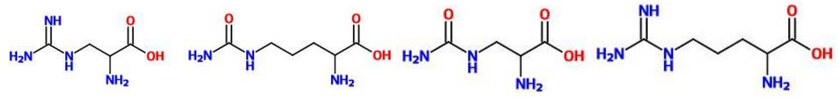


Materials and Methods

Material Modification

Poly-L-lysine (PLL) → Modified Poly-L-lysine





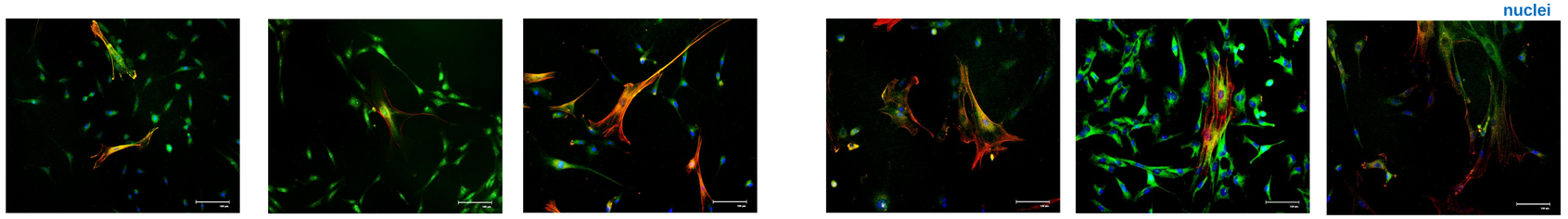
A 2-amino-3-guanidinopropionic acid | **B** Citrulline | **C** Albizzin | **D** Arginine

Results

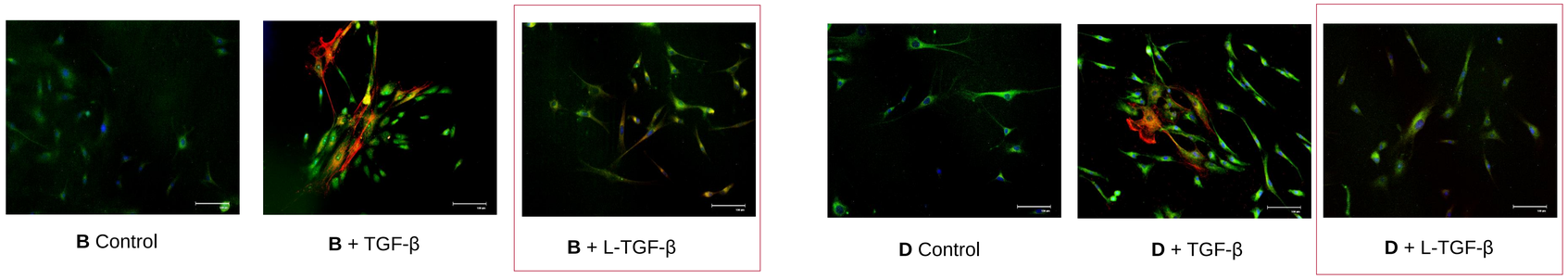
Fibroblast to myofibroblast differentiation

Mouse NIH-3T3 fibroblasts were stimulated *in vitro* with TGF-β and L-TGF-β, then stained for tubulin, α-smooth muscle actin, and nuclei. A control with no stimulation was also performed for each material.

α-smooth muscle actin
tubulin
nuclei



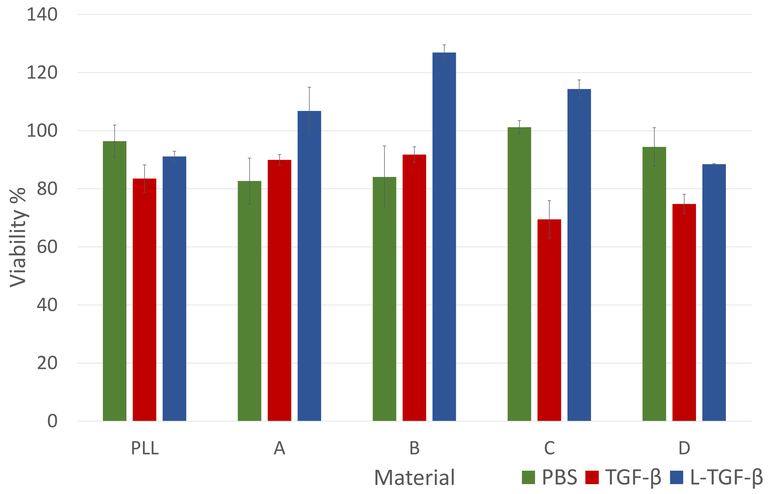
A Control | **A** + TGF-β | **A** + L-TGF-β | **C** Control | **C** + TGF-β | **C** + L-TGF-β



B Control | **B** + TGF-β | **B** + L-TGF-β | **D** Control | **D** + TGF-β | **D** + L-TGF-β

NIH/3T3 – modified PLL cytocompatibility

Fibroblasts were stimulated *in vitro* with TGF-β and L-TGF-β on modified PLL-coated surfaces. Viability > 70% indicates cytocompatibility. All samples are compared to a control of fibroblasts on tissue culture plastic in the presence of the indicated stimulant.



Conclusions and Future Work

- Materials B and D inhibited myofibroblast formation to a large extent when fibroblasts were stimulated with L-TGF-β
- Results suggest that longer carbon chains may be more influential than chemical end groups
- All materials tested were shown to be cytocompatible
- A better understanding of the differentiation process was achieved

Future work could include cell co-culture to investigate the influence of materials on fibroblasts in the presence of different cell types, and *in vivo* studies could eventually be conducted to evaluate material effects.

References
1. Anderson, J. M., Rodriguez, A. & Chang, D. T. Foreign body reaction to biomaterials. Semin. Immunol. 20, 86–100 (2008).
2. Li, A. G. et al. Elevation of transforming growth factor beta (TGF b) and its downstream mediators in subcutaneous foreign body capsule tissue. J. Biomed. Mater. Res. Part A 82, 498–508 (2007).
3. Batra, V. et al. Bronchoalveolar lavage fluid concentrations of transforming growth factor (TGF)-β1, TGF-β2, interleukin (IL)-4 and IL-13 after segmental allergen challenge and their effects on alpha-smooth muscle actin and collagen III synthesis by primary human lung fibroblasts. Clin. Exp. Allergy 34, 437–444 (2004).
4. Bygd, H., Forsmark, K., Bratlie, K. The significance of macrophage phenotype in cancer and biomaterials. Clinical and Translational Medicine. 2014

Acknowledgements: This work was supported by the National Science Foundation under Grant No. CBET 1227867 and the Roy J. Carver Charitable Trust Grant No. 13-4265 and an Iowa State University Honors Grant. The authors also acknowledge support from NSF ARI-R2 (CMMI-0963224) for funding the renovation of the research laboratories used for these studies.