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

Background

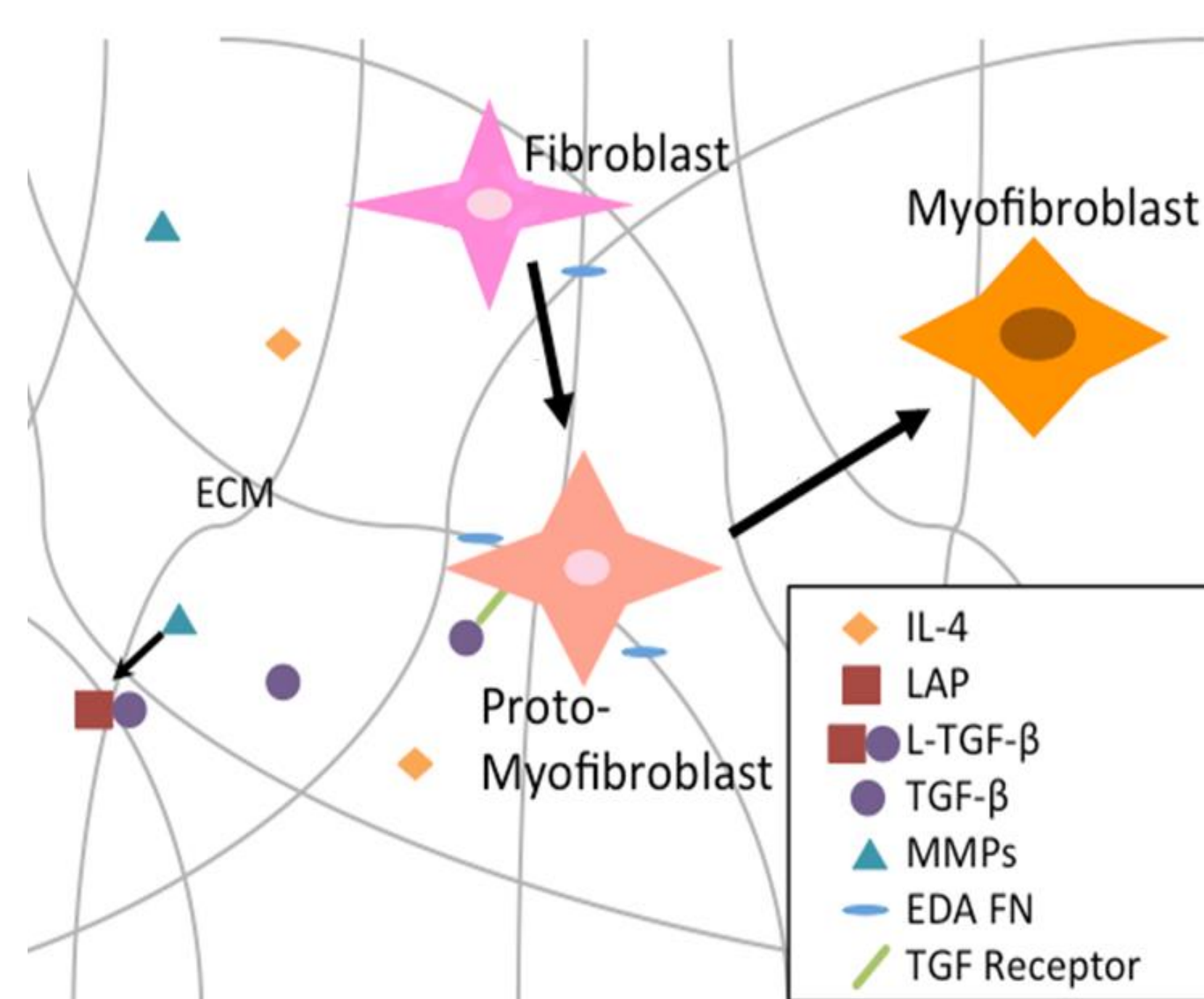
The **foreign body response** to implanted devices is responsible for encapsulation of the device¹, often hindering its function for patients.

- **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 capsule¹
- **TGF- β must be activated from its latent form (L-TGF- β) by MMPs**

Goal

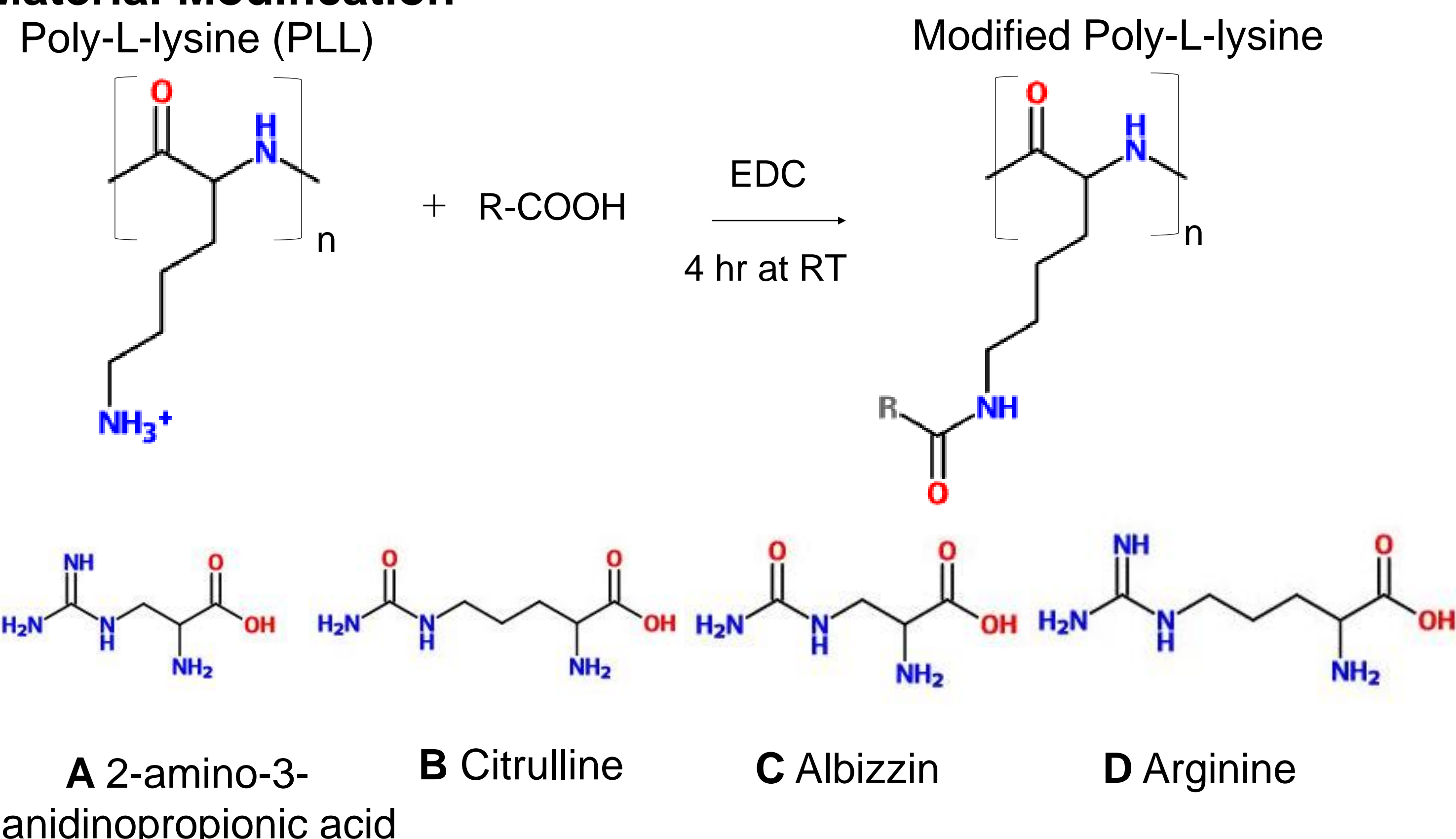
Reduce the thickness of the fibrous capsule formed in response to implanted devices.

- 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

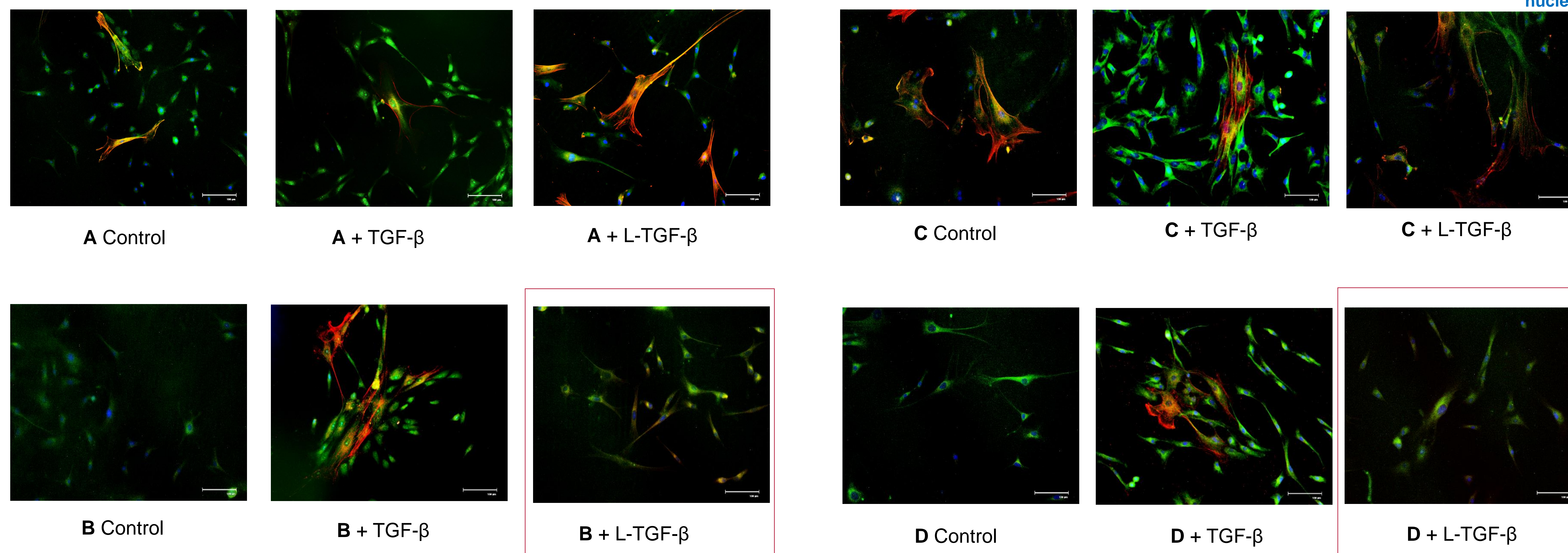
Material Modification



Results

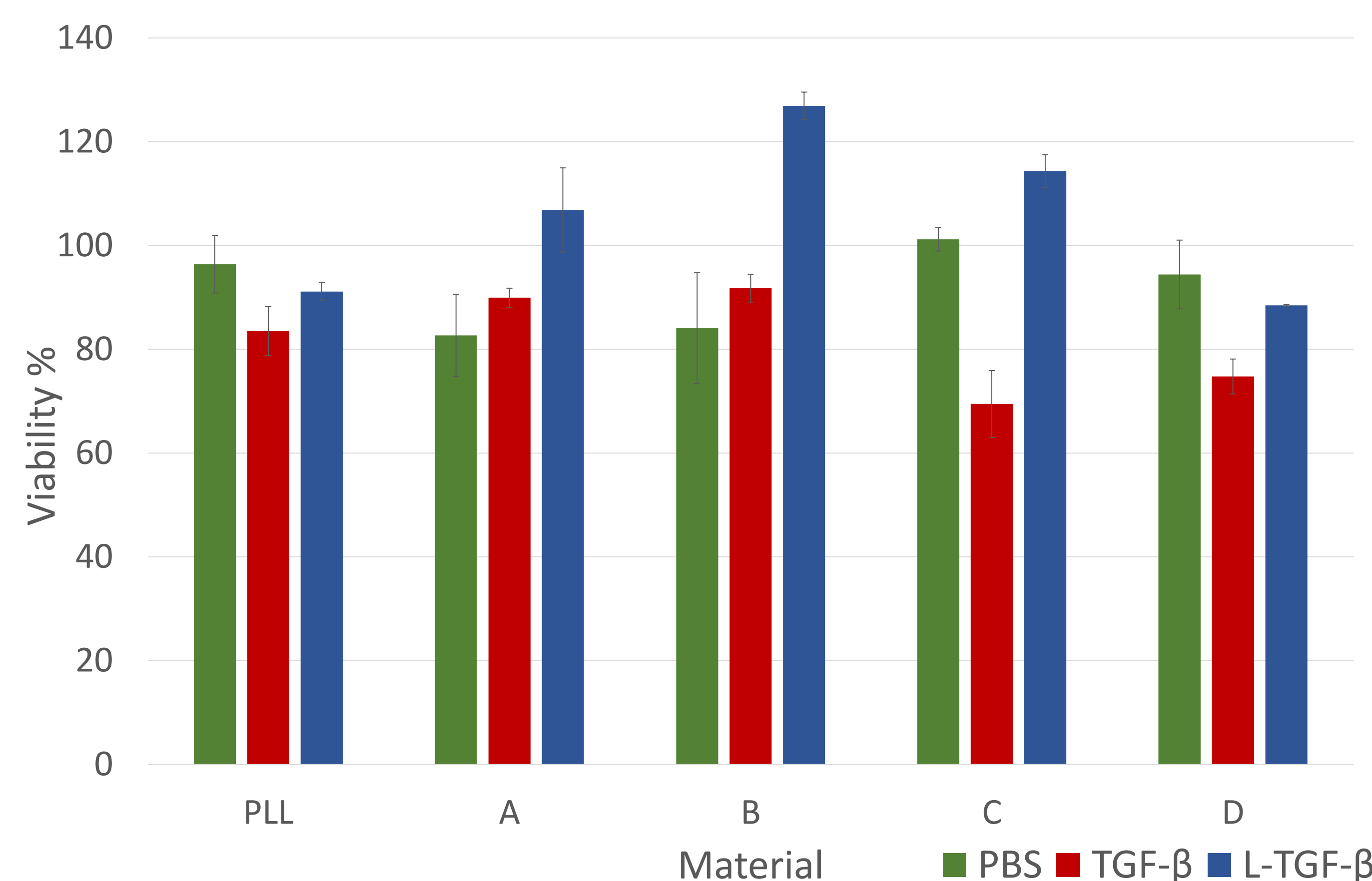
Fibroblast to myofibroblast differentiation

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.



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

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2. Li, A. G. et al. Elevation of transforming growth factor beta (TGF- β) 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)- β 1, TGF- β 2, 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