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, often hindering its function for patients.

- Transforming growth factor β (TGF-β) is involved in fibrous capsule formation.
- TGF-β leads to the differentiation of fibroblasts into myofibroblasts.
- Myofibroblasts secrete large amounts of collagen and produce α-smooth muscle actin, a cytoskeletal protein that enables myofibroblasts to contract collagen to form a dense, acellular, fibrous capsule.
- 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**

<table>
<thead>
<tr>
<th>Material</th>
<th>Modification</th>
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<tbody>
<tr>
<td>Poly-L-lysine (PLL)</td>
<td>+ R-COOH</td>
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<tr>
<td>Modified Poly-L-lysine</td>
<td>EDC 4 hr at RT</td>
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**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.

**Results**

**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.

**References**

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