535f Modulation of Astrocyte Behavior Via Transforming Growth Factor & Beta-1 Conjugated Surfaces

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Implantation of deep-brain recording devices, to restore lost functionality, is a traumatic event which inevitably elicits reactive gliosis. Gliosis involves the proliferation, hypertrophy, and process extension of astrocytes in the vicinity of the trauma. The resulting physical component of reactive gliosis involves the development of a glial scar composed primarily of reactive astrocytes and the extracellular matrix products they produce. As a result of glial scar formation, the ability to transmit signals to or from the target neuron is lost due to scar tissue increasing the distance of the neuron from the implant. Surface modifications capable of decreasing scar tissue formation should result in improved long-term implant-neuron communication.

Surface modifications influencing astrocyte proliferation represent a method of mitigating glial scar development. Potentially, the severity of glial scar formation could be minimized, for example, by limiting the number of astrocytes actively participating in reactive gliosis. Transforming growth factor-beta one (TGF-β1) has been shown to decrease the rate of astrocyte proliferation. Covalent bonding of the cytokine to dextran surfaces maintains the efficacy of TGF-β1 toward astrocyte proliferation over the long-term since the growth factor cannot diffuse away or become internalized by the astrocytes.

Astrocyte culture proliferation was measured via colorimetric assays against in solution concentrations of TGF-β1 for determining the optimum concentration of TGF-β1 for proliferation inhibition. This experiment demonstrated a 44.9% ± 32.6% ($p < 0.0003$) decrease in proliferation at 10 ng/mL TGF-β1. A predictive receptor-ligand model based on mass action kinetics was developed to equate three-dimensional (in solution) TGF-β1 concentrations to two-dimensional (surface bound) TGF-β1 concentrations. TGF-β1 was bound to immobilized dextran surfaces. Poly-L-lysine coated surfaces were treated with oxidized dextran. The dextran was re-oxidized with sodium metaperiodate to generate aldehyde binding site locations to which TGF-β1 was covalently bound via a Michael addition reaction. The resulting surfaces inhibited *in vitro* proliferation by 53.8% ± 25.2% ($p < 0.0003$). These results demonstrate that covalently bound TGF-β1 retains its ability to inhibit astrocyte proliferation.