Extracellular Matrix Coatings Decrease the Foreign Body Response to Silicon Microelectrode Arrays Chronically Implanted in Rat Motor Cortex

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Statement of Purpose: Microelectrode recording devices show promise to provide volitional control of prosthetic devices. However, such devices perform inconsistently over long indwelling periods, presumably due to the foreign body response (FBR). In the brain, this response is dominated by persistent neuroinflammatory sequela. Available evidence has suggested that decellularized extracellular matrix (ECM) derived from various tissue sources is capable of modulating the activation state of macrophages and accelerating wound healing. Here we investigate the utility of cell-specific ECM coatings as a means to modify the FBR for neural recording devices chronically implanted in the mammalian cortex.

Methods: Open-cell polyurethane foams (Tecoflex) were fabricated, pretreated with fibronectin and seeded with primary astrocytes and cultured for several weeks. Following culture, the cells and polymer were removed using a weak aprotic solvent and the remaining cell-derived material was rinsed in DI water, frozen and lyophilized. The ECM was characterized by Mass Spectroscopy and immunohistochemical methods. Silicon microelectrode arrays were coated with acid solubilized ECM solutions via repetitive dip coating process. Planar silicon coated electrodes and uncoated controls were implanted stereotactically in motor cortex (perpendicular to midline) of adult male Sprague-Dawley rats (n=6). After an 8-week indwelling period, animals were transcardially perfused and their brains post-fixed in 4% paraformaldehyde. The brains were then serially sectioned and the FBR was characterized using a quantitative immunohistochemical approach. All procedures were conducted in accordance with the University of Utah Animal Care and Use Committee (IACUC).

Results: Astrocyte derived ECM was shown to contain various ECM constituents. In general, the freeze dried product was a white lacy solid that could be ground into a powder and brought into solution under acidified conditions. Eight weeks after implantation ECM coated microelectrodes showed a lower overall distribution in markers for the FBR. As illustrated in Figure 1, the distribution of CD68 and GFAP was significantly different within the first 100µm as determined by a K-S statistical test. Mean GFAP immunoreactivity was also significantly lower in this range. NeuN manual cell counts showed a decrease in neuronal cell density of approximately 50% with no apparent difference between control and ECM coated.

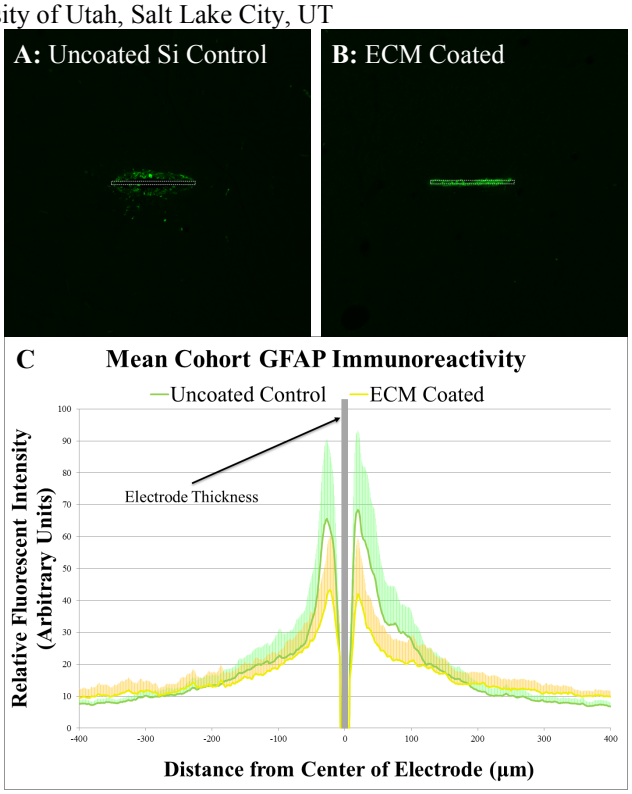

Figure 1. Representative immunoreactivity of CD68 which showed the mean cohort profile had a broader distribution surrounding the **(A)** uncoated silicon compared to **(B)** ECM coated (n=5, $p<0.001$). **(C)** Differences in the spatial distribution of GFAP immunoreactivity for control (green) and ECM coated microelectrode arrays (yellow) (n=5, $p<0.001$).

Conclusions: We show that astrocyte-derived ECM coatings may be a useful tool for altering the distribution and intensity of FBR biomarkers to any device implanted in the central nervous system. Current research is focused on investigating underlying mechanisms of action including accelerated hemostasis and modulation of inflammatory sequela following implantation. Research in progress is aimed at identifying alternative cell sources of ECM, whose use may improve the biocompatibility of a variety of chronic indwelling devices.

References: Brown BN, et al., Biomaterials. 2009;30:1482-1491. Wolchok JC and Tresco PA, Biomaterials. 2010;31:9595-9603. Skousen JL, et al., Prog Brain Res. 2011;194:167-180. Tanaka J, et al., Neurosci Res. 1999;34:207-215.