**Development of a biomimetic 3-dimensional spinal cord model system to study inflammation-mediated astrogliosis.**

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Spinal cord injury is one of the severest traumatic life-changing events to affect the human body frequently incurring devastating physical loss of voluntary control and sensory function. Due to the poor functional outcomes, research has identified many of the pathophysiological processes that occur following SCI and is characterised, in part, by the formation of a complex inhibitory scar composed mainly of astroglial cells at the site of injury.

Developing therapeutic approaches to target injury-responsive and scar-forming astroglia is hampered by a) their complex interactions with other injury responsive glial cells (e.g. microglia) through multiple signalling pathways, b) the spectrum of reactive subtypes that are predicted to develop and c) the current lack of sufficiently complex model systems capable of replicating their complex 3D tissue environment.

We propose to develop a reduced 3D bioengineered spinal cord cell scaffold (SCCS) containing evenly seeded human astrocytes and neurons. The scaffold, composed of the extracellular matrix proteins hyaluronan and collagen, and so designed to mimic the architectural features of the human spinal cord will be subjected to specific mechanical injuries. Using this system, we aim to investigate the neuroinflammatory pathways that may contribute to the scar forming response of astrocytes. The deliverables from the project will identify key targets and/or pathways responsible for enhancing the astroglial response to injury and inform the design of therapeutic DNA- and RNA-containing nanoparticle cargoes. Subsequently, the SCCS will serve as the test bed for these new therapies and help direct future research.



**Astrocytes**

**Neurons**

**Nuclei**

Figure 1. Immunostained 2D co-cultures of human derived astrocytes (GFAP, red) and neurons (β-tubulin III, green) counterstained with the nuclear stain DAPI (blue). Both cell types will be seeded into the spinal cord cell scaffolds.

**25µm**