Abstract:

Spinal cord injury is a devastating condition affecting the every-day life of 250,000- 400,000 victims and their families in the US. Recent clinical evidence for the neuroprotective effects of pharmacological treatments in the acute phase as well as experimental evidence for regeneration of central axons upon injury gives promise for an effective treatment of SCI. Regeneration of the principal neurons in the spinal cord depends on the extracellular (soluble and contact) signals reaching the neurons from their environment. Recently, an *in vitro* system was developed in the Hybrid Neuronal Systems Laboratory at Clemson, which has been shown to promote the growth and differentiation of motoneurons and DRG cells. Using this system the extracellular environment (both soluble factors and growth substrate) could be modified in a systematic and effective way and preliminary results indicated that it is a good model for spinal cord injury. In this study we are proposing the adaptation of this *in vitro* system for pharmacological screening, where not only soluble neurotrophic factors can be tested, but with the modification of the growth substrate we can model specific conditions after spinal cord injury (membrane bound growth inhibitory factors) and drugs acting on contact signaling receptors can be screened. This model utilizes surface chemistry to create patterns of cultured cells where the axons of motoneurons and DRG cells are directed in parallel tracks, which could enable quantification of axonal regrowth after injury. The serum-free growth media and the composition of the growth substrate will be systematically modified to find the optimal conditions for neuronal survival and axonal regeneration. The effect of two growth inhibitory proteins (neurocan and tenascin-R) will be studied in detail. Antibodies as well as possible receptor antagonists will be screened in a systematic way. Results obtained during this study will be used to prepare for the submission of an NIH K02 career development grant in collaboration with Prof. James J. Hickman at Clemson University.