Project #7: **Ravi Bellamkonda** and **Chunyang Xiong:** *The effects of CSPG mediated inhibition on neuronal cell signaling and cytoskeletal mechanics*

Astroglial scar tissue formed after physical injury to the central nervous system (CNS) presents a major impediment to CNS regeneration. Chondroitin sulfate proteoglycans (CSPGs) present in astroglial scar tissue have been strongly implicated in scar-mediated inhibition. Neurite inhibition by CSPGs results in the development of dystrophic growth cones, culminating in cytoskeletal and membrane protein dysfunction. The Rho family of GTPases – including RhoA, Rac1 and CDC42 – has been widely implicated in growth cone guidance. The laboratory of one of the PIs (Dr. Bellamkonda) has shown that modulation of the Rho GTPases, CDC42 and Rac1 results in alleviation of CSPG-mediated inhibition, by the likely alteration of cytoskeletal mechanics. Transduction of constitutively active (CA) forms of CDC42 and Rac1 along with C3 transferase, an inhibitor of RhoA activiation into neurons, resulted in greater neurite crossing into CSPG rich regions. While it is generally accepted that RhoA plays an important role in CSPG mediated inhibition, the effects of RhoA activation in regenerating axons are poorly understood. In this proposal, we aim to expand upon our significant findings, and test the hypothesis that CSPG induced activation of RhoA in neuronal growth cones may trigger inhibitory effector cell-signaling cascades, leading to altered cytoskeletal mechanics and changes in tractionforces *in vitro*. In this collaboration, the Bellamkonda lab will provide neuronal cell biology expertise, and the Chunyang lab will provide traction force microscopy expertise, which will be used to dynamically detect the force exerted by neurons growing on a soft substrate.