Project 4: Testing clinically relevant matrices for Schwann cell transplantation following spinal cord injury

Cell therapy strategies to repair the injured spinal cord are promising new breakthroughs with the recent clinical trials in acute and chronic spinal cord injury (SCI) subjects [1]. Following an insult to the mammalian spinal cord, a series of complex responses follow that contribute to an aggravated expansion of the initial injury, and result in dramatic functional deficits [2]. The formation of fluid-filled cavities contributes, in part, to the regenerative failure and functional deficits that follow SCI. Cell transplantation strategies rely on reducing cavitation following damage, re-bridging the injured tissue and creating more favorable conditions for axonal regeneration. From the various cell types proposed to be used in SCI repair, Schwann cells (SCs) have been extensively studied and are currently undergoing safety and efficacy evaluation in clinical trials in the Miami Project to Cure Paralysis. SCs are the myelinating glia of the peripheral nervous system, and can be obtained from SCI patients, expanded in culture, and autologously transplanted into the lesioned spinal cord. These cells were found to be neuroprotective, reduce cavitation, promote axon regeneration and myelination, and modestly improve hindlimb movements in animal models [3, 4]. Nevertheless, one of the hurdles that may be limiting the therapeutic potential of SC implants, as well as other cell types, is the poor survival rate of the transplanted cells in the injury site [5]. Previous reports have shown that after a contusion injury in rats, there is about an 80% SC loss 3 weeks after transplantation due to necrosis and apoptosis [6, 7]. The traumatic nature of cell isolation procedures, the detachment from its extracellular matrix (ECM) before transplantation, and the injury environments are some factors that contribute to this significant cell death.

One possible approach to improve transplanted SC survival, therefore maximizing its therapeutic potential, is to implant them in ECM-derived substrates, such as an injectable matrix, instead of the culture media suspension approach. Most commercial ECM matrices, however, are tumor-derived and have undefined and variable growth-factor composition. For these reasons, they are not clinically applicable and it still remains of the utmost importance to identify clinically relevant injectable matrices for achieving greater survival and efficacy of cellular implants after SCI. **The goal of this project** is to evaluate the potential of ECM-derived matrices in supporting SC survival after injury, while fostering neuronal regeneration through the graft. It will be a project involving concepts and techniques from biomaterials and biomedical research, and envisioning future translational studies for clinical applications.