NASCIC
SCI RESEARCH
ADVOCACY COURSE

Module 7 – Neurorepair

Introduction to Neurorepair

In module 6, we covered the goals and strategies relevant to neuroprotection that aim to protect tissue from being lost during secondary injury cascades. The following three modules will cover the therapeutic goals and strategies aimed at restoring function through modulating nervous tissue.

The current module, Module 7, will talk about neurorepair. We will discuss the mechanisms that inhibit axonal regeneration, current strategies to promote the re-growth of the cut/injured axon through the lesion back to its normal target, and lastly touch on the hurdles presented when implementing regenerative therapies.

In Module 8, neuroreplacement is addressed. Neuroreplacement methods seek to replace or restore the function of dead/damaged neurons by introducing new cells into the environment. Module 8 will introduce stem cells, as well as strategies of cell replacement in SCI that aim to improve function.

Lastly, Module 9 will describe neuroplasticity, which will detail the process of re-wiring of neural circuitry with the aim of improving functions affected by SCI. Topics, such as the internal mechanisms for reconstruction of neural circuits and current activity-based therapy, epidural spinal stimulation and brain computer interface will be discussed. The next 3 modules can become interconnected and, in combination, provide therapeutic benefits to an individual with SCI. Thus, as we move throughout these modules, it is important to note that some topics may be brought up several times, due to its applicability in another treatment method/purpose.

To begin Module 7, the objective of neurorepair is to allow for axons that have been damaged from injury to regenerate through and beyond the lesion, and to make meaningful connections that can restore function.

What defines axonal regeneration? R**egeneration** refers to re-growth of the cut/injured axon through a lesion back towards its normal target. Regeneration is different than sprouting, which is defined as the splitting of an uninjured axon into multiple branches which can occur above a lesion, into a lesion, or below the lesion in axons that have been spared from injury. The growth of sprouting axons is distinctly different from axon regeneration and can be difficult to differentiate in experimental models. Sprouting from spared axons will be talked about in Module 9 (Neuroplasticity), however both sprouting and regeneration aim to increase communication to and from the brain.

The lack of repair following spinal cord injury is due to both neuron cell intrinsic factors and the extrinsic injury environment. As understanding grows about the complex interplay between different cell types and the extracellular environment at the site of damage, researchers are increasingly optimistic that they will find a way to kick-start the regeneration that is suppressed in the CNS.

So, why is it so challenging to cause axon regeneration? Let's break this down into three major players of axon growth. 1) extracellular inhibitors, 2) extracellular growth enhancers (growth factors and guidance cues), and 3) intracellular growth inhibitors/activators. Research into axon regeneration seeks to identify what molecules inside and outside of a cell inhibit regenerative potential, and which have the ability to promote regeneration.

The complex factors that prevent the spinal cord from repairing itself might mean that not one approach will be sufficient. It seems likely that a combination of treatments will be needed to support neuronal regeneration and restore function and independence to people with spinal-cord injury. When used in combination with neuroprotection and rehabilitation that seeks to retrain neural circuits, neurorepair therapies may lead to functional improvements for people with an SCI.

In this module, you will learn:

- how neurorepair is inhibited in the CNS and promoted in the PNS
- how researchers are using this information to develop and test neurorepair therapies
- controversies within the field