

Background

The peripheral nervous system consists of forty-three pairs of motor and sensory nerves; these nerves connect the brain and spinal cord to the rest of the body [1]. The peripheral nervous system controls sensation, movement and motor coordination. Additionally, the nerves in the peripheral nervous system are very fragile and are easily damaged [1]. Peripheral neuropathy is the condition in which the peripheral nervous system is damaged. When there is damage at the peripheral nervous system the nerves malfunction and nerve signaling is disrupted [2].

Schwann cells have a remarkable plasticity that allows them to mount an adaptive response to nerve injury and promote regeneration [3]. Schwann cells must be kept in a reactive state to support regeneration. Furthermore, axon regeneration must be accelerated to prevent chronic denervation changes in Schwann cells and denervated muscle. There was a study that demonstrated that overexpression of activating transcription factor 3 (ATF3) in dorsal root ganglion sensory neurons accelerates regeneration of axons [4].

Aim

To propose a model that can overexpress ATF3 which accelerates axonal regeneration and thus prevents denervation changes in Schwann cells which promote regeneration.

Research Model

To understand the role of accelerated axonal regeneration on nerve regeneration, I will use a transgenic mice model to overexpress ATF3. ATF3 is implicated in the acceleration of axonal regeneration in dorsal root ganglion sensory neurons. Overexpression of ATF3 should result in an accelerated axonal regeneration.

The mice will be put under anesthesia and the sciatic nerve will be crushed with forceps for fifteen seconds. This is done to demonstrate a sciatic nerve crush injury. ATF3 will be transduced into an AAV vector. The AAV vector with ATF3 will be microinjected directly into the dorsal root ganglionic neurons. The expression of ATF3 will be observed in the peripheral nervous system to determine whether it will accelerate axonal regeneration and thus prevent Schwann cell denervation changes.

Applications

Accelerating axonal regeneration will prevent Schwann cell denervation changes. This is important because Schwann cells are critical in supporting regeneration of peripheral nerve regeneration. Understanding the importance of axonal regeneration is critical for the generation of therapeutic methods to enhance peripheral nerve regeneration.

References

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