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Suppression of AMIGO3 promotes dorsal root ganglia neuron axon regeneration after spinal cord injury

Sharif Almutiri[1], **Ann Logan**[2] and **Zubair Ahmed**[2]
[1]Shaqra University, Saudi Arabia
[2]University of Birmingham, UK

Unlike the peripheral nervous system, the spinal cord which forms part of the central nervous system (CNS) is unable to regenerate. Nogo-A, myelin associated glycoprotein (MAG), and oligodendrocyte-derived myelin glycoprotein (OMgp) is one of the major inhibitory proteins in the CNS which contributes to the non-regenerating nature of CNS axons. They bind with a common Nogo-66 receptor and activate axon growth cone collapse through the Rho GTPase pathway. However, manipulating the extracellular environment in the CNS after injury can induce limited axon regeneration. In this study, we demonstrate by manipulating expression of extracellular protein molecules-AMIGO3 (an amphoterin-induced gene open reading frame) that axon regeneration in the CNS is possible. Data from immunohistochemistry in regenerating and non-regenerating spinal cord injury models showed that low levels of AMIGO3 expression correlated with regenerating sciatic nerve (SN) and preconditioning SN+DC lesion models. Knockdown of AMIGO3 in dorsal root ganglion neuron (DRGN) cultures promotes DRGN neurite outgrowth. Non-viral delivery of an AMIGO3 shRNA plasmid to knock down AMIGO3 expression in injured dorsal columns (DC), demonstrated significant DC axon regeneration. Moreover, AMIGO3 when tagged with green fluorescent protein (GFP), targeted large diameter DRGN after injection and was anti-inflammatory, revealing a novel function of AMIGO3 in regulating inflammation in the CNS after injury. The mechanisms by which AMIGO3 supresses or promotes axonal regeneration is not yet known, but we conclude that AMIGO3 plays a major role in DRGN axon regeneration and could be harnessed to promote regeneration of injured neurons after spinal cord injury.

Biography

Sharif Almutiri completed a PhD in University of Birmingham, School of clinical and experimental medicine, College of medical and dental science 2017. He completed his Master of Science in Cell and Tissue Engineering, a College of Science and Technology in Medicine, from Keele University, UK in the year 2011. He completed a bachelor's degree from Gassim University, medical applied science (medical microbiology) 2007.

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