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PII: S0012-1606(16)30595-4
DOI: http://dx.doi.org/10.1016/j.ydbio.2017.05.011
Reference: YDBIO7441

To appear in: *Developmental Biology*

Received date: 15 September 2016
Revised date: 3 February 2017
Accepted date: 11 May 2017

Cite this article as: Marcos Julian Cardozo, Karolina S. Mysiak, Thomas Becke and Catherina G. Becker, Reduce, Reuse, Recycle - Developmental Signals i Spinal Cord Regeneration, *Developmental Biology* http://dx.doi.org/10.1016/j.ydbio.2017.05.011

Reduce, Reuse, Recycle - Developmental Signals in Spinal Cord Regeneration

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Abstract

Anamniotes, fishes and amphibians, have the capacity to regenerate spinal cord tissue after injury, generating new neurons that mature and integrate into the spinal circuitry. Elucidating the molecular signals that promote this regeneration is a fundamental question in regeneration research. Model systems, such as salamanders and larval and adult zebrafish are used to analyse successful regeneration. This shows that many developmental signals, such as Notch, Hedgehog (Hh), Bone Morphogenetic Protein (BMP), Wnt, Fibroblast Growth Factor (FGF), Retinoic Acid (RA) and neurotransmitters are redeployed during regeneration and activate resident spinal progenitor cells. Here we compare the roles of these signals in spinal cord development and regeneration of the much larger and fully patterned adult spinal cord. Understanding how developmental signalling systems are reactivated in successfully regenerating species may ultimately lead to ways to reactivate similar systems in mammalian progenitor cells, which do not show neurogenesis after spinal injury.

Keywords

neural tube, regeneration, development, signalling pathways, spinal cord injury, CNS

Introduction

How animals are capable of reconstructing a functional tissue after a disruptive injury is a fundamental question in regenerative biology. One principle appears to be that mechanisms that regulate cell proliferation, differentiation or death during development are redeployed after injury.

Mammals can functionally regenerate a few organs, such as the liver, but the central nervous system (CNS) regenerates very poorly [e.g.(Hugnot and Franzen, 2011)]. In contrast, some adult vertebrates can regenerate many organ systems successfully, including heart, limbs and CNS (Gemberling et al., 2013). Teleost fishes, larval *Xenopus* and salamanders are the leading models that can successful regenerate spinal cord after an injury (Diaz Quiroz and Echeverri, 2013; Edwards-Faret et al., 2017). Recently, zebrafish larval models of spinal cord injury (SCI) have been introduced, taking advantage of tissue transparency, and transgenic and mutant lines that allow for time-lapse and drug screening analyses (Briona and Dorsky, 2014; Ohnmacht et al., 2016).