

The Effect of Retinoids on the Regenerating Axolotl Spinal Cord

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Currently, there are approximately 265,000 individuals in the United States who suffer from incapacitating spinal cord injuries (SCI). The available therapies that are utilized—including drugs, electrical stimulation, and stem cell applications—have demonstrated inadequate effects in rectifying the severity of the injury. In mammals, penetrating spinal cord injuries (from shrapnel, bullets, knives, or splintered bone in humans) involve a scar in which the surrounding meninges (connective tissue coats) direct the action of astrocytes within the cord to form a composite glial and meningeal scar. This scar may act to prevent secondary damage to neurons from invading inflammatory molecules. However, the scar also prevents those neurons from making new functional connections across the lesion site. In contrast, within Urodeles (amphibians including newts and salamanders), the penetrating injury response involves the meninges interacting with the underlying ependymal cells (that line the central canal), which will remodel the lesioned cord and promote axonal extension and neurogenesis via differentiation of respective stem cells. Interestingly, the meninges happens to be a rich source of retinoids, which are known to serve critical roles in neural development and regeneration, such as modifying gene expression to drive neuronal differentiation and neurite outgrowth. In addition, retinoids applied to ependymal cells in culture facilitate re-epithelialization of the tissue; ependymal cells co-cultured with reactive meninges also re-epithelialize. Furthermore, our lab aims to better characterize the effect of retinoids on Urodele spinal cord regeneration by employing antibody labeling-concurrent with horseradish peroxidase staining of both intact and regenerating paraffin-embedded Axolotl spinal cord tissues obtained from adult and juvenile animals—to target protein expression of specific components of the pathway; in addition, cell culture techniques will be utilized to observe the effect of those components on re-epithelialization of spinal cord tissue. Currently, Cellular Retinoic Acid Binding Protein II (CRABP II) and Cellular Retinol Binding Protein I (CRBP I) are being investigated. Our results demonstrate that CRABP II is heavily expressed in the pia mater meningeal layer; CRBP I, however, is expressed in three locations: the pia mater meningeal layer, the nuclei and cytoplasm of gray matter neuroblasts, as well as processes derived from neuroblasts and ependyma. Moreover, the morphogenic nature of the retinoids may possess a significant role in the regeneration-permissive interaction of the meninges and ependyma of the Axolotl spinal cord.