Internship Proposal

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Project Title:
Caharacterization of the extracellular matrix properties of spinal cord after lesion in Acomys versus Mus.

Level:

Master Student

Project Summary:

Lesions to the brain and spinal cord remain a major unmet medical condition. The main obstacles to treat these conditions is the formation of a scar at the injury site and the intrinsic inability of adult neurons to regenerate. The Nerve Regeneration group (i3S) has recently discovered that the spiny mouse (Acomys) is a unique exception and is able to regenerate and recover function after full spinal cord transection. To understand the mechanism underlying regeneration in Acomys, we have performed RNAseq of the spinal cord injury (SCI) site of Acomys and the closely related non-regenerative Mus musculus. The results revealed that some of the most differentially regulated genes between Mus and Acomys, belong to the extracellular matrix (ECM) category (unpublished data). This internship aims at investigate the differentially regulated ECM-related genes and its potential contribution to different biophysical properties of the Acomys SCI site in comparison with Mus, contributing to its regenerative capacity. The knowledge gained with this analysis will enable us to proceed to in vivo proof-of-concept experiments where we will modify the Mus spinal cord environment in an Acomys-like manner, to enable this species to become regeneration-competent.

Work to be developed by the student:

The Acomys ECM-remodeling, indicated by our previous RNAseq data, and the byophysical consequences of

such alterations will be accessed as follows:

1.1. Initially, 5 selected ECM-related genes (based on its expression levels and profile) differentially

The knowledge gained with this analysis will enable us to proceed to in vivo proof-of-concept experiments where deregulated in Acomys after injury, will be validated by

immunohistochemistry using spinal cord sections from

we will modify the Mus spinal cord environment in an Acomys-like manner, to enable this species to become Acomys and Mus, collected at the same time points post-SCI as RNAseq was done (already available).

regeneration-competent.

1.2. As tissue stiffness is altered after CNS injury/repair in other organisms, and differences in ECM-related proteins are likely to produce similar effects, the Acomys spinal cord will be compared with that of Mus for its mechanical properties. For that, naïve and injured (at 1 day, 1 week, 3 weeks post-injury) spinal cords of both species will be subjected to atomic force microscopy (AFM)-based indentation. the resulting wide range of mechanical parameters, including force, pressure, tension, adhesion, friction, elasticity, among others, will allow a deep characterization on tissue.

References:

Nogueira-Rodrigues, J., et al. (2022). "Rewired glycosylation activity promotes scarless regeneration and functional recovery in spiny mice after complete spinal cord transection." Dev Cell 57(4): 440-450 e447.

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