Functions of HDAC8 in Schwann cell development

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Schwann cells (SCs) are the myelinating glial cells of the peripheral nervous system (PNS), they surround axons, forming a myelin sheath that provides axonal insulation, saltatory nerve conduction, tissue homeostasis and neurotransmission. The development of Schwann cells is tightly regulated at the transcriptional level in every step of differentiation and involves the transcriptional control of the major factors involved in myelination.
A previous work in our group demonstrated that histone deacetylase 1 (HDAC1) and HDAC2, two chromatin remodeling enzymes that remove the acetyl group from the lysine residues of histone tails, play a crucial role in the regulation of gene transcription during SC differentiation. My project is focused on HDAC8, which is highly expressed in the PNS during development, to understand the mechanism of action that drives SC differentiation and survival.
To perform these analyses, I compared the expression of crucial inducers of myelination in the sciatic nerve of control mice and of HDAC8 knockout (H8KO) mice obtained with the Dhh-Cre mouse line that leads to SC-specific gene ablation starting at the SC precursor stage.
The analyses revealed that Sox10, Oct6 and Krox20, the three major inducers of myelination, do not show any detectable expression change between control and H8KO sciatic nerves.
The expression of the transcription factor Pax3 and his direct target P0, a transmembrane glycoprotein essential for the formation and stabilization of the multilamellar structure of the compact myelin, are upregulated in H8KO nerves from birth to the adult stage. Similarly, the analyses on myelin basic protein (MBP), another constituent of the myelin sheath, show that the protein is strongly upregulated in H8KO animals from birth until the adult stage.
On the other hand, the proliferation marker Sox2 is also upregulated at birth, but in contrast to Pax3, P0 and MBP, this regulation is not observed at later time points.
These data, obtained through Western Blot (WB) and immunostaining (IF) techniques, suggest that HDAC8 acts as a myelination break during Schwann cell development. These analyses will be continued to determine whether the lack of HDAC8 leads to hypermyelination and/or aberrant myelin formation. This question will be addressed by using electron microscopy.
The next steps for this project include the analysis of the mechanism of action by which HDAC8 regulates the expression of Pax3, P0, MBP and Sox2.

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