Characterization of the role of the SOX2 transcription factor in neurons of the visual thalamus: insights into developmental visual disorders

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Abstract

The visual thalamus (dorsolateral geniculate nucleus, dLGN) is fundamental for vision. This brain nucleus receives neuronal input from the retina *via* the optic nerve, and its projection neurons in turn connect to the cortical visual area, where eye-derived signals are elaborated. The transcription factor SOX2 is highly expressed and plays a crucial role within differentiated dLGN neurons; indeed, defective differentiation of dLGN neurons leading to abnormal thalamocortical projections and affected visual area specification were observed in Sox2 thalamic conditional knockout mice. To understand the molecular mechanisms underlying these defects, RNAseq of dissected neonatal dLGNs followed by CUT&RUN analyses have identified not only several genes deregulated following Sox2 thalamic ablation (DEG), but also hundreds of reproducible SOX2-bound regions (peaks). We also found that genes differentially expressed in the Sox2 thalamic mouse mutant, compared to controls, and directly bound by SOX2, are highly enriched in functional categories related to neuronal development and function. SOX2 is known as a key factor in neural progenitors; our work is shedding new light on a novel role of Sox2 in differentiating neurons.
We plan to characterize the role of SOX2 target genes in dLGN neurons initially by manipulating their expression in *in vitro* cultures of dLGN neurons and determining how their downregulation affects cell morphology and differentiation. We will then study how these SOX2 target genes affect the formation of circuits in the visual system using co-cultures of retina-thalamus-cortex and *in vivo* studies in both mice and zebrafish.