Sox2 expression in thalamic neurons is required for the development of the visual system

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Visual system development involves the formation of neuronal projections connecting the retina to the thalamic dorsolateral-geniculate nucleus (dLGN), and the thalamus to the visual cerebral cortex. Patients carrying mutations in the *SOX2* transcription factor gene present severe visual defects, thought to be linked to SOX2 functions in the retina. We show that Sox2 is strongly expressed in mouse postmitotic thalamic projection neurons in the dLGN. Cre-mediated deletion of Sox2 in these neurons causes reduction of the dLGN, abnormal distribution of retino-thalamic and thalamo-cortical projections and secondary defects in cortical patterning. Reduced expression, in mutants, of Sox2 target genes encoding ephrin-A5 and the serotonin-transport molecules SERT and vMAT2 (important for establishment of thalamic connectivity) likely provides a molecular contribution to these defects. In addition, Sox2 thalamic mutants have abnormalities that closely mirror those found in COUP-TF1 mutants. We found that Sox2 and CoupTf1 are co-expressed in neurons in the dLGN and we are searching for genes that could be co-regulated by Sox2 and COUP-TF1 and could be affected in our Sox2 mutants. A role for Sox2 in eye development had been previously described and we have now identified its importance for the development of another component of the visual system: the dLGN. These findings unveil thalamic SOX2 function as a novel regulator of visual system development and a plausible additional cause of brain-linked genetic blindness in humans.