Research Week 2020

Isl1 is Required for the Specification and the Morphological Maturation of Starburst Amacrine Cells

Yessica Santana, Teresa Stackhouse, Patrick Kerstein

OHSU

Keywords

cell fate, neurodevelopment, retina, starburst amacrine cell, transcription factor

Abstract

During neuronal development, neuronal subtype differentiation is regulated by transcription factors (TF's) which control effector genes that define cell fate. TFs can regulate initial neuronal specification, the development of cell features (morphology, neurotransmitter expression, physiology) or both. The mammalian retina consists of 5 classes of retinal neurons with each type containing many subtypes. Specific transcriptional pathways that direct development for each subtype are unknown. The most diverse class of retinal neurons are amacrine cells (ACs), with over 45 distinct subtypes. Within the AC population, the TF Isl1 is expressed in a single subtype: starburst amacrine cells (SACs). Isl1 is also expressed in other retinal neuron classes, and pan-retinal deletion of Isl1 results in a loss of these retinal neurons, thus confounding conclusions about Isl1's role in SAC development. To examine Isl1's role in SACs, we developed two approaches to selectively delete Isl1 at distinct stages of development. The first deletes Isl1 from AC precursors using a Ptf1aCre;Isl1cKO mouse line, allowing us to examine its role in the initial specification of SACs. The second approach uses a ChATCre;Isl1cKO mouse line to delete Isl1 after SACs are specified and migrate to their correct target area, but before the completion of dendritic growth. This approach allows us to examine how Isl1 can regulate SAC-specific features. Preliminary data indicates that deleting Isl1 in Ptf1aCre;Isl1cKO results in an absence of SACs. If deleted in ChATCre;Isl1cKO, SACs adopt aberrant dendritic morphology and lamination. Together, these data suggests Isl1 is required for the initial specification of SACs and the subsequent development of proper morphological maintenance. Detailing the specific roles TFs have in neuronal subtype specification and differentiation is important for understanding how neural circuitry develops and how morphological properties contribute to overall circuit function.