HIGHLIGHTS

Highlighted article: "*prdm1a* Regulates *sox10* and *islet1* in the Development of Neural Crest and Rohon-Beard Sensory Neurons" by E.C. Olesnicky, L. Hernandez-Lagunas, K.B. Artinger

Neural crest cells are a multipotent, stem cell like population that arises at the border between the neural and non-neural ectoderm. The interaction between neural and non-neural ectoderm allows neural plate border cells to become specified as neural crest cells. Following the initial induction, a cascade of transcriptional regulators, termed neural crest specifiers, are expressed and function to promote epithelial-mesenchymal transition from the neural tube, enabling neural crest cells to migrate throughout the embryo. Neural crest cells give rise to a variety of different tissues, including melanocytes, neurons and glia of the peripheral nervous system, and cartilage and bones of the face. A primary sensory neuron population, termed Rohon-Beard (RB) sensory neurons, also arises at the neural plate border. RB neuron specification requires a unique and overlapping set of transcriptional regulators to those used in neural crest cell specification. Although many genes have been shown to play a role in specification of these two distinct populations, critical gaps remain in understanding the connectivity of these processes, since many players within the neural crest gene regulatory network have been identified based solely on gene expression.

Prdm1a (Blimp-1) is a zinc finger DNA-binding transcription factor that is involved in many aspects of cell fate specification during development, including gastrulation, formation of head structures and slow twitch muscle development. Importantly, in zebrafish and mouse, mutations in *prdm1a* lead to defects in neural crest and posterior pharyngeal arch development, suggesting conservation of function between species. In zebrafish, *prdm1a* is necessary for neural crest specification and RB sensory neuron formation, as mutations in *prdm1a* display an absence of RB sensory neurons and a reduction in neural crest cells. Thus, *prdm1a* functions as a neural plate border specifier, in that it is required for the formation of cells at the neural plate border. While it is clear that *prdm1a* is important for the development of RB neurons and neural crest cells, the mechanism of action and the gene regulatory network incorporating *prdm1a* is currently unknown.

In the report by Olesnicky *et al.*, the authors describe experiments designed to understand the gene regulatory network in which *prdm1a* acts as a central player to specify neural crest and RB sensory neuron cell fate. A microarray analysis between *prdm1a* mutant embryos and wildtype embryos at 25 hours post fertilization was performed and a series of potential downstream targets were identified. While many known genes were identified in the array, additional novel players involved in the development of RB sensory neurons and neural crest were identified. The authors then focused on two transcription factors, *sox10* and *islet1*; they demonstrate that the expression of these two genes is reduced in *prdm1a* mutants and that over-expression of *prdm1a* mRNA in wildtype embryos increases their expression. Importantly, by performing epistatic rescue analyses with *sox10* and *islet1* in the *prdm1a* mutant background, they determined that *sox10* substantially rescues the neural crest phenotype in *prdm1a* mutants, and *islet1* partially rescues RB sensory neurons. This suggests that *sox10* acts as a primary effector of *prdm1a* in neural crest cell development, whereas *islet1* lies downstream of *prdm1a* in RB sensory neuron development. This study demonstrates the importance of *prdm1a* in the specification of cells at the neural plate border and places it centrally as an important regulator of these cell types. This study further illustrates the importance of using epistatic rescue analyses to construct gene regulatory networks, and it effectively used this approach to elucidate the genetic interactions required for neural crest and RB sensory neuron specification.

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