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Making sense of transcriptional networks regulated by Genomic screen homeobox 1 and 2 in the zebrafish nervous system

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Homeobox transcription factors like Genomic screen homeobox 1 and 2 (Gsx1 and Gsx2) regulate complex molecular genetic networks that direct neurodevelopment across vertebrates. The Bergeron lab is studying the unique and overlapping roles of these two transcription factors using the zebrafish model system. Zebrafish are an accessible, vertebrate genetic model system with a comparatively "simple" nervous system, rapid neurodevelopment, many orthologues of human disease-related genes, and defined and tractable behavioral responses to sensory stimuli throughout their lifespan starting at just 18 hours post fertilization (hpf). We are the first basic research lab to uncover novel roles for Gsx1 in establishing a functional visual system through studies of gsx1 zebrafish mutants. This work allows us to predict ways in which eye to brain neural circuit connections might be reestablished reliably in disease states such as glaucoma in which these connections degenerate over time, leading to vision loss. In addition, we are investigating phenotypes in our gsx2 zebrafish mutants that recapitulate human patient phenotypes of diencephalic-mesencephalic junction dysplasia syndrome (DMJDS) that is due to recessive Gsx2 loss of function missense and nonsense mutations. Intriguingly, several genes are regulated similarly in zebrafish gsx2 mutant and DMJDS patient transcriptome datasets. Typically, transcription factor loss of function is assumed to have very broad overarching effects on central nervous system (CNS) development and function, but we have a more nuanced view of this and transgenic tools in development that will aid us in teasing apart these complex networks and what they regulate from genes to behavior across the CNS.

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