ROLE OF WNT/PLANAR CELL POLARITY SIGNALING
IN MOUSE FACIAL BRANCHIOMOTOR NEURON MIGRATION

Derrick M. Glasco

Dr. Anand Chandrasekhar, Dissertation Supervisor

ABSTRACT

Neuronal migration is essential for the formation of distinct neural layers and functional neural networks in the developing central nervous system. As a model, we study the caudal migration of facial branchiomotor neurons (FBMNs) from rhombomere 4 (r4) to r6 within the developing mouse hindbrain. Since Wnt/planar cell polarity (PCP) signaling components had been implicated in zebrafish FBMN migration, we tested whether they also were required in mice.

FBMNs failed to migrate caudally in *Vangl2 (Looptail)* mutants, *Vangl2* knockout embryos, and *Ptk7* mutants, indicating a specific role for *Vangl2* and Wnt/PCP signaling in FBMN migration. However, FBMNs migrated normally in *Dishevelled 1/2* double mutants and in zebrafish embryos with disrupted *dishevelled* signaling. These results suggest strongly that the caudal migration of FBMNs is controlled by multiple components of the Wnt/PCP pathway, yet may not require the central signaling molecule Dishevelled.

Interestingly, in *Celsr1 (Crash)* mutants, many FBMNs migrated rostrally instead of caudally, indicating a specific role for *Celsr1* in the directionality of FBMN migration. To better understand how *Celsr1* functions, we inactivated *Celsr1* in specific hindbrain tissues and found that it functions within the ventricular zone of rhombomeres 3 through 5 to regulate FBMN directionality. Using anterograde labeling with lipophilic dyes, we also found that the starting positions of individual FBMNs within r4 correlated with the direction of migration in *Celsr1*$^{Crsh/+}$ mutants. Together, these results indicate that *Celsr1* is required in the ventricular zone of multiple rhombomeres to regulate the direction of FBMN migration, and provides insight as to how only a subset of FBMNs is affected in *Celsr1* mutants.