Examining Patterns of Rostral Migration in Celsr1 and Wnt5a Double Mutants

During development, neuronal differentiation and migration are important for building the neural circuits needed for cognitive and motor function. Our lab focuses on the Facial Branchiomotor (FBM) neurons and their stereotyped migration within the hindbrain since the system is evolutionarily conserved and well-studied. Many components of the Wnt/PCP (Planar Cell Polarity) pathway are involved in the initiation of FBM neuron migration, but potential roles in regulating the direction of migration are poorly understood. Our experiments focus on the roles of Wnt/PCP genes *Celsr1* and *Wnt5a* in controlling the direction in which FBM neurons migrate. Proper caudal migration of FBM neurons originates at the r3/r4 boundary. Our model hypothesizes that WNT5A can act as a chemoattractant to induce inappropriate rostral migration of FBM neurons into rhombomere 3 (r3). In proposing *Wnt5a's* role, mutant mice were generated that lacked expression of *Celsr1*, and were found to exhibit an inappropriate rostral migration phenotype. In an effort to further validate this model, double mutant mice lacking *Celsr1* and *Wnt5a* were generated. They exhibited a phenotype that lacked rostral migration, supporting *Wnt5a'*s role as a chemoattractant.

Since the double mutant embryos have open neural tubes, further investigation is needed to ensure that the failure of rostral migration is not a consequence of deformed tissues within the mutant brain. To rule out this possibility, I am examining the expression of the *Krox20* and *Hoxb1* genes, which are expressed in r3 and r5, and r4, respectively, in double mutant embryos. As part of this process, I have begun performing RNA in situ hybridization using mouse embryos.