Investigating how *protocadherin10a* in zebrafish influences neural crest derived melanocytes during migration.

Jason Williams, Christy Rossi, Laura Hernandez-Lagunas, Kristin Bruk Artinger.

Cell Biology, Stem Cells and Development Graduate Program, and Department of Craniofacial Biology, University of Colorado Anschutz Medical Campus.

Neural crest derived melanocyte precursors migrate along discrete pathways to reach their final destination in the skin. A mechanism by which neural crest cells undergo directed migration is via contact inhibition of locomotion (CIL), where weaker adhesion between cells is required for cells to move collectively forward. How neural crest cells maintain a weaker adhesion is not well understood. Cell adhesion proteins such as Protocadherins, similar to classic cadherins in that they function in cell adhesion and cell guidance, are good candidates to mediate a weaker adhesion required for contact inhibition. Here we tested the hypothesis that *pcdh10a* functions in zebrafish neural crest derived melanocyte precursors migration by regulating actin distribution thereby promoting CIL. Through expression and loss of function analysis, we have determined that *protocadherin10a* (*pcdh10a)* is required for zebrafish neural crest and melanocyte precursor migration.*pcdh10a* is expressed in a subset of migrating neural crest cells and in *dct*+ melanocyte precursors during migration. Loss of *pcdh10a*function results in the development of fully melanized melanocytes within the ventral pathway adjacent to the notochord and fail to reach their final position in the skin. Live cell imaging analysis suggests two phenotypes in melanocyte precursor migration: 1) dorsally located cells aggregate and cluster together; and 2) cells that are able to migrate ventrally detach from the migrating stream. In addition, actin localization in *pcdh10a*-/- neural crest cells migrating in the ventral pathway is disrupted in that actin localization along the medial cell membrane closest to the neural tube is increased. These data in combination suggest that *pcdh10a* controls migration via CIL, and in the absence of pcdh10a, a stronger adhesion between neural crest cells is observed, resulting in clumping of cells during migration and differentiation of melanocytes in ectopic locations.