**Specific Aims**

Neurofibromatosis is a genetic disorder resulting in tumor growth in the brain, spinal cord, nerves and skin. Typically Neurofibromatosis manifests itself with café au lait spots, freckling in armpits or groin area, and neurofibromas on or under the skin. Children with neurofibromatosis also have learning disabilities. Neurofibromatosis Type 1 is caused by an autosomal dominant mutation in the NF1 gene that plays a role in the Ras and cAMP pathways, necessary for cell proliferation and differentiation, and cell-cell communication. Loss of NF1 leads to disregulation of the Ras and cAMP pathways leading to tumor growth and learning disabilities. The role for NF1 in the Ras and cAMP pathways as it relates to learning is unclear.

I **hypothesize** that mutations in NF1 regulate the Ras and cAMP pathways, which are necessary to maintain proper neuronal connections. Zebrafish are an excellent model organism to study neurofibromatosis because it is easy to study neuron function and learning. Since zebrafish are see-through in their embryonic stage along with having their neural circuits developed enough for learning assays by 5dpf. My **long-term goal** is to understand how neurofibromatosis functions in a pathway that leads to learning.

**Aim 1**: Identify which protein domain of NF1 is necessary for learning, through either the Ras or cAMP pathways.

**Rationale**: Once the necessary domain for learning is identified we will have a better understanding of how to treat NF1 learning disabilities. The Ras pathway and the cAMP pathway are two very different drug targets.

**Approach**: The conserved protein domains of NF1 will be analyzed using SMART and PFAM. The protein domains that interact with the Ras and cAMP pathways will be determined using these programs. A knockdown zebrafish (MOs) will be made for both the N and C terminus, each encompassing one of the two domains. Learning assays will be preformed on 5dpf zebrafish, whichever of the two have learning disabilities new knockdowns will be made from the protein domain area and the surrounding area of the protein. New learning assays will be preformed, and whichever zebrafish do not learn determine the area of the protein that contains the domain that functions with learning.