**Specific Aims Draft #2**

Emberger Syndrome (ES) is a rare autosomal dominant disorder characterized by the co-occurrence of edema in the lymph nodes and a predisposition to acute myeloid leukemia (AML). Other symptoms include widespread warts, deafness, and minor physical anomalies such as neck webbing and slender fingers. *The mechanisms responsible for the variable phenotypic expression of ES are not yet fully understood*. While there are multiple treatments to help improve the lives of patients with ES, a cure is unknown. ES is caused by mutations in the *GATA2* gene, which encodes the GATA2 protein. GATA2 is necessary for the development and function of hematopoietic stem cells. In ES patients, *GATA2* mutations result in haploinsufficiency, which is when an organism has only one functional copy of a gene and it is not capable of producing wild-type conditions by itself.

***The long-term goal*** of our research is to understand the pathology underlying Emberger Syndrome and *GATA2* deficiency. In order to do that, we must first understand the complete role of GATA2 in the abnormal phenotypes observed in ES patients. Our primary goal is to further understand the role of GATA2 in the lymphatic system. **Here we will test the hypothesis that mutations in *GATA2* affect expression levels of genes associated with lymph nodes.** To test our hypothesis, we will pursue the following aims:

**Specific Aim 1:** To identify how well conserved GATA2 is across model organisms with and without lymphatic systems.

**Approach:** Clustal Omega can be used to compare the differences between each species sequence.

**Hypothesis:** GATA2 will be highly conserved in organisms with similar lymphatic systems. GATA2 will be less conserved in organisms without a lymphatic system.

**Specific Aim 2:** To determine which lymphatic system genes are expressed differently in the model organisms with and without GATA2.

**Approach:** RNA Sequencing can be used to identify gene expression in the lymphatic system for both wild type and mutant organisms.

**Hypothesis:** Organisms with the mutant GATA2 will be lacking expression in various genes that are significantly expressed in wild type organisms.

Determining which lymphatic system genes are directly affected by GATA2 mutations will hopefully establish a narrow list of genes for future research on the pathological processes underlying the edema of the lymph nodes in ES. This would allow for more confident genetic screenings to confirm the presence of ES, which would maximize opportunities for enhancing the lives of patients, and hopefully finding a cure.