Emberger Syndrome (ES) is a rare autosomal dominant disorder characterized by the co-occurrence lymphedema with a predisposition to acute myeloid leukemia (AML). Lymphedema is the primary symptom in which fluid is retained and swelling of extremities occurs [1]. Other symptoms associated with ES include warts, deafness and physical anomalies such as neck webbing and slender fingers [2]. While there are multiple treatments to help improve the lives of patients with ES, including complete decongestive therapy (CDT), which decreases swelling and increases lymph drainage from the congested areas, a cure is unknown [3]. ES is caused by a series of eight mutations in the *GATA2* gene, which is a transcription factor necessary for the development and function of hematopoietic stem cells and the regulation of body fluid levels [4]. In ES patients, *GATA2* mutations lead to haploinsufficiency, which is when a patient only receives one functional copy of a gene. Although research has identified the mechanism of GATA2 haploinsufficiency, *how GATA2 regulates the function of genes involved in hematopoiesis remains unclear.*

***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 development and function of hematopoietic stem cells. Here, we will test the hypothesis that mutations in *GATA2* regulate genes that affect the function of hematopoietic stem cells. To test our hypothesis, we will pursue the following aims:

**Specific Aim 1:** Identify how well conserved GATA2 is across model organisms with and without circulatory systems. **Approach:** Build a tree with homologs that have GATA2 with and without a circulatory system. Then use Clustal Omega to identify specific amino acids in conserved domains that are only found in the species with circulatory systems. **Hypothesis:** Specific amino acids in conserved domains only found in species with circulatory systems might be involved in the binding of partners that regulate hematopoiesis. **Rationale:** Mutations in *GATA2* lead to an accumulation of abnormal white blood cells (myeloblasts) that restricts the production of normal blood cells.

**Specific Aim 2:** Characterize the GATA2 interacting protein LMO2 and determine its cellular role as it pertains to the development of hematopoietic stem cells. **Approach:** Use STRING to determine LMO2 interactions across species and determine the different processes it may be involved in. **Hypothesis:** Proteins that LMO2 only interacts with in species with circulatory system are directly involved in the development of hematopoietic stem cells. There will be no interaction with GATA2 in species without circulatory systems. **Rationale:** LMO2 interacts with proteins that regulate red blood cell development, which is absent in species without circulatory systems.

**Specific Aim 3:** Determine factors that regulate the development of hematopoietic stem cells that interact with GATA2. **Approach:** Use RNA Sequencing to determine gene expression in the circulatory system for both wild type and mutant GATA2 organisms. **Hypothesis:** Genes involved in the regulation of hematopoiesis will decrease in expression in mutant GATA2 organisms. **Rationale:** Mutations in GATA2 cause abnormal phenotypes in hematopoiesis in humans.

Identifying and characterizing GATA2 interacting proteins that regulate hematopoiesis will provide insight into the pathological processes underlying Emberger Syndrome. Understanding these protein interactions and how they are disrupted in ES will help establish a better basis for research on potential treatments that could enhance the lives of patients.