2016 Million Dollar Bike Ride
Pilot Grant Program

**Application Title:** Identification of the Genetic Causes of Generalized Lymphatic Anomalies

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Patients with generalized lymphatic anomalies (GLA) experience severe symptoms, but the genetic understanding of their condition is lacking, limiting development of diagnostics and novel therapeutics. Lymphatics maintain tissue fluid balance, modulate immunity, and regulate intestinal fat uptake. Recent studies suggest lymphatic malformations, a lymphatic anomaly subtype, arise from somatic mutations, where only abnormal cells carry a mutation (mosaicism). We hypothesize that GLA is caused by somatic mutations in the lymphatic endothelium. We have isolated affected lymphatic endothelial cells from GLA patients and pre/postnatal congenital chylothorax patients and will subject them to Whole Exome Sequencing and variant cohort analysis to determine if they carry somatic mutations for GLA. These studies have the potential to identify new genes and pathways that function in lymphatic development and homeostasis. Information gained from these studies will improve diagnosis and help to devise personalized, effective therapies for GLA patients.