

## Sphingosine-1-Phosphate In Sickle Cell Disease

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Principal Investigator: Julie Saba MD, PhD

Co-Investigators: Elliot Vichinsky, MD

### Synopsis:

**HYPOTHESIS:** Sphingosine-1-phosphate (SIP) is a natural lipid molecule present in all cells of the body, including platelets and other blood cells. Erythrocytes, platelets, neutrophils and mononuclear cells all produce SIP, and it is maintained in these cells at high levels for prolonged periods. (1) SIP is released into the bloodstream from platelets and other cell types, where it contributes to lymphocyte trafficking, induces platelet aggregation and stimulates endothelial cell proliferation, migration and angiogenesis. Serum SIP has also been shown to be a predictor of obstructive coronary artery disease, suggesting that it may be a useful indicator of ischemic tissue injury. We hypothesize that circulating SIP levels may be altered in patients with sickle cell disease, due to ischemic tissue injury, increased platelet activation, hemolysis and abnormal vascular flow, all of which could lead to release of SIP into the circulation. We further hypothesize that elevated SIP levels and signaling may contribute to some clinical complications associated with hemoglobinopathies, including stroke, vaso-occlusive crisis, acute chest syndrome, and end organ failure.

### SPECIFIC AIMS:

1. To determine whether circulating SIP levels in patients with sickle cell disease are higher than in normal controls.
2. To determine whether elevated circulating SIP levels are associated with specific clinical complications of sickle cell disease including vaso-occlusive crisis, stroke and acute chest syndrome.
3. To establish the feasibility of performing a large study based on preliminary data obtained in the current study.