Title: Association of Cell-Derived Microparticles with Osteonecrosis of the Femoral Head in Sickle Cell Disease

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Synopsis:

Sickle cell disease (SCD) is the most common cause of osteonecrosis of the femoral head (ONFH) in childhood. Clinical symptoms peak during adolescence, resulting in significant physical impairment and chronic pain. Patients frequently go on to require total hip replacement at an early age. Despite the relative frequency of ONFH in SCD, few predictors or biomarkers indicating progression of this clinical complication exist. The mechanisms leading to the development of ONFH in SCD are poorly understood, but are undoubtedly related to intravascular coagulation and microcirculatory thrombosis.

Microparticles (MPs) are small membrane vesicles that are released from various blood and endothelial cells during activation or apoptosis. Microparticles (MP) are emerging as an important surrogate marker of endothelial dysfunction and thrombosis, with potential predictive and prognostic value for SCD-related complications. Increased levels of cell-derived (endothelial, leukocyte, red cell and platelet) MP have been associated with several diseases characterized by endothelial dysfunction and thrombosis, including ONFH from other causes. Erythrocyte-derived microparticles are elevated in SCD patients at baseline and increase further during vaso-occlusive pain episodes. However, it is not known what role they may play in SCD-associated ONFH. To test the hypothesis that cell-derived microparticles contribute to the pathophysiology, and as such may act as biomarkers, of ONFH in patients with SCD, we propose to determine whether circulating MP are associated with the development of ONFH in SCD by assessing their relative quantity and cellular origin in SCD patients with ONFH compared to SCD patients without ONFH.