Characterization of Adipose Tissue in the Setting of HIV-infection and Aging Using Lipidomics

By 2030 it is estimated that 73% of people living with HIV (PLH) will be 50 years or older, with as many as 78% of such patients with cardiovascular disease, 17% diabetes, and 17% with malignancies. It has been hypothesized that PLH have an accelerated form of aging manifested by an increased prevalence of age-related diseases, including cardiovascular disease, frailty, renal insufficiency, bone loss, and polypharmacy with many diseases occurring a decade earlier than in HIV-negative individuals. Chronic inflammation is often cited as the etiology of age-related diseases-- both Aging and HIV-infection are associated with pro-inflammatory environments. Therefore, investigating the underlying inflammatory mechanisms that contribute to the development of age-related diseases in the setting of HIV-infection can help us understand how inflammation contributes to development of age-related diseases. HIV-infection can serve as a model. We have been collecting fat pad biopsies from young and older, HIV-negative and HIV-positive adults in an effort to understand how adipose tissue contributes to the pro-inflammatory environment. Preliminary data from our single cell RNA sequencing data is demonstrating an upregulation of ferroptosis, and increased expression of HMOX- within innate immune cells (macrophages and monocytes), and adipocyte progenitor cells in the setting of HIV and aging. Ferroptosis is an iron dependent form of cell death that is triggered by the lipid peroxidation of polyunsaturated fatty acids (PUFAs) in the cell membrane. Ferroptosis has emerged as an important cellular mechanism that is thought to contribute to the diseases of aging. HMOX-1 is a protein that can modulate both inflammasome activation, ferroptosis, and is strongly associated with metabolic disease and insulin resistance. In Aim 1 we are proposing using untargeted lipidomics to evaluate adipose tissue from young and older HIV-negative and HIV-positive subjects. Untargeted lipidomics will be used to evaluate the lipid layer (adipocytes) and sorted cells from the stromal vascular fraction, including innate immune cells and Adipocyte progenitor cells. Using untargeted lipidomics will allow us to confirm the upregulation of ferroptosis via identification of PUFAs. In Aim 2 we will further validate Ferroptosis and lipid targets identified via untargeted lipidomics using assays such as qPCR, Immunohistochemistry, multicolor flow cytometry, etc. Overall, this pilot grant will allow us to generate preliminary data for a future R01 proposal.