Investigator:	**Sushma Cribbs** Phone: (404) 321-6111 ext. 204336 Email: skomaku@emory.edu
Primary Research Interest:	Other
Description of Research:	This proposal will test the hypothesis that PGE2 activity is upregulated in HIV positive individuals, which impairs alveolar macrophage immune functions thereby increasing the risk for pneumonia. Furthermore, blockade of EP2 and EP4 receptors will diminish this risk. This project is a a 2-year follow up study of HIV positive and negative veterans from the Atlanta VA. Eligible participants will undergo a procedure to obtain samples of fluid from their lungs (lung lavage) to measure PGE2 and lung immune functions. All participants will also undergo serial blood sampling every 6 months to assess the association of PGE2 levels with systemic immune response. Alveolar macrophages obtained through lung lavage will be treated with EP2 and EP4 receptor blockers to determine if macrophage immune functions are improved. This proposal will also investigate lung metabolomics. In this proposal, lung metabolites will be measured to study the correlation with lung immune markers. Specifically, prostaglandin metabolism will also be assessed by performing serial metabolomics analyses on blood and exhaled breath condensate (EBC) samples every 12 months and correlated with immune functions. EBC is an inexpensive and non-invasive method to evaluate the lung environment so a novel aspect is the comparison of lung metabolites between EBC and lung lavage. In addition, metabolomics analyses will be done on the alveolar macrophages both pre and post- treatment with EP2 and EP4 receptor blockers
Relevance to VA:	Lung infections take an enormous toll among the veteran population, including HIV-infected veterans. The Veterans Administration (VA) is considered the largest provider of HIV health care in the US. In 2011, over 25,000 HIV positive veterans received health care in the VA (an increase of 3.8% since 2007) and approximately 1 out of every 250 veterans in health care at the VA is living with HIV/AIDS. Although rates of ART use and receipt of other treatments such as vaccinations have improved, many HIV positive veterans continue to suffer from lung diseases. The Veterans Aging Cohort Study (VACS) includes more than 45,000 HIV positive veterans who were matched to over 90,000 HIV negative veterans. This study specifically showed that pulmonary infections, particularly bacterial pneumonia, were significantly more likely among HIV positive patients with an incidence of 28.0 per 1,000 person years (95% CI, 27.2–28.8) compared with 5.8 per 1,000 person years (95% CI, 5.6–6.0) among HIV negative individuals (p=0.001). This project will help answer his proposal will help answer outstanding questions about 1) the key biologic pathways by which an infectious insult, HIV, affects the lung, 2) define targets for new treatments and possibly preventions against lung infections which are a common cause of increased death among all veterans and 3) possibly identify new biomarkers of lung health that will reduce complications and death from lung infe