

## ASP-INFECTIOUS DISEASES SOCIETY OF AMERICA YOUNG INVESTIGATOR AWARD IN GERIATRICS



### AWARD RECIPIENT

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### PROJECT

"INFLUENCE OF SEX STEROIDS AND AGING ON HIV-1 CHEMOKINE CORECEPTOR EXPRESSION IN WOMEN"

### MENTORSHIP TEAM

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Women represent almost one-half of all individuals living with HIV-1 in the world. Women also represent 25% (300,000) of individuals living with HIV-1 in North America and are most commonly infected through heterosexual sex. There is a misperception that older women are not at risk for HIV-1 infection. However, new infections in the United States among women over the age of 40 significantly increased from 1999 to 2004, while the incidence in other age categories decreased. As survival rates of HIV-1-infected individuals improve due to the introduction of antiretroviral therapy, the number of postmenopausal women with HIV-1 will increase. Knowledge of the impact of aging on the pathogenesis of HIV-1 infection in older women is urgently needed.

One of the principal changes associated with postmenopause in women is loss of estradiol (E2) production. Existing data suggest that hormonal milieu may alter female susceptibility to HIV-1 infection, although specific changes within the female genital tract have not been well characterized. In addition, irrespective of sex, aging is associated with more rapid HIV-1 disease progression. Lymphocyte chemokine receptor 5 (CCR5) density, immune activation, and chemokine production are all associated with susceptibility to HIV-1 infection and disease progression in older adults.

In the present study, we aim to investigate the influence of aging and hormonal milieu in women on these markers through two clinical studies:

1. A study of chemically induced menopause in HIV-1 seronegative women of reproductive age who are randomized to receive E2 or placebo.

2. A study of physiologic E2 replacement in both HIV-1 seropositive and seronegative postmenopausal women.

With these three cohorts of women, we plan to evaluate the hypothesis that in the presence of E2, cluster of differentiation 4 co-receptor T cell susceptibility is increased through increased CCR5 cell surface expression, decreased chemokine expression, and increased immune activation. The global aim of the proposed research is to determine the independent effects of aging and E2 on factors thought to be related to HIV transmission on postmenopausal women's susceptibility to HIV-1 infection as well as the risk of transmitting HIV-1 to sexual partners.

At the conclusion of the ASP-Infectious Diseases Society of America Young Investigator Award in Geriatrics, I will be uniquely trained to apply research techniques in an interdisciplinary environment to optimize future studies evaluating the relationship between sex hormones and HIV-1 pathogenesis as it relates to older adults. The additional funding and training offered through this award will provide opportunities to integrate myself into a network of researchers who are committed to translational research in both the fields of HIV-1 and geriatrics. In addition, this project will provide preliminary data that could be used to develop a unique R01 proposal focused on the effect of sex hormones and aging on HIV-1 disease pathogenesis. Finally, a better understanding of the effects of sex hormones and aging on HIV-1 disease pathogenesis may lead to changes in clinical services and management of hormone replacement in postmenopausal women.