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NIH GRANT SUPPORTS UCSF RESEARCH EXPLORING EARLY HIV INFECTION

A team led by researchers at the UCSF Positive Health Program has been named to receive \$15 million over five years to expand understanding of the complex interactions between HIV and the immune systems of newly infected patients following HIV transmission.

The grant is being awarded by the National Institute of Allergy and Infectious Diseases, an arm of the National Institutes of Health.

“The program will provide an important platform for innovative research into HIV transmission and early infection in patients and aims to provide new clues for developing a vaccine and improving therapeutic outcomes,” said the grant’s primary investigator, Frederick Hecht, MD, professor of medicine at the UCSF Positive Health Program at San Francisco General Hospital Medical Center.

The research will be based on two clinical cohorts of recently infected patients: the UCSF Options Project in Northern California (<http://www.ucsf.edu/options/>) and the Projeto AMPLIAR cohort in Southern Brazil. The Brazil project was developed through the work of Ricardo de Souza, MD, from the Universidade de Caxias do Sul, Brazil in Brazil, and Christopher Pilcher, MD, from UCSF’s Positive Health Program.

“The inclusion of the Brazil cohort allows us to look at two HIV subtypes simultaneously. Subtype C predominates in Sub-Saharan Africa and subtype B predominates in North America, though both are common in Southern Brazil. This provides us with a natural research study for understanding competing HIV subtypes,” said Hecht.

The overall grant aims to understand the viral and host factors that favor or block HIV transmission on a biological level and the factors that favor good control of early HIV infection by newly infected patients. The program is composed of four projects.

One project, led by Hecht, will focus on the transmission and persistence of two types of HIV resistance mutations. Some are caused by infection with HIV variants that have resistance mutations caused by exposure to antiretrovirals. Understanding how easily these mutations occur and how long they persist is important for long-term forecasting of the effectiveness of antiretroviral regimens in populations.

The other types of resistance mutations are those that allow the virus to escape an infected patient’s specific T-cell immune responses. HIV mutates constantly, thereby

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escaping attack from the body's targeted T-cell defenses that are meant to kill the virus, and eventually eludes effective control in most individuals. Understanding this process could assist in vaccine development.

A second project, led by Steven Deeks, MD, of the Positive Health Program, examines properties of the outside of the HIV virus—the envelope—and how they influence HIV transmission and evolve in a newly infected individual after transmission. These envelope properties determine which cells most easily will succumb to infection with the virus. In addition, the envelope properties of HIV may affect the virus's capacity to damage the immune system and determine how readily it is transmitted.

A third project, led by the UCSF-affiliated Gladstone Institute of Virology and Immunology's Robert Grant, MD, MPH, is focused on superinfection, which is infection with a second HIV virus on top of a preexisting infection. The project will study how readily this occurs in early HIV infection—which appears to be the most vulnerable period for superinfection—and what factors may prevent it.

The fourth project, led by Douglas Nixon, MD, PhD, of the UCSF Division of Experimental Medicine, tests whether new immune responses, following HIV transmission to a newly infected patient, help to reverse some of the mutations that allowed the virus to escape immune responses in the HIV-individual who transmitted the virus.

The UCSF Positive Health Program (<http://php.ucsf.edu>) is a component of the AIDS Research Institute (ARI, <http://ari.ucsf.edu>) at UCSF. UCSF ARI houses hundreds of scientists and dozens of programs throughout UCSF and affiliated labs and institutions, making ARI one of the largest AIDS research entities in the world.

UCSF is a leading university that consistently defines health care worldwide by conducting advanced biomedical research, educating graduate students in the health professions and life sciences, and providing complex patient care.

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