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The Wistar Institute and partners receive HIV cure research grant to test novel immunotherapies

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The Wistar Institute is pleased to announce that the National Institutes of Health (NIH) has awarded a nearly $23 million Martin Delaney Collaboratories for HIV Cure Research grant to the BEAT-HIV: Delaney Collaboratory to Cure HIV-1 Infection by Combination Immunotherapy (BEAT-HIV Delaney), a consortium of top HIV researchers led by co-principal investigators **Luis J. Montaner, D.V.M., D.Phil.**, director of the HIV-1 Immunopathogenesis Laboratory at The Wistar Institute Vaccine Center, and **James L. Riley, Ph.D.**, research associate professor at the Perelman School of Medicine at the University of Pennsylvania.

The Philadelphia-based BEAT-HIV Delaney project is one of six grants awarded by the Delaney initiative, joining a highly-selective group of U.S.-led teams charged with advancing the global efforts to develop a cure for HIV. The five-year award promotes a preeminent partnership of more than 30 leading HIV investigators from The Wistar Institute, the University of Pennsylvania, Philadelphia FIGHT, Rockefeller University, VA San Diego Healthcare System, Johns Hopkins University, the University of Nebraska-Lincoln, and the University of Utah working with government, non-profit, and industry partners to test combinations of several novel immunotherapies under new preclinical research and clinical trials.

With 37 million people now living with HIV worldwide and 17 million receiving antiretroviral therapy, the **Martin Delaney Collaboratories for HIV Cure Research** initiative reflects the interest in HIV cure research that has grown into a global priority over the last five years and follows President Obama's call for increased HIV cure research.

"The lifelong stigma, economic burden on society, strain on healthcare resources, and sheer toll on human life across the globe makes finding a cure a top priority," said Montaner. "Together we're building on our teams' extensive established efforts to move forward and make those next transformative steps that will bring us closer to an HIV cure."

Three Research Pillars

Incorporating three distinct areas of study, the goals of the BEAT-HIV Delaney project are to investigate where HIV hides after therapy and test novel clinical strategies aimed at an HIV cure that eliminates the hidden virus. The first area of study or "pillar" will identify where and how HIV hides so researchers can better assess if proposed clinical strategies can eradicate the virus. This pillar links three research teams who will measure HIV in the body, determine how HIV persists after therapy, access new areas in the body that have not been studied before where HIV may hide, and distinguish HIV by "fingerprinting" or "barcoding" to determine the fate of each infected cell. The BEAT-HIV Delaney research team plans to develop clear criteria to evaluate reductions in the virus beyond what is measured in the clinic.

The second pillar focuses on stimulating the immune system with which we are all born (innate immunity) through a combination immunotherapy approach using highly-potent antibodies against HIV together with pegylated interferon alpha 2b. The researchers plan to conduct the first human clinical trial combining these two therapeutic strategies (which have been tested separately and have shown activity in reducing HIV in humans) with the expectation that a boosted innate immune system empowered with unique antibodies to target HIV-infected cells will achieve greater reductions in HIV than observed previously. In addition, the researchers will look to develop novel DNA-based delivery systems that may make administering anti-HIV treatments more simple and effective than by transfusions.

The third pillar will bring together two promising gene therapy strategies, independently tested in humans, with the goal of engineering, growing and administering killer cells that are uniquely empowered to find and kill HIV-infected cells. The proposed gene therapy strategy is based on the success of small human trials of killer T-cells (Chimeric Antigen Receptor [CAR] T-cell therapy). Earlier studies showed that killer T-cells can be generated and administered safely. The research team will repeat these studies and for the first time safeguard the new killer cells from being attacked by HIV when "activated" by removing the CCR5 protein. HIV needs this protein to infect and kill the killer cells, so removing it can "protect" killer cells so they can continue to proliferate and kill HIV-infected cells. The ability of cells to remain unaffected by HIV in the absence of CCR5 has already been shown clinically, but this strategy has not yet been joined with gene therapy in making killer cells.

"The results of this trial are expected to show for the first time what the long-term effects of these killer cells can be in finding and eradicating HIV," said Riley.

Source:
Wistar Institute