amfAR Awards New HIV Cure-Focused Research Grants Totaling $2.4M

High number of applications for amfAR's Target Grants shows fierce competition for HIV research funding.

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amfAR, The Foundation for AIDS Research, has awarded new Target Grants to support innovative research projects aimed at curing HIV, funding five grants in a single round for the very first time. This brings total funding for new grants and fellowships in recent months to more than $3.1 million. In an indication of the fierce competition among scientists for research support, especially in the wake of substantial cuts to federal funding of HIV research, amfAR received the highest number of grant submissions since 2005.

"All five of these outstanding research teams proposed innovative, well-supported and carefully crafted studies that received high marks from our grant reviewers," amfAR's incoming CEO Kyle Clifford said. "We are deeply grateful to the generous donors who make these grants—and the potential breakthroughs they could lead to—possible."

The only successful HIV cure strategy to date has involved high-risk stem cell transplantation in 10 people living with both HIV and certain blood cancers, and cannot be replicated on a global scale. An effective cure strategy needs to be scalable, accessible and applicable to the largest number of people possible. The new amfAR grantees are working on a range of approaches to eradicating HIV or controlling the virus in the absence of antiretroviral therapy (ART), while striving to fulfill these criteria. Each project is awarded $480,000 over two years.

Francesco Simonetti, MD, PhD

Johns Hopkins University, Baltimore, MD

Dr. Simonetti's project hinges on a "self-destruct" mechanism embedded in HIV-infected cells. This sensor detects HIV's protease enzyme, a protein the virus needs to mature. Once activated, the sensor causes infected cells to undergo a form of cell death called pyroptosis. Dr. Simonetti's team has shown that efavirenz, a common HIV drug, can activate this sensor and reduce the size of the HIV reservoir. The researchers now plan to test new compounds that can amplify its activity.

Why is this important for HIV cure?

This project introduces a new way of attacking HIV: by repurposing an existing anti-HIV drug to trigger a built-in “self-destruct” mechanism in infected cells.

If successful, this study will:

1. Provide a therapeutic approach that is potentially effective against all viral strains.
2. Offer a globally applicable path toward a cure.

Rachel Rutishauser, MD, PhD

University of California, San Francisco

Brad Jones, PhD

Weill Cornell Medicine, New York

Drs. Rutishauser and Jones will employ an immunotherapy used to treat certain blood cancers—CAR T cell therapy—to target HIV. Typically, this therapy requires collecting cells from a person’s body, genetically modifying them to recognize and target disease cells, and reinfusing them into the body. Instead, the researchers plan to reprogram the cells inside the body, using a delivery system based on targeted nanoparticles. They will use a new type of engineered T cell called TRAC-HIT, which can recognize and kill HIV-infected cells far more effectively than previous CAR T cell approaches.

Why is this important for HIV cure?

This innovative in vivo editing approach addresses key barriers of cost, complexity and scalability that have limited cellular therapies so far.

If successful, this study will:

1. Provide a practical and globally deployable treatment.
2. Represent an approach that empowers a person’s own immune system to maintain long-term HIV control without daily ART.

“HIV cure work—including studying the virus and figuring out how to target immune responses to the virus—is immensely relevant to so many other fields of study, including other infectious diseases, cancers, autoimmune/inflammatory diseases, and neurologic disorders.” —Dr. Rachel Rutishauser

Mirko Paiardini, PhD

Emory University, Atlanta, GA

Pilot studies led by Dr. Paiardini and colleagues showed that tazemetostat, an anti-cancer drug, is able to target a pathway that directly controls how infected cells evade the immune system. Blocking a cellular protein named EZH2, tazemetostat made it easier for the immune system to find and eliminate HIV-infected cells. Virus levels were reduced, and exhausted immune cells were rejuvenated. The present study will test tazemetostat in an animal model.

Why is this important for HIV cure?

Dr. Paiardini will test tazemetostat in a close model of HIV infection in humans, to see if it can safely reduce the HIV reservoir when given alongside ART.

If successful, this study will:

1. Repurpose an already approved anti-cancer therapy for HIV cure, targeting a pathway that directly controls how infected cells evade the immune system.
2. Rapidly move into clinical testing.

Sharon Lewin, PhD

University of Melbourne, Australia

Thumbi Ndung'u, PhD

Africa Health Research Institute, South Africa

A cure that is widely applicable needs to be effective against the different subtypes of HIV. While subtype B predominates in North America, Western Europe and Australia, this strain is rare in sub-Saharan Africa and Asia, where most people with HIV live. Bringing together HIV cure scientists based in Australia, Uganda, South Africa and the U.S., Drs. Lewin and Ndung'u are investigating whether or not an approach already found to be effective on HIV subtype B can work on non-subtype B.

Why is this important for HIV cure?

This project builds directly on an earlier amfAR-funded breakthrough in which Dr. Lewin's team used lipid nanoparticles (LNPs) to safely "wake up" dormant HIV without broadly activating the immune system.

If successful, this study will:

1. Optimize this potent HIV-specific LNP system and adapt it for use in people living with non-subtype B HIV in Africa.
2. Bring together HIV cure scientists based in Australia, Uganda, South Africa, and the US.

"amfAR is willing to take a little more risk than most funders. I think this is a fantastic addition to the ecosystem as without a little bit of risk taking in backing new ideas, we won't have the breakthroughs we need." —Dr. Sharon Lewin

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Nadia Roan, PhD

Gladstone Institutes, San Francisco, CA

Possu Huang, PhD

Stanford University

Drs. Roan and Huang have developed a groundbreaking tool called TRACeR, an engineered protein construct that can recognize fragments of HIV displayed on the surface of infected cells. In this innovative approach, Drs. Roan and Huang plan to use TRACeRs first to create a detailed atlas of active reservoir cells across multiple tissues, and then to convert the TRACeRs into therapeutic molecules designed to guide killer T cells to eliminate infected cells.

Why is this important for HIV cure?

This project targets a special subset of HIV-infected cells that remain active even under ART, contributing to a variety of health complications in people with HIV.

If successful, this study will:

1. Identify and directly attack active HIV reservoir cells with precision tools that work regardless of viral strain.
2. Not only reduce the risk of viral rebound, but also lower inflammation and improve long-term health for people living with HIV.

"We are very excited to be funding these research projects, which demonstrate a diverse and imaginative range of approaches to curing HIV and show the continued vitality of the cure

research field and dedication of the scientists within it," said Dr. Andrea Gramatica, amfAR VP and director of research. "These innovative projects could yield critical new insights that get us closer to a cure for the more than 40 million people living with HIV today."

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