

## The Continuing Challenge of HIV-AIDS Research

AIDS treatment was transformed in the mid-1990s by the introduction of powerful antiviral drug combinations. These breakthrough therapies, which were first tested on The Rockefeller University campus, have dramatically reduced HIV-associated deaths in the United States and Western Europe. While the progress of the past few years has been remarkable, the existing drug regimens are not likely to end AIDS in any region affected by the epidemic, rich or poor.

In the United States, the rate of new infections is rising in some risk groups, and drug-resistant strains of HIV are spreading. In the hardest-hit nations of Africa, AIDS is taking millions of lives and leaving a generation of orphans. Epidemics in parts of Asia and Eastern Europe could repeat Africa's tragedies.

The laboratories and research clinics of The Rockefeller University are racing against time to develop the medical tools that will be needed to stem the worldwide AIDS epidemic. These tools include:

- >> Simplified antiviral treatment.
- >> Topical agents to block HIV transmission from one person to another.
- >> Cell-based therapies to stimulate HIV immunity in those infected.
- >> New strategies that combine therapeutic immunization and antiviral drugs.
- >> A vaccine that can confer lifelong protection against HIV.

AIDS investigators at Rockefeller are members of the Christopher H. Browne Center for Immunology and Immune Diseases, a consortium of laboratories working on basic and clinical immunology, as well as infectious diseases. Several are also investigators at the Aaron Diamond AIDS Research Center for the City of New York, which formalized its affiliation with The Rockefeller University in 1996.

**The Rockefeller University** is a world-renowned center for research and graduate education in the biomedical sciences, chemistry and physics. Founded by John D. Rockefeller in 1901 as the nation's first institute for medical research, the University has a unique laboratory based structure that encourages interdisciplinary research and collaboration. A total of 21 scientists associated with the University throughout its history have received the Nobel Prize in medicine or chemistry — including Paul Greengard in 2000 and Günter Blobel in 1999. In addition, 17 Rockefeller scientists have received Lasker Awards, five have been named MacArthur Fellows and 11 have garnered the National Medal of Science. More than a third of the current faculty are elected members of the National Academy of Sciences.

**The Rockefeller University Hospital** was founded in 1910 to translate basic science into better medicine. Throughout the years, the Hospital has been the site of many seminal research breakthroughs, including the discovery that genes are made of DNA. In the 1950s, the Hospital served as the model for the clinical research facility created by the National Institutes of Health in Bethesda, Maryland. Today, The Rockefeller University Hospital is the largest private General Clinical Research Center funded by the NIH.

For more information about *DirectEffect*, contact:

Selena Ching  
The Rockefeller University  
1230 York Avenue, Box 164  
New York, NY 10021-6399  
Phone: 212-327-8910  
Fax: 212-327-7752

[www.rockefeller.edu](http://www.rockefeller.edu)



# direct effect

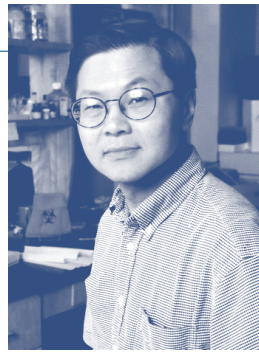
The HIV-AIDS  
Research Support Program at  
The Rockefeller University

## >> *What is DirectEffect?*

Founded in 1993, *DirectEffect* is a volunteer group dedicated exclusively to raising funds for HIV and AIDS research at The Rockefeller University in New York City. Unlike other programs of its kind, *DirectEffect* contributes every dollar it raises to basic and clinical research. To date, the program has attracted more than 1300 contributors and raised more than \$7 million for AIDS research at the University.



At The Rockefeller University Hospital, the outpatient clinic, inpatient unit, and research laboratories are undergoing major renovations.



**David D. Ho, M.D.**

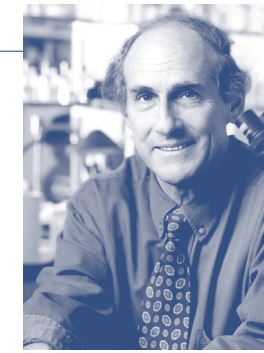
David Ho is the Irene Diamond Professor at Rockefeller and the Scientific Director/CEO of the Aaron Diamond AIDS Research Center. The Ho group pioneered the first life-extending treatments for HIV, using quantitative analyses to model the dynamics of viral infection and predict optimal combinations of antiviral drugs that were tested in patients at The Rockefeller University Hospital. The Ho group also helped to identify the central molecular gateway HIV uses to infect T cells, providing targets for drug discovery. Their newest work includes:

- >> Development of candidate vaccines to protect against HIV infection. Preparations are under way for a clinical trial in China.
- >> Identification of defensins as anti-HIV molecules. Research on defensins could lead to completely new classes of HIV drugs.
- >> Intensive study of the earliest stages of HIV infection—work that is critical to vaccine and drug development.

**The Rockefeller University Hospital** is the site of all clinical research supported by *DirectEffect*. At the Hospital, the Steinman group is examining dendritic cell function in people who have HIV as well as people who don't. These studies are a basis for experimental therapies designed to boost cellular immunity against infection. Dr. Ho and his Diamond Center associates, who conducted their first successful tests of combination antiviral treatments at the Hospital, have several patient-based research projects under way.



**Martin Markowitz, M.D.**, an associate professor of clinical investigation at The Rockefeller University, directs the Diamond Center's clinical programs. His



**Ralph M. Steinman, M.D.**

Ralph Steinman, the Henry G. Kunkel Professor at The Rockefeller University, directs the Christopher H. Browne Center for Immunology and Immune Diseases. Dr. Steinman discovered the dendritic cell, which plays an essential role in alerting T cells to the presence of invading microbes. When the invader is HIV, however, it appears that dendritic cells fail in their normal vigilance. In fact, they transmit HIV to the T cells that the virus infects. Understanding this dendritic cell failure and how it might be corrected is a priority in the Steinman laboratory, which is now investigating:

- >> Vaccines designed to block HIV's infiltration of the immune system via dendritic cells. A model system used in these studies is SIV, the HIV-like virus that infects non-human primates.
- >> Tolerance, a natural mechanism of the immune system that HIV exploits to "silence" immunity. Tolerance is mediated by dendritic cells.
- >> Use of specially treated dendritic cells to boost immunity against HIV in individuals already infected.

group focuses on optimizing existing treatments and designing new medication strategies and vaccines. Their current projects are aimed at:

- >> Assessing new antivirals, such as drugs that block HIV from entering cells.
- >> Developing more potent drug combinations and "patient friendly" treatment regimens.
- >> Ascertaining the effectiveness of early intervention with antiviral drugs and therapeutic vaccines.
- >> Evaluating the results of discontinuing combination drug therapy.
- >> Monitoring transmission of drug-resistant HIV.