ADARC

News from THE AARON DIAMOND AIDS RESEARCH CENTER

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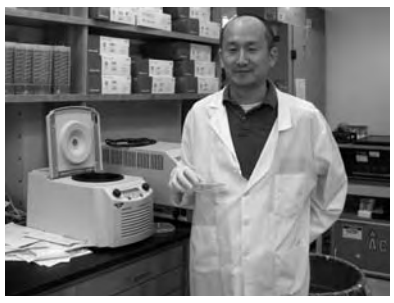
IN THE LAB:

ADARC SCIENTIST PROFILES

Robert Gifford, *Assistant Professor, grew up in a fishing village in northeast Scotland. While studying zoology at Glasgow University, he became interested in the phenomenon of emerging disease. He pursued a master's degree in the molecular biology and pathology of viruses, and a Ph.D. researching retroviral evolution at Imperial College.*

At ADARC Dr. Gifford researches viral evolution across radically different timescales, from the progression of drug resistance during HIV-1 infection, to "paleovirological" studies that address the evolution of viruses across millennia. His research has two major themes, both linked to the recent, exponential advances in gene sequencing technology. Dr. Gifford is seeking to use the vast quantities of vertebrate genome sequence data currently being generated to explore the molecular fossil record of viruses. He is developing network technologies and software tools to facilitate sharing and analysis of viral gene sequences for use in public health and medicine.



Masahiro Yamashita, *ADARC Scholar, grew up in Osaka and studied biology at Kobe University. He received his Ph.D. from Kyoto University, where he started working on HIV-1 and human T-cell leukemia virus (HTLV). His postdoctoral training at the Fred Hutchinson Cancer Research Center in Seattle was on the molecular biology of HIV-1.*

Dr. Yamashita researches the molecular basis for HIV replication and the differences between HIV and other retroviruses that are responsible for its pathogenesis. He focuses on HIV's critical ability to infect non-dividing cells—such as resting CD4+ T cells and macrophages. At ADARC he studies the cellular defense system that recognizes the incoming capsid, or protein shell, of HIV-1. His work raises the possibility that humans encode a broad range of capsid-dependent antiviral genes and that HIV's ability to evade such defenses enables the virus to infect non-dividing cell types. With data that reveals this viral evasion may have promoted HIV-1 adaptation in humans, Dr. Yamashita will continue to illuminate the molecular details underlying these host-pathogen interactions, and examine how diverse strains of HIV interact with cellular machinery to achieve infection.

Photo: Leo Sorel

President Clinton honored at Irene Diamond Award Gala

More than 350 business and community leaders joined ADARC in honoring President Bill Clinton with the inaugural Irene Diamond Award at a gala dinner in New York's Jazz at Lincoln Center on October 15. The Gala raised $1.15 million for ADARC's mission to defeat HIV/AIDS through scientific research. Actress Lucy Liu hosted the evening, which included appearances by Wynton Marsalis, Magic Johnson, Dr. David Baltimore and Dr. David Ho.

The Irene Diamond Award is a tribute to ADARC's founder Irene Diamond. Her determined idealism led her to establish ADARC in 1991 to pursue scientific solutions to the epidemic at a time when AIDS research was acutely underfunded. Mrs. Diamond's philanthropy was inspired by her sense of personal responsibility to those affected, and her faith in the power of committed individuals to be catalysts for public good.

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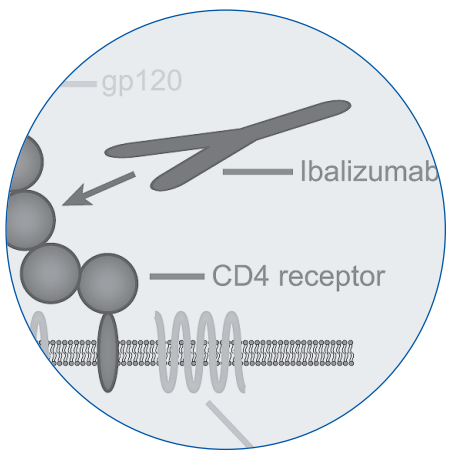
ADARC'S VISION



"Ibalizumab shows promise to become a centerpiece in the field of HIV prevention."

See article on page 3

A *Identified a molecule that serves as a central gateway for HIV's entry into CD4 cells.*

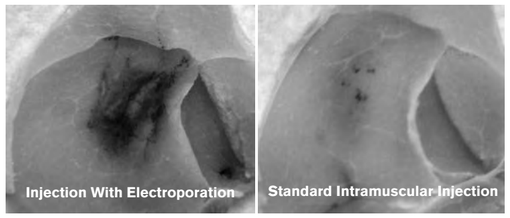
D *Introduced antiretroviral combination drug therapy that has saved millions of lives worldwide.*

A ADVANCING AIDS RESEARCH

R *Proved that HIV begins replicating at an unrelenting rate from the moment of infection, attacking the immune system if left untreated.*

C *Detected HIV in a 1959 blood sample, putting a time frame on the epidemic and providing new insights into the evolution of the virus.*

Electroporation Boosts HIV Vaccine Response



Ichor Medical Systems

Expression levels of green fluorescent protein in rat muscle following DNA administration with and without electroporation.

Brief electrical impulses may boost the protective effect of DNA-based HIV vaccines, according to experiments ADARC conducted in partnership with San Diego-based Ichor Medical Systems. DNA vaccines against HIV use genetic material from the virus to elicit an immune response. "Compared to other approaches, these vaccines are easier to make, cheaper and more stable at high temperatures," said Dr. Sandhya Vasan, who managed the trial. However, DNA vaccines administered by routine intramuscular injection have shown disappointingly weak immune responses in several trials.

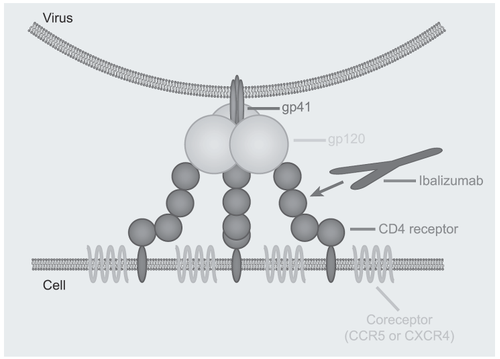
One limiting factor is that DNA cannot effectively penetrate the cell membrane when injected into the muscle. This limitation can be overcome with electroporation, a procedure that applies pulsed electricity to increase the amount of vaccine delivered to cells. In a recent clinical trial, ADARC scientists used electroporation to administer ADVAX, a DNA vaccine engineered from HIV-1 genes. This was the first time electroporation was tested on healthy volunteers. ADARC tested electroporation's safety and tolerability, as well as its effect on the immune response. The trial enrolled 40 volunteers in groups that received different doses of vaccine or placebo with either electroporation or a standard injection. The results show that electroporation is safe and tolerable.

The procedure, which employs a handheld device to deliver electricity in discrete doses, feels like a "punch in the arm" according to volunteers. "Electroporation didn't hurt as much as I imagined, it's an interesting experience and holds promise for a new, more effective method," observed one.

Preliminary data from the trial indicates that the immune response appears to be far stronger and broader among volunteers who received electroporation. While no one in the injection group had a detectable immune response, three of eight people who received electroporation and a low dose of the vaccine showed a response, and everyone who received the highest dose via electroporation had a response.

"This is the first clinical trial of electroporation in healthy volunteers for a preventive vaccine. It can be applied to many diseases and different vaccines, not just HIV." Dr. Sandhya Vasan

ADARC Launches New HIV Prevention Strategy



Neal Pacle

Ibalizumab binds to domain two of a CD4 cell, blocking HIV's entry while still allowing the cell to fight other pathogens.

In partnership with TaiMed Biologics, Children's Hospital of Philadelphia and Tulane University, ADARC is embarking on a groundbreaking new study aimed at preventing HIV infection. The project is funded by a $6.9 million grant from the Bill & Melinda Gates Foundation, and led by Dr. David Ho.

Dr. Ho's laboratory will test ibalizumab, a monoclonal antibody that binds to the CD4 cell receptor, the principal gateway by which HIV enters cells. In recent studies ibalizumab has proven to be a powerful anti-HIV therapeutic in treating infected individuals. Unlike conventional vaccines, it neutralizes a variety of viral strains from all over the world. Its potency, breadth of HIV inhibition and excellent safety profile are indications it could one day become a potent weapon in the fight to prevent HIV.

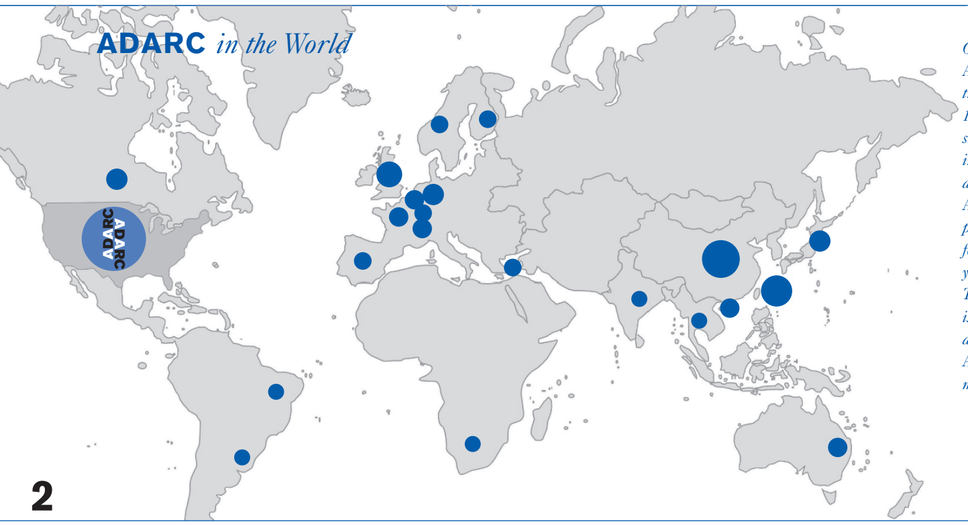
ADARC will be the first to test ibalizumab as a prevention method in healthy individuals. Dr. Ho and his team of scientists are confident studies to be conducted at ADARC will prove its safety and effectiveness. The challenge will be to make it cheaper and more easily deliverable to the millions who could benefit. Currently, ibalizumab must be given intravenously, and because of its relatively short half-life, patients need repeated infusions to maintain its protective effect. ADARC scientists will conduct bench work to develop stronger versions of the antibody so it can be administered less frequently.

Dr. Sandhya Vasan, an investigator in Dr. Ho's lab, hopes the antibody can be reformulated for subcutaneous injection, so that it can be released slowly over a longer period of time. "Imagine the impact in the developing world if just a few shots a year could prevent HIV," she says.

Dr. Ho believes this engineering problem will be quicker and easier to solve than the vaccine discovery problem. "Ibalizumab shows promise to become a centerpiece in the field of HIV prevention," he said. With over two million new HIV infections every year, time is of the essence.

Dr. Ho's work with ibalizumab was featured in the January 25 issue of Time magazine. The story can be viewed at www.adarc.org/timearticle.

ADARC *in the World*



Over the past 20 years, ADARC has been a training ground for over 100 scientists who now study HIV/AIDS in 80 independent laboratories around the world. ADARC is proud to provide a nurturing home for the development of young investigators. Today, our scientific team is more international and diverse than ever: ADARC scientists represent more than 30 nationalities.

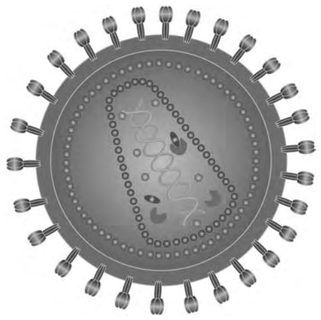
ADARC *Promise*

"Vaccine research is essentially a discovery problem, which by nature is slow and unpredictable. Many in the field agree that we should not expect a vaccine in the next ten years, so ADARC is going back to basics with a promising new approach." Dr. David Ho

Ho with a model of the antibody that he believes may prevent HIV infection.

Henry Leutwyler/AUGUST

ADARC *Discovery*



ADARC Clinical Trials

The Clinical Program is a vital part of ADARC's mission. Through clinical trials, scientists put research into practice. Trials conducted in the Clinical Program take place at The Rockefeller University Hospital.

ADARC's trials have benefited millions of people living with HIV worldwide. The Center leads studies that include HIV-positive patients, as well as healthy volunteers.

The decision to participate in a clinical trial is an important one. ADARC staff ensure trial participants receive accurate information and provide help, support and a friendly environment through the duration of the trials.

Dr. Martin Markowitz, Clinical Director, leads studies that test the safety and efficacy of new drugs or treatments in HIV-positive patients, or seek to understand how the virus interacts with the host.

For more information on trials open to HIV-positive patients, please contact Don Garmon at (212) 327-7290 or dgarmon@adarc.org.

ADARC *News In Brief*

Irene's Vision

ADARC at 20: Irene's Vision, a new film by award-winning director Renata Simone, was premiered at the Irene Diamond Award Gala in October. This short documentary tells the story of ADARC's establishment by philanthropist Irene Diamond, and its mission, accomplishments and vision for how science will provide solutions to the epidemic.

The film can be viewed online at www.adarc.org/irenesvision. To request a DVD copy, please contact Gary Gailor at ggailor@adarc.org.

Discovery Seminars

ADARC supporters and friends now have an opportunity to learn firsthand about recent developments in HIV/AIDS research and scientific progress in our laboratories. The Center's Discovery Seminars feature private briefings in non-technical terms by ADARC scientists who are extending the field's research frontiers. Previous seminars featured Dr. Paul Bieniasz speaking about his work to reconstruct an extinct retrovirus, and a thought-provoking discussion with Dr. Martin Markowitz on the possibility of a cure for HIV/AIDS.

For an invitation to upcoming Seminars, please contact Melissa Haber at mhaber@adarc.org.

Walter Wang Joins ADARC Board

Walter Wang, President and CEO of J-M Eagle, the world's largest producer of plastic pipe, has joined the Board of Directors of The Aaron Diamond AIDS Research Center.

Mr. Wang is active in numerous civic organizations, including the Committee of 100 and Young Presidents' Organization, and helped underwrite Bill Moyers' PBS special Becoming American, a documentary series about Chinese who made contributions to the United States. In 1998, he was presented with the Model Overseas Chinese Young Entrepreneur Award by the President of Taiwan, and in 2006 he was awarded the Ellis Island Medal of Honor.

Mr. Wang and his wife Shirley helped ADARC launch the China AIDS Initiative in 2005 and advocate tirelessly for this important cause. Together, the Wangs have made prodigious contributions to the betterment of society through personal and corporate support of educational, medical and humanitarian relief initiatives around the world. Most recently Mr. Wang co-chaired ADARC's inaugural Diamond Award Gala honoring President Bill Clinton.

"Walter's presence and support are giving new momentum to ADARC's mission to advance fundamental HIV research, and to develop new vaccines and therapies against AIDS," said Dr. David Ho.

Photos: Leo Sorel

From top left, clockwise: Jane Silver and Dr. Gerald Friedland; Wendy Keys, Donald Pels, Rafael Viñoly; Dr. David Ho, Lucy Liu, Magic Johnson; Gina Lin Chu, President Clinton, Walter Wang.

Gala continued from page 1

Dr. David Ho remembered Mrs. Diamond's courage, compassion and intellectual curiosity, which compelled her to fight the epidemic by establishing the first private laboratory dedicated to HIV/AIDS research—an investment that realized dramatic returns when a few years later ADARC pioneered antiretroviral therapy.

Magic Johnson attested to the impact of ADARC's breakthroughs on the lives of people affected by HIV/AIDS. He presented the Irene Diamond Award—Rafael Viñoly's striking design with a single red rose embedded in a crystalline diamond—to President Clinton, and recognized his tireless efforts to bring life-saving antiretroviral therapy to millions.

President Clinton emphasized the critical link between scientific advances pioneered at ADARC and his own work lowering the cost of medications and providing access to treatment in developing nations through the Clinton HIV/AIDS Initiative. His remarks can be viewed at adarc.org/clintonremarks.

Nobel Laureate David Baltimore, former chairman of ADARC's Scientific Advisory Board, spoke of key ADARC breakthroughs that have redefined our understanding of HIV and changed the course of clinical care for patients. He introduced an original documentary film by Renata Simone about Irene Diamond's role in establishing ADARC, and its history, accomplishments and mission. *ADARC at 20: Irene's Vision* can be viewed at adarc.org/irenesvision.

ADARC is grateful to the many friends and benefactors whose support made the inaugural Irene Diamond Award Gala a success. Funds raised will directly support innovative research into HIV's structure and function, development of next-generation therapeutics and vaccines, and new prevention strategies.

We hope you will be inspired by Irene Diamond's and President Clinton's commitment to the cause. To make a gift, please visit www.adarc.org/onlinegiving or contact Gary Gailor, ggailor@adarc.org, 212.448.5069.

You Can Help ADARC's Scientists Fight HIV/AIDS

Private giving is vital to the Center's research mission, allowing rapid exploration of new ideas that have not yet attracted government funding. As costs rise and the pace of science increases, ADARC counts on your support to sustain the research environment critical to new discovery. Your contribution is an investment in the people and promise of ADARC.

Please join us in the fight.
Send your check to:

The Aaron Diamond AIDS Research Center
455 First Avenue, 7th Floor
New York, NY 10016
T: 212.448.5069

If you prefer to give online, please visit
www.adarc.org/onlinegiving

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AIDS Research Center
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455 First Avenue, 7th Floor
New York, NY 10016

Address correction requested