

Discovery

The Newsletter of
the Institute of
Human Virology

FROM LABORATORY TO CLINIC



(From left to right) Dr. Roberto Trujillo; Dr. Robert Gallo, Director of IHV; Ing. José Antonio González-Treviño, President of the UANL, and Jesús Zacarías-Villarreal, Assessor of the State Government for Medical Services.

Message From The Director IHV Teams with Africa, China & Mexico

The Institute of Human Virology (IHV) has recently teamed with Africa, China and Mexico in an international effort to address the global AIDS epidemic by building partnerships, expanding resources, training professionals and empowering patients.

The IHV in April established IHV-Nigeria to assist Africa's most populous nation in the fight against HIV/AIDS. The new entity, located in the Nigerian capital Abuja, is an extension of IHV's primary facility in Baltimore and shares a common mission of care, treatment, training and research. The Institute of Human Virology-Nigeria Asokoro Training Laboratory Center, a state-of-the-art facility, was inaugurated on Dec. 9.

Nigeria, with an estimated population of nearly 140 million, is widely considered a frontline in

ROBERT C. GALLO, M.D.
Director of
the Institute



efforts to stem the tide of HIV/AIDS in Africa, where the disease has claimed millions of lives. An estimated nearly 5 percent of Nigerians are infected with HIV.

In August, the IHV and China's Center for Disease Control and Prevention signed an agreement to work together to develop new treatments and a preventive vaccine for HIV. The agreement also calls for the IHV to train Chinese medical researchers and doctors in its Baltimore laboratories and at research institutions in China. The IHV and the National AIDS/STD Center of China's CDC will also work together on scientific
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Expert on Virus-Host Cell Membrane Fusion Joins IHV

While shared mechanisms of action exist across organisms and species, viruses that imitate 19th century whalers are surely unprecedented. In their efforts to gain entry into and infect host cells, viruses like HIV and influenza cluster around a host cell, each casting a microscopic, viral protein 'harpoon' (a fusion protein) designed to penetrate the 'blubber' (cell membrane), reel the cell closer, and enable the fatal strike—penetration of viral contents into the cell.

Viral penetration across cell membranes, ultimately mediated by formation of transient "fusion pores" via unknown mechanisms, has become the life's work of Gregory Melikyan, a recent addition to the Vaccine-Basic Science Division of the IHV. A native of Armenia, Melikyan obtained his Ph.D. from Moscow University, building on a pre-existing interest in biophysics and lipid bilayers—the sandwich-like configuration of lipids (fats) that, together with proteins and other biomolecules, comprises outer cell membranes and intracellular structures.



GREGORY MELIKYAN

Structurally, a lipid bilayer is organized with hydrophilic (water-loving) 'heads' facing outward (sandwich
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research and clinical programs to enable the world's most populous nation to address a growing number of infections. According to the United Nations, China has 840,000 people infected with HIV.

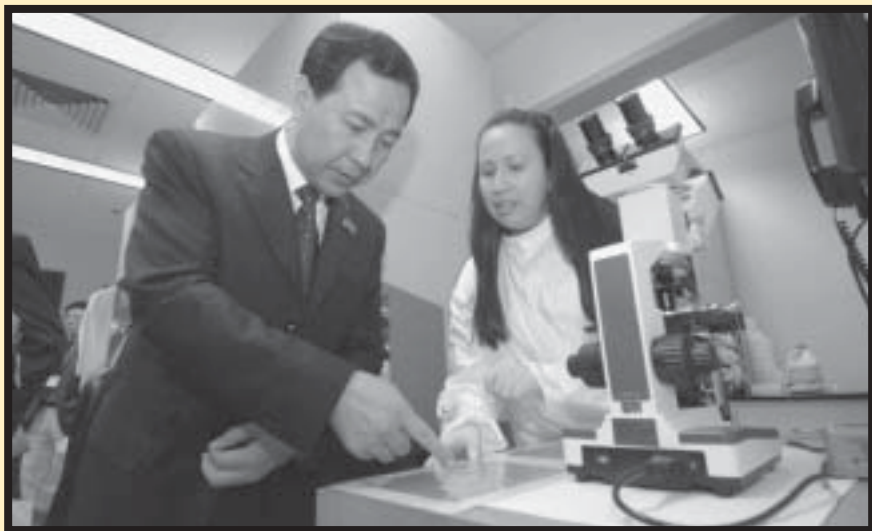
While the disease in China remains confined mainly to high-risk groups such as intravenous drug users, former blood plasma donors and commercial sex workers, it is vital for the country to stop the epidemic from spreading to the general population. The country faces shortages in the number of doctors trained to diagnose and treat HIV/AIDS.

Dr. Robert Gallo, director of the IHV and a co-discoverer of the virus that causes AIDS, describes the partnership with China as "an historic milestone in international HIV/AIDS cooperation...with two hemispheres of the globe joining to solve the problem of HIV/AIDS."

Dr. Yu Wang, Director of the Chinese Center for Disease Control and Prevention, concurs. "International



Dr. Yu Wang at press briefing



A partnership with China's CDC will enable the IHV to train Chinese medical researchers and doctors in its Baltimore laboratories and at research institutions in China.

collaboration is part of China's AIDS control effort and this agreement lifts the collaboration between scientists to a new level."

In October, the IHV also partnered with Universidad Autonoma of Nuevo Leon (UANL) in Monterrey, Mexico to focus on the fight against HIV/AIDS in Latin America.

UANL will be forming IHV-Mexico to conduct basic research, clinical research, training, care and education. IHV-Mexico, to be directed by the IHV's Dr. Roberto Trujillo, will be located in a new facility on the campus of UANL. IHV will assist UANL by providing its expertise from having operated a similar Institute for the past nine years in Baltimore.

According to the United Nations, Latin America has more than 1.7 million people infected with the AIDS virus.

The Institute has entered a number of international collaborations in an effort to help build resources and provide train-

ing in order to increase the availability of scientists and medical personnel globally.

The IHV has collaborated with scientists internationally since its opening almost 10 years ago with great results. In February 2004, the Institute was one of the first organizations to receive federal funding from the President's Emergency Plan for AIDS Relief recognizing leaders in their field and empowering them to expand their efforts internationally in regions hardest hit by the AIDS epidemic.

"These and similar efforts must be maintained and encouraged at all costs... Careful planning, help with infrastructure, training in the use of these complex drugs, and assistance in fostering biomedical research in developing nations are all needed," stresses Dr. Gallo.



An architectural rendering of a new institute to open in Monterrey, Mexico.

Discovery is a quarterly newsletter of the Institute of Human Virology. Copies are available upon request. Please send comments to:

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Gallo receives Tovi Comet-Walerstein award in Israel

On Nov. 30 Dr. Gallo received the prestigious Tovi Comet-Walerstein Award from Bar-Ilan University Safdie Institute for AIDS and Immunology Research in Ramat Gan, Israel.

The award is given annually to a distinguished scientist whose contribution was unique to basic and/or applied research and was widely recognized as a major breakthrough for future research and treatment.

The award recognized Dr. Gallo as the pioneer of the field of human retrovirology in 1980 by discovering the first human retrovirus (HTLV-1) and showing it to cause a particular form of human leukemia. A year later, he and his group of researchers discovered the second known human retrovirus (HTLV-2), which was followed in 1984 by the landmark discovery by Dr. Gallo and his colleagues of HIV. Gallo's team provided the first results to show that HIV was the cause of AIDS and developed the life-saving HIV blood test.

"Dr. Gallo's vision has been unprecedented in the field of virology and he has made scientific research – and



Here, Dr. Gallo is presented with an honorary degree from the National University of Ireland, along with musician Bob Geldof, Professor Carole Pateman and renowned filmmaker Neil Jordan.

the opportunity to help put an end to deadly diseases – his life's work," said

Safdie CAIR Director Professor Benjamin Sredni.

Gallo Bylines Articles in Newsweek and The Lancet

Dr. Gallo has been the requested author of several articles, editorials and opinion pieces that appeared recently in prestigious journals including The Lancet and Newsweek magazine.

In The Lancet, Gallo challenges the position that failed efforts to develop a preventive vaccine indicate a need to abandon the approach. His position is that it is not time to give up on HIV vaccines but rather to change the way we pursue them. His contribution outlines seven major scientific obstacles blocking the effort, including vaccine

design and the lack of a truly useful animal model for studying HIV infection.

"HIV- preventive vaccine research should clearly ignore empirically driven approaches and rely exclusively on rational approaches that are based on solid knowledge of HIV biology," Galls states. "I suggest after years of wandering, we have only begun to travel this path. A shift in emphasis to solving key scientific problems that have plagued the field is necessary."

In the Newsweek essay, sold internationally, Gallo contends that HIV/AIDS is a medically solvable problem but that what works in one locale will be differ-

ent from what works elsewhere.

"The choices of therapeutic drugs for different regions should be evidence-based, not pre-determined. Treatment programs should tolerate flexibility in the use of alternative approaches that may be sensible in some developing countries even if they appear less than optimal in the United States and other developed nations... Careful planning, help with infrastructure, training in the use of these complex drugs, and assistance in fostering biomedical research are all needed."

IHV welcomes new Board of Advisors members

The Institute of Human Virology wishes to welcome three new members to its Board of Advisors. They include an NBA Hall of Fame athlete and coach, a wildly successful restaurateur, and an Asian expert on interferon who built and directed the Institute of Molecular and Cell Biology in Singapore.

The newest board members arrive as the Institute goes into its 10th anniversary year, having recently celebrated the spin-off of its first biotech company as well as a growing patient base of more than 4,000 in the metropolitan Baltimore area and a growing international presence with scientific partnerships and collaborations established with Africa, China and Mexico.

“Mirroring the IHV’s multidisciplinary approach to addressing the worldwide HIV/AIDS pandemic through a combination of research, treatment and prevention, these individuals represent a vast diversity of skills and insights that will help shape and mold the vision, performance and long-term success of the Institute,” says Dr. Robert Gallo, founder and director of the IHV.

Chris Tan

Founding Director of the Institute of Molecular and Cell Biology in Singapore, Chris Tan saw staffing increase from 35 scientists in 1987 to more than 500 by 2003 and oversaw an annual budget of about \$40 million.

“My remit was to continually convince the government of Singapore the value of establishing a strong research culture, which to them was unfamiliar territory,” reflects Tan. “In the 10 years following its inception, the IMCB became a leading international research institute capable of competing with labs worldwide in cell biology, infectious diseases and neurobiology.

Articles and editorials appeared in *Nature*, *Science*, the *Economist Intelligence Unit*, *Business Week*, *Nikkei Keizai Shimbun*, *Asahi Shimbun*, *Fortune Magazine* and *Time Magazine*, reporting the IMCB as an international player in biomedical research. The IMCB’s success eventually spurred Singapore to undertake biomedical R&D as a pillar for its knowledge based economy and this has since resulted in the establishment of Biopolis, where 2,000 biomedical research scientists are housed in newly built space of 2 million square feet.



Lenny Wilkens

Wilkins is the all-time coaching wins leader without ever coaching a Hall of Fame player in his prime or at his best. It may be the most remarkable record in sports. It can be argued no one has done more with less in NBA history than Lenny Wilkens. He doesn't shout for attention or demand it; he earns it with results, which is the way it should be.

-- Sam Smith, ESPN

Lenny Wilkens holds the rare distinction of having



coached all teams that he represented during his 15 seasons as an NBA player: Seattle, Portland, Cleveland and Atlanta. He began his coaching career in 1969 as player/coach for the Seattle Supersonics and has coached the Portland Trailblazers, Cleveland Cavaliers, Atlanta Hawks, Toronto Raptors, and the famed New York Knicks.

Wilkins was a nine-time NBA All-Star as well as MVP of an All-Star Game. He was enshrined in the NBA Hall of Fame as a player in 1989 and selected to the NBA’s all-time Top 10 Coaches and 50 Greatest Players List in 1996, the only NBA representative recognized both as Hall of Fame player and coach. Wilkins also coached Seattle to a World Championship in 1978-79, was NBA Coach of the Year in 1994 and led the 1996 USA Basketball Dream Team to the gold medal in the Atlanta Olympic Games. He coached the Knicks to first place in the Atlantic Division in 2004-5.

General Manager, Public Speaker, Author, Fundraiser, Board of Directors and Television Analyst are all roles that Wilkins has excelled at, though he has no plans to slow the pace. “As role models, it’s important for us to give back to the communities in which we work and live,” he says.

Franco Nuschese

Hospitality entrepreneur and native Italian Franco Nuschese is president of Georgetown Entertainment Group LLC, the management company for Cafe Milano in Georgetown, Sette Osteria near Dupont Circle, and Sette Bello in Arlington, Va.

Nuschese was born in Minori on Italy’s fabled Amalfi Coast on March 7, 1961 and he mastered the art of blending hospitality and entertainment skills during a career that included training in Europe and early marketing experience at Caesars Palace in Las Vegas.

Nuschese came to Washington, D.C., in 1991, when he was general manager of Bice, an Italian restaurant in the Penn Quarter. He opened Café Milano in Georgetown the following year and the restaurant soared to top-status rank, attracting Hollywood celebrities, politicians, diplomats, classical and popular entertainers, professional athletes, international journalists and famous broadcasters.

Nuschese created two Italian restaurants at the MGM Grand Hotel and Casino in Las Vegas in 1995; he opened Sette Osteria in 2004 and his newest restaurant, Sette Bello, opened this fall in the Clarendon section of Arlington.

Proud of his heritage, Nuschese is active in organizations that support the Italian culture in America and participates and donates to various civic and charitable organizations within the Washington, D.C., metropolitan area. Nuschese also is a member of the advisory board for LifeLink MD, Inc. and the board of the Washington National Opera. He is on the boxing committee for the D.C. Sports and Entertainment Commission and is a trustee of The American Academy of Hospitality Sciences.



IHV Researcher Receives Innovator of the Year Award



DR. NIEL CONSTANTINE
IHV Laboratory of Viral Diagnostics director

Dr. Niel Constantine was presented with the Top Innovator of the Year Award by The Daily Record at a recognition event hosted in Baltimore in September 2005.

The award recognizes the researcher's work in developing a blood test that can detect microscopic levels of prions, protein particles known to cause mad cow disease and other incurable and always fatal neurological disorders.

Currently, the protein can be detected in brain tissue but not in blood because of its very low concentration levels.

"This new test should allow us to detect prions and disease before symptoms appear," explains Dr. Constantine, adding that the technology could result in a safer blood supply and safer food consumption for the public. "In cattle, it can be

envisioned that a simple hoof-stick would provide the sample for surveillance testing."

Dr. Constantine is Director of the Laboratory of Viral Diagnostics at the IHV; his findings have been published in the *Journal of Virological Methods*.

2006 Annual Meeting

The 2006 Annual International Meeting of the Institute of Human Virology will be held Nov. 17 - Nov. 21 in Baltimore, MD.

Check www.ihv.org, for more information in upcoming weeks and to register online.

Site features will include:

- Meeting information
- Session titles
- Speaker schedule
- Hotel information with online registration
- Guidelines for submitting abstracts
- Scholarship information
- Reception and banquet details

Important Deadline:

May 20, 2006

Abstracts Submissions

Scholarship Submissions

Expert on Virus-Host Cell Membrane Fusion and Love of Lipids Joins IHV, *continued from page 1*

"bread") and hydrophobic (water-avoiding), long 'tails' facing inward (sandwich "filling"). Other molecules and gross structures (transporters and ion channels) exist anchored or floating freely in this fluidly dynamic lipid "soup", much like ocean buoys.

On a micro-scale, viral entry requires Herculean feats: forced proximity of virus and cell outer membranes; a progression of conformational changes in viral fusion proteins (gp120 and gp41, for HIV); subsequent fusion into a bridge-like, pore structure; pore enlargement; and, passage of a large, viral capsid through the pore.

Melikyan studies how conformational intermediaries of fusion proteins promote pore formation, examining the extent to which their formation can be blocked, either by neutralizing antibodies or by inhibitors that target both initial viral binding (to host cell CD4 receptors and coreceptors) and subsequent fusion protein conformational changes—namely, gp41 refolding into a so-called "six-helix bundle" (6HB).

The rearrangement and merging of membrane lipids to form fusion pores "is catalyzed first by insertion of the hydrophobic portion of a viral fusion protein (gp41 for HIV) into the cell membrane, followed by gp41 refolding (into 6HB) and fusion pore formation," says Melikyan.



Recently, Melikyan has developed sensitive fluorescent microscopy and functional testing methods that enable him to monitor individual virus-cell fusion and pore formation events, in real time, simultaneously tracking membrane fusion and delivery of viral contents—an advantage over past techniques that provided measures of only productive virus-host interactions.

"Fusion pores are actually unstable; most form and then collapse,"

says Melikyan. Only a small percentage of pores will enlarge, within a matter of seconds to minutes." The relatively long life of small pores was the most surprising aspect of his discovery, suggesting that "additional factors might be required to promote pore growth, in living organisms."

"Now, we can definitively dissect the three major steps of pore formation: merging of cell-virus membranes, small pore opening, and pore enlargement," he adds. Obtaining such mechanistic, molecular knowledge of key fusion intermediaries is the goal of his future work. Melikyan is certain "these studies will both advance our understanding of the mechanism(s) by which fusion proteins promote virus entry and aid the development of novel entry inhibitors."

THE INSTITUTE OF HUMAN VIROLOGY (IHV) at the University of Maryland was established to create and develop a world-class center of excellence focusing on chronic diseases and virally linked cancers. The IHV is dedicated to discovery, research, treatment, and prevention of these diseases and cancers. Its unique structure seeks to connect cohesive, multidisciplinary research and clinical programs so that new treatments are streamlined from discovery to patient. The IHV serves patients locally and the scientific community globally.

Making AIDS vaccine a reality as published in The Baltimore Sun

By Margaret I. Johnston and Anthony S. Fauci, Dec. 1, 2005

World AIDS Day today is an opportunity to bow our heads in remembrance of the more than 25 million men, women and children who have died of HIV/AIDS. It also is a chance to renew our resolve to end this deadly scourge.

More than two decades after experts first recognized the threat posed by this disease, 40 million people worldwide - a nearly incomprehensible number - are living with HIV/AIDS, and 14,000 people are newly infected with HIV each day.

To beat back this modern plague, we must collectively recommit ourselves to global efforts to care for HIV-infected individuals and their families and to redouble our efforts in HIV prevention. The ultimate defeat of HIV/AIDS will require a multifaceted effort but will be difficult, if not impossible, without a safe and effective preventive HIV vaccine.

In the past five years, the U.S. National Institutes of Health (NIH) alone has dedicated \$2 billion toward HIV vaccine research. The Global HIV/AIDS Vaccine Enterprise, a consortium devoted to HIV/AIDS vaccine research, has been endorsed by the Group of Eight industrialized countries and provides needed focus on this issue. Progress is being made.

Cutting-edge science has led to novel vac-

cine approaches that have shown promise in the laboratory and in animal tests. About 25,000 people have volunteered to participate in more than 90 HIV vaccine clinical trials worldwide. Each trial brings us a step closer to ending the pandemic.

But all this effort will be for naught if the public continues to believe myths about HIV/AIDS vaccine research. The tragic truth is that if scientists discovered the ideal vaccine candidate tomorrow, many Americans would not be prepared to help prove its effectiveness - a critical step in licensing a safe vaccine.

To conduct a meaningful, large-scale trial, tens of thousands of healthy, HIV-negative volunteers will need to roll up their sleeves and receive an experimental vaccine. Finding volunteers for vaccine trials is often daunting. But it will be nearly impossible if Americans continue to believe misinformation about HIV vaccine trials.

According to a recently published study by the National Institutes of Health in Bethesda, only half of those surveyed knew that the HIV vaccines being tested could not cause HIV infection. More than half of respondents expressed skepticism about the safety measures built into vaccine trials. Equally disturbing, a majority of those surveyed reported that they would not be supportive of a friend or loved one volunteering for a preventive HIV vaccine trial.

Such attitudes cripple vaccine trials. It is critical that communities most affected by the HIV pandemic and policy-makers inside and outside the government help dispel these myths. Credible spokesmen and women must repeat - over and over again in media trusted by the public - that volunteers in preventive vaccine trials cannot contract HIV from the vaccines being tested. The overriding importance of clinical trials, and the way in which they safeguard volunteers, must be conveyed.

Finding a vaccine for HIV/AIDS and ending the HIV/AIDS pandemic rests in no small measure with each of us, as researchers, advocates, volunteers, family and friends. Despite the extraordinary efforts of thousands of scientists worldwide, there is still no effective HIV vaccine.

On this World AIDS Day, let us recommit ourselves to doing everything in our power to find an HIV vaccine. We must roll up our sleeves, literally and figuratively.

sanofi pasteur

The vaccines business of sanofi-aventis Group

DISCOVERY would like to thank its corporate sponsor, sanofi pasteur, for continued support of the IHV and its mission.



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