

Discovery

Laboratory • Clinic • Community • World

Summer/Fall 2012



AIDS Researchers Discover New Cell

This past July, researchers at the Institute of Human Virology (IHV) of the University of Maryland School of Medicine announced that they had identified a new behavior for the human macrophage that provides new explanations for several features of HIV biology, including how the virus persists within the body indefinitely, how quiescently infected CD4+ T-cells arise, and how the infection leads to depletion of CD4+ T-cells. The research team found that macrophages cultured from human blood can function as “nurse cells” and in this capacity, generate and release newly formed cells. The new cells released include a previously unknown small cell, termed “self-renewing monocytoid cell” (SRMC) that is highly susceptible to infection with HIV. This small cell can develop into another nurse macrophage that can, in turn, produce another small cell. This nurse macrophage/small cell developmental cycle can continue in culture for several generations, even during continuous production of HIV. Current anti-HIV drugs cannot inhibit HIV maintained through this process, because they act to prevent new infection. The nurse macrophage/small cell cycle does not require infection of new cells and for this reason, it may help to explain, along with latently infected long-lived cells, how “wildtype” HIV strains—those lacking drug resistance mutations—are maintained within the body during years of uninterrupted anti-HIV therapy. The researchers emphasized that although working with HIV led them to recognize nurse macrophage behavior, all of the phenomena observed can be seen in uninfected, as well as HIV-infected macrophage cultures.

Amazingly, nurse macrophages can also produce CD4+ T-cells, which are released as resting cells. These cells are a specific subtype of CD4+ T-cells, the subtype preferentially targeted by HIV. The researchers observed a dramatic decline in T-cell production in HIV-infected macrophage cultures, as well as release of resting CD4+ T-cells that contained HIV DNA, but were not producing the virus. These findings suggest that nurse macrophages may represent a source of latently infected CD4+ T-cells, and that compromise of nurse macrophage production of CD4+ T-cells,



Dr. Susanne Gartner

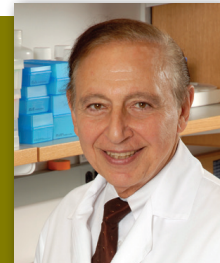
brought about by HIV infection, may contribute to the CD4+ T-cell decline that characterizes AIDS. Dr. Susanne Gartner, the leader of the Institute’s stem cell research team, notes, “Thus far, the experiments have been performed using macrophages obtained from blood, and then cultured in the laboratory. We are now trying to determine if these phenomena are operational in vivo—within the human body.” Dr. Robert C. Gallo, Director of the IHV adds, “The concept that a cell can be produced within another cell, a ‘mother’ cell, is new—at least in human biology—and thought-provoking, and

continued on page 3

Director’s Message:

The Institute of human virology (IHV) is proud to continue the Annual International Meeting, now in its 14th year since its inception. Continuing the tradition from more than 30 years of scientific conferences, our meeting continues to be a forum for outstanding science in the fields of human viruses and cancer. This year’s meeting opened with two outstanding sessions. On Sunday morning, we heard from many of our international partners in Africa who are building indigenous research programs in close collaboration with IHV. Success of these programs makes a durable footprint in the ground of our outstanding global outreach and education effort, and was recognized by kind remarks from Dr. Jay Perman, President of the University of Maryland, Baltimore (UMB). This first day also highlighted truly remarkable advances in clinical science of HIV, and the future for therapy was outlined by our Baltimore colleague and this year’s winner of the IHV Lifetime Achievement Award for Excellence in Medical Education, Dr. John Bartlett.

continued on page 2



Director's Message continued



IHV Meeting attendees.

Monday saw us getting into the weeds of basic research on HIV pathogenesis followed by a session new to this year's meeting, on Structural Biology of Immunity and Viruses. These sessions showed how scientists working in HIV research have pushed the envelope of basic understanding in the most essential interactions of viral pathogenesis and are applying the tools of structural biology to understanding of viruses and the immune system. The meeting continued on Tuesday with a full day program on Preventive HIV Vaccine. Several speakers described outstanding research aimed at understanding the successes and failures of earlier human clinical vaccine trials. It is not too much to say that we are witnessing a revolution in the science of vaccine, where empirical testing of candidate immunogens is now being replaced by antigen design guided through a detailed understanding of each step in the immune response. We learned the difficulties of triggering an initial antibody response to the HIV envelope glycoprotein and reviewed efforts to overcome this barrier. Lessons learned in the vaccine program are moving rapidly to successful prevention of



IHV Lifetime Award Winners, Prof. Yi Zeng, Dr. Waldmann, Dr. Bartlett and IHV's Dr. Redfield.

HIV transmission, and will impact efforts to develop vaccines against many other pathogens which have avoided our best efforts until now.

An important activity of our Annual Meeting is to recognize outstanding colleagues who have contributed greatly in the areas of human viral disease. Nominated and voted on by IHV faculty this year, we bestowed the IHV Lifetime Achievement Award for Public Service to Prof. Yi Zeng from the Chinese Centers for Disease Control, for his lifetime of studying viral causes of human cancer. Dr. Zeng was honored by a talk from Lishan Su at the University of North Carolina who described new models for studying HIV and hepatitis viruses. Dr. Thomas Waldman from the National Cancer Institute was honored with the Lifetime Achievement Award for Scientific Contributions. Speaking on behalf of Dr. Waldman was Dr. J Berzofsky, also from the National Cancer Institute, who described their years of collaborative research. Dr. John Bartlett of Johns Hopkins, as mentioned, was honored with the Lifetime Achievement Award for Excellence in Medical Education and was recognized by a talk from our own Dr. Robert Redfield who discussed strategies for global implementation of antiretroviral therapy. These Award winners were recognized again during the Gala Banquet on Tuesday evening, with personal comments from close friends and colleagues. That evening was hosted by our new IHV Board Chair, Terry Lierman and we were treated to a dinner speech by U.S. Senator Benjamin Cardin (D-Md).



Dr. Gallo and U.S. Senator Benjamin Cardin.

The final morning session of the meeting focused on Viral Oncology. Here we learned how several viruses regulate DNA damage pathways during induction of malignant disease and we reviewed new information on Hepatitis C Virus, Human T-cell Leukemia Virus, and a new oncogenic mechanism driven by structural proteins of HIV.



IHV Director, Dr. Robert Gallo and NIAID Director, Dr. Antony Fauci.

Despite significant financial challenges, we continue to present the Annual International Meeting as a representation of the important international leadership of IHV in treatment, prevention and research on human viral diseases and cancer. Long known as a meeting with outstanding scientific content and opportunities for collegial interaction, the IHV Annual Meeting continues to be an important part of our Institute's calendar. I am very grateful to members of IHV who work



NCI Director, Dr. Harold Varmus.

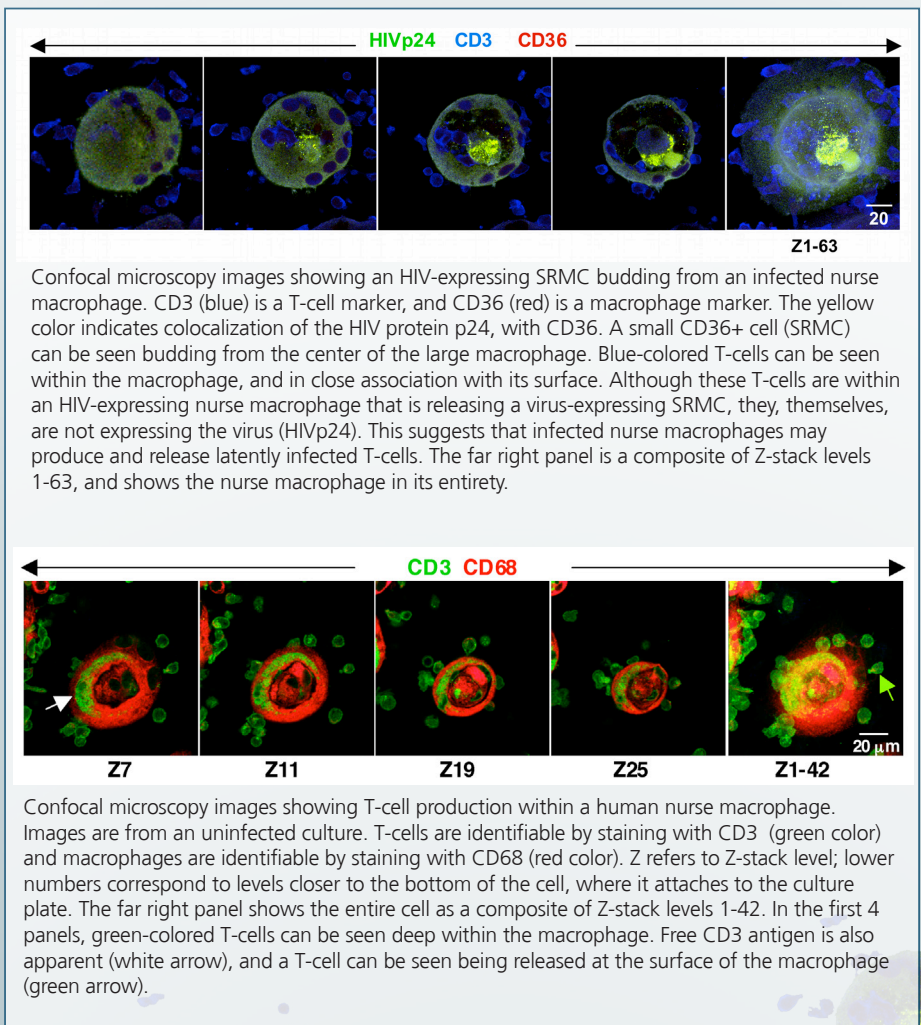
year-round, especially David Pauza, Deborah Mullins and Lauren Moscato, and to our corporate and government sponsors without whom this meeting would be impossible. Now we shift our attention to IHV's 15th Annual International Meeting in Moscow, Russia.

AIDS Researchers Discover New Cell

continued from cover page

it makes sense that a virus would exploit this process as a survival strategy. Of course, the phenomena must be documented directly in patients, but it is likely that these concepts will ultimately impact several fields. In fact, this observation in vitro does demonstrate that at least some macrophages have a capacity never before described." Gartner and her coauthors at the Institute, Drs. Yiling Liu and Senthilkumar Natesan, began this work while they were members of the Department of Neurology at Johns Hopkins University.

The paper describing this work is published in PLoS ONE. It can be accessed through the following link: <http://dx.plos.org/10.1371/journal.pone.0040139>



University of Maryland Students, Faculty, and Staff join thousands at M&T Bank Stadium for

1st Project Homeless Connect



Aaron Burgess, (SSW—UMB) and Sarah Southard, (SOP—Shady Grove), review a case before escorting a client to an HIV testing station. Photo by Ed Fishel

On Thursday, August 2, the University of Maryland's Founding Campus participated in Baltimore's first Project Homeless Connect at the M&T Bank Stadium. Through its Preparing the Future program (www.jacques.umaryland.edu/PTF), the JACQUES Initiative of the Institute of Human Virology at the School of Medicine partnered with the campus' Office of Interprofessional Student Learning & Service Initiatives to provide free, rapid HIV testing and linkage to care services. The mission of Project Homeless Connect is to provide a single location where multidisciplinary service providers collaborate to serve and empower people who are homeless and at risk of homelessness. Under the supervision of Alexandra (Allie) Reitz and Harriet Kapilikisha of the JACQUES Initiative, HIV testing and linkage to care services were provided by a multi-disciplinary group of 21 students from five of our campus' professional schools including medicine, nursing, social work, law and pharmacy. The group encountered 84 citizens for HIV testing and linkage to care and worked alongside of medical providers from around the city, including our campus' medical center.

In 2011–2012, over 100 medical and nursing students participated in the pilot of the Preparing the Future program, whose goal is to normalize, routinize and integrate HIV into the future practice of emerging professionals. The Preparing the Future program inspired a campus-wide event on April 16, 2012, the University of Maryland Leadership in HIV Summit: Preparing the Future. The event drew 400 campus leadership, faculty, students, policy makers and community members in a forum that featured student displays reflecting how being better informed about HIV has impacted their lives, a campus-wide plenary, breakout sessions and a community partnership town hall. Preparing the Future is currently being expanded to other disciplines at the University of Maryland to include Dentistry, Law, Pharmacy and Social Work and the model is being shared nationally. Participation in this event was spearheaded by Matt Zeitler, a second year medical student who participated in the pilot program.

At the August 2 event, medical and nursing students trained in the first year of Preparing the Future carried out the HIV testing. Students from pharmacy, social work and law provided testing support. Allie Reitz, Coordinator of Community & External Affairs of the JACQUES Initiative said, "The students worked as an integrated



Jl staff Harriet Kapilikisha and Alexandra (Allie) Reitz review the volunteer schedule for the day. Photo by Ed Fishel

team with dignity, poise and respect – it did not matter what discipline they were from, they complemented each other with the common goal of providing a service to a community in need."

The Mayor's Office of Human Services, United Way of Central Maryland, KPMG and Beta Alpha Psi organized this event in partnership with local providers. Project Homeless Connect is a national model that has been replicated in more than 260 cities across the U.S. During the event, volunteers act as one-on-one guides for homeless individuals as they navigate an array of services, including everything from housing to haircuts to health insurance. The 2011 biennial Point-in-Time homelessness survey counted 4,088 individuals who were homeless on a single night in Baltimore City.

For more information about the JACQUES Initiative of the Institute of Human Virology and the Preparing the Future program, please visit their website at www.jacques.umaryland.edu.



Group photo of student volunteers and JI staff at Project Homeless Connect.

the JACQUES Initiative's Project SHALEM



A volunteer demonstrates how the rapid HIV test works to a client at City Uprising HIV Outreach Day. Photo by Cricket Barrazotto



The JACQUES Initiative's Chris Williams, Director of Case Management and Mental Health, provides on-site case management services at City Uprising HIV Outreach Day. Photo by Cricket Barrazotto



A volunteer goes over paperwork with a client at City Uprising HIV Outreach Day. Photo by Cricket Barrazotto

Since 2009, the JACQUES Initiative's Project SHALEM continues to directly impact Baltimore through unique and purposeful outreach that includes HIV testing, linkage to care and supportive services through trained volunteers. In Phase 1 it engaged volunteers from the faith-based community. Phase 2 launched in September 2012, engaged the University of Maryland Baltimore professional schools through a project called Preparing the Future (PTF) with the goal of training emerging professionals to normalize and routinize HIV in their future practice through a didactic and hands on curriculum. Project SHALEM has been successful in mobilizing the community, evidenced by the provision of HIV testing

and linkage to care for more than 8,800 individuals through a workforce of trained volunteers.

Each year, the JACQUES Initiative participates in a city-wide event called City Uprising. This year's City Uprising HIV Outreach Day event encountered over 900 individuals, reached 44 people living with HIV and made more than 150 case management referrals to HIV positive and negative individuals for services such as food and shelter. There were a total of 513 volunteers who served on that day alone, more than 60% from the faith-based community and almost 20% from our campus including students, hospital staff and IHV staff.



The front entrance of the Esperanza Center with 2012 volunteers. Photo by Cricket Barrazotto

This past summer, members of the Global Virus Network (GVN), which include foremost experts in every category of virus and represent more than 20 countries, concluded a conference in Naples, Italy. Members presented current research, identified the most serious and imminent global virus threats to public health, and discussed both what is required and how to best deal with these viruses.

Members of the GVN identified viruses transferred from animals to humans, such as avian and swine influenzas, as the most imminent and potentially pandemic threats to public health.

Dr. Ilaria Capua of Italy's Veterinary Public Health Institute (IZSve), and a leading researcher of animal-borne viruses, warned that the rapid spread of what is presently a mild form of avian flu (H9N2) is combining with a far more virulent and deadly form of avian flu, which could cause the emergence of a lethal chimeric virus. "We are sitting on a ticking time bomb, and it is imperative that the members of the Global Virus Network advocate for funding to increase surveillance and research in this field," said Dr. Capua.

Members of the GVN also determined that nature, not humans, is the public's foremost bioterrorism threat. Dr. Ab Osterhaus, Professor at Erasmus University Rotterdam, Netherlands said, "The recent claim that publishing a paper on bird flu would provide terrorists with a means to kill is absurd, and frankly, just not possible for terrorists to recreate. We must remember that all of these dangerous flu mutations are already present in regions of Southeast Asia." Osterhaus added, "What is most important is that scientists work together on these issues, which is exactly the



Dr. Peter Palese presents in Naples, Italy.

function the GVN serves. In this way, the relevant mutations in the virus could be spotted in humans as soon as they emerge." Additionally, one of the world's foremost influenza experts, Dr. Peter Palese of Mount Sinai Medical Center in New York, said "We must share information and early results so we can develop safe and effective vaccine—anything less is useless."

Dr. Rino Rappuoli, Global Head of Vaccines Research at Novartis Vaccines and Diagnostics based in Siena, Italy, spoke about his foundation he launched to supply vaccines against diseases that particularly target poor populations. Rappuoli presented an inspiring talk about how vaccines have made the biggest contribution to the increased life expectancy that we enjoy today and to our modern quality of life. He said, "We are not yet adequately prepared for new and existing viral threats, and our mission at the GVN is to fill that gap. The GVN represents leading experts and researchers in every classification of human virus, and is uniquely capable of assisting governments and organizations in focusing their resources on research and public policy to address viruses which pose a serious and imminent threat to public health."

"It is only a matter of time before our next virus epidemic or even pandemic," said Dr. Robert C. Gallo, who is Director of the Institute of Human Virology at the University of Maryland School of Medicine and is most widely known for co-discovering HIV and developing the HIV blood test. "We are not yet adequately prepared for new and existing viral threats, and our mission at the GVN is to fill that gap. The GVN represents leading experts and researchers in every classification of human virus, and is uniquely



Dr. Robert and Mary Jane Gallo in Naples, Italy.

capable of assisting governments and organizations in focusing their resources on research and public policy to address viruses which pose a serious and imminent threat to public health.”

The GVN was co-founded in March 2011 by Gallo, currently Chair of GVN’s Scientific Leadership Board, and by Dr. Reinhard Kurth of the Ernst Schering Foundation in Germany and Dr. William Hall of University College Dublin in Ireland. GVN will seamlessly share information through cutting-edge technology including developing a virtual bio bank and developing a Rapid Action Fund to provide resources for research of the most dangerous, high-risk pathogens. Additionally, the GVN seeks to build and maintain clinics adjoined to bio-containment facilities in six of the world’s continents, as well as a Global Rapid Response Research Team, to be mobilized in the event of viral threats. Lastly, the GVN will sponsor fellows who are expected to conduct high-priority research in medical virology at GVN Centers.

“Scholarly exchange is fundamental to international collaborations that will link our activities far into the future,” said Gallo. “GVN scientists will also have the unique opportunity to move between centers to implement research programs or bring specific expertise to a local problem.”



GVN Italy Participants.



Naples Group Photo.

Terry Lierman Appointed Chair of Institute's Board of Advisors

Brings vast entrepreneurial and political experience to role on board

On October 9, Dr. Robert C. Gallo, director of the Institute of Human Virology (IHV) at the University of Maryland School of Medicine, announced that Mr. Terry Lierman is the new Chair of the Institute's Board of Advisors. Mr. Lierman is renowned on Capitol Hill for his political skills as well as his passionate support of improved health care and funding for medical research, and was most recently the Chief of Staff to U.S. Rep. Steny Hoyer (D-Md.), currently the Minority Whip of the U.S. House of Representatives.

"Terry has an extraordinary commitment to health care and research, both as an advocate for patients and as the founder of a number of companies and organizations that focus on the advancement of medical science," said Dr. Robert C. Gallo, who pioneered the field of human retroviruses with his discoveries of HTLV-1 and HTLV-2, co-discovered HIV as the cause of AIDS, and developed the HIV blood test that has saved many thousands of lives. "In addition, Terry has been frequently noted as one of the most influential persons in Washington, DC. I am looking forward to Terry's contributions to the Board as he applies his terrific leadership skills, vast entrepreneurial and political experience, and broad capabilities for problem-solving and bringing people together."

IHV is the first center in the United States to combine the disciplines of basic science, epidemiology and clinical research in a concerted effort to speed the discovery of diagnostics and therapeutics for a wide variety of chronic and deadly viral and immune disorders—most notably HIV. The unique structure of the Institute seeks to connect cohesive, multi-disciplinary research and clinical programs so that new treatments are streamlined from discovery to patient. Through the U.S. President's Emergency Plan for AIDS Relief (PEPFAR), IHV treats

more than 750,000 HIV positive patients in seven African and two Caribbean nations and implements training and prevention programs to develop and enhance PEPFAR countries' health care infrastructures. Locally, IHV also treats more than 5,000 HIV positive patients in Baltimore while scientific collaborations span the globe. The IHV Board of Advisors, along with the IHV Scientific Advisory Board, provides oversight and guidance to advance the interrelated missions of the Institute.

"I have had the privilege and opportunity to combine politics, policy, and management, and to create a wide variety of ventures to promote better health care," noted Mr. Lierman. "As the new Chair of the IHV Board of Advisors, I am thrilled to be able to support the exceptional work of Dr. Gallo and the world-class scientific and patient care teams at IHV as they seek breakthrough discoveries in medical science and create new models of patient care."

Mr. Lierman began his career in the health field at the U.S. National Institutes of Health (NIH) in 1971, where he assisted in budget and policy development, grants, and contracts. Over the last four decades he has combined his entrepreneurial and political talents in a variety of ventures from serving in leadership positions on the staff of the U.S. Senate Appropriations Committee, founding companies and non-profit organizations that advanced health care advocacy, to leading the Maryland Democratic Party. He is currently leading a new venture capital company, Health Ventures International, and chairing CSGI, Inc., the parent company of CTIS, a global health information technology company.

Mr. Lierman replaces former Maryland Lt. Governor Kathleen Kennedy Townsend as the Chair of the IHV Board of Advisors. Ms. Townsend will continue to serve as an active leader on the board.



About Terry Lierman

Terry Lierman began his career in the health field at the National Institutes of Health, where he assisted in budget and policy development, grants, and contracts. He then moved to the U.S. Senate Committee on Appropriations, where he was the Staff Director of the Labor Health and Human Services (HHS) Appropriations Subcommittee as well as the full Committee.

Mr. Lierman founded several companies and organizations, including the Children's Research Institute at Children's Hospital National Medical Center, National Coalition for Cancer Research, the National Organization on Fetal Alcohol Syndrome (NOFAS), and the Pancreatic Cancer Action Network (PANCAN). He was the Chair of the Maryland Democratic Party and served as the Chief of Staff to the House of Representatives Majority Leader and Democratic Whip Congressman Steny H. Hoyer.

Mr. Lierman is presently on Venture Capital Boards, President of Energy One, and the Founder of Summit Global Ventures. He now Chairs the Institute of Human Virology, and serves on the Boards of the GVN (Global Virus Network), as well as the Council for a Livable World and Peace PAC.

The Washington Post

A PEPFAR for D.C. and Baltimore

By Robert C. Gallo, Published: July 20

Since 2004, the **President's Emergency Plan for AIDS Relief (PEPFAR)**, which provides resources for prevention, treatment and training in the fight against HIV/AIDS, has been saving lives in more than a dozen underdeveloped countries, including many nations in Africa. With HIV infection rates in some U.S. cities reaching Third World levels, it is past time for a similar program targeting the communities with the highest rates of new infections in the United States. The return on investment would come not only in lives saved but in a reduction in overall health-care costs.

It is no secret that the HIV/AIDS problem in the Washington-Baltimore corridor is dire. An estimated 47,000 people live with HIV in the region, and there were close to 3,000 new cases in 2010. How can it be that our nation's capital region has infection rates that are comparable to those of many of the countries supported by PEPFAR? The answer is simple: We are failing to make full use of what we know works.

When my lab showed that HIV was the cause of AIDS and developed the blood test for the virus in 1984, I never would have imagined that in 2012 the infection rates in U.S. inner cities would be so high. That's why I am calling on President Obama and the U.S. Congress to create a domestic PEPFAR, to take full advantage of the power of diagnosis and treatment as part of a comprehensive prevention strategy to move us toward Obama's vision of an AIDS-free generation. With such a program in place for targeted regions of the United States, we can decrease new infection rates, build stronger links between patients and the care they need, and help people live longer, healthier lives on anti-retroviral medication.

Treatment for HIV has become a powerful tool in HIV prevention. By suppressing the virus with medication, people infected with HIV are far less likely to spread the disease. Nationally, however, less than a quarter of those with HIV infections achieve viral suppression. Worse, many who are infected remain undiagnosed, while others who are diagnosed do not receive care. As a result, the disease can spread.

We have a long way to go before we fully achieve the hope of treatment as prevention, but we have to start somewhere. Given all we now know about treatment, there is no reason for anyone living in the industrialized world to die from AIDS. But to begin the path towards an AIDS-free generation, the rate of new infections must fall.

The good news is that taking on this challenge will not be a burden as the country grapples with its budget problems. The Centers for Disease Control and Prevention estimates that a \$10 billion investment today will save \$66 billion over the long term. Currently, the cost to treat one new HIV infection is \$360,000 over the lifetime of the infected person. The 835 newly diagnosed cases of HIV in 2010 recently reported for the District added more than \$300 million to the long-term health-care costs of the city. Isn't it obvious? Not only do we have a moral obligation to combat the HIV epidemic here in the United States, but we have a fiscal responsibility as well.

Four years ago, in a 2008 Post op-ed, I noted that a domestic PEPFAR could also help enhance health-care infrastructure in our inner cities. Over the past decade, federal and state officials have allocated enormous sums to fight bioterrorism while Americans continue to die from AIDS. We need to recognize that investing in the infrastructure of our health systems to help neutralize the AIDS epidemic would, at the same time, strengthen America's ability to handle a bioterrorism attack, particularly in regions of the country that are medically and educationally disadvantaged.

Last year, Maryland Gov. Martin O'Malley and D.C. Mayor Vincent C. Gray requested that the president implement a domestic PEPFAR pilot program targeting the Baltimore-Washington region. I join them and again strongly encourage the Obama administration to support such efforts—but not to limit them to Baltimore and the District.

The writer, a professor at the University of Maryland School of Medicine, directs the Institute of Human Virology in Baltimore.

Grants & Awards



Wuyuan Lu, Ph.D., Professor, Institute of Human Virology, received a three year \$583,000 award from the National Institutes of Health entitled "High-throughput screening for HIV assembly and maturation inhibitors". The proposed research aims to develop a sensitive fluorescence polarization assay that can be automated for high-throughput screening for small molecule

inhibitors of dimerization of the C-terminal domain of the HIV-1 capsid protein. Such inhibitors may become additional weapons in the arsenal to fight HIV infection by specifically targeting HIV assembly and maturation.



C. David Pauza, Ph.D., Professor, Institute of Human Virology, received a two year \$422,000 award from the National Institutes of Health entitled "T-follicular helper cells in Env-immunized macaques." Current vaccines elicit transient protection against HIV but fail to sustain the durable immunity needed to stop epidemic spread of the virus. Our goals are to look for defects in fundamental steps in the process of generating long-term

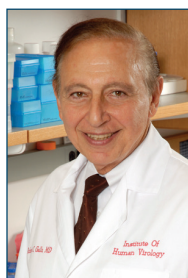
antibodies, that have not been evaluate in previous animal or human vaccine studies. We focus on T follicular helper cells (Tfh), which are required for the generation of B-cell memory. Tfh generation and function are impacted by exposure to HIV proteins including vaccine antigens. We are developing new strategies to mitigate the impact on Tfh that will increase the durability of protective immune responses against HIV.

C. David Pauza, Ph.D., Professor, Institute of Human Virology and Xiaoping Zhu, DVM, Associate Professor, University of Maryland, College Park are Multiple PIs of a four year \$3,032,000 award from the National Institutes of Health entitled "FcRn-targeted mucosal HIV vaccine." Subunits of HIV are ineffective for immunization across mucosal surfaces due to poor uptake or inactivation. To overcome this obstacle, we are exploiting properties of the Fc receptor neonatal (FcRn), a natural transport receptor for moving antibodies across mucosal barriers. Fusion proteins consisting of HIV envelope glycoprotein gp120 and the Fc segment from IgG, transit mucosal epithelial cells via FcRn, and are delivered to underlying antigen presenting cells and lymphocytes. Fusion proteins are covalently modified with adjuvant for efficient co-delivery across the mucosal barrier. Novel fusion proteins carrying their own adjuvants may be effective vaccines against HIV immunity and could be used for a broad spectrum of pathogens which enter through the mucosal route.



Hau Cheng, M.D., Associate Professor, Institute of Human Virology. Dr Cheng, is a new PI to IHV since July 2012. He brings a two year grant from the National Institute of Allergy and Infectious Disease entitled titled, "Linking IKKbeta activation to anti-autophagy in viral protein Tax-mediated oncogene".

This research focus on determining the critical steps of HTLV-1 Tax in deregulating autophagy during T cell transformation. Increasing evidence shows that dysregulation of autophagy by oncogenic viruses plays a key role in cell transformation and tumorigenesis. This data provides insights into the role of the viral oncoprotein Tax deregulated autophagy in T cell transformation. The role of lipid rafts in Tax-mediated autophagic process will enhance knowledge on autophagy regulation at pathological conditions.



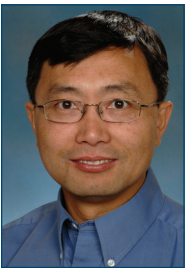
Robert C. Gallo, M.D., Professor and Director, Institute of Human Virology, received second year funding in the amount of \$1,000,000 from the Henry M. Jackson Foundation (the US Army Medical Research & Material Command for the Advancement of Military Medicine) entitled "Safety and Immunogenicity of FLSC". The Military HIV Research Program (MHRP) in collaboration

with the Institute of Human Virology and Profectus Biosciences will evaluate the safety and immunogenicity of the full length single chain (FLSC) subunit prior to evaluating combinations with either an ALVAC-HIV (V cp1521) Prime, or a new ALVAC construct expressing FLSC.

Robert C. Gallo, M.D., Professor and Director, Institute of Human Virology and Davide Zella, Ph.D., Assistant Professor, Institute of Human Virology, received a one-year \$220,000 grant from the ForST Foundation (Rome, Italy) entitled "Analysis of the Effects of H2S as a Major Component of the Thermal Waters on Endothelial Functions During Mycoplasma Infection". The goal of this study is to investigate the effects of exogenous H2S on endothelial cell biology in vivo and in vitro cell models infected with M. fermentans and to investigate the effects of exogenous H2S on pro-inflammatory molecules levels and endothelial cells/leukocytes interaction.



Anthony L. DeVico, Ph.D., Professor, Institute of Human Virology, received a two-year \$107,822 subrecipient agreement from Dr. Siba K. Samal, University of Maryland, College Park entitled "Newcastle Disease Virus Vectors HIV Vaccine". This funding is from NIH/NIAID and Dr. DeVico will provide expertise and guidance on HIV envelope structure, antigenicity and immunogenicity.



Yongjun Guan, Ph.D., Assistant Professor, Institute of Human Virology, received a one-year \$71,708 subrecipient agreement from Dr. Zhixin Zhang, University of Nebraska Medical Center entitled "Accumulation of VH Replacement Products in HIV Patients". This funding is from NIH/NIAID and Dr. Guan will perform ELISA assays and HIV neutralizing antibody analysis to determine if

the enriched VH-replacement products encode anti-HIV-1 or HIV neutralizing antibodies.



Lai-Xi Wang, Ph.D., Professor, Institute of Human Virology, received a two-year \$422,125 grant from NIH/NIAID entitled "Synthetic Variable Domain Glycopeptides for Neutralizing Epitope Characterization". HIV/AIDS is a serious global epidemic that threatens human health and social stability. The goal of this research aims to characterize the neutralizing epitopes of broadly

neutralizing antibodies, which will provide important insights in HIV-1 vaccine design.



William A. Blattner, M.D., Professor and Associate Director, Institute of Human Virology, received a five year \$2,500,000 award from the Centers for Disease Control and Prevention entitled "Nigerian Alliance for Health Systems Strengthening (NAHSS)" to build capacity in the area of sustainable clinical quality in Nigeria. Dr. Blattner is partnering with Healthqual International, IHV Nigeria, Solina Health and GHIL, Ltd.

to develop NigeriaQUAL, an innovative, technical quality improvement program that equips both tertiary, secondary and primary sites and state and local government to make data driven decisions to improve patient care. NigeriaQUAL will bring quality management, quality improvement and performance measurement to the clinic level through Quality Improvement

Teams that employs the Plan, Do, Study, Act cycle that identifies gaps, analyzes problems and develops interventions to solving challenges at the clinic level.

William A. Blattner, M.D., Professor and Associate Director, Institute of Human Virology, received a three year \$2.9M award from the National Institute of Health entitled TRUST. TRUST is a prospective cohort study that employs a network-based recruitment strategy to link Nigerian Men having Sex with Men (MSM) to prevention and comprehensive HIV medical services. The study will evaluate Respondent Driven Sampling (RDS) as a recruitment tool, define barriers to HIV counseling and testing and service engagement for MSM, and quantify acceptability of test and treat practices. Additionally, TRUST will measure optimal service delivery models for this most at risk population. The outputs of the TRUST include an expanded understanding of the extent of MSM social and sexual networks, the drivers of risk practices, and the assessment of the quality of HIV and medical services delivered in a nontraditional venue.



Robert Redfield, M.D., Associate Director, Institute of Human Virology, Professor of Medicine, Director of the Infectious Diseases Division, the University of Maryland School of Medicine, received a five-year \$ 3,823,159 subcontract from the African Medical and Research Foundation under a cooperative agreement grant funded by the United States Agency for International Development ("USAID"), entitled, "APHIAplus

IMARISHA Project in Kenya". Under this award, IHV will work to increase the demand for and availability of an integrated package of quality high-impact interventions at facility levels. This support will be provided to the Northern Arid Lands region with approaches within the region tailored to the individual counties of Marsabit, Isiolo, Samburu, Garissa and Tana River.

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Complimentary copies are available upon request.

Questions/Comments?

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William Blattner, MD



Blattner and Redfield Build HIV/AIDS Business Model in Africa and Caribbean

IHV Engages Globally in the Largest Public Health Initiative

In October, William Blattner, MD, and Robert Redfield Jr., MD, associate directors and co-founders of the Institute of Human Virology (IHV) and professors in the Department of Medicine at the School of Medicine, were named the 2012 UMB Entrepreneurs of the Year.

On Tuesday, Oct. 23, Drs. Blattner and Redfield, joined by IHV director Dr. Robert Gallo, School of Medicine Dean Al Reece and University President Jay Perman, described their experiences at an event from 4 p.m. until 6 p.m. in the University of Maryland BioPark conference center. They detailed their success in building a sustainable business model and infrastructure in nine African and Caribbean nations, and treating nearly 500,000 patients with antiretroviral medications and close to 3 million people with prevention interventions and HIV testing.

A foundation of their social entrepreneurship success is a high-impact service delivery model that has trained 35,000 in-country health care professionals who have delivered more than 100 million doses of medication.

In uncharted waters, Blattner and colleagues in the IHV established the Institute of Human Virology Nigeria (IHVN) not for profit corporation as the mechanism that allowed \$294 million in grant funding to the University in the last nine years. The impact of this effort is best measured in the clinical care, treatment, and prevention services to 944,004 Nigerians who were

counseled and tested for HIV; 896,555 mothers who were screened to prevent infections of their babies; 139,857 patients who received antiretroviral therapy; and 22,639 health care workers who were trained. The partnerships developed with the IHVN and multiple Nigerian universities position the University of Maryland, the Institute of Human Virology, and the School of Medicine for sustained benefit to our global research, clinical, and educational mission.

Since 2004, the IHV's Division of Clinical Care and Research, under the leadership of Redfield, has been awarded more than \$189 million for the development of a consortium known as AIDSRelief. Redfield has built dedicated teams of more than 200 faculty and staff who are providing emergency response training, building local health care capacity, and strengthening key institutional partners in Ethiopia, Guyana, Haiti, Kenya, Nigeria, Rwanda, Tanzania, Uganda, and Zambia.

These teams are committed to making a sustainable impact on current global health priorities, providing care and treatment for more than 500,000 people, making a significant overall contribution to the U.S. PEPFAR (President's Emergency Plan for AIDS Relief) program. The PEPFAR is the largest public health program in global history, now operating with a budget of \$48 billion. Based on the success of this business model, Redfield's teams have been awarded 24 additional international grants.

Robert Redfield Jr., MD

