



Measuring the Progress of Immune Reconstitution in HIV Disease

In 2013, persons with HIV have access to antiviral therapy able to control disease. Most patients achieve virus suppression, or recovery of their CD4 T cell count disease symptoms. Many researchers are now looking beyond the status quo to imagine strategies for disease-free survival without prolonged therapy, affording a cure for HIV. However, HIV disease is a combination of ongoing virus growth and accumulated immune deficits. The Institute of Human Virology's (IHV) David Pauza believes that "cure" must account for both aspects of HIV disease, eliminating virus growth and repairing damage done to the immune system.

The process of regaining immune system capacity during prolonged therapy is known as immune reconstitution. The extent of immune reconstitution is often measured by rising CD4 T cell counts and better responses to vaccination and improved resistance to common infections among most patients. For a small fraction of patients, immune reconstitution is slow or not apparent even with potent antiviral therapy. Even when CD4 counts and immune responses to common vaccines come back during treatment, we do not know whether patients can regain a capacity for natural control over HIV, using their own immune system and independent of antiviral drugs. To understand how immune reconstitution is controlled, why it does not occur in some cases and how we can rebuild immunity and acquire control of HIV, Dr. Pauza believes we need to study biological mechanisms underlying the response to treatment.

Two very distinct theories were proposed to explain increasing CD4 T cell counts during antiviral therapy. Nearly two decades ago, it was suggested that the small population of CD4 cells present when treatment was started, could increase in numbers and account for immune reconstitution. However, the immune system relies on complex cell populations capable of responding to complex threats in the environment. Immune reconstitution based on growth of pre-existing cells would increase the CD4 count, but not recover lost functions. Some immune deficits, perhaps anti-HIV responses, might never recover if that

continued on page 4

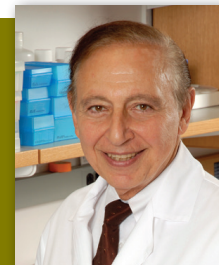
Director's Message:

This year is the 30th year since the period between 1983-1984 representing the

original publications describing a new retrovirus later called HIV, and papers showing HIV as the cause of AIDS.

The first scientific contribution to the field was the epidemiology carried out principally by U.S. Centers for Disease Control (CDC) and the description of the disease by clinicians. This gave rise to laboratory scientists including our own group focusing on the possible etiology of the new disease.

The papers in this period provided the most important step forward, namely, identifying the causative agent and convincing the scientific community globally that HIV was the cause of AIDS. On the practical side, the first practical contribution from the field of laboratory HIV research was the development of the blood test. The development of the blood test not only preserved our blood supply preventing blood transfusion-associated HIV infection, but it also enabled public health officials and physicians to follow the disease for the first time. Previously, of course, they could only follow it by waiting for patients to fully



continued on page 2

Director's Message continued

develop AIDS. Thus, the epidemic could now be scientifically studied for the first time.

But that is not where the practical advances from the blood test ended. It also provided a system where we could continuously grow the virus in tissue culture cell lines for drug testing and indeed AZT (see later) came soon thereafter (by testing in the system). Still another major contribution of the blood test is that it enabled verification. We knew at that time that if we were left only to isolating the virus, verification would be very difficult. And, for most of us, verification is essential for being able to move a field. As I once heard, "It is not the first to wave a flag, but who moves a field."

Why was this the case? In order to link the virus to the disease by virus isolation it would take a large number of patients – our group and the Pasteur group eventually did that very thing, but it would take more than a couple of groups carrying out a number of isolations which would be specific to AIDS patients or people in high-risk groups. The reasons for this were easy to foretell. First, material from patients with AIDS was not widely available. Second, material was not even allowed in some institutions because of fears. Third, many laboratories wouldn't work on it because of additional fears of infection. Fourth, by the time a person had AIDS if one was to use their blood there was hardly any T cells left making it exceptionally difficult. Fifth, not many laboratories in the world were custom to the utilization of IL-2, which we had found in, and reported in, 1976. It was principally a tool of immunology labs and in just a few virology laboratories. Growing T cells in culture from primary sources was essential for the isolation of the virus. We could calculate then that verification was unlikely to come this way. But in striking contrast, the blood test was simple, safe, sensitive, highly reproducible, inexpensive, and rapid, the result of that was confirmation globally almost overnight. And, for the first time there was almost uniform agreement of the cause of AIDS by the late spring of 1984.



Dr. Robert Gallo gives special remarks as Guest of Honor this past May at a conference entitled "30 Years of HIV Science: Imagine the future" held in Paris. The event was attended by the world's top HIV/AIDS researchers and was co-hosted by the National Institutes of Health and the Institut Pasteur.



IHV Board Chair Terry Lierman, Dr. Grant Colfax, Director of the Office of National AIDS Policy at the White House, Dr. Robert Gallo and IHV Associate Director Dr. William Blattner during a White House visit to the IHV this past spring.

The second practical advance coming forward from laboratory-based research on HIV and AIDS was therapy. As indicated above, the continuous cell line production of virus was used to test drugs – beginning with Burroughs Wellcome supply of several nucleoside analogues, AZT was found by Sam Broder working in Marv Reitz's laboratory in my group. Marv is now in IHV's Basic Science and Vaccine Development Division. Broder and his Japanese postdoctoral colleague, Hiroaki Mitsuya, were then able to bring this to the clinic while Broder and Bob Yarchoan of NCI carried out the first clinical trials. AZT was no panacea, but it opened the doors to the pharmaceutical industry. Many companies came rushing in supplying additional nucleoside analogues and non-nucleoside analogues that block reverse transcriptase.

The third major advance was the development of protease inhibitors which when coupled with reverse transcriptase inhibitors allowed many clinical groups to show that it was really possible to make this infection highly controllable in people so they could live long lives for the first time. These are medically historical events because prior to AZT and the HIV field, there was really no strong evidence for any systemic antiviral drug. AZT had shown that even though not a perfect drug, a decline in virus was associated with a decline in signs and symptoms of virus replication.

For almost ten years now, we have been refining therapy adding more to the triple drug cocktail including new classes such as entry inhibitors and integrase inhibitors. Yet there has been no additional fundamental breakthrough that could affect people's lives from around the world because what is needed now is nothing less than cure and prevention.

Let me go to the positive things that have occurred. We will always need new drugs, because of resistance and toxicities, and new approaches are constantly going on including the ones I just mentioned. For prevention we have seen the wonderful results

continued on page 5

Preparing the Future: A Collaborative Community Model for the Nation

Preparing the Future is a program of the IHV's JACQUES Initiative

More than 330 students from medicine, nursing, pharmacy, social work, law and dentistry trained to date in a program that aims to address the goals of the National HIV/AIDS Strategy (NHAS).

In a city where one of every 40 people older than 13 is HIV positive, the Institute of Human Virology's JACQUES Initiative (JI) at the University of Maryland School of Medicine, Baltimore has mobilized a "model" program of unprecedented health, psychosocial, and legal resources called Preparing the Future (PTF) that could make HIV testing and linkage to care more routine and normalized, say federal officials.

A central component of PTF brings together students into teams from the University's dentistry, law, medicine, nursing, pharmacy, and social work schools to address the goals of National HIV/AIDS Strategy (NHAS), including identifying new infections of HIV and increasing access to care for people living with HIV, says Jamie Mignano, MSN, MPH, RN, Director of JI Development and Information Dissemination. The PTF program has so far educated and trained 334 students. Each student takes a basic HIV classroom course, then performs community service to test and counsel patients on seeking appropriate care and medications, says Neha Pandit, PharmD, Assistant Professor at the School of Pharmacy and one of the PTF instructors. At its current pace, the program will test more than 7,000 people for HIV in 2013.

The program is supported by a grant from Gilead Sciences' HIV FOCUS Program, for the JACQUES Initiative, which is in the Clinical Care and Treatment Division of the Institute of Human



Students from medicine, nursing, social work, and pharmacy work in interprofessional teams at "Community, A Walgreens Pharmacy" site.



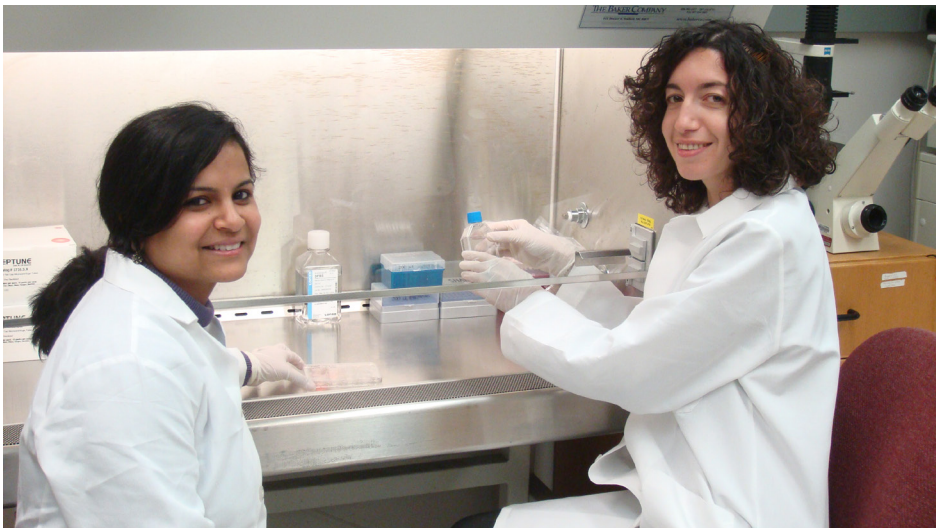
Alexandra "Allie" Reitz, JI's Academic Coordinator trains PTF students to document use the HIV Testing Encounter Form at "Community, A Walgreen's Pharmacy."

Virology (IHV), led by Dr. Robert Redfield. IHV's JI staff coordinate the didactic and hands-on curriculum for the PTF students, equip current providers to routinize HIV testing in their clinical practice and facilitate linkage to care for persons identified as HIV positive. The Director of the White House Office of National AIDS Policy, Grant Colfax, MD, says that such a "commitment to a multidisciplinary approach to fighting the epidemic could be a model for other communities across the country." The PTF is "about a lot of communication and a lot of community," says Pandit. "And it is about explaining to patients what it means to be on medications, to stay adherent to medication, and what are some of the things that make the progression to good HIV care."

The program also includes the University of Maryland Medical Center, the hospital on the UMB campus. All patients admitted in the Department of Medicine are now routinely offered HIV tests, with streamlined linkage to care and supportive services, in partnership with JI. "The goal is to capture a good number of the patients with a potential of several thousand a year tested," says Mangla Gulati, Assistant Professor of Medicine, General Internal Medicine. "It is very timely and we have very engaged patients and very engaged residents who are very excited and open with the patients about it." PTF is also a good match with existing efforts in UMB's School of Dentistry, which has recruited both dental students and dental hygiene graduate students for the program. The School has operated the PLUS Clinic since 1989, where students work closely with faculty members to treat HIV-positive patients. Also, in partnership with the IHV's JI, the School has implemented protocols for offering routine HIV testing and linkage to care in its extensive public dental clinics. Valli Meeks, DDS, MS, RDH, Associate Professor, teaches students that proper infection control is vital for all patients, not just those suffering from HIV. And

continued on page 8

Measuring the Progress of Immune Reconstitution in HIV Disease *(continued from cover)*



Dr. Suchita Chaudhry and Dr. Christiana Cairo

model were true. A second theory argued that adult, HIV-positive patients retain some capacity to generate new T cells that can enter the blood CD4 population, increase the CD4 count and also increase complexity. This concept was unexpected because adults normally lose function of their thymus gland—the major source for new CD4 T cells, during early years of life.

Despite many studies, there was no clear proof for either mechanism of immune reconstitution and even less understanding about why some patients fail to reconstitute. Now, a publication from Dr. Pauza's laboratory directly addressed this question and provided for the first time, a definitive answer about the mechanism for immune reconstitution in patients treated for HIV disease. The paper "The gamma delta T cell receptor repertoire is reconstituted in HIV patients after prolonged antiviral therapy" by Drs. Suchita Chaudhry, Christiana Cairo and David Pauza of IHV, with our co-author Dr. Vanessa Venturi from Sydney, Australia, was published in the March 21 issue of the *Journal AIDS*.

For several years, Dr. Pauza's group in IHV's Basic Science and Vaccine Development Division has conducted intensive studies

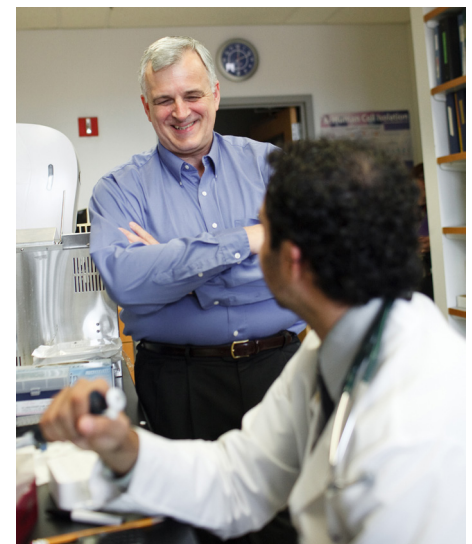
on a circulating T cell population known as gamma delta T cells. Much like CD4 T cells, each gamma delta T cell has a unique identifying structure on its surface known as the T cell receptor. Using DNA sequencing approaches, Dr. Pauza's group can measure the complexity of gamma delta T cell populations by counting the number of individual T cell receptor sequences found in blood samples from individual people. They reasoned that T cell receptor sequence data would allow them to discriminate between immune reconstitution by growth of pre-existing cells or new cell synthesis. Growth of pre-existing cells would not change the complexity of T cell receptor sequences, because new cells with new receptor sequences were not added to the population. If new cells are being synthesized, even at a slow rate, IHV scientists can recognize their contribution to increasing CD4 count and elevating complexity among T cell receptor sequences. Because of the way T cells are generated in the body, what is true for gamma delta T cells must also be true for CD4 T cells.

Working with Dr. Robert Redfield and Dr. Mohammed Sajadi from the IHV Clinical Division, Dr. Chaudhry obtained blood

samples from consenting, HIV+ volunteers who had reconstituted CD4 T cells after prolonged, successful antiviral therapy. Gamma delta T cell receptor sequences were determined by DNA sequencing and compared to similar data from age and gender-matched, uninfected control subjects. Because of the smaller size and lower complexity of gamma delta T cell populations, we needed only thousands of events or "shallow sequencing" of the T cell receptor pool. Due to unique features of gamma delta T cells, many individuals share common receptor sequences and we can evaluate the "health" of each individual gamma delta T cell receptor repertoire based on the presence or absence of these common sequences. Heavy number crunching to compare T cell receptor sequences among individuals was done in collaboration with Dr. Vanessa Venturi in Australia. Our data and extensive analyses, established similarities or differences between treated patients and uninfected volunteers.

Work from the Pauza group with Dr. Venturi, showed that immune reconstitution is accompanied by increasing complexity of T cell receptor sequences among gamma delta T cells. They did not find evidence for the simple model of immune reconstitution via growth of pre-existing cells. Because

continued on page 9



Dr. David Pauza

Director's Message continued (continued from page 2)



Participants of the "30 Years of HIV Science: Imagine the future" gather for a group photo this past May.

of Salim Abdool Karim and his colleagues in South Africa with microbicides demonstrating proof of principle and showing that under the proper education and medical follow up microbicides can indeed work.

On a wider scale today there is much more of a push for frequent testing and immediate therapy. This is certainly a good slogan to reduce or get rid of this epidemic—"Test, Test, Test, Treat, Treat, Treat." Indeed this is to say we are still on the hunt for a preventive vaccine. I do not believe that three of the four clinical trials were adequately thought through before they were initiated. The first vaccine trial left something to be desired since an unmodified gp120 almost always gives a type specific form of immunity. Thus, one is anticipating this would not be very effective. But at least in one major aspect it was in the right pathway, i.e. the development of antibodies to try to block infection right at the beginning. Two other trials using adenovirus were based on delivering viral genes within the cell and having them presented in the right configuration that stimulates killer T cells. This interesting approach has serious deficits, in that it allows infection to occur and supposes that the killer T cells will remove the remaining infected cells. Most of us would feel that this is hardly likely because infection is established in a day or two, and virus is spreading, variants are emerging and it would be unlikely that a CTL alone, approach could contain it.

Everyone knows about the U.S. Army Thai Trial (RV144) written about in these pages and everywhere else in the virological literature many times over. This trial clearly had a positive result but a modest one. As I see it, the trial could have been far more effective if the antibodies it induced could be maintained. There have been erroneous presentations including newspaper articles that the recent failed trial that was based on stimulating a cellular immune response was essentially the same as this Army trial in Thailand that gave partial protection. This is not the case—because, the Army trial also included an approach, as I've already indicated, that would induce antibodies, and I think they were inducing the correct kinds of

antibodies and one which we deliberately have been trying to develop as an IHV candidate vaccine for some years now (which is based only on induction of the right antibodies). I do not want to end the discussion of vaccines saying that we have the only approach or that the Army approach was the only approach. That is far from the truth. My own thinking is that there will be more than one pathway that could be successful. We think and we hope that we are on one of those right pathways.

There are also new developments that have occurred in France headed by Jean-Marie Andrieu which are very different, imaginative, and possibly important which need to be repeated. Right now those data are available only in primate studies, but the results were certainly unique and interesting. Finally, we have the exciting positive results of the microbicide trial conducted by Salim Abdool Karim and his colleagues in South Africa.

Can we cure HIV infection? That is to say, can we eliminate all virus from an infected person so that no therapy is needed, or at least can we reach a point where we are sure that therapy is no longer needed even if there are some residual small amounts of virus-infected cells? Much publicity has been given to the so-called Berlin patient and to the baby recently achieving a cure. However, there is no final proof that they are completely HIV-free. Rather, they have achieved (at least) a functional cure in that therapy is no longer needed. Both cases do not have much practical value for the entire field as far as I can see. Nonetheless, there are some molecular biological advances that make some approaches to a cure seem within the realm of possibility. In my view a practical removal of the epidemic will be the success of the "Test, Test, Test, Treat, Treat, Treat" notion described above and the full testing of the vaccine candidates that are based on good rationale. The "cure" will likely occur from the molecular biological approaches that lead one to the theoretical possibility of a cure. This will be a discussion in more detail in a future Discovery publication.

IHV to Partner with Russia and Global Virus Network for 15th Annual International Meeting



Dr. Alexey Mazus

Alexey Mazus, MD is Chief Expert on HIV/AIDS for the Russian Federation and Head of the Moscow Center for HIV/AIDS Treatment and Prevention. One of eight federal centers for HIV/AIDS, Moscow Center is the largest and provides treatment and care for more than 25,000

patients with HIV, in addition to supporting HIV diagnostic services for the Moscow region. As the Chief Expert on HIV/AIDS for the Russian Federation, Dr. Mazus works to optimize HIV therapy and prevention for his country and leads efforts to guide the evolution of treatment practices. He kindly agreed to Co-Host the IHV International Annual Meeting with Dr. Gallo, and has been working closely with IHV Associate Director David Pauza, PhD to coordinate the scientific program and logistical support needed for this important event. The Annual International Meeting continues its commitment to cutting edge research on HIV/AIDS but with an expanded focus on other viruses of importance in human disease including hepatitis viruses, measles, influenza, Dengue fever, and Human T cell leukemia virus 1 discovered by Dr. Gallo. Dr. Mazus also will incorporate workshops on comorbidities of HIV/AIDS, a problem of increasing importance world-wide, that will be important to participants attending from all eight of the Russian Centers for HIV/AIDS Treatment and Prevention. Dr. Mazus looks forward to this meeting for the international exchange of ideas and information that will advance all of our efforts to combat HIV/AIDS and other human viral diseases.

As part of his commitment to this area, Dr. Mazus has agreed to head the Russian Center of the Global Virus Network, a growing international organization started by Dr. Gallo, and bring together leading virologists in his country to ensure their participation in this international effort to promote human health. Because he was willing to co-host the IHV Meeting and promote the development of GVN in Russia, the Annual International Meeting expanded the breadth of human viral diseases under discussion and incorporated a panel of virology experts many of whom represent or lead GVN Centers.

- 1. IHV is thrilled to partner with Russia's Ministry of Health to host its 15th Annual International Meeting in Moscow. Why did you decide to host the IHV and GVN meetings in Russia?**

The decision to hold the IHV and GVN meetings in the capital of Russia was not made by chance. From the very beginning of the epidemic the Moscow Government realized the significance and complexity of this challenge for the city healthcare. Compared to other regions of Russia, Moscow has quite a number of factors that affect the spread of HIV infection. Among these, include a complicated emigrational situation, social contrast of the population, and social behavior in the capital megapolis.

At the same time, some serious positive advances should be noted: considerable intellectual and financial potential, a well developed system of epidemiological control, an accessible system of outpatient and inpatient care for the HIV-infected patients, and an effective system of informing the population on prevention of HIV infection. Annually, the budget allocates considerable financial means ensuring the necessary provision of diagnostics and treatment to all categories of HIV-infected citizens, as well as preventive measures among healthy population.

Solid success has been achieved by the Moscow Healthcare system by strategic direction, such as prevention of mother-to-child (MTC) virus transmission. We managed to achieve the maximum coverage of the HIV-infected pregnant women with prevention programs, due to which over 97% of children of these women are born healthy. Nowadays we can speak about the attained stabilization of the epidemics growth rates in the city. Moscow is one of the more safe capitals in Europe according to the HIV incidence level.

At the same time we clearly realize that there is a long way to final victory over the HIV/AIDS epidemic. In this sense, the whole world looks with hope at the scientists working on the creation of the vaccine, and until then we have to provide decent quality of life for HIV-infected patients. Naturally, here we mean i.e. the creation of inexpensive, affordable and effective antiretroviral drugs. Considering the above, holding this meeting is absolutely justified.



- e. Ensuring safe blood donation and medical procedures;
- f. Creating conditions for the social support for HIV-infected people and their families.

A comprehensive system of medical care for HIV-infected has been created in the Russian Federation:

- a. A network of specialized medical institutions has been created (over 100 centers for the HIV prevention and control and over 1000 laboratories of HIV diagnostics);
- b. A Unified system of HIV/AIDS epidemic monitoring is working (Federal Government statistic monitoring); Medical surveillance, diagnosis and treatment of HIV-infected individuals is carried out in accordance with approved standards of the RF Ministry of Healthcare;
- c. The programmes of palliative care for patients with HIV infection have been introduced into practice: the joint prevention projects are being implemented in cooperation with public and non-governmental organizations.

Annually since 2006 (the launching of the “Health” project), from 23 to 25 million people are being examined for the detection and diagnosis of the human immunodeficiency virus-infected, which amounts to 16-17% of the population. Recently, as a result of the consistent work, the moderate development of the epidemic process is observed in the Russian Federation, which is characterized by the annual growth of new cases, not exceeding 7%, which is lower than the indices for the Central and Western Europe (8.1%—data of Euro HIV Index 2009).

2. Please discuss how Russia supports free government programs available to all persons with HIV upon the recommendation of their physician, including treatment administered through eight regional centers.

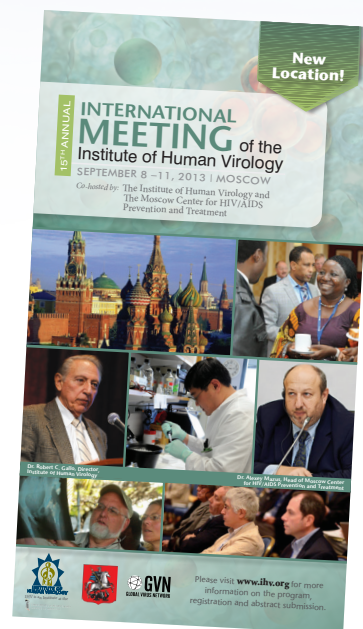
The RF Government, the Russian government and public organizations carry out realization of the global initiative on ensuring universal access to HIV prevention, treatment and care under HIV by 2010, which is supported by the Group of Eight, and the UN Joint Programme on HIV/AIDS. In the Russian Federation the main Government courses of HIV epidemic counteraction are determined by the priority national project in the field of Healthcare “Health” (HIV, hepatitis B and C prevention, detection and treatment of HIV-infected patients):

- a. Informative measures directed at HIV prevention among the various groups of population;
- b. Maintaining the high level of the population screening with the aim of the early detection of HIV infection and prevention of the further transmission of the infection;
- c. Ensuring 100% access to the medical care for the HIV-infected citizens of the Russian Federation with the application of the high technological methods of diagnosis of immune and virological status and provision of contemporary drugs;
- d. Support of measures directed at preventing MTC HIV transmission at all healthcare institutions of the Russian Federation;

3. Please describe the growth and development of HIV testing programs in Russia.

The task to achieve the maximum possible coverage of HIV testing has been set. Presently, 100% access to consulting and HIV testing has been provided for the population. The law determines the HIV testing is compulsory for:

- donors of blood, organs and tissues
- workers of certain professions: personnel providing medical care to HIV patients
- foreign citizens coming to the Russian Federation for the period over three months
- army recruits
- prisoners



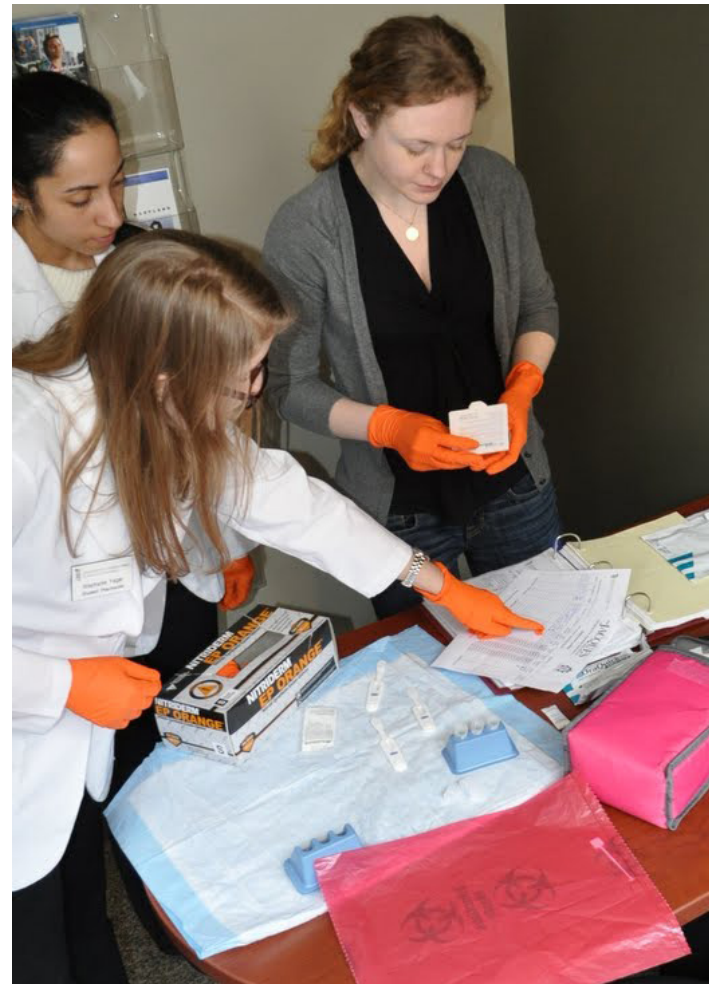
continued on page 9



Preparing the Future: A Collaborative Community Model for the Nation (continued from page 3)

Throughout the 2012-2013 academic year, teams of interprofessional students from all the schools have discussed thousands of cases with each other as they tested and counseled people at locations such as Walgreen's Community Pharmacy on Baltimore's busy downtown Howard Street. Recently, a delegation from the White House Office of National AIDS Policy visited the Institute of Human Virology on April 30 for an update on the University's innovative Preparing the Future program. Colfax, the Office Director, says he "very much enjoyed" the visit, adding, "I know [Preparing the Future] will continue to be an important partner as we implement the National HIV/AIDS strategy."

The JACQUES Initiative (Joint AIDS Community Quest for Unique and Effective Treatment Strategies) was initiated by IHV in 2003 in memory of Joseph William Jacques, PhD well known contributor to the field of HIV and AIDS activism.



PTF students run controls prior to initiating HIV testing for the day at "Community, A Walgreens Pharmacy."

Pharmacy student collects demographic information from individuals seeking HIV testing at "Community, A Walgreens Pharmacy."

she hopes that students in the PTF, as well as those in the PLUS Clinic, learn lessons in tolerance as well as dentistry. "I tell them: Before assuming you can't treat an HIV patient, look at the whole picture. . . . It is still a little bit of a stigma, but it is changing."

Indeed, the PTF is as much about creating broad awareness of HIV issues among all UMB graduates as it is about testing and helping patients, says Derek Spencer, MS, CRNP, Executive Director of the JI. "You have to expect the students to come in with their own biases. Many go through a transformation, a new openness. The questions they ask they couldn't ask before. We are making a big difference." Mignano says HIV "is a chronic disease that is treatable, like high blood pressure or diabetes. And students are learning how to address a public health crisis, that with treatment has potential positive impacts on the health of the entire community."

Through the PTF, the University's Francis King Carey School of Law contributes to a special a clinic held each Tuesday at the JACQUES Initiative by law students and preceptor attorneys. They meet with new HIV patients to discuss insurance, benefits, financial support, and more. Jeff Weaver, a Physicians' Assistant, says it is an "amazing" collaboration. "I tell them what I learned about the patient and they see the patient on the spot," Weaver says. "It is another professional side of HIV health. Every individual school and profession has their own ethical and professional background and they can come together and better help the patient."



Staff of "Community, A Walgreen's Pharmacy" located at 6 N. Howard Street. The group opens their doors to the community weekly for HIV education, testing and linkage to care by the PTF program.

Measuring the Progress of Immune Reconstitution in HIV Disease *(continued from page 4)*

gamma delta T cells and CD4 T cells derive from the same starting population and the behavior of one predicts the other, they are confident that their results are directly applicable to mechanisms for immune reconstitution of CD4 T cells; both depend on a slow, steady process of new cell synthesis even in adults with HIV.

Dr. Pauza's work provided proof for the role for new cell synthesis in immune reconstitution and created a quantitative approach for measuring changes in T cell population complexity during the course of antiviral therapy. This approach can also be used to study patients who fail to reconstitute CD4 cells. We need to know whether these individuals have slower rates of cell synthesis or their new cells do not survive in circulation. With quantitative approaches for measuring changes in T cell populations, IHV can tackle the need for designing and testing therapeutic strategies that will improve immune reconstitution for all patients with HIV.

The overriding question remains: Will HIV patients recover a natural ability for controlling HIV in the absence of antiviral therapy and how will we recognize this ability if it appears? New methods for evaluating immune reconstitution coupled with innovative treatments to increase this process, may repair immune responses to a point where they control HIV and contribute to a cure for this disease.

IHV to Partner with Russia and Global Virus Network for 15th Annual International Meeting *(continued from page 7)*

The voluntary HIV testing is offered according to the clinical indication:

- pregnant women (twice during pregnancy)

High risk group people:

- having multiple sexual partners
- having sex with sex workers
- having sex with IV drug users
- sharing syringes or needles
- using non-sterile needles for piercing or tattooing

HIV testing in the public system is free for all citizens.

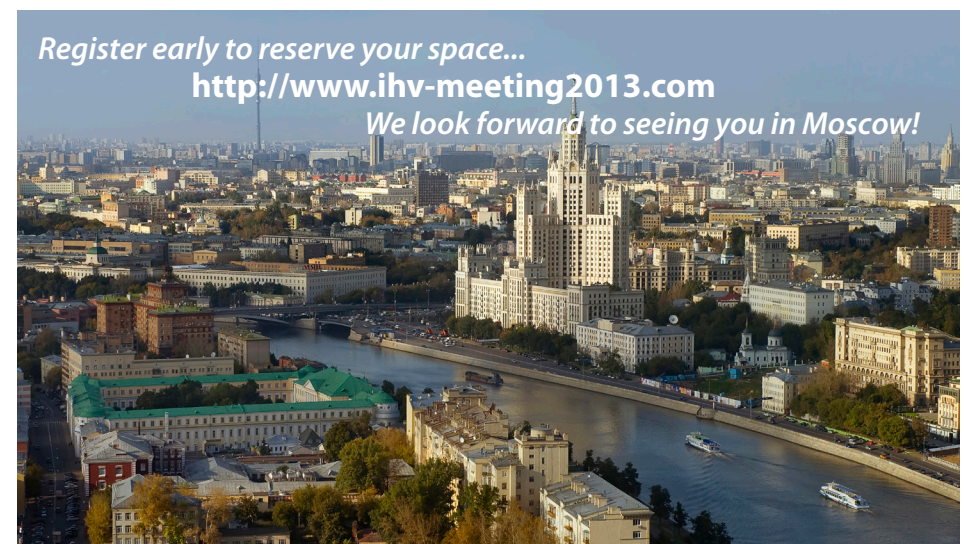
4. *What are the special challenges to implementing national HIV care in the Russian Federation?*

We come across with the same problems which exist in many other developed countries, but I would like to draw attention to the specific traits of our country. Despite the well-developed prevention system, it is necessary to strengthen the participation of voluntary public organizations in attracting and informing HIV-positive people (including people of the high risk groups) into the healthcare system.

Another problem is the necessity of the anti-retroviral drugs production in Russia, which will enable to reduce the cost of therapy and the pressure to the Federal budget (different levels of budgets). Further, there is a need to create funds for the support of HIV-infected individuals and private business participation in the programs of prevention, social and economic impact of the epidemics.

5. *What will the International Meeting accomplish for Russia and for the world?*

This truly outstanding meeting will serve to concentrate attention on the key problems and to put the right priorities of the scientific medical community. It will enable acceleration of the introduction of advanced technologies into practical medicine, and it will enhance the integration of home specialists into the international scientific medical community.





IHSV Board Members and Sharon Stone, pictured to the left.

Franco Nuschese, Sharon Stone, and Dr. Robert Gallo, pictured below.



Actress Meets IHSV Board Members

This year's spring IHSV board meeting was one to remember. President of Georgetown Entertainment and IHSV Board Member Franco Nuschese hosted the IHSV Spring Board Meeting at his restaurant, Café Milano, in the heart of Georgetown. Many celebrities are known to frequent the establishment, and on this night the IHSV Board met actress Sharon Stone.

Gray Recruits Gallo for Miami AIDS Walk



Dr. Robert Gallo and The Honorable Robert Gray

In April, IHSV Board Member Robert K. Gray hosted Dr. Robert Gallo in Miami as he participated as Grand Marshal of the 25th anniversary of AIDS Walk Miami, a 5K walk to benefit Care Resource, a community organization that provides

medical, dental, psychological, and other kinds of help to more than 15,000 people who have or are impacted by HIV or AIDS. Twenty-five years since the first Miami AIDS Walk Miami, Miami-Dade County ranks number one in the nation with the highest number of new AIDS cases per capita.

In a brief speech before the walk, Dr. Gallo spoke about the importance of testing and treating the epidemic, and the need for a U.S. strategy similar to that of the U.S. foreign program, the President's Emergency Plan for AIDS Relief (PEPFAR). More than a thousand people participated in the Miami Beach walk to raise funds for South Floridians living with HIV or AIDS.



Dr. Gallo interviews with local media

Malone and Townsend Share U.S. History



Dr. Sharon Malone



*The Honorable Kathleen
Kennedy Townsend*

Dr. Sharon Malone and The Honorable Kathleen Kennedy Townsend—together, you may know them as two of the key members that comprise the Institute of Human Virology's Board of Advisors. But those closest to them know of the unbreakable bond these two women and their families share through a period of American history never to be forgotten.

It was 1963—a year in which civil rights remained at the forefront of societal discussion, symbolized by civil rights activists being aggressively attacked in Birmingham with police dogs and merciless water sprayed from fire hoses. The date was June 11 and all eyes were pointed directly on the University of Alabama who were in the midst of monumental integration. Ms. Townsend's uncle, John F. Kennedy, was President of the United States and her father, Robert F. Kennedy, was the U.S. Attorney General. Alabama's then governor, George Wallace, widely known for his extreme segregationist and discriminatory platforms, had been court-ordered to cooperate with the enrollment of two African-American students to the University of Alabama. While the entire nation tuned in, John F. Kennedy's administration diplomatically diffused what had the potential to be a catastrophic event during America's civil rights movement. After George Wallace had issued a reactionary court order and devised a plan

to federalize the Alabama National Guard, Wallace begrudgingly stepped down and acquiesced to John F. Kennedy's stance in support of civil rights.

The two African-American students would be making prominent history, becoming the first African-American students to enroll at the University of Alabama. One of these students, Vivian Malone Jones, was the sister of our very own Dr. Sharon Malone. Ms. Jones, then a 20-year-old transfer from an all-black college, had the courage to venture into uncharted territory and in two years of stepping foot onto the school's campus, she became the first African-American to graduate from the University of Alabama.

Today, Dr. Sharon Malone and The Honorable Kathleen Kennedy Townsend serve on the IHV's Board of Advisors to, among other things, combat HIV and AIDS. They continue to further each of their family's long lasting legacies in support of the African-American community, who in Baltimore and across the nation, are disproportionately affected with HIV and AIDS.

The link they share is shaped by their past and their present. While they reflect on the legacies left behind by their families, they are working toward a better tomorrow, one that includes an end to deadly viral and immune disorders.

Awards & Grants

Award: In February 2013, **Dr. Robert Gallo**, Director of the Institute of Human Virology, was inducted as an honorary member of St. George's University (Commonwealth of Grenada) Gamma Kappa chapter of the Delta Omega Honorary Society in recognition of his enormous contributions to the field of public health. Dr. Gallo also presented the University's fifth annual Keith B. Taylor Memorial Lecture/13th Annual WINDREF Lecture.



Speaking on the topic "Viruses and Epidemics with a Focus on HIV/AIDS: Our Attempts to Control Them," Dr. Gallo provided an overview of viral epidemics that have swept the globe over the last century.



L to R: Dr. Cal Macpherson, Director WINDREF and Vice Provost for International Program Development at SGU, Dr. Gallo, and Dr. Omur Cinar Elci, Chair of the Department of Public Health and Preventive Medicine



Award: In March 2013, **Dr. William Blattner**, Associate Director of the Institute of Human Virology and Chair of the Baltimore Commission on HIV/AIDS Prevention and Treatment, was commended by Mayor Stephanie Rawlings Blake for his tireless dedication, compassion and leadership to the Commission.



Grant: **Dr. Lai-Xi Wang**, Professor, Institute of Human Virology, received a four-year \$1,197,300 renewal grant from NIH/NIGMS entitled "Convergent Chemoenzymatic Synthesis of Glycopeptides and Glycoproteins". The goal of the proposed research is to develop a general and highly efficient

chemoenzymatic method for making diverse omogeneous glycopeptides and glycoproteins of biomedical significance. The proposed study is expected to provide important new tools in chemoenzymatic synthesis and the knowledge gained will speed up glycoprotein therapeutic applications.



Awards: In March 2013, **Dr. Robert Gallo**, Director of the Institute of Human Virology, was honored as a Charter Fellow of the National Academy of Inventors. Later that month, Dr. Gallo was conferred an honorary degree from Xi'an Jiaotong University in China. This is Dr. Gallo's 31st honorary degree.

Discovery is published biannually. Complimentary copies are available upon request.

Questions/Comments?

Contact Nora Grannell, Director of Public Relations & Marketing, NGrannell@ihv.umaryland.edu

Editor: Nora Grannell • Design: mmgraph llc • Printing: Gasch Printing

Dr. Diane Griffin—Keynotes Greenebaum Annual Lecture



L to R: Dr. David Pauza, Dr. Robert Gallo, Dr. Maria Salvato, Dr. Diane Griffin, Mr. Stewart Greenebaum, Dr. Robert Redfield, Mrs. Marlene Greenebaum, Mr. Dave Wilkins, Mr. Michael Greenebaum, Dr. Joseph Bryant and Dr. William Blattner

The Eighth Annual Marlene and Stewart Greenebaum Lecture hosted guest lecturer, Diane Griffin, MD, PhD. Griffin is the Alfred and Jill Sommer Professor and Chair in Molecular Microbiology and Immunology at Johns Hopkins Bloomberg School of Public Health, The Johns Hopkins University. Griffin is also director of the Johns Hopkins University Global Virus Network (GVN) center of excellence.

With close to two hundred in the audience on November 11, Griffin's Greenebaum Lecture was titled "Virus Clearance: It Isn't Easy." Greenebaum, a close friend and IHV Board of Advisor member, sponsors this annual IHV series insisting that the key note speaker be someone who has made substantial scientific contributions, while caring for the betterment of the human condition.

IHV Welcomes New Board of Advisors Members



Peter Angelos is a renowned trial lawyer, nationally noted for his legal career representing those who have suffered from harmful products, medical malpractice, and personal injury. A former member of the Baltimore City Council, Angelos is perhaps best known to sports fans as the lead owner, Chairman and CEO of the Baltimore Orioles. A longtime proponent and

advocate for the City of Baltimore, Angelos was one of the first attorneys in the United States to accept and litigate asbestos cases, and he has made successful recoveries for thousands of workers and their families. He was chosen by the State of Maryland after a national bid process to conduct what became the State's successful lawsuit to recover billions of dollars for Maryland from the tobacco industry. Angelos has a long and diverse record of civic involvement, and has been widely honored for his commitment to higher education and charitable causes.



Mayor Stephanie Rawlings-Blake was sworn in as Baltimore's 49th mayor on February 4, 2010 and elected to her first full term as Mayor in November 2011. The Mayor has focused her administration on growing Baltimore's population by 10,000 families over the next decade by improving public safety and public education and by strengthening city neighborhoods. Additionally, Mayor

Rawlings-Blake was elected to a top leadership position in the Democratic National Committee to serve as Secretary, and serves in key leadership positions in the U.S. Conference of Mayors. Rawlings-Blake served as City Council President from January 2007 to February 2010. She was first elected to the City Council in 1995, at the age of 25—the youngest person ever elected to the Baltimore City Council. She represented the council's 5th District from 1995 to 2004 and the 6th District from 2004 to 2007, serving communities throughout West and Northwest Baltimore. From 1998 to 2006, Rawlings-Blake was an attorney with the Baltimore Office of the Public Defender.



Edward D. "Chip" Robertson, Jr. is the former Chief Justice of the Missouri Supreme Court. He is a partner at the trial law firm, Bartimus Frickleton Robertson and Gorny, and concentrates on appellate practice, complex cases, and litigation strategy. Robertson is involved in numerous national class actions, and serves as a mediator in other cases.



Ray Lewis was a first-round pick out of the University of Miami in 1996 for the Baltimore Ravens. He led the team to a Super Bowl victory in 2000, and was named Defensive Player of the Year that same season. In 2013, Lewis led the Ravens to another Super Bowl victory and retired in 2013. Lewis has been involved in charitable activities throughout his professional career,

including founding the Ray Lewis 52 Foundation - a nonprofit corporation whose mission is to provide personal and economic assistance to disadvantaged youth. Lewis is involved in pressing political, business, and philanthropic leaders for a stronger commitment to disability sports both in Baltimore and in the developing world. Lewis was honored with a JB award (named in honor of CBS broadcaster James Brown) during the 2006 off-season and received the "Act of Kindness" Award for his work in the community.



James P. Pinkerton has been a Contributor to the Fox News Channel since 1996 and is a regular panelist on "Fox News Watch," the highest-rated media-critique program on television. He is a contributing editor to The American Conservative magazine. In addition, he is the co-chair of the RATE (Reforming America's Taxes Equitably),

a group working to reform the US corporate income tax. He is also a consultant to the American Road and Transportation Builders of America, and has worked for companies and groups including BMW, the Auto Alliance, and AT&T. Earlier in his career, he worked in the White House domestic policy offices of Presidents Ronald Reagan and George H.W. Bush and in the 1980, 1984, 1988 and 1992 presidential campaigns. In 2008 he served as a senior adviser to the Mike Huckabee for President Campaign. He is a former columnist for Newsday, and is the editor of SeriousMedicineStrategy.org. He has written for publications ranging from The Wall Street Journal, The New York Times, The Washington Post, The Los Angeles Times, USA Today, National Review, The New Republic, Foreign Affairs, Fortune, The Huffington Post, and The Jerusalem Post. Today he also writes regularly for Foxnews.com. He is the author of What Comes Next: The End of Big Government-and the New Paradigm Ahead (Hyperion: 1995). Married to the former Elizabeth Dial, he is a graduate of Stanford University

IHV Remembers Two Prominent Board Members

Dr. Hilary Koprowski

(December 5, 1916–April 11, 2013)



Dr. Hilary Koprowski died at age 96.

This 1961 photo shows Dr. Hilary Koprowski, a pioneering virologist who developed the first successful oral vaccination for polio. Koprowski died April 11 at his suburban Philadelphia home.

Former IHV Scientific Advisory Board Chair, Hilary Koprowski, passed away April 11. He was a longtime chair and friend. Koprowski was a great virologist and immunologist formerly of the Wistar Institute, where he was its Director and where he made Wistar into an internationally renowned research center (during his tenure) on the University of Pennsylvania campus and affiliated with University of Pennsylvania. Koprowski created the world's first polio vaccine and an effective rabies vaccine. Most recently, he served as President of Biotechnology Foundation Laboratories, Inc., and Head of the Center for Neurovirology at Thomas Jefferson University.

Richard "Dick" Hug

(January 11, 1935–May 4, 2013)



Richard "Dick" Hug died at age 78.

Former IHV Board of Advisors member, Dick Hug died peacefully May 4. Most notably known for his political fundraising for three Maryland gubernatorial campaigns and his civic duties, Hug was an immense supporter of the IHV. He was a former member of the University System of Maryland Board of Regents and a 1956/1957 graduate of Duke University (BS, MF). Hug began his business career with Koppers Company, Inc. He was named a corporate vice president of Koppers in 1973. For the ensuing 22 years, he served as president, chairman and chief executive officer of Environmental Elements Corporation, a company specializing in air pollution control systems for the utility and industrial markets and listed on the New York Stock Exchange since 1991. In 1995, Mr. Hug retired but remained a director, principal stock holder and chairman emeritus until the company's sale in 2006. He has been politically active in recent years serving as finance chairman for the 1994 and 1998 campaigns of Ellen Sauerbrey and the 2002 and 2006 Maryland gubernatorial campaigns of Robert Ehrlich. Mr. Hug also served as Maryland's finance chairman for the Bush for President Campaign in 2000 and 2004, and was awarded "Pioneer," "Team 2000," and "Super Ranger" status during the campaigns.



**725 West Lombard Street
Baltimore, Maryland 21201-1009
www.ihv.org**



**The Institute of Human Virology is a center of the University of Maryland School of Medicine
and is affiliated with the University of Maryland Medical Center.**

For more information call 410.706.8614 or visit www.ihv.org

www.ihv.org for more information on the program, registration and abstract submission.'"/>

SAVE THE DATE!!

**Moscow, Russia
September 8-11, 2013
Radisson SAS Slavyanskaya Hotel**



Radisson Hotel in downtown Moscow, Russia.