



DISCOVERY



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HAITI and Redfield

It was 4:53 p.m. in Haiti on Tuesday, January 12, 2010 when the disastrous 7.0 earthquake struck Port-au-Prince, the country's capital city. In minutes, the city was leveled – an entire working government nearly wiped out under rubble. The already strained healthcare system was decimated as well. Two of the country's top nursing schools, students and their faculty were also lost in the earthquake's wreckage. 90% of the city's hospitals, including physicians, patients, medicine and equipment are still buried and entombed in debris. Basically, anyone in a building as the ground began to shift under them was working against life's odds, and those in makeshift housing in the outskirts of the capital region were beating those odds.

Fortunately, the Institute of Human Virology's (IHV) Haitian colleagues and local offices survived the earthquake. Since 2004, IHV – in partnership with Catholic Relief Services (CRS) and through the President's Emergency Plan for AIDS Relief (PEPFAR) – has been providing care and treatment to 30% of Haiti's HIV/AIDS

patients. Through the years IHV has trained and employed 18 national Haitians to diagnose and treat HIV/AIDS patients, educate the public on the pandemic, and implement other important public health initiatives based upon IHV's programs and mission.

Hit harder by the powerful tremor was Port-au-Prince's St. Francois de Sales Hospital as it was nearly unsalvageable following the mass calamity. St Francois is the largest private teaching hospital and a key partner with IHV in HIV care and treatment of patients and medical training for Haitian health care professionals. In



Dr. Guesly Delva checks on a woman whose leg was amputated. Dr. Delva, an infectious disease fellow from the IHV is part of the Maryland team to treat the injured at St. Francois de Sales, one of Haiti's oldest hospitals. As a native of Haiti, he felt compelled to return to his homeland to help. After looking at the injured in Port au Prince and working with patients, he says: "I feel a sense of desperation." There's so much to do. I know probably we're not going to have enough time or resources to relieve all of the pain or suffering."

the wake of the earthquake, 85% of the hospital was destroyed, 120 of the patients and medical

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DIRECTOR'S MESSAGE: Emotion Enters Biomedical Science - HAITI and Japan's Dr. Tokuda

Robert C. Gallo, MD

As virtually everyone in the world is aware, the suffering in Haiti has been unbearable. Numerous people and organizations across the world have tried to give their help in one way or another.

Whether assisting in country or from the other side of the world, it will never be enough relief.



Nonetheless, the University of Maryland, Baltimore should have a sense of pride for the great work done by IHV's team in Haiti led by IHV's Dr. Robert Redfield (Associate Director of IHV and Director of the IHV Clinical Care and Research Division) and the University of Maryland Medical Center's Shock Trauma team led by Dr. Thomas Scalea.

IHV's presence in Haiti precedes the January earthquake. For over six years, our work in Haiti led by Dr. Redfield and individuals of

his staff, in partnership with Catholic Relief Services (CRS), has helped treat and care for HIV infected people through the President's Emergency Plan for AIDS Relief (PEPFAR) funding of approximately \$614 million over 10 years. IHV-AIDSR relief provides technical stewardship of the overall program in two Caribbean and seven African nations including Guyana, Haiti, Ethiopia, Kenya, Nigeria, Rwanda, Tanzania, Uganda, and Zambia. As a faith-based consor-

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DIRECTOR'S MESSAGE *Continued from page 1*

tium, AIDSRelief builds upon on-the-ground faith-based health networks to treat poor and under-served populations with lifesaving anti-retroviral therapy (ART). Additionally, Redfield and his staff have been training about 20 Haitian nationals to diagnose and treat HIV/AIDS – which as many know can only be treated by infectious disease specialists familiar with that region's strain of HIV/AIDS and the population's adherence, or lack thereof, and specific ART drug therapies.

Needless to say Redfield immediately felt the need to visit our various clinics in Port-au-Prince following the massive quake. He has spent time in Haiti's capital city during the midst of this catastrophe and Redfield and his staff have given of themselves generously. When Redfield came back from Haiti, I asked him to tell us about his experiences. I cannot retell those stories in this article, but I can testify that they were numbing and unimaginable in the magnitude of their horror. Those of us at IHV have been very proud of Redfield and his team for their clinical work, clinical investigations, and for their role in the PEPFAR program in bringing ART to developing nations, but at no time were we prouder than learning about their continued efforts during this Haitian tragedy.



Dr. Tarao Tokuda

Very separate but somewhat related to this story for its pull on ones emotions, were the experiences I had on my recent trip to Japan. During this visit, I lectured in different cities across Japan. At the end of the trip I had the opportunity to meet the sponsor of this trip, who also happens to be an asset to the foundation of Japan's health care delivery system, Dr. Tarao Tokuda (Tarao means "tiger" in Japanese). Dr. Tokuda's story is one that can give hope and inspiration to anyone.

Born relatively poor in a southern island of Japan, Tokuda witnessed his brother die of an infection. Tokuda learned later that the



Dr. Robert Redfield, Associate Director of the IHV, and Catholic Relief Services Chief of Party, Anna Van Rooyen, look over a patient's x-ray at the St. Francois de Sales hospital in Port-au-Prince, Haiti.

PHOTO BY SARA A. FAJARDO/CATHOLIC RELIEF SERVICES

infection would have been curable if doctors were available to his poor family in his remote village. As a young teenager, Tokuda decided he would devote his life to ensuring people in poverty had equal opportunities to medical care. His parents sold land to help pay for his continued education and fulfill his goal of becoming a doctor and bringing medical care to the poor by forming hospitals with unique missions. Tokuda's dream came true after placing his life's future in the hands of fate and borrowing money against life insurance. And so it began. One hospital succeeded and led to the construction of another and another, and so on. Tokuda began fulfilling his mission that no one would be turned away no matter how poor.

I knew of Tokuda's self-sacrificing journey in life before I met with him in Japan. I also knew Tokuda was suffering from amyotrophic lateral sclerosis which left him without speech, but with sight. He is also paralyzed, even unable to swallow. During our meeting, he had an "interpreter" who watched Tokuda's eyes as he focused on something like an alphabetical chart to interpret and then communicate with others. But I wasn't prepared. Being in his presence while his assistants helped him bear his physical pain, was

surreal. After introductions, he began to tell me his philosophy, his story.

Takuda said that he believes God has purposely kept him alive with this disease for the past 7 years (despite usually causing fatality at 1 to 2 years) so he can continue to grow his work around the world, including North Africa and the poorer countries of Eastern Europe. After sharing his philosophy on his life, I thought to myself that Tokuda is a true philanthropist. Later, I visited the Tunisian embassy in Tokyo and heard first-hand about the extraordinary work Tokuda performs in their country. As I was leaving, I noticed Tokuda never lost his glowing smile. His good-bye words were, "God keeps me alive because he knows I have many more things to do."

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Dr. Anthony Amoroso of the IHV works with St. Francois de Sales hospital residents in Port-au-Prince, Haiti.
PHOTO BY SARA A. FAJARDO/CATHOLIC RELIEF SERVICES

staff were buried alive, and most of the hospital equipment and supplies were lost. Members of the IHV/CRS team working with the St. Francois Hospital staff pulled 35 surviving patients out of the rubble and began to re-establish the hospital in the courtyard just outside of the demolished St. Francois site.

Dr. Robert Redfield, Director of Clinical Care and Research and Associate Director at the IHV said, "This earthquake is clearly the greatest loss of human life in history. In addition, several hundred thousand people sustained several fractures and trauma related injuries which required urgent surgical attention."

Within a week of the earthquake Dr. Guesly Delva, an IHV Infectious Disease Fellow, and Dr. Martine Etienne, Director of Community Based Treatment Support Services for IHV-AIDSRelief, went to Haiti to locate family members and begin to organize the University's medical response team. Dr. Redfield followed several days later with Dr. Andrew Pollak, Associate Professor of Orthopedics and Chief of the Division of Orthopedic Traumatology, to further assess how the IHV and the University of Maryland Medical System could best help at the time of crisis. After touring devastated IHV-AIDSRelief clinics in Port-au-Prince, the team developed

a response plan that led to the deployment of weekly medical teams since January 28. Due in large part to IHV's existing relationships in country, a collaborative team of 22 health care professionals from the University of Maryland School of Medicine/IHV and University of Maryland Shock Trauma Medical Center were the first team of relief workers sent to Haiti.

IHV's Dr. Anthony Amoroso, also a member of the relief team said, "For the first two days we organized the hospital into traumatic triage, admission, outpatient follow-up and pre and post operative care, and had the operating rooms cleaned and functional. By the second day surgeries were being performed and I'd say around 100 patients were brought in from the street and surrounding camps with large ulcerative traumatic wounds, gangrene, and fractures with minimal or no previous care; and this was a full 3 weeks after the earthquake." Amoroso continued, "It was an experience of a life time and I am grateful to have been given the opportunity to help. It also was physically and mentally exhausting but I'll be going back in April."

Only a few health emergency aid organizations including the University of Maryland, Baltimore team committed to a long-term presence to sustain the desperate need for immediate and on-going medical care. While it is admirable that many organizations are entering Haiti and performing life-saving procedures in the short-term, many patients are returning to hospitals post-surgery with severe infections due to the lack of continuity in care. UMB teams, including Dr. Redfield's IHV team, will donate their time away from their own families to ensure Haitians receive the proper medical care they so desperately need for survival.



Dr. Robert Redfield, Associate Director of the IHV, hands out lollipops to young patients at the St. Francois de Sales Hospital in Port-au-Prince, Haiti.
PHOTO BY SARA A. FAJARDO/CATHOLIC RELIEF SERVICES



University of Maryland Shock Trauma Center orthopedic surgeon, Cullen Griffith, right, helps to wheel a patient to the salvaged radiology department at St. Francois de Sales hospital in Port-au-Prince, Haiti.
PHOTO BY SARA A. FAJARDO/CATHOLIC RELIEF SERVICES



Hospital workers dig through rubble at the St. Francois de Sales hospital in Port-au-Prince, Haiti on Friday, January 15, 2010 in the aftermath of the 7.0 magnitude earthquake that struck earlier that week.

IHV Researchers Hunt for an Infectious Cause of Some Human Lung Cancers

Lung cancer kills more people than any other type of cancer. Although smoking is known to be the major cause of bronchial lung cancer, there are other forms of lung cancer. Epidemiological studies have found that HIV infection is associated with their increased risk, independent of smoking. This finding has led researchers at the Institute of Human Virology (IHV) of the University of Maryland School of Medicine to hypothesize that some lung cancers may have an infectious cause, and they are attempting to find such a causative agent.

"When HIV influences the incidence of cancer, most of the time it's turned out to be a viral induced cancer or at least a virus playing a role in that cancer," says Dr. Robert Gallo, Director of the IHV. "We became interested because of our long interest in viral oncology and because we are involved in a viral oncology at the University's Greenebaum Cancer Center, particularly with Dr. Martin Edelman, Director of Medical and Thoracic Oncology," he says. "It's not long ago that people thought no cancer had an infectious cause," but now it's estimated that between 20% and 25% of all cancers have a viral cause or a role with other factors, he adds.

HIV has previously been associated with certain cancers like Kaposi sarcoma and non-Hodgkin lymphoma. In both cases, the cancers are associated with the expression of tumor-inducing viral oncogenes, and their occurrence is dependent on immune system suppression that may increase the expression of latent viruses. However, the advent of highly-active antiretroviral therapy and longer life spans caused a shift from the occurrence of these AIDS-related malignancies to other types of cancer, including lung cancer. The increased incidence of these cancers has led researchers to search for their cause.

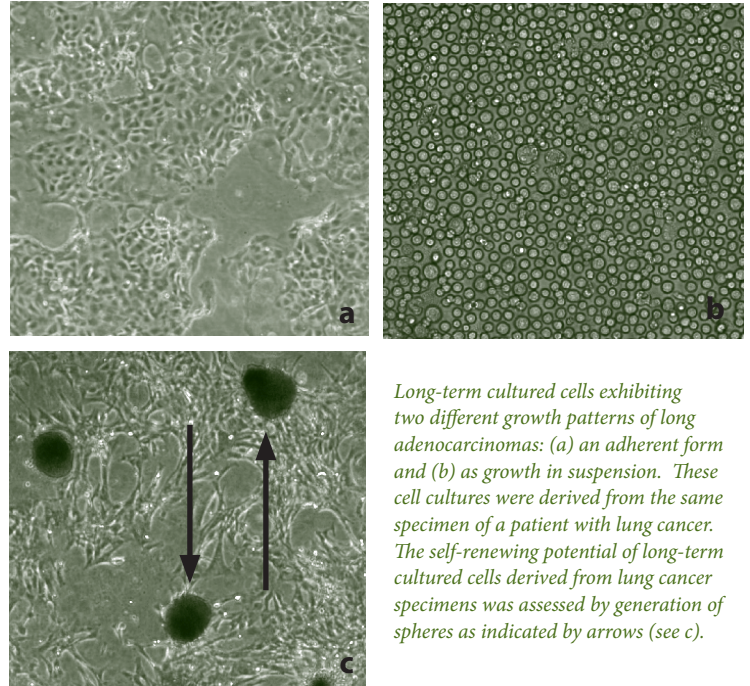
Apart from the association with HIV, another indication that there might be a microbial cause for human lung cancers came from a naturally occurring lung cancer in sheep, says IHV senior researcher Dr. Mika Popovic, who is conducting the study along with IHV's Director of Animal Models, Dr. Joseph Bryant, Gallo and other IHV scientists. It was discovered that this lung cancer is caused by Jaagsiekte sheep retrovirus (JSRV). Interestingly, JSRV-induced sheep tumors bear strong similarities to human lung cancer adenocarcinomas, leading IHV researchers to look for a similar infectious cause of human lung cancers.

To achieve their research goals, Popovic is extracting and culturing tumor cells from patients with lung cancer. "Virus infection frequently induces changes in the cells," he says. For example, viral infection can create giant, multinucleated cells, and as such Popovic identifies and cultures these cells before analyzing them for any infectious agents.

Apart from potential virus-modified cells, "Popovic is trying to pull out stem cell-like cells of the cancer," that are thought today to be the driving cells of the disease, says Gallo. These 'cancer stem cells' are thought to constitute just a small portion of tumor cells, but have stem cell-like characteristics that allow them to regenerate the whole tumor.

Once he has these cells, "the ultimate marker of a cancer stem cell is that you inoculate it into immunodeficient mice and see whether it generates a tumor," says Popovic. And so far, the cells he extracted have successfully generated human lung cancer tumors in mice.

Popovic has currently extracted cells from 5 patients with lung cancer,



Long-term cultured cells exhibiting two different growth patterns of long adenocarcinomas: (a) an adherent form and (b) as growth in suspension. These cell cultures were derived from the same specimen of a patient with lung cancer. The self-renewing potential of long-term cultured cells derived from lung cancer specimens was assessed by generation of spheres as indicated by arrows (see c).

and has established 3 cell culture lines. "We have short and long term cultures, as well as primary cultures for characterization, and that's where we are," he says. In the past "people have not had much success in culturing cells from lung cancer," says Gallo, but "Popovic has plenty of experience, talent, and the necessary patience to make advances." Now that Popovic has managed to grow them, "he's looking for different types of viruses," says Gallo.

Because of the link between JSRV and sheep lung cancer, the researchers definitely wanted to include retroviruses in their search, says Gallo. To identify retroviruses, Popovic looks for the expression of the viral enzyme reverse transcriptase, whose expression increases dramatically during retroviral infection. Popovic also uses polymerase chain reaction (PCR) to screen peripheral blood cells, mononuclear cells, or cells from pleural effusions extracted from patients. PCR is used to try to amplify regions of DNA specific for different viruses, including human papilloma viruses, Herpes viruses, Cytomegalovirus, and JSRV. According to Gallo, in the future the researchers could also sequence patients' genomes to look for any information in the DNA that might indicate a virus.

Once the researchers find a virus, they will need to characterize it and find out how it is associated with lung cancer. This would involve a combination of serological assays and molecular biology techniques. Among other things, to be associated with the disease a virus should be present in the lesions caused by the disease, says Popovic.

Finding a viral or other infectious cause for lung cancer would have a major impact on the treatment and prevention of lung cancer. "If we discover a virus that's novel, or we find an old virus and can link it positively to that kind of tumor, the implications would be obvious—anti-viral therapy, methods for early diagnosis, or prevention by vaccine," says Gallo.

New Peptides Could Lead to Better Anti-Cancer Therapies

Scientists are always trying to develop new strategies in the on-going fight against cancer and infectious diseases. Now researchers at the Institute of Human Virology (IHV) of the University of Maryland School of Medicine have synthesized novel compounds that may help specifically kill cancer cells by allowing p53, a key “tumor suppressor”, to be activated in them.

p53 is a key regulator of cancer in humans. It helps prevent tumors from developing by blocking the growth and killing of cells with damaged DNA, such as cancer cells. However, to its detriment MDM2 and MDMX are two proteins that bind to the p53 protein and help temporarily inactivate it. This is sometimes useful in preventing unnecessary cell death, but not when the cell has become a cancer cell. In this case, it will promote cancer development and spread.



Dr. Marzena Pazgier

In recent work, IHV researcher Dr. Marzena Pazgier and her colleagues in IHV Senior Investigator, Dr. Wuyuan Lu’s laboratory, synthesized 12-amino acid long peptides that help block the binding of MDM2 and MDMX to p53, reactivating this protein and leading to the death of tumor cells. These compounds may eventually lead to the development of novel anti-cancer drugs.

To identify peptides that bind to MDM2 and MDMX, the researchers used a phage display library. Random combinations of 12 amino acids were displayed on the outer capsule of bacteriophages, a virus which infects bacteria. The target protein, in this case MDM2 or MDMX, was incubated with the bacteriophages, and researchers identified the phages and therefore the peptides that bind specifically to the protein.

Amino acids can have two mirror image conformations, L and R. Initially the researchers looked for L-peptides, which are made up of L-amino acids, the conformation that’s found in our proteins. The researchers used the phage display library on the L versions of MDM2 and MDMX, and identified a potent inhibitor, PMI, that blocks the binding of p53 to those proteins.

However, “the problem with L-peptides is that they are unstable in human cells and can be degraded by proteases in the cells,” says Pazgier. This normally occurs in our cells with our normal proteins when they have been “cut” to the small size we call peptides. However, as a drug they are not very useful. To generate stable compounds that could eventually lead to anti-cancer drugs, Pazgier and her colleagues began to focus on D-peptides. “D-peptides are completely stable,” says Pazgier.

Creating these D-peptides was not trivial—the researchers had to screen a phage display library against the D version of the target protein. Unlike L-proteins, D-proteins can’t be made by bacteria, and have to be chemically synthesized from scratch, which is both difficult and costly, says Pazgier. “It’s only a few labs that can do this synthesis.”

However, Lu’s laboratory at the IHV had the technology and expertise to synthesize these proteins, and the researchers were able to use D-MDM2 to identify peptides that bound to it. They then created mirror images of the L-peptides, to get D-peptides that would work against the L version of MDM2, i.e., the natural state of MDM2..

Chemically synthesizing the proteins had other advantages too. “Synthetic proteins are much, much easier to crystallize than proteins, derived by other means,” says Pazgier (Figure 1). And the

best way check how a peptide works is to check its crystal structure with the target protein to see how they bind, she adds.

Figure 1. Crystals of the p53-binding domain of MDM2 (A) and MDMX (B) in complex with PMI

Both MDM2 and MDMX have a binding pocket where both p53 and the peptides bind, notes Pazgier, and the L-peptides and p53 bind very similarly, since they exist in the L form. However, the D-peptides don’t quite bind the same way, so a D version of PMI didn’t fit as well

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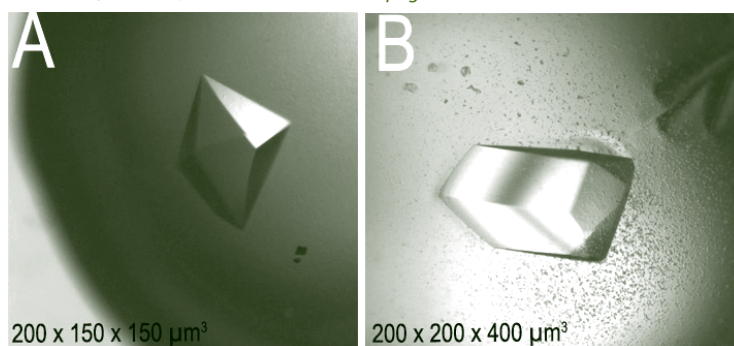


Figure 1

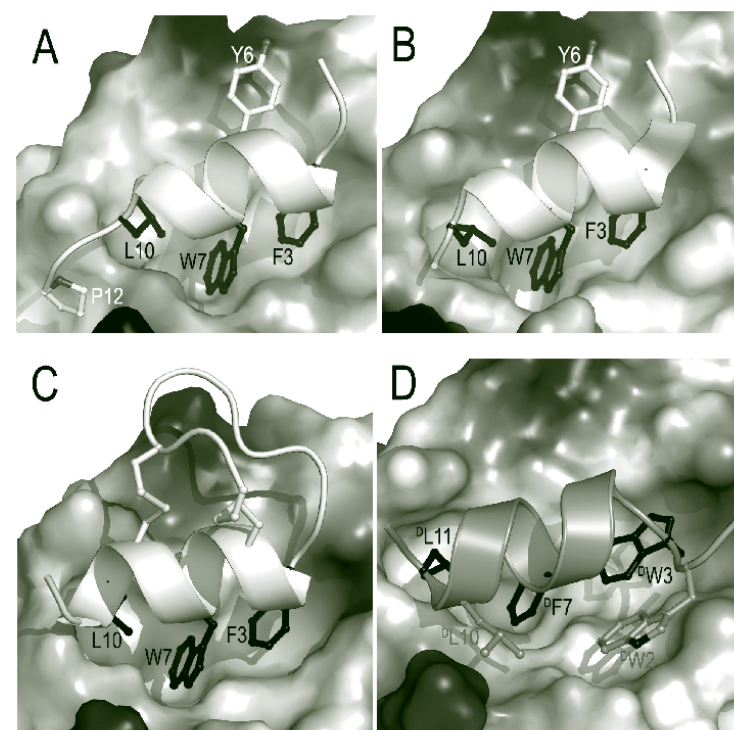


Figure 2

Gallo and Board Member Moynahan Descend Upon the Emerald Isle

By Dr. Rosarii Griffin, Director Centre for Global Development through Education Mary Immaculate College, Limerick, Ireland

On Wednesday 20th January 2010, the Graduate Entry Medical School hosted a public lecture by Dr. Robert Gallo, co-discoverer of the AIDS virus and director of the Institute of Human Virology (IHV) at the University of Maryland School of Medicine on the theme of 'Viruses, Epidemics and Putting an End to Deadly Diseases in the 21st Century' in the Jean Monet Lecture Theatre, University of Limerick. Dr. Gallo, speaking to a packed auditorium, gave a riveting lecture for over an hour and a half long, keeping his audience captivated and keen to learn more.

Dr. Gallo began his presentation by stating that he wished to concentrate the talk on the concepts around various viruses and epidemics, and on putting an end to deadly diseases in the 21st Century, rather than on the detail in respect of the 'science' of these viruses. Nevertheless, Dr. Gallo, fondly referred to as 'Bob' by his colleagues, gave a presentation with detailed information on both. Even for scientific neophytes, such as myself, Dr. Gallo was able to explain the most complicated and complex chemical equations and reactions, with the help of diagrams and graphs, reducing the complexity of his theories to simple comprehensible concepts for those who were not from a scientific background, but who nonetheless would be interested in the complexity of his discoveries.

Dr. Gallo began his talk explaining where the term 'virus' comes from (meaning 'poison'), how viruses are constituted molecularly and chemically, and then put the discovery of viruses in its historical and medical context. He then proceeded to explain the difference between Endemic, Epidemic and Pandemic citing a conversation he had earlier on in the week with RTE Radio One presenter Mr. Pat Kenny, and various issues raised there in relation to the Swine Flu 'pandemic.' Dr. Gallo believed the World Health Organization acted responsibly to threats of its spreading, against media criticism that it was driven by the pharmaceutical industry. He pointed out that it was a case of 'damned if you do, and damned if you don't' citing U.S. Department of State Secretary Hilary Clinton's visit to Haiti as a good example of this (if she didn't go, it would be perceived poorly, but the fact that she did go also generated criticism as the plane she travelled in could have been used to bring supplies to Haiti – illustrating Dr. Gallo's point beautifully).

Then Dr. Gallo went into more complex



(Top) Left to right: John MacNamara, Tim Moynahan, Rosarii Griffin, Robert and Mary-Jane Gallo
(Left) Mary-Jane Gallo and Tim Moynahan



detail in respect of the various viruses, the issues around their mutation, the use or otherwise of vaccinations, and the difficulty it can be to prove anything is the case unless one has a critical mass of evidence that one can safely say, 'yes, this is the cause of HIV-AIDS.' He also went on to show how the scientific establishment has been proved wrong on more than one occasion, particularly when it came to illustrating that viruses can and do contribute to, if not cause, certain cancers. And, by illustrating viruses particular 'make up' i.e. they have no metabolism, per se, so therefore,

one is struggling to come to terms with how to counteract, or prevent, their impact on other good cells' nuclei. The answer seems to lie in the prospect of developing an 'enveloping' vaccination to prevent the virus from penetrating other good cells genetic makeup. For this reason, the human genome project may well be one of the ways forward in the 'curing' or at least, prevention of HIV-AIDS as well as other such viruses. Another point of interest was Dr. Gallo's reference to the need for education along with intervention in the Sub-Saharan context in reference to the HIV-AIDS pandemic. He emphasised that these must go hand-in-hand if progress is to be achieved. In doing so, he made specific reference to the negative impact of the former President of South Africa's Mbeki denial of the HIV-AIDS pandemic which ravaged the country to devastating effect.

It was a testimony to Dr. Gallo's genius that one could hear a pin drop during the entire presentation. Even when it was completed, Dr. Gallo was gracious enough to take questions from the floor, and in doing so, gave considered, thoughtful and sensitive answers to questions varying from

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New Grants and Supplements



Jean K Carr, PHD

Jean K Carr, PHD, Associate Professor, Division of Epidemiology and Prevention, Institute of Human Virology, has received an ARRA supplement in the amount of \$90,804 from NIH/NIAID for her R21 entitled “HIV-1 subtype B transmission in a heterosexual incident cohort.” The supplement will enable Carr to extend her exploration of founder viruses in HIV infections to those in Nigeria.

Lori Fantry, M.D., MPH, Medical Director of the Evelyn Jordan Center, Associate Professor of Medicine, the University of Maryland School of Medicine, received a one-year \$10,000 grant from the Baltimore City Health Department for her work entitled “Ryan White Part A – Enhancement of Clinical Quality Management, EJC.” The Evelyn Jordan Center (EJC) Health Maintenance Project will enhance the EJC electronic medical record (EMR) through the use of reminders to perform health maintenance and more user friendly methods to document health maintenance.



Lori Fantry, M.D.



George K. Lewis, Ph.D.

George K. Lewis, Ph.D., Professor and Co-Director, Division of Basic Science and Vaccine Research, Institute of Human Virology, received a five-year \$2,955,849 grant from the National Institute of Allergy and Infectious Diseases for his work entitled “Broadly Neutralizing Monoclonal Antibodies Against HIV-1.” The goal of this research is to identify novel monoclonal antibodies (mAbs) that broadly recognize

the HIV-1 envelope glycoprotein (Env) and block infection in vitro to guide vaccine development.

Wuyuan Lu Ph.D., Professor, Division of Basic Science and Vaccine Research, Institute of Human Virology, received a two-year \$412,500 R21 supplement from National Institute of Allergy and Infectious Diseases for his R21 grant entitled “D-peptide inhibitors of HIV assembly and maturation.” This research aims to develop a novel class of D-peptide inhibitors as additional weapons in the arsenal to fight HIV infection by specifically targeting HIV assembly and maturation. Lu also received a \$137,078 supplement from the National Institute of Allergy and Infectious Diseases for his grant entitled “Inhibition of anthrax Lethal Factor by alpha-defensins,” to replace aging equipment and fund two researchers.



Wuyuan Lu Ph.D.



David Pauza, Ph.D.

his grant entitled “Mechanisms for SIV evasion of vaccine immunity: Role of FasL-mediated death.” These supplemental funds will allow additional data collection needed to improve statistical significance and information about cell-mediated immunity in AIDS.

Maria Salvato, Ph.D., Professor, Division of Basic Science and Vaccine Research,



Maria Salvato, Ph.D.

Institute of Human Virology, received a \$75,000 supplement from the National Institute of Allergy and Infectious Diseases for her grant entitled “A Lassa Vaccine in Primates with AIDS.” These funds will be used to look for vaccine integration into primate germline and somatic tissues, and to determine whether integration impacts host immunity and disease.



Robert Redfield, M.D.

the University of California San Francisco for his work entitled “Solid Organ Transplantation in HIV: Multi-Site Study.” The primary aim of this study is to evaluate the safety and efficacy of solid organ transplantation in people with HIV disease by conducting a prospective, multi-center cohort of HIV-positive patients who undergo kidney or liver transplantation.

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 one-year \$85,000 grant from Associated Black Charities for his work entitled “Ryan White MAI – EMA Medical Case Management, IHV.” The Jacques Initiative program at the IHV will be able to better coordinate services to improve client’s health outcomes including linkages to medical care, mental health, substance abuse, and housing, etc.

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 one-year \$424,000 continuation award from DHMH – Infectious Disease and Environmental Health Administration for his work entitled “HIV Prevention Training.” IHV

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New Peptides Could Lead to Better Anti-Cancer Therapies

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as the L version. “It’s like you have right hand and left hand glove, and they don’t fit the same,” says Pazgier. By getting a crystal structure of the D-peptide bound to MDM2, and using mutagenesis to modify the peptide to make it fit better in the binding pocket, the researchers were able to make the interaction tighter (Figure 2).

Figure 2. Close-up views of MDM2/MDMX-peptide inhibitor binding sites. The pictures were drawn based on the crystal structures determined by IHV researchers of MDMX and MDM2 in complex with identified peptide inhibitors that block the binding of p53 to those proteins. Shown are as follows: (A) MDMX and (B) MDM2 in complex with 12-amino acid long L-peptide inhibitor PMI, (C) MDM2 in complex with 18 amino acid long L-peptide Stingin-1 and (D) MDM2 in complex with 12-amino acid long D-peptide inhibitor D-PMI.

While most previous work had been done on MDM2, blocking both MDM2 and MDMX from binding to p53 would be crucial for releasing p53 fully and helping treat cancer. The D-peptide that the researchers made against MDM2 turned out to be a weak inhibitor of MDMX, for which there aren’t many inhibitors. The researchers now plan to screen their phage display library against D-MDMX as well. “By doing that we’ll get the best fit for MDMX.”

The researchers will also optimize their D-compounds against both MDM2 and MDMX. “This is like the starting point, it’s a very exciting story for us right now,” says Pazgier. Structural studies provided a detailed insight into D-peptides interactions with MDM2 and validated the binding mode of D-peptides as a novel class of p53 activators; however additional structure-based optimization studies are needed to gain the full benefit from them in the future.

Another issue that is key to developing peptides of any kind of anti-cancer drugs is getting the peptides across cell membranes into the cell. To achieve this, the researchers plan to try newer methods that have shown promise in getting L-peptides across membranes. “If we find a good delivery system, we will have new drug candidates in the future,” says Pazgier.

“Wuyuan Lu, Marzena Pazgier and their colleagues have made an exciting, scientific collaboration,” said IHV Director Robert Gallo. “There is a real chance that their work will lead to a novel approach for treating many cancers. The technical challenges they still have to face are formidable, but if any group can do it I would bet on them – in fact, I have!”



IHV’s Terry Muzzy (left) and Samantha Watts (right) strike a pose with the Baltimore Orioles Bird

IHV Holiday Party

Every December, IHV staff and faculty from each of IHV’s HIV/AIDS clinics organize a large holiday dinner for patients and their families filled with gifts for children, local celebrities and entertainment. This year was no different. The Hilton Hotel’s Camden Yards Ballroom could barely contain the number of guests and fun-filled activities.



IHV Clinical Faculty and Staff



From left to right, Lydia Cornelius, Jada Carr, Sheila Lee, Jasmine Lee and Carlisle Harvey

Gallo and Board Member Moynahan Descend Upon the Emerald Isle *Continued from page 6*

the impact of HIV-AIDS on families, to the use of primates in laboratory experiments. Even when dealing with such a serious topic as HIV-AIDS, Dr. Gallo managed to inject his talk with humor and light-hearted jokes, and off the cuff remarks which went down well with his Irish audience. My interest in attending this lecture, as Director of the Centre for Global Development through Education, was from the perspective of our Centre's work in Lesotho, a country ravaged by HIV-AIDS.

Also in attendance was Mr. Tim Moynahan (Attorney) from Connecticut and Chair of The Robert Gallo C. Foundation for AIDS & Virus Research. The Foundation was established to support the work of Gallo and his colleagues at IHV, including counteracting the spread of the HIV-AIDS pandemic in Africa. While IHV is engaged in many countries in Africa, it has concentrated efforts in Nigeria for the past fifteen years. However, Dr. Gallo did point out in his lecture, that the HIV-AIDS pandemic is growing even in his home city of Baltimore, with rates in part of the city as high as that found in parts of Sub-Saharan Africa. Nevertheless, Dr. Gallo is hoping to extend his activities in Africa, with the possibility of looking at places such as Lesotho in the future. In fact, Dr. Gallo hinted that his Institute was interested in setting up partner institutes in places like Limerick, and maybe Dublin, to further the research through collaborations, which his institute at the University of Maryland School of Medicine has already begun.

One of the most interesting points which arose from Dr. Gallo's lecture, that unlike other diseases, such as Polio, one can safely vaccinate against such diseases, as the body retains memory cells which learn to cope with a recurring infection. The problem with HIV-AIDS, is that by the time such

'memory cells' have been activated, it is already too late. HIV-AIDS infection, like a diamond (he joked) is 'forever.' This was particularly worrying. What Dr. Gallo and his team are attempting to do is to create a vaccination whose memory will last to prevent any future infection. Currently, this is not the case. However, he believes it can and will be done, and HIV-AIDS will be cured in the near future. Dr. Gallo also spoke about the prevalence of other diseases too, such as STD related infectious viruses, various influenzas (including SARS, Avian flu and Swine Flu) and Polio, to mention just a few of the wide range of viruses in our world.

In an encouraging note to science students and graduates present, Dr. Gallo suggested that this may be a great opportunity for the University of Limerick to become a Centre of Excellence, particularly in relation to virology (an area of science he believes is at risk of becoming neglected due to the 'short term' memory of the world of various pandemics). If this were to happen in the manner outlined, not alone would Limerick benefit, but Ireland in general would be given a chance to showcase the innovativeness of its scientists and graduates in becoming leaders in 'high-end' knowledge creation and the knowledge society, especially within the science and technological arena.

Dr. Gallo was joined in the audience by his wife Mary-Jane (Hayes) Gallo, Mr. Tim Moynahan (Chair of the Gallo Foundation) and John McNamara of University of Limerick (UL). Dr. Gallo was introduced by Prof. Paul Finucane of the Graduate Medical School and he was also presented with a gift in appreciation for his talk by Prof. William T O'Connor of the Graduate Medical School, UL.

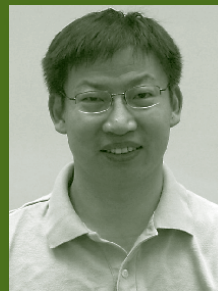
New Grants and Supplements *Continued from page 7*

has been working in collaboration with the Infectious Disease and Environmental Health Administration for the last 15 (fifteen) years to facilitate training programs aimed at building the skills of staff working with populations at high risk for contracting HIV.

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 one-year \$124,828 continuation award from DHMH – Infectious Disease and Environmental Health Administration for his work entitled "Routine Rapid Testing in an Emergency Department." IHV has been working in collaboration with the Infectious Disease and Environmental Health Administration for the purpose of providing HIV Testing and Referral (Routine HIV Testing) to non-critical patients presenting for care at the University of Maryland Medical Center Emergency Department.

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 one-year \$101,500 continuation award from DHMH – Infectious Disease and Environmental Health Administration for his work entitled "Expanding Rapid

HIV Testing in Perinatal Settings." IHV has been working in collaboration with the Infectious Disease and Environmental Health Administration for the purpose of using nursing expertise to provide consultation and education to health care providers regarding perinatal HIV/AIDS and HIV testing with the ultimate goal of increasing the amount of documented HIV testing, especially rapid testing, that is conducted in perinatal venues across the state.



Lai-Xi Wang, Ph.D.

Lai-Xi Wang, Ph.D., Professor, Division of Basic Science and Vaccine Research, Institute of Human Virology, received a one-year \$37,500 pilot grant from the University of Maryland, Marlene and Stewart Greenebaum Cancer Center for his work entitled "Construction of Tumor-Associated Glycopeptide Antigen Library for Immunological Studies and Vaccine Development." The goal of this research is to characterize the antigenic structures of the tumor-associated mucin MUC1 by constructing a library of synthetic MUC1 glycopeptide antigens corresponding to the tandem repeats - consisting of 20 amino acids with five potential O-glycosylation sites.

The Institute of Human Virology (IHV) at the University of Maryland School of Medicine is a world-class center of excellence focusing on chronic viral diseases, most notably HIV/AIDS, and virally linked cancers. IHV is dedicated to fundamental and clinical research leading to improved treatment and prevention of these diseases. Our unique structure connects cohesive, multidisciplinary research and clinical programs to streamline new treatments from discovery to patient. IHV serves the global scientific community and treats patients at clinics in Maryland, across Africa and in the Caribbean.

New Appointments



Isaac Witz, Ph.D.

Isaac Witz, Ph.D. is with the Institute of Human Virology as a part-time Visiting Professor in the faculty of the Department of Microbiology and Immunology at the University of Maryland School of Medicine through October 31 of this year. Dr. Witz, on sabbatical from Tel Aviv University was awarded in 2008 the IHV Lifetime Achievement Award for Scientific Contributions for pioneering the entire field of the important role of the microenvironment in cancer.

Yi Zeng, M.D. is with the Institute of Human Virology as an Adjunct Professor in the in the faculty of the Department of Medicine at the University of Maryland School of Medicine through June 30, 2010. Dr. Zeng is also a Professor of Virology at the Institute of Virology, Chinese Academy of Preventive Medicine and a member of the Chinese Academy of Science. Zeng has been a strong advocate on HIV/AIDS-related issues in China and is currently the President of the China AIDS Foundation.



Yi Zeng, M.D.

NEW LOCATION

12TH Annual International Meeting

of the **INSTITUTE OF HUMAN VIROLOGY**

October 4-8, 2010
Tropea, Calabria, Italy



Dr. Giovanni Laborie,
Rector, University of Calabria

Please join world experts to discuss HIV biology, therapy and vaccines; HIV and cancer; epitope/target discovery; HIV and malignant diseases in Africa.

Visit www.ihv.org for more information on our 2010 location, program, registration and abstract submission.



Dr. Robert C. Gallo,
Director, Human Virology

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