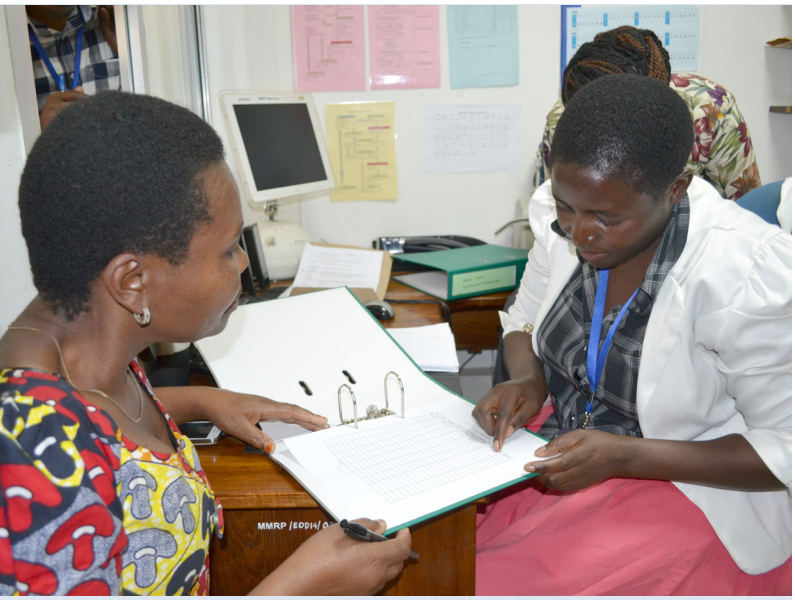
MHRP EXCHANGE

Spring 2017

NEWS FROM THE U.S. MILITARY HIV RESEARCH PROGRAM AT THE WALTER REED ARMY INSTITUTE OF RESEARCH

New Multi-site Phase 2 Ebola Vaccine Study Begins in Africa



Clinicians participate in an Ebola vaccine protocol training exercise in Mozambique.

In March, MHRP and WRAIR initiated a Phase 2 clinical trial to evaluate the safety and immunogenicity of a prime-boost Ebola vaccine regimen in both healthy and HIV-infected volunteers. The study's first vaccination was in Uganda in March, and the other trial sites in Nigeria, Kenya, Tanzania and Mozambique planned to begin the study by the end of may.

This study, which will enroll a total of 500 volunteers in Africa, includes two vaccine candidates, Ad26.ZEBOV from Crucell Holland B.V., one of the Janssen Pharmaceutical Companies of Johnson & Johnson; and MVA-BN-Filo from Bavarian Nordic, which will be given sequentially as a "prime boost" regimen. The study will also test a vaccination schedule beginning with Ad26.ZEBOV and then boosted with MVA-BN-Filo.

"It is critical that we know these vaccines are safe and immunogenic in the communities where they will be used in Africa," said Lt. Col. Julie Ake, an infectious disease physician, MHRP Principal Deputy and protocol chair for the international study.

This is the fifth Ebola vaccine study conducted in Africa by WRAIR and MHRP.

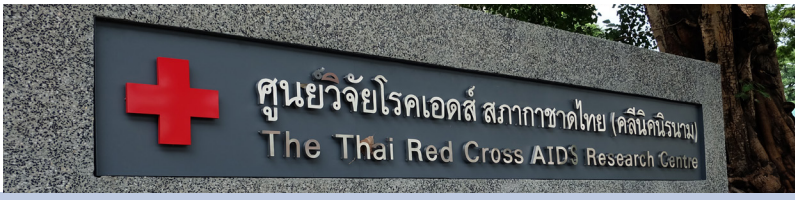
Study Provides Clues to T Cell Responses in Acute HIV Infection

A new study has shown that potent HIV-specific CD8+ T cells that are able to kill HIV-producing cells and reduce seeding of the HIV reservoir are only detected at peak viremia in acute HIV infection. Findings from the study, which was led by MHRP, were published in the February issue of *Science Translational Medicine*.

HIV-specific CD8+ T cells are white blood cells that kill cells infected with HIV. CD8+ T cells play a critical role in controlling HIV viremia and could be important in reducing overall numbers of HIV-infected cells in approaches to eradicate HIV.

Researchers studied HIV-specific CD8+ T cells in samples from MHRP's unique RV254 acute infection study, a cohort of individuals who are recruited at the earliest stages of acute HIV infection, usually within weeks of infection, and placed on ART immediately. RV254 is led by Dr. Jintanat Ananworanich, MHRP's Associate Director for Therapeutics Research, and conducted in collaboration with the Thai Red Cross

"Fully differentiated HIV-specific CD8+ T cells were still present two weeks after ART initiation, but their numbers decline drastically," said Dr. Lydie Trautmann, MHRP's Chief of Cellular Immunology and senior author of the paper. "Interventions aiming at prolonging their survival might have profound impact on the HIV reservoir size."



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WRAIR
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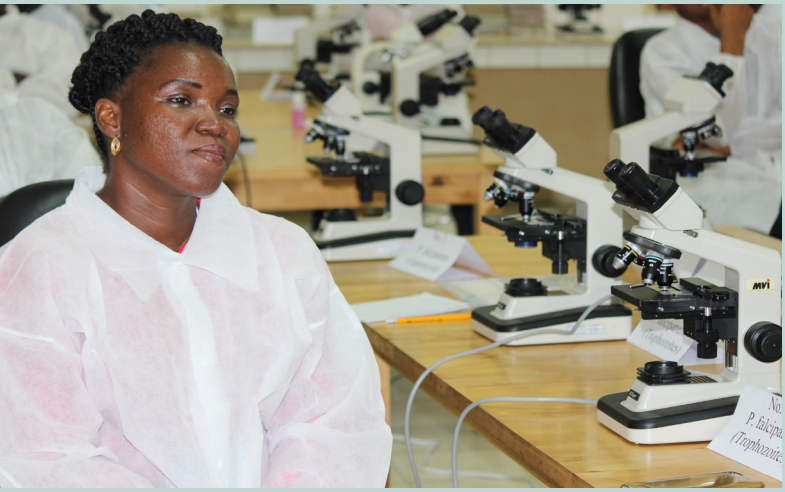
Clinical Training Course in Liberia Boosts Biopreparedness Efforts in West Africa



The Joint West Africa Research Group (JWARG) in April held a week-long clinical course in tropical and emerging infectious diseases for clinicians and lab professionals in Monrovia, Liberia. This training was to strengthen clinical skills needed to enhance research capability in West Africa.

The course included training on several specific diseases of concern in Liberia, including Ebola, Lassa fever, malaria, typhoid, and HIV, as well as training on sepsis from any cause. Lectures also addressed clinical response to infectious disease threats, including diagnostics, prevention, treatment and ethics.

"This initiative is a unique collaboration between military and civilian partners in West Africa," said U.S. Ambassador to Liberia Christine Elder. "Each group brings unique perspectives and strengths to the table, enabling the Group to develop strategies and capabilities that will help prepare the region for future disease outbreaks."

The training follows on the establishment of Liberia's first clinical microbiology lab in 40 years at Phebe Hospital, implemented in late 2016 with support from JWARG. Prior to that, Liberia had no advanced microbiology diagnostic capabilities. This improved capability is critical to the management of infectious diseases.

JWARG efforts in Liberia will enhance the capabilities of West African physicians, scientists, and institutions to conduct clinical research. It will also build and strengthen research capabilities in the region, provide an effective surveillance mechanism and also broaden understanding of relevant infectious disease threats.

> *"This initiative is a unique collaboration between military and civilian partners in West Africa."*

Col. Nelson Michael Selected as One of Vice Motherboard's 'Humans of the Year'

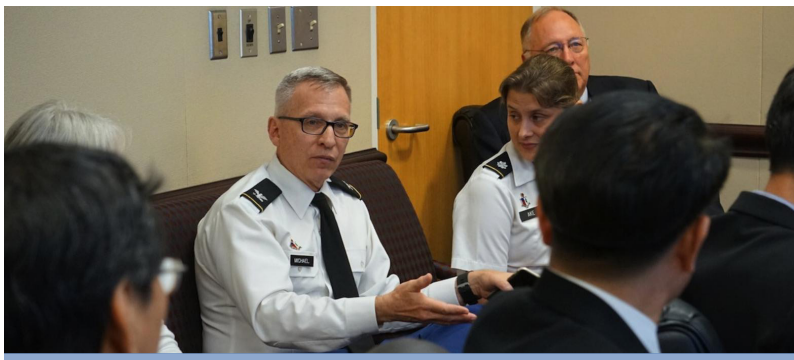
Online science and tech magazine *Motherboard* has selected MHRP's director Col. Nelson Michael as a "Human of the Year" for his work developing vaccines for HIV and other emerging diseases, namely Ebola and Zika.

In their selection, *Motherboard* aimed to "focus on a few enterprising individuals in science and tech in particular — people whose names you may not recognize right away, but whose work has the potential to touch your life and change the world in a positive and novel way."

Dubbing Col. Michael "The Vaccine Hunter," the *Motherboard* profile praises both his recent work in helping to develop WRAIR's Zika vaccine candidate and his decades of work on HIV.

"It's been extremely helpful to me to work on Ebola and Zika because these are, frankly, easier nuts to crack," Col. Michael says in the profile. "I don't want to say it's easy but the honest truth is, in the history of making vaccines, the Superbowl is a vaccine for HIV."

Col. Michael was interviewed by *Motherboard* reporters for an article last year about WRAIR's Zika Purified Inactive Virus (ZPIV) vaccine candidate, which progressed from concept to human trials in less than one year.



Col. Michael, Director of MHRP, was called "The Vaccine Hunter" by the magazine Motherboard.

Dr. Carl Alving Inducted as National Academy of Inventors Fellow

Earlier this month, Dr. Carl Alving, MHRP's Chief of Adjuvant and Antigen Research, was inducted as a 2016 Fellow of the National Academy of Inventors (NAI) in a ceremony at the Kennedy Library and Museum in Boston.

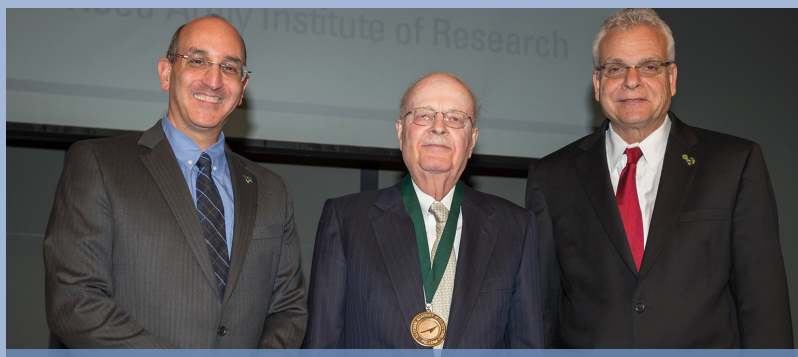
NAI elects as Fellows academic inventors who have "demonstrated a prolific spirit of innovation in creating or facilitating outstanding inventions that have made a tangible impact on quality of life, economic development, and the welfare of society."

Dr. Alving has been with the Walter Reed Institute of Research since 1970. He has been an author or coauthor on approximately 300 scientific publications (more than 250 peer-reviewed papers) in the fields of adjuvants, antigens, antibodies, complement, lipid biochemistry and immunology and liposomes as drug carriers and carriers of vaccines. He has created adjuvants for many types of experimental vaccines, including vaccines to malaria, HIV, meningococcal infection, heroin addiction, biological threat agents and prostate and intestinal cancer. He holds 31 U.S. patents.

"The research and scientific environment at the Walter Reed Army Institute of Research that fostered an environment of creativity and innovation led to this national recognition," said Dr. Alving.

"Technology transfer activities that resulted from these activities have supported and benefited many military missions."

With the election of the 2016 class, there are now 757 NAI Fellows, representing 229 research universities and governmental and non-profit research institutes. The 2016 Fellows are named inventors on 5,437 issued U.S. patents, bringing the collective patents held by all NAI Fellows to more than 26,000 patents.



Dr. Carl Alving, center

MHRP Well Represented at CROI 2017

MHRP gave a plenary presentation, five oral presentations, and 17 posters plus a press conference on one of those posters at the premier HIV conference of the year CROI (Conference on Retroviruses and Opportunistic Infections), held in Seattle 13-17 February.

MHRP's Dr. Jintanat Ananworanich's opening plenary presentation was "The Emerging Potential for HIV Cure for Infants, Children, and Adults." MHRP's expanding HIV cure research portfolio stems from two unique infection cohorts in East Africa and Thailand that provide crucial insight into the earliest, critical days of infection and immune response.

Site Updates

MHRP Conducts Protocol Training at Partner Sites in Germany
Members of MHRP's Clinical Operations Office (COO) and International Laboratory Program (INLAP) in April traveled to Germany for a site assessment visit and protocol training for RV464, a protocol that includes cohort and site development for acute HIV infection studies in Germany.

RV464 is designed to establish and characterize an acute HIV infection cohort in a German high-risk population, describe the underlying immunology and virology of acute and chronic HIV-1 clade B infection and prepare the site for future HIV-related clinical trials.

68 Nigerian Army Reference Hospital Yaba Achieves 5-star Rating
In April, auditors from the African Society for Laboratory Medicine (ASLM) completed a Strengthening Laboratory Management Toward Accreditation (SLMTA) assessment of 68 Nigerian Army Reference Hospital Yaba in Lagos, Nigeria, and awarded the lab a 5-star rating.

With this rating, the Nigerian Ministry of Defence/Walter Reed Program-Nigeria now has two labs with 5-star ranking. The first was the 445 Nigerian Air Force Hospital Ikeja, also in Lagos, around two years ago, which was the first lab in the country to achieve this level.

Mbeya site completes enrollment for HVTN study
MHRP's site in Mbeya, Tanzania completed enrollment in March into HVTN 111, a Phase 1 clinical trial to evaluate the safety and immunogenicity of an HIV clade C DNA adjuvenated vaccine in healthy, HIV uninfected adult participants. A total of 28 participants were enrolled in just under 4 months.

Participants in Uganda PEPFAR OVC Program Graduate to Become Counselors

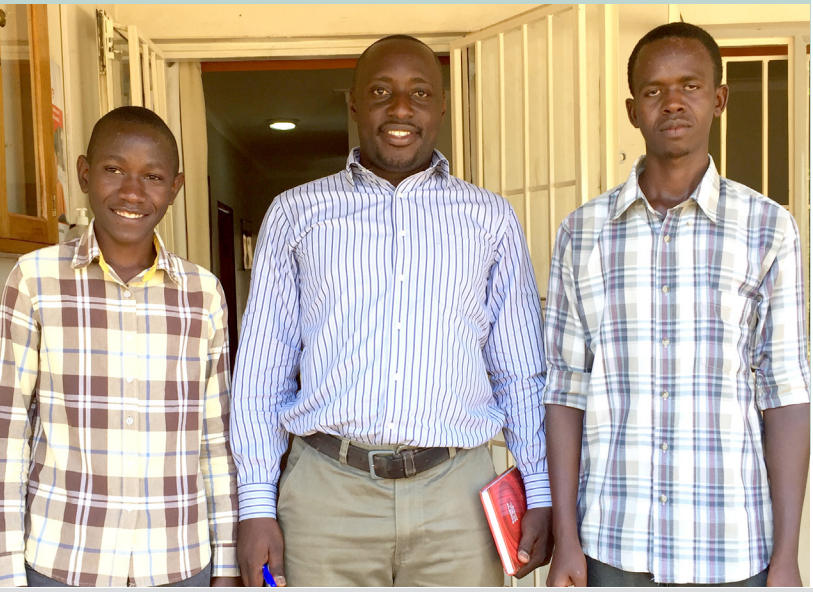
Two young men from Uganda's Kayunga District have graduated from Makerere University Walter Reed Project's Orphans and Vulnerable Children (OVC) programs and now work as counselors for the Presidents Emergency Plan for AIDS Relief (PEPFAR) program working with children and adolescents. The program benefits from their experience as former participants, and the job helps Richard and Semel support themselves.

Richard and Semel were identified and enrolled in support programs in infancy and benefitted from MUWRP OVC support through adolescence. They have unique insights into the many struggles children in the program face.

OVC services aim to help orphans and vulnerable children at high risk for HIV infection. Some examples of program support include provision of school fees, vocational training for parents, treatment linkage and adherence and healthy living counseling.

As a peer mentors, these young men help ensure that the kids with HIV stick to their medical regimens. Semel also works to prevent adolescents from becoming HIV infected through his work at the Youth Center, where PEPFAR-funded HIV education counseling and testing is offered in a supportive environment.

As they advanced through MUWRP OVC programs Richard and Semel were mentored by MUWRP PEPFAR staff member Chris, who now calls them his "brothers." Once they aged out of the OVC program, Richard and Semel attended training and are now formally part of the program's staff.



Dual-use Heroin Vaccine Elicits Immune Response in Mice

A novel combination vaccine designed to treat heroin addiction and target HIV was found to elicit immune responses in mice and dull their response to injected heroin in a recent preclinical trial. Findings from the study were published in the online journal *npj Vaccines* in May.

A team of U.S. government researchers led by scientists from WRAIR created a dual vaccine formulated with three main components: a segment of a protein expressed on the surface of HIV; a synthetic molecule that resembles heroin and its degradation products; and a potent adjuvant to stimulate the immune system. Mice immunized with this vaccine had high antibody titers against the HIV surface protein as well as heroin and its derivatives.

Dr. Gary Matyas

The heroin component induces antibodies that bind to the drug in the bloodstream, preventing the drug from crossing the blood-brain barrier. "This would block the euphoria and addictive effects," said Dr. Gary Matyas, Chief of Adjuvants and Formulations for the MHRP. "We hope to give people a window so they can overcome their addiction."

> *"We hope to give people a window so they can overcome their addiction."*

Since the onset of the HIV epidemic, scientists and public health advocates have attempted to curb the high prevalence of HIV among intravenous drug users. Heroin addicts in particular have a higher rate of HIV infection. In 2012, the National Institute of Drug Abuse awarded a $5 million grant to MHRP and WRAIR scientists to support the research and development of a combination heroin/HIV vaccine.

"WRAIR fosters an environment of creativity and innovation that allows us to work on novel approaches like this dual vaccine," said MHRP's Dr. Carl Alving, corresponding author and Chief of MHRP's Laboratory of Adjuvant and Antigen Research. He added, "While these are very early studies in mice, we think that a dual vaccine directed to heroin—and eventually HIV—is feasible."

Further developmental work to optimize the heroin component of the vaccine for humans is underway.

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Please submit your questions and comments via email to communications@hivresearch.org. Editors: Lisa Reilly, Jamie Livengood

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