

# MHRP EXCHANGE



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

## RV144 Vaccine Efficacy Increased Against Certain HIV Viruses

### New Research Reinforces Results from Thai Study

Scientists used genetic sequencing to discover new evidence that the first vaccine shown to prevent HIV infection in people also affected the viruses in those who did become infected. Viruses with two genetic “footprints” were associated with greater vaccine efficacy. The results were published recently in the journal *Nature*.

“This is the first time that we have seen pressure on the virus at the genetic level due to an effective HIV vaccine,” said Morgane Rolland, Ph.D., a scientist at the U.S. Military HIV Research Program (MHRP) and lead author of the study. The analysis revealed evidence of a vaccine-induced immune response on two sites of Env-V2 region located on HIV’s outer coat. For viruses carrying these two particular signatures, the vaccine efficacy increased to 80 percent.

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*Morgane Rolland, Ph.D., Bioinformatics Section Chief, Department of MHRP’s Molecular Virology and Pathogenesis Department co-lead the study that used genetic sequencing to uncover new evidence that the first vaccine shown to prevent HIV infection in people also affected the viruses in those who did become infected.*

## MHRP Scientist Awarded \$5 Million Grant to Develop a Combination Anti-Heroin/HIV Vaccine

*Dr. Gary Matyas (R), with NIDA Director Dr. Nora Volkow (L), at the press conference to announce the NIDA 2012 Avant-Garde Award to develop a combination heroin/anti-HIV vaccine.*



Dr. Gary R. Matyas received the 2012 National Institute on Drug Abuse’s (NIDA) Avant-Garde Award for Medications Development. Matyas proposes to develop an effective, safe and easily manufactured combination anti-heroin/HIV vaccine that could treat heroin addiction while at the same time prevent HIV infection in those receiving the vaccine. Matyas will receive \$1M per year for five years to support his research.

“Heroin use is strongly associated with a high-risk of HIV infection and represents an increasingly important worldwide health problem,” stated Matyas. “The possibility of creating a combination heroin-HIV vaccine provides an important opportunity to address both a unique treatment for heroin abuse as well as continuing the quest to develop an effective preventive HIV vaccine.”

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# Testing the First Ebola/Marburg Vaccine in Africa

## One Trial Participant's Experience

The Makerere University Walter Reed Project (MUWRP), MHRP's site in Uganda, has a varied research portfolio that includes an Ebola/Marburg vaccine developed at the NIAID's Vaccine Research Center.

In a recent interview with MUWRP staff member, Lillian Mutengu, a vaccine study participant discussed his reasons for participating in the trial. Jackson Otim Oyugi spoke with Ms. Mutengu on his last clinic visit.

**Lillian: So Otim, you are one of our participants in the Ebola/Marburg vaccine trial. What attracted you to join the study?**

**Otim:** My joining this study goes back a long way. Ebola claimed the life of a close relative of mine, Dr. Lukwiya Mathew, who died in the line of duty. [Dr. Lukwiya was a Medical Officer at the Gulu District Hospital where he contracted the disease while caring for those infected with Ebola]. When that happened...it kind of sounds like a Hollywood script of sorts [chuckles]...I said I would give back to make sure that a cure or treatment for this disease is found. Participating to finding a vaccine for this deadly disease was a way for me to make a contribution.

**Lillian: How has your experience been?**

**Otim:** I suppose it has been okay, all said and done. I was told, for example, I got the real experimental vaccine and it's been quite interesting, I think.

**Lillian: How interesting?**

**Otim:** Interesting because I thought...wow, Mathew, this is something I could do for the cause. Having got the "real deal"...it was a great feeling and I only wish I could do more.

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*Jackson Otim Oyugi (center) is the cousin of the first medical officer to die in the line of duty during Uganda's Ebola outbreak in 2000. Today, he is giving back by participating in Africa's first Ebola/Marburg vaccine trial.*

## Public-Private Partnership Developed to Accelerate Vaccine Progress

The Pox-Protein Public-Private Partnership (P5) seeks to build upon the results of RV144 to advance and ultimately license HIV pox-protein vaccine candidates that have the potential to achieve a broad public health impact.

In 2009, the RV144 Thai vaccine trial provided the first evidence in humans that a safe and effective preventive HIV vaccine is possible. Although efficacy was 31.2% at the end of the study, there was a higher early effect (60%) at 12 months.

The P5 comprises a collaborative team across four continents to accelerate progress towards an effective and durable HIV vaccine. Members include the U.S. National Institute of Allergy and Infectious Diseases/Division of AIDS, Bill & Melinda Gates Foundation, HIV Vaccine Trials Network, U.S. Military HIV Research Program, Sanofi Pasteur, Novartis Vaccines and Diagnostics.

The P5 is working on product development, regulatory planning and access agreements, and will continue to collaborate with government and communities within the host countries.

## RV144 Moving Forward

### Fall 2010

Using samples from RV144, 25 U.S. and international collaborators initiated intensive laboratory studies in an effort to define the immune mechanisms mediating the protection against HIV infection.

### Spring 2012

Data gleaned from extensive laboratory studies on correlates of risk of HIV infection shed new light on the immune responses that may have played a role in protecting some volunteers in RV144.

### Fall 2012

Results of genetic sequencing revealed evidence of a vaccine-induced immune response in RV144 participants who became infected with HIV. (see page 1)

### Underway

MHRP is leading a small clinical study (RV305) in Thailand to evaluate re-boosting in volunteers who participated in the RV144 study.

# RV144 Vaccine Efficacy Increased Against Certain HIV Viruses

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“These findings reinforce both the RV144 result and the previous study showing that antibodies directed at the V1V2 region reduce the risk of infection. Taken together the work suggests that the Env-V2 region could be a critical target for future HIV vaccines,” noted Col. Jerome Kim, senior author on the study.

Researchers examined HIV genome sequences from 110 volunteers who participated in the Thai HIV vaccine trial, RV144, and who subsequently became infected with HIV. Results indicated that the HIV viruses infecting trial participants were different in persons who received vaccine compared to those who received placebo.

Researchers focused their analysis on the V2 portion of the HIV virus after a study published earlier in 2012 in the New England

Journal of Medicine found that antibodies specific to the V1V2 region of the HIV genome correlated with lower risk of infection.

This new genetic sequencing study showed that the viruses that broke through or escaped from these immune responses have genetic differences in the same V2 region, indicating that the vaccine exerted pressure in this region.

HIV viruses that escape from antibodies and manage to infect a person have genetic footprints, or mutations, that can prevent them from being recognized by the immune system. These changes can be seen in the

genetic sequence of the virus. The research team sequenced more than a thousand full-length viruses to look very carefully at which changes corresponded to “escape” mutations.

“These findings reinforce both the RV144 result and the previous study showing that antibodies directed at the V1V2 region reduce the risk of infection.”

## Nigeria Unveils 2012 National HIV Vaccine Plan

Nigeria’s National Agency for the Control of AIDS (NACA) revealed a new 2012 National HIV Vaccine Plan in September in Abuja. This collaborative plan aims to elevate Nigeria’s contribution to the international effort to eradicate HIV/AIDS.

“With its large population and unique HIV subtypes, I believe that Nigeria should be in the forefront of the current global quest for an effective vaccine,” said Dr. Ogonnaya Njoku of MHRP’s program in Nigeria, Walter Reed Program-Nigeria (WRP-N). WRP-N is contributing to enhanced research capacity in Nigeria—one of the plan’s objectives—with vaccine cohort studies around Nigeria.

In addition to WRP-N leadership, the Executive Director of the African AIDS Vaccine Program based in Kampala, Uganda and other international experts working within Nigeria were instrumental in the development of this plan.



### Underway

P5 Scientists are developing, analyzing and selecting protein components of the vaccine candidates to use in future studies. They aim to improve and prolong the level of protection.

### Upcoming

MHRP will begin a second clinical study (RV306) in early 2013 using the RV144 vaccine regimen to compare additional vaccine boosts and gather more immunogenicity data in 460 new volunteers.

### Upcoming

The P5 is planning an efficacy trial in heterosexual adults in Southern Africa that will evaluate a prime-boost vaccine adjusted to target the most common subtype of HIV in the region (C).

### Upcoming

The P5 is planning an efficacy trial in a high-risk population of men who have sex with men (MSM) in Thailand to improve upon the RV144 result and extend its relevance to at-risk populations.

## Unprecedented Study Captures Data from Earliest Stages of HIV Infection



*A potential volunteer is screened for eligibility to participate in the Early Capture HIV Cohort Study at one of MHRP's research sites in Kenya.*

MHRP initiated an ambitious research program in 2010 to follow a group of high-risk volunteers to gather information on acute HIV infections. The acute, or first stage, of HIV infection immediately follows exposure to the virus, and occurs long before an individual knows they are infected. During this stage, the virus begins to replicate and invade the immune system.

Through this unprecedented study, called the Early Capture HIV Cohort Study (ECHO), researchers collect frequent samples from acutely infected persons before they show detectable HIV antibody. Valuable information and mucosal samples from this study will allow scientists to study the virus that is transmitted and replicated, and characterize the immune responses in the

first weeks and months of infection. Many researchers believe that understanding this early period will help provide clues to developing an effective vaccine, and the events during this early era are critical to determining long-term disease course. This program also provides a potential platform to pursue research for a cure for HIV.

As of August 2012, ECHO had recruited approximately 1,800 volunteers in East Africa and Thailand and collected samples and data for 71 individuals who become infected after joining the study. MHRP will work with leading researchers worldwide to examine the samples from this study, which they hope will shed new light on how to shut HIV down early in the infection process.

## New Data from MHRP Study Impacts Rapid Hepatitis C Test Used on Battlefield

Data from a study published in August in the journal *Transfusion* found that significant differences in reliability exist among rapid test kits used to identify hepatitis C (HCV) under adverse conditions on a battlefield. Preliminary data from the study led the U.S. military to halt the use of the rapid test most commonly used in Iraq and Afghanistan to detect HCV in donated blood prior to an emergency blood transfusion.

“This research directly impacts care for the warfighter on the battlefield,” said LTC Robert O’Connell, M.D. of the U.S. Military HIV Research Program and lead author of the study. “Emergency blood transfusion is a life-saving procedure commonly used on today’s battlefields; having reliable rapid tests to detect diseases like hepatitis prior to a transfusion is imperative for the health and well-being of our injured service members.”

Researchers selected five rapid tests for a comprehensive evaluation. Twenty-nine tests were initially identified,

however, only five met pre-determined criteria to undergo comprehensive evaluation. Criteria included availability, ability to produce a positive result from an infected sample and/or instability in varied temperature environments.

Results suggest that a brand of rapid test other than what the military had been using to detect HCV in the field was superior and provided more accurate results in conditions similar to what is experienced on the battlefield.

Current U.S. military clinical practice guidelines indicate the use of non-FDA compliant blood products voluntarily donated by other service members during mass casualties and after the stored blood supply is exhausted in order to prevent hemorrhagic shock. Accordingly, several measures are in place to protect this blood supply and include rapid diagnostic testing in the field for HCV as well as for hepatitis B and HIV.

“...having reliable rapid tests to detect diseases like hepatitis prior to a transfusion is imperative for the health and well-being of our injured service members.”

# Testing the First Ebola/Marburg Vaccine in Africa

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**Lillian: Before you were told you got the vaccine and not the placebo, how did you feel about the whole process of joining the first vaccine trial on the continent against one of the most deadly viruses in the world?**

**Otim:** When we came in for the briefing, we were told that much as it's the first time its being conducted on the African soil, its been thoroughly tested in the United states. Though it's a little daunting obviously, for lack of a better word. But like I said, the doctors were open in giving us information even when some of us asked annoying questions. Much as there was that little nagging fear at the back of my mind, I refused to pay much attention to it because I felt re-assured.

**Lillian: Did you share information about your participation in the study with your family?**

**Otim:** All people at home knew.

**Lillian: And they were supportive?**

**Otim:** Yes. Everybody knew about Mathew and all that. So, they did not object. They were only waiting to see the outcome and now, at the end of the study, they are much more excited than they were at the beginning.

**Lillian: How did your family react?**

**Otim:** My mum particularly was a little worried, but I re-assured her that we would be monitored. After getting the vaccine, I remember that day, I went with people from here [MUWRP] to my home so that in case of any emergency arising from the vaccination, they said they would come right back for me. All that made me feel confident and re-assured my mum.

**Lillian: Any other experience you would like to share with me about your study participation?**

**Otim:** On the whole, it's been a great experience.

# Collaborating to Improve Malaria Diagnostics in Tanzania

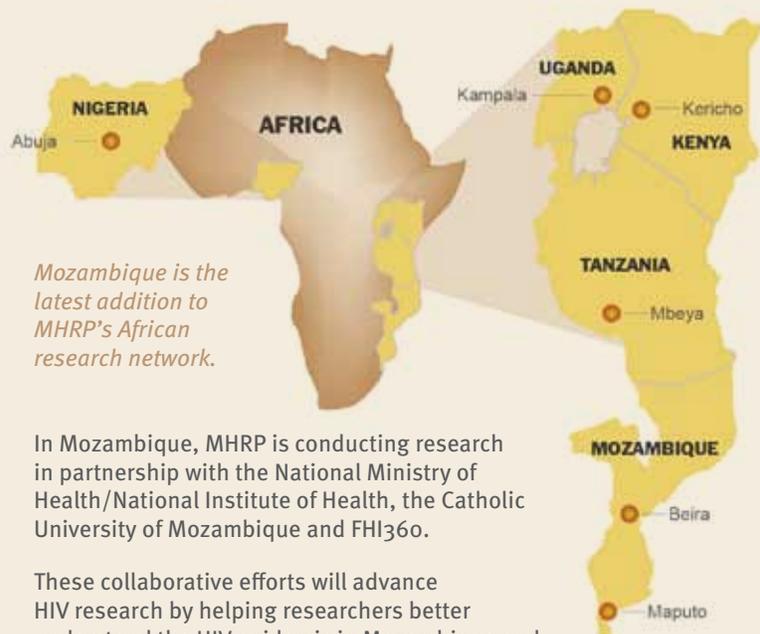


The Walter Reed Program-Tanzania (WRP-T) is working closely with the Malaria Program at the Walter Reed Army Institute of Research (WRAIR) to build capacity within Tanzania to strengthen malaria diagnostic capabilities on the mainland and on Zanzibar.

This collaborative program leverages WRP-T's established infrastructure, strong local relationships and experience in capacity building with WRAIR's expertise in malaria diagnostics and quality assurance and control. Some of these programs are part of the U.S. President's Malaria Initiative (PMI).

WRP-T recently organized and conducted a 2-week malaria microscopy training to improve and strengthen malaria microscopy skills of laboratory practitioners in district hospitals. WRP-T has worked in Tanzania since 2005 providing PEPFAR-funded HIV services, and recently expanded to support PMI and other initiatives to improve malaria diagnostics and research in Tanzania.

# MHRP Expands its Research Network to Mozambique



In Mozambique, MHRP is conducting research in partnership with the National Ministry of Health/National Institute of Health, the Catholic University of Mozambique and FHI360.

These collaborative efforts will advance HIV research by helping researchers better understand the HIV epidemic in Mozambique and increase capacity in the country to perform future HIV vaccine trials that test vaccine candidates against the predominant HIV subtype (C) circulating in this part of the world.



# PEPFAR

U.S. President's Emergency Plan for AIDS Relief

## PEPFAR Spotlight

MHRP executes President's Emergency Plan for AIDS Relief (PEPFAR) programs at its research sites in Africa and with military communities in Kenya, Tanzania and Nigeria under the Department of Defense HIV/AIDS Prevention Program (DHAPP), which supports HIV prevention, care, and treatment activities for military personnel in 68 countries.

### New Reference Laboratory Commissioned in Nigeria

The government of Nigeria commissioned a new Defence Reference Laboratory (DRL) in September that was built in partnership with the Department of Defense Walter Reed Program-Nigeria.

"The DRL is a critical piece for healthcare, enabling world-class diagnostic and laboratory monitoring services for military personnel and the civilian population living in the surrounding communities," said U.S. Ambassador to Nigeria, Terrence McCulley, who attended the event along with other high-ranking officials from the Nigerian military.



*The U.S. Ambassador to Nigeria, Terrence McCulley, helped commission Nigeria's new Defence Reference Laboratory.*

### Mobile Circumcision Clinic Reaches Under-served Communities in Uganda



*Scan the code to view a video about Africa's only mobile circumcision clinic.*

To reach high-risk men in under-served communities, the Makerere University Walter Reed Project (MUWRP) developed a mobile clinic to provide Medical Male Circumcision (MMC). Operating 5-days a week with full time staff, the mobile clinic travels to remote locations, such as fishing villages. Since 2010, MUWRP has circumcised 14,000 men through its mobile and permanent clinics and trained 400 clinicians.

### African Militaries Gather for HIV Prevention Conference



*US Global AIDS Coordinator Eric Goosby greets Mozambique Prime Minister Aires Bonifacio Ali at the 2012 International Military HIV/AIDS Conference in Maputo, Mozambique.*

Earlier this year, representatives from 75 militaries gathered in Mozambique for the International Military HIV/AIDS Conference. Co-hosted by the Mozambique Armed Defense Forces and the DoD HIV/AIDS Prevention Program, the 4-day conference provided a platform to share best practices. "All of these prevention tools are especially important to be implemented by militaries because it enables a nation to keep a strong and healthy defense force," said Michael Grillo, DHAPP Prevention Education and Training Director.

The Secretary of Defense has identified HIV/AIDS pandemics in foreign militaries as a national security issue. Pursuing HIV/AIDS prevention activities with foreign militaries has clear ties to security interests, regional stability, humanitarian concerns, counterterrorism, and peacekeeping efforts because the spread of the virus is a major destabilizing factor in developing societies.

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