

MHRP EXCHANGE



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

Introducing MHRP's New Website: hivresearch.org

Introducing a redesigned hivresearch.org—MHRP's new website and central hub for news and updates on our HIV vaccine research and recent findings. The new website has been streamlined to enhance user experience and promote easy access to information on our latest research.

Browse through a timeline of MHRP's landmark RV144 trial, or read biographies of our top researchers and their labs. Dive deeper into our HIV cure and vaccine research and stay up-to-date with the latest news from countries in our international network.

Visit www.hivresearch.org today! Like what you see? We'd love to hear from you! Email communications@hivresearch.org and let us know what you think!

New HIV Vaccine Trial Begins at Two MHRP Sites

In August, MHRP sites in Uganda and Thailand initiated a Phase II study of an HIV vaccine candidate that uses Ad26 prime with an MVA and protein boost. The inserts of this vaccine are mosaic constructs and the protein boost is subtype C. Although the protein is subtype-specific, the mosaic inserts are intended to provide broad response so the final vaccine can be deployed globally. The study, called A004, is the critical path study to down-select for a final regimen to advance to efficacy testing. In addition to contributing sites and collaboratively designing the study and development plans, MHRP provides the MVA being tested in A004. The study is funded and sponsored by Janssen, a division of J&J.



Staff at MUWRP in Uganda hold an information session for potential volunteers for a new vaccine study called A004.

IN THIS ISSUE

- 2 Host Genetics Played Role in RV144 Protection
- 2 Insights into the HIV Epidemic in the U.S. Military
- 3 New Ebola Vaccine Study Begins in Nigeria
- 4 Infection with Multiple HIV-1 Variants Leads to Poorer Clinical Outcomes

Host Genetics Played A Role in RV144 Protection



Rasmithomas, Ph.D.

New findings from an RV144 follow-on study published in *Science Translational Medicine* provide key insights into the role that host genetics played in protecting against HIV-1 infection during the landmark “Thai Study.”

MHRP researchers tested whether specific variants of immune response genes called HLA were associated with greater protection against the virus. “We found that antibody responses correlated with increased or decreased risk of

acquiring HIV only in the presence of specific host HLA alleles,” said senior author Dr. Rasmithomas. By identifying this specific allele, or gene variation, researchers hope to more clearly determine the mechanism of protection.

HLA class II molecules play an important role in antibody response, so MHRP researchers tested variation in these genes for interactions with the two vaccine-induced correlates of risk identified in RV144. This study showed that particular HLA class II genes modulated the quantity and quality of vaccine-induced antibody responses to affect HIV acquisition and vaccine efficacy.

According to MHRP Director Col. Nelson Michael, “This study confirms the importance of host genetics to the interpretation of correlates of protection of HIV vaccines and informs approaches to develop more effective next-generation products.”

MHRP Welcomes Dr. Lydie Trautmann



Lydie Trautmann, Ph.D.

MHRP welcomes Lydie Trautmann, Ph.D. as the new Chief of Cellular Immunology.

Dr. Trautmann joins the program after more than five years with the Vaccine & Gene Therapy Institute of Florida where she collaborated on acute HIV infection research with Dr. Jintanat Ananworanich. She says she was inspired to join MHRP by the chance to work more closely with these unique acute cohorts.

“Human immunology is hard. You need to work with strong cohorts in order to have any meaningful data and if you want to find an answer you have to start at one point and work backwards,” Trautmann said.

Joining MHRP is, “an opportunity to work with unique cohorts and a strong group of researchers working toward the same goal of studying acute HIV infection. We all have complementary expertise and, if we work together, we can make an HIV vaccine a reality.”

Dr. Trautmann’s lab is currently focused on HIV cure and remission studies. She says understanding the complexity of acute HIV infection is key to creating a viable vaccine.

She and her team are working to define the impact of treatment initiation in acute infection and the quality of the immune memory response. By researching whether the memory response is better in the extremely early, middle or late stages of acute infection, Dr. Trautmann and her team hope to provide crucial insight into immunology which could elevate vaccine development.

New Findings Give Shape to HIV Epidemic in the U.S. Military

The repeal of the Don’t Ask, Don’t Tell policy allows scientists to fully characterize epidemic for the first time.

New results of the comprehensive HIV characterization program among U.S. Army service members helps paint a detailed portrait of the HIV epidemic within the military since the repeal of Don’t Ask, Don’t Tell (DADT). The findings were published online ahead of print in *JAIDS* in an article titled, “Sexual Risk Behaviors of HIV Seroconverters in the U.S. Army, 2012-2014.”

Epidemiologists found the majority of HIV-infected Soldiers had engaged in same-sex relations and were African-American. “More frequent testing and pre-exposure prophylaxis may be warranted in certain high-risk groups,” said Shilpa Hakre DrPH, MPH, first author on the paper. “We also found infrequent condom use, which needs to be addressed to avoid secondary infections.”

Though the findings mirror larger trends within the HIV epidemic across the United States, they are significant because the repeal of DADT has enabled service members to disclose same-sex relations with health care providers. This, in turn, has allowed epidemiologists to track demographic and behavioral characteristics among those service members infected with HIV.

Researchers hope findings from the study will help health care providers target prevention programs to high-risk populations within the Army.

New Ebola Vaccine Study Begins in Nigeria



Staff of the Clinical Research Centre, WRP-N and MHRP pose with Director General MOD HIP at the commissioning of the Ebola vaccine study in Abuja, Nigeria.

MHRP recently began a new Ebola vaccine study at its site in Abuja, Nigeria in collaboration with the Nigerian Ministries of Defence and Health.

The vaccine used in the study (RV429) is the monovalent chimpanzee adenovirus Type 3 (ChAd3) candidate developed at NIAID and is being further developed GlaxoSmithKline (GSK). First vaccinations began on 21 August.

Since 2005, MHRP's program in Nigeria—the Walter Reed Program-Nigeria—has been working closely with the Nigerian Ministries of Defence and Health to enhance HIV prevention, care and treatment through the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) in Africa's most populous nation. MHRP has also been building a sustainable research infrastructure in Nigeria for future HIV vaccine trials.

This is the first MHRP/WRAIR vaccine study to be conducted in Nigeria and WRAIR's fourth Ebola vaccine study to date.

Successful Lab Audit in Mozambique

MHRP's collaborators in Mozambique—the National Institute of Health, Polana Çanico Health Research and Training Center (CISPOC) in Maputo—recently successfully completed a Good Clinical Lab Practice (GCLP) audit and are GCLP compliant. Successfully completing this audit demonstrates that the CISPOC laboratory operates within the framework set forth by the GCLP guidelines and strengthens the reliability, quality and validity of the work performed within the lab. The CISPOC team dedicated many hours and worked diligently to meet these standards, which enables them to participate in HVTN studies. MHRP provided technical support to CISPOC as they worked towards compliance.

MHRP/WRAIR Ebola R&D

WRAIR's unique research capabilities came to the forefront during the West African Ebola Outbreak of 2014. While Ebola research is not its primary mission, the Institute quickly redirected resources to support this urgent global health crisis, contributing training, diagnostics and countermeasure research and development, including:

- Completed Phase I Clinical Testing VSV-EBOV Vaccine Candidate at WRAIR (*NEJM*)
- Conducted First Ebola Vaccine Clinical Trial in Africa (*The Lancet*)
- Testing ChAd3 vaccine in Uganda Phase I study
- Recently Began ChAd3 Vaccine Study in Nigeria
- Developed Lab Tests to Support VSV-EBOV Ebola Vaccine Clinical Studies
- Published Paper on Largest Long-term Follow-up Study on Ebola Survivors (*Lancet ID*)

Functional Cure Studies: Protocol Training in Tanzania



MHRP staff conduct protocol training for RV398 at our research site in Mbeya, Tanzania. This upcoming MHRP study will be conducted at MHRP sites in East Africa in the RV217 cohort and will evaluate the efficacy of VRC01 in acutely infected individuals.



MHRP's African Cohort Study (AFRICOS) enrolled its

2,000th volunteer in September. This prospective observational HIV-focused cohort characterizes HIV outcomes at 11 MHRP PEPFAR-supported clinics in four African countries: Uganda, Kenya, Tanzania and Nigeria. The study is funded by PEPFAR.

Infection with Multiple HIV-1 Variants Leads to Poorer Clinical Outcomes

A new study shows the number of HIV-1 variants at the beginning of infection affects viral load, according to a paper published in the journal Nature Medicine.



Morgane Rolland, Ph.D.

In this study, MHRP researchers and collaborators analyzed large sample sets from two important HIV vaccine efficacy trials—the Step HIV vaccine clinical trial (HVTN 502) and RV144, the landmark vaccine clinical trial conducted in Thailand—to evaluate whether genetic characteristics of the founder viral populations could influence markers of clinical outcomes. Specifically, they examined

viral loads and CD4 T-cell counts against measures of HIV-1 diversity.

In both studies, data collected up to one year post HIV-1 diagnosis showed that subjects who had multiple founder viruses had significantly higher mean viral loads.

“This study emphasizes the value of vaccine efficacy trials for gathering rich datasets—even if a trial fails to show efficacy, the data may be used to investigate important questions regarding HIV pathogenesis which informs next steps for HIV vaccine development,” according to Col. Nelson Michael, MHRP Director.

“Our results brings into sharp focus how the earliest interactions between virus and host have a profound impact on the course of the entire disease,”

- Morgane Rolland, Ph.D., senior author

MHRP Study Indicates Increase in HIV Subtypes in Kenya



Recent analysis of data from Kenya shows a rise in both the number and complexity of inter-subtype recombinants of HIV-1, which could pose a significant challenge for vaccine development. Findings from an MHRP-led analysis of the epidemiology of HIV-1 subtypes within a tea plantation community in Kenya were recently published in the journal *PLOS One*. When compared to other MHRP-led studies in Kenya, the tea plantation cohort contained a higher proportion of recombinant incident infections. Researchers worry that increases in diversity among viral subtypes—driven by high rates of genetic mutation and recombination—could continue to complicate the picture for vaccine scientists.

gp145 Env Product Advances

Researchers with MHRP, along with outside collaborators from eight institutes, recently published a paper in the *Journal of Virology* on their work with a novel acute HIV-1 Subtype C gp145 Envelope product. Currently, the product pipeline for HIV vaccines is insufficient and limited by inadequate capacity to produce large quantities of vaccine to standards for human clinical trials. Such products are required to evaluate critical questions of vaccine formulation, route, dosing and schedule, as well as to test Env vaccine efficacy. This subtype C Env gp145 protein is currently undergoing good manufacturing practice production for use as a reagent for preclinical studies and for human clinical research. This product will serve as a reagent for comparative studies and may represent a next-generation candidate HIV immunogen.

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Please submit your questions and comments via email to communications@hivresearch.org. Editor: Lisa Reilly

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The U.S. Military HIV Research Program (MHRP)—centered at the Walter Reed Army Institute of Research (WRAIR)—is at the forefront of the battle against HIV/AIDS to protect U.S. troops from infection and reduce the global impact of the disease. Its international network includes research sites in Kenya, Uganda, Tanzania, Nigeria, Mozambique and Thailand.

WWW.HIVRESEARCH.ORG