MHRP EXCHANGE

MHRP
U.S. MILITARY HIV RESEARCH PROGRAM

Spring 2019

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

2003 RV144 HIV vaccine trial begins, involving many international partners and more than 16,000 volunteers from Thailand

2009 RV144 results announced and published in NEJM. The vaccine regimen was found to be safe and modestly effective (31.2% efficacy). It is the first, and so far only, time an HIV vaccine has shown efficacy.

2010 MHRP initiates intensive international laboratory studies using RV144 samples in search for correlates of risk

A public-private collaboration, called the Pox-Protein Public-Private Partnership (P5), forms to further develop the vaccine regimen tested in RV144

2012 Correlates of risk are identified and published in NEJM, providing clues to how the vaccine protected volunteers and informing future HIV vaccine efforts

MHRP researchers at AFRIMS in Thailand begin immunogenicity studies aimed at sustaining or increasing RV144's higher earlier efficacy seen at 6-12 months (60%) through additional boosts

2016 AFRIMS announces results from immunogenicity studies, identifying ideal interval for late boosts; subsequently published in JID

P5 initiates the HVTN702 HIV vaccine study in Southern Africa, using a similar pox-protein vaccine

2020 Results expected from HVTN702

RV144: 10th Anniversary

This November marks 10 years since the announcement of results from the MHRP-led RV144 "Thai Study," the first clinical trial to show an HIV vaccine regimen was safe and modestly effective in preventing HIV infection.

RV144 tested the "prime-boost" combination of two vaccines: ALVAC® HIV vaccine (the prime) and AIDSVAX® B/E vaccine (the boost). The trial showed that the regimen lowered the rate of HIV infection by 31.2 percent compared to placebo.

These study results, announced by the Army in 2009, showed that a preventive HIV vaccine is possible, and the landmark trial continues to provide scientific direction to help guide vaccine development and testing.

"It's difficult to overstate the reinvigorating effect RV144 had on the field of HIV vaccine research," said MHRP Director Dr. Robert Gramzinski. "RV144 allowed researchers to discover correlates of risk, provided targets for improved vaccine development and formed a foundation for the HIV vaccine candidates currently undergoing efficacy testing." Results from HVTN702, which uses a modified version of the RV144 regimen, are expected in late 2020.

RV144 stakeholders learned the results in September 2009. Results were subsequently published in the New England Journal of Medicine.

WRAIR
Walter Reed Army Institute of Research

PEPFAR DREAMS Student: 'This Is What It Means to Be Empowered'

At age 15, having completed only four years of primary education, a young woman named Winnie in a small town in Uganda found work as a barmaid to help support herself and her family. Friends convinced her to take on sex work, and she eventually agreed to have unprotected sex with customers willing to pay more money.

"When I became pregnant the story changed, I wouldn't get customers anymore and so decided to give sex trade a break," she said. After she gave birth and her baby was one year old, she couldn't cope financially and returned to sex work.

After relocating to Mukono, Uganda, two friends with whom she previously worked and who had also migrated to Mukono visited her. They told her about a program in Mukono targeting young girls like them that would give them options other than sex work.

"When they told me about the DREAMS program, I made up my mind to join. Since then, I have never regretted my decision," Winnie said.

PEPFAR's DREAMS public-private partnership aims to help young women become Determined, Resilient, Empowered, AIDS-free, Mentored and Safe through education, vocational training and other evidence-based interventions. In the Mukono DREAMS program, implemented by MHRP partner the Makerere University Walter Reed Project, Winnie learned the importance of safe sex practices and had the opportunity to take an HIV test.

"At first I feared to take a test, but I was given very good counselling and later agreed," Winnie said. "Lucky enough I tested HIV negative and praised my God."

Winnie prides herself in having learned the importance of saving under the DREAMS program.

"At first I saw it as impossible. Already I was getting very little money because I had left the business of sex trade and was working in a hair salon using the skills I had learnt in the safe space. However, after saving for one year, am excited about my accumulated savings." Winnie plans to use her savings to start up her own hair dressing business salon.

"This is what it means to be empowered," Winnie said. "Under DREAMS we have learned many life skills including hair dressing, sweater making and bead making. I feel that with all these skills that I have learned, I will not go without food, my child cannot fail to get good clothing or fail go to school."

MHRP Leadership Transitions

MHRP welcomes Dr. Sandhya Vasan as the new Director of the HJF component of MHRP, providing key leadership for MHRP's wide array of basic and clinical studies. "We are thrilled to have Sandy join our leadership team at MHRP," said MHRP Director Dr. Robert Gramzinski. "She is a highly qualified research physician with broad experience in basic and translational laboratory work, non-human primate research, and extensive clinical research experience in the U.S. and abroad."

Most recently, Dr. Vasan was MHRP's Associate Director for HIV Vaccine Research, and prior to that she served MHRP at AFRIMS in Bangkok for seven years as Science Director and head of the Nonhuman Primate Laboratory.

Dr. Vasan obtained her undergraduate degree in engineering at MIT before completing her MD at the Harvard-MIT Division of Health Sciences and Technology at Harvard Medical School. From 2002-2011, Dr. Vasan conducted Phase 1 clinical trials of HIV vaccines and adjuvants and related immunology research at the Aaron Diamond AIDS Research Center and the Rockefeller University.

In her new role, Dr. Vasan will also serve as the Principal Investigator representing HJF for MHRP's cooperative agreement with the DoD. Dr. Merlin Robb will remain involved with MHRP scientifically and programmatically but will step into a new position as HJF's Vice President and Chief Medical Advisor.

Three Neutralizing Antibody Lineages Identified

A new longitudinal analysis illuminates early events in the development of three neutralizing antibody lineages in an HIV-1-infected individual, insights which may help inform vaccine design. Researchers, led by scientists with MHRP and the Vaccine Research Center at the National Institutes of Health, published their findings this spring in the journal *Immunity*.

Neutralizing antibodies against HIV-1 are likely to be a major component of the protective immune response elicited by an effective vaccine. However, the lack of longitudinal and early samples in infection has limited the ability of such studies to uncover the earliest events in the development of these antibodies.

In the new study, researchers analyzed longitudinal samples from an HIV-1 infected individual who was part of MHRP's RV217 acute infection cohort. This prospective study has captured samples from some of the earliest stages of HIV infection, along with blood samples before infection.

"By revealing some of the early events in the development of MPER-targeted antibodies, and identifying a candidate immunogen to elicit them, this work has yielded insights that may guide efforts in lineage-based vaccine design," said co-author Dr. Shelly Krebs, chief of MHRP's B cell biology core.

Thai Collaborator Speaks at LGBT Pride Month Event

As part of its observance of LGBT awareness month, Ms. Doi Nakpor visited the Walter Reed Army Institute of Research to speak about her transgender community organization, Sisters, in Pattaya, Thailand, and discuss how their collaboration helps support MHRP's research.

HIV Cure, Vaccine Strategy Meetings

In February MHRP hosted more than 200 researchers from around the world for two days of annual meetings and discussion focused on the program's collaborative acute HIV infection cohorts and HIV vaccine research.

Participants at the acute HIV science meeting reviewed findings and ongoing research stemming from MHRP studies RV217 and RV254. These pioneering cohort studies, based primarily in East Africa and Thailand, provide insight into crucial stages of early HIV infection and form a foundation for HIV remission trials.

Investigators shared findings from studies that examine the interaction of HIV prevention measures and early antiretroviral therapy with acute infection dynamics and immune response.

The also discussed analytical treatment interruption and viral rebound in the cohorts, covering topics ranging from early rebound biomarkers to study ethics.

At the day-long vaccine science meeting, MHRP researchers and collaborators discussed strategies to advance the development of an effective HIV vaccine building on the success of the Army-led RV144 HIV vaccine trial.

Investigators provided updates on MHRP's ongoing HIV incidence cohort studies in Africa, Thailand and Germany. These three cohorts are pulled from populations affected by different subtypes of the HIV virus. Research from these diverse cohorts will be critical in MHRP's efforts to advance a globally effective HIV vaccine.

Researchers also presented MHRP's planned research into new vaccine technologies and platforms to be studied, including late boosts, improved vaccine protein constructs, fractional dosing and testing of the Army-developed ALF adjuvant.

U.S. Army, Partners to Launch New HIV Vaccine Efficacy Trial

The U.S. Army Medical Research and Development Command (USAMRDC) is part of a global partnership preparing to launch Mosaico, the first large-scale Phase 3 efficacy study of an investigational mosaic-based HIV-1 preventive vaccine.

The HIV vaccine efficacy trial aims to prevent infections by the wide range of viral strains responsible for the HIV pandemic. The trial will enroll 3,800 individuals in eight countries across North America, South America and Europe. It is expected to commence later this year. MHRP played a role in early studies leading up to Mosiaco and will provide technical support in the new trial.

Mosaico will be the third HIV vaccine efficacy trial in progress worldwide. Partners in the Mosaico study include Janssen Vaccines & Prevention B.V., part of the Janssen Pharmaceutical Companies of Johnson & Johnson; the National Institute of Allergy and Infectious Diseases (NIAID); the HIV Vaccine Trials Network (HVTN) based at the Fred Hutchinson Cancer Research Center; and the U.S. Army Medical Materiel Development Activity (USAMMDA), which is part of USAMRDC.

Data from the earlier Phase 2a ASCENT trial, presented at IAS 2019, suggest that using a combination of mosaic gp140 and clade C gp140 proteins broadens immune responses that may enhance protection against clade B, informing the decision to use the expanded regimen in Mosaico. In the military most HIV infections are sub-type B, and with service members being deployed world-wide, a vaccine that protects against all subtypes would be ideal.

Dr. Trevor Crowell Awarded ACTG Honor

In June Dr. Trevor Crowell was honored with the 2019 John Carey Young Investigator Award. The AIDS Clinical Trials Group (ACTG) awards the honor to investigators who have made significant contributions to the advancement of knowledge about HIV and its complications and demonstrated a cooperative spirit with colleagues and commitment to service.

MHRP Scientist Co-edits Journal Issue Focused on Viral Genetics

MHRP's Chief of Viral Genetics and Systems Serology Dr. Morgane Rolland has co-edited, together with Dr. Josh Herbeck, an edition of *Current Opinion in HIV and AIDS* devoted to HIV-1 phylogenetics. Dr. Rolland authored an editorial and review for the issue, focusing on how research into viral diversity can increase understanding of the epidemic and contribute to improved HIV vaccine candidates.

"HIV-1 epitomizes viral diversity with extensive variability across circulating strains and continuous diversification," Dr. Rolland explained in the editorial. Phylogenetic analyses have shown that nine subtypes exist for the main group of HIV-1 viruses as well as almost a hundred circulating recombinant forms and unique recombinants.

Phylogenetics research can provide insights in HIV epidemiology by providing new opportunities to uncover risk groups and transmission patterns not identified with more traditional methods. According to her review, Dr. Rolland also posits that incorporating findings based on the analysis of HIV diversity and evolution can help design better vaccine candidates.

HIV Study Opens in Jordan

In May the Walter Reed Army Institute of Research opened a protocol that will be the first observational HIV study conducted in the Kingdom of Jordan.

MHRP is collaborating on RV505, a study that seeks to understand the evolving HIV epidemic in Jordan; gathering information on HIV risk factors, outcomes, genotypes and drug resistance profiles.

This is the first study to come out of the Partnership for Research in the Middle East (PRIME), a WRAIR collaborative initiative led by the Emerging Infectious Diseases Branch (EIDB) with the Jordanian Royal Medical Services. and the Jordan Ministry of Health.

PRIME, headed by Dr. Kayvon Modjarrad, launched in 2017 with with initiatives focused on training, improving biopreparedness and upgrading laboratories and equipment. Future research activities will focus on emerging infectious diseases including studies on Severe Acute Respiratory Infections, survivors of locally reportable diseases and acute febrile illness.

PRIME
Partnership for Research in the Middle East

Keystone Symposia 2019

More than a dozen MHRP researchers and collaborators presented at this year's Keystone Symposia on HIV Vaccines and Functional Cures and the Eradication of HIV in Whistler, British Columbia.

- Dr. Jintanat Ananworanich gave the first public presentation of findings from RV405, a study evaluating AD26 and MVA vaccines administered therapeutically in early-treated acute HIV cohorts.
- Postdoctoral fellow Samantha Townsley received a scholarship to attend the symposia and present on IgG-mediated autoreactivity and neutralization breadth, and Dr. Shelly Krebs was invited to give an oral presentation on B cell priming and antibody responses in Rv144.
- Dr. Rasmi Thomas co-chaired a workshop on immunology of an HIV cure, and Dr. Diane Bolton co-chaired a workshop on T-cells in HIV vaccination and acute infection.

Exchange is published by the Communications Department of the U.S. Military HIV Research Program through a cooperative agreement with the Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc. Contents of this publication are not necessarily the official views of, or endorsed by, the U.S. Government or the Department of Defense. Depiction of individuals in photographs does not indicate HIV status.

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

For more information visit: www.hivresearch.org. Connect with us on Facebook and Twitter!