MHRP EXCHANGE

MHRP U.S. MILITARY HIV RESEARCH PROGRAM

Spring 2018

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

WRAIR Celebrates 125th Anniversary

WRAIR Walter Reed Army Institute of Research | 125 YEARS 1893-2018

The Walter Reed Army Institute of Research (WRAIR), MHRP's parent institute, is celebrating its 125th anniversary with events throughout the year in 2018.

In January 1893, Brig. Gen. George M. Sternberg, the Army surgeon general – a physician remembered today as the nation's first bacteriologist – established a new duty station: the Army Medical School. At the first school of public health and preventive medicine in the United States, Army medical officers were trained in the art and science of military medicine, focusing primarily on the prevention of infectious disease – which was, at the time, the most significant threat to soldiers' health.

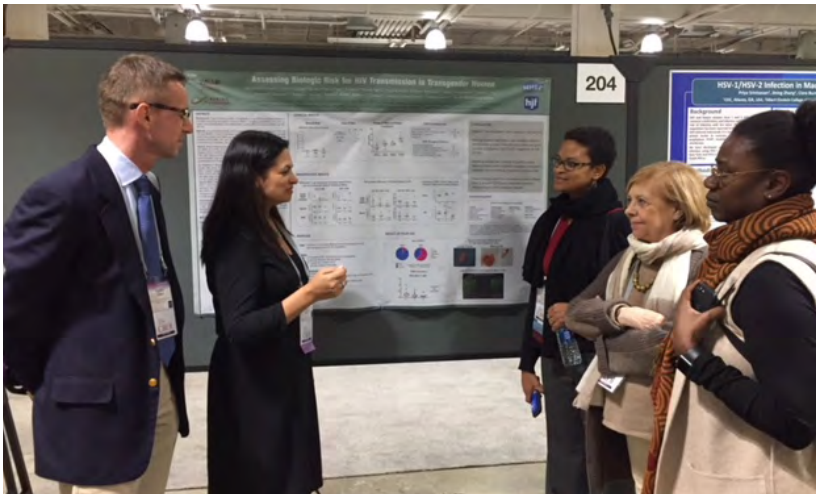
Since 1893, the School has expanded and evolved into the Walter Reed Army Institute of Research (WRAIR), now in Silver Spring, Md. To commemorate the anniversary, WRAIR will host an infectious disease symposium on June 22. Family day will be an internal celebration, and another symposium for the Center for Military Psychology and Neuroscience will be held in the fall.

Assessing Risk for HIV Transmission in Transgender Women

High HIV infection rates in transgender women (TGW) are largely attributed to increased behavioral risk factors; however, effects of hormone therapy on the immune system and injectable fillers or sex reassignment surgery on immune activation may alter HIV risk.

MHRP, AFRIMS, and the Thai Red Cross are conducting research to examine and characterize the biologic risks of HIV susceptibility among TGW. Dr. Sandhya Vasan, MHRP's Science Director at AFRIMS, Thailand, presented early findings from a pilot study at the 2018 Conference on Retroviruses and Opportunistic Infections.

The pilot study showed differential T cell distribution in the female genital tract between TGW and cisgender women, and potential differences in the distribution of sigmoid target cells for HIV between TGW and MSM. Additional studies are currently underway to further characterize differences across groups.



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Soldier Health • World Health

DREAMS Work in Mbeya Provides a Path Out of Prostitution

Joyce was just 12 years old when her parents divorced, leaving her mother to raise her and her three siblings in a village near Mbeya, Tanzania. Without land to farm or another reliable source of income, Joyce's mother struggled to put food on the table, and by the time Joyce was 15, she had entered into sex work to help support her family.

Joyce was forced to drop out of school when she became pregnant at 16. By 18, she had two babies, with little ability to prevent future pregnancies or knowledge of how to protect herself from disease.

Joyce's brother took her from her village to Mbeya, with hopes of giving her a second chance at life. In Mbeya, she met a peer educator and was enrolled into the DREAMS initiative funded by PEPFAR through the Henry Jackson Foundation Military Research International (HJFMRI) and MHRP.

PEPFAR's DREAMS public-partnership aims to help young women like Joyce become Determined, Resilient, Empowered, AIDS-free, Mentored and Safe through education, vocational training and other evidence-based interventions. After enrolling in DREAMS, Joyce received education on gender-based violence, family planning, HIV/AIDS prevention and joined a dressmaking class.

With skills learned from DREAMS' entrepreneurial training, she set up a roadside food stand selling roasted corn, sending money to her mother and children back in her village. She managed to save $112 to buy her own sewing machine to start a tailoring business, and hopes to be able to return to school one day.

Now a DREAMS Ambassador, Joyce hopes to be able to help other girls and young women in and around her community.

"As an Ambassador, I get the opportunity to make a change in the lives of other girls who are going through the life I once had; a dark life with no guidance and ambition," she says. "I am happy that the girls I have reached are now able to avoid unwanted pregnancies and protect themselves from unsafe sex and HIV. I will always be a DREAMS Ambassador inside and outside of Tanzania – helping young girls."

Jordan Study set to Launch

PRIME
Partnership for Research in the Middle East

A new MHRP initiative called the Partnership for Research in the Middle East (PRIME) has begun site development and training activities for what will be the first observational HIV study conducted in the Kingdom of Jordan.

PRIME is headed by Dr. Kayvon Modjarrad and was founded on a military-to-military partnership between WRAIR and the Jordanian Royal Medical Services. Program activities began last year with initiatives focused on training, improving biopreparedness and upgrading laboratories and equipment.

The upcoming study, RV505, will seek to understand the evolving HIV epidemic in Jordan; gathering information on HIV risk factors, outcomes, genotypes and drug resistance profiles. The study, led by MHRP's Dr. Paul Scott, is expected to start this summer.

Future PRIME research activities will focus on emerging infectious diseases including studies on Middle East Respiratory Syndrome (MERS), survivors of locally reportable diseases and acute febrile illness.

Partner Site in Germany Prepares to Open Study

A new study called BRAHMS, a collaboration with the University of Duisburg-Essen's Institute for HIV Research, is set to open April at sites in Germany. It will be a prospective observational cohort that aims to characterize a population at high-risk for HIV infection. The study, headed by MHRP associate Dr. Hendrik Streeck (pictured), also aims to assess risk factors associated with incident HIV infection and determine willingness to participate in a future HIV vaccine trial.

Social Science Research in Acute HIV Cohort Seeks to Understand Volunteers' Perspectives

The RV254/SEARCH10 cohort, headed by MHRP's Dr. Jintanat Ananworanich, is an acute HIV cohort in Bangkok, Thailand made up of individuals who are diagnosed in the very early stages of HIV infection and begin antiretroviral therapy (ART) immediately.

A recent paper in the Journal of Medical Ethics reports on insights gleaned from in-depth interviews with members of this cohort about their decision to participate in an HIV remission study with analytical treatment interruption (ATI).

Led by Dr. Gail Henderson, a professor of social medicine at the University of North Carolina School of Medicine, this social science and ethics research seeks to understand the decision-making process of RV254/SEARCH10 cohort members who agree and decline to participate in ATI studies. Interviews revealed central themes about volunteers' decisions to join:

- While acknowledging risks of ATI, most perceived they were given an opportunity to interrupt treatment, to test their own bodies and increase normalcy in a safe, highly monitored circumstance.
- They were motivated by potential benefits to themselves, the investigators and larger acute cohort and others with HIV.
- Volunteers believed their own trial experiences and being able to give back to the community were sufficient to offset participation risks.

Importantly, researchers found that volunteers' perceived benefits are individual and may differ from the benefits imagined by researchers. Future publications will address the thoughts and reasoning of members of the cohort who decline to participate in ATI studies.

A central tenet of MHRP's work towards HIV remission is to conduct social and behavioral research in an ongoing effort to explore perceptions of remission trials by those invited to participate, and issues of voluntary and informed consent.

Recent MHRP Publications

Viral sequencing

HIV Type 1 Subtype CRF01_AE is dominant in Thailand where the Army-led RV144 vaccine trial was conducted. To study immune correlates of protection in ongoing trials, CRF01_AE derived reagents are essential. Research led by Dr. Sodsai Tovanabutra, Chief of MHRP's Viral Sequencing Core, presented a novel panel of full-length CRF01_AE infectious molecular clones (IMCs) with a reporter gene, generated from different Fiebig acute stages of infection and from chronic infection. These IMcs will be useful for immunological studies, to include different functional humoral responses to HIV-1, and may be used to detect responses to envelopes of differing antibody sensitivities. Findings were published in *JAIDS*.

Full-length gene sequencing

A paper published in the journal *HLA* describes a novel method to generate high-resolution HLA types by full-length next-generation sequencing of HLA genes. This method also enabled identification of two novel HLA alleles with frequency of greater than two percent from the MHRP cohorts in Thailand and Africa. Understanding HLA diversity is important, as they impact vaccine efficacy, disease outcomes and transplantation. Research was led by MHRP's Dr. Rasmi Thomas and her host genomic laboratory.

Acute infection

A new study has shown a relationship between the levels of a gut-homing protein called alpha-4 beta-7 occurring at the time of HIV infection and health outcomes in people. The study, led by researchers at the Centre for the AIDS Programme of Research in South Africa (CAPRISA), was published in Science Translational Medicine. Researchers looked at data from MHRP's RV254/SEARCH10 clinical trial at the Thai Red Cross in Bangkok, Thailand and found that starting antiretroviral therapy (ART) soon after HIV diagnosis did not completely prevent the depletion of $CD4+$ T cells from the gut or facilitate reconstitution of the depleted cells.

Opioid vaccine

MHRP researchers reported that an experimental heroin vaccine induced antibodies that prevented the drug from crossing the blood-brain barrier in mice. The vaccine, co-developed by intramural scientists at National Institute on Drug Abuse (NIDA), produced antibodies against other commonly abused opioids, including hydrocodone, oxycodone, hydromorphone, oxymorphone and codeine. The vaccine appeared to dampen the impact of heroin at a high-dose, which might indicate a potential to prevent overdose. Findings were published in the *Journal of Medicinal Chemistry*.

Army-developed Zika Vaccine Induces Strong Immune Response in Three Phase 1 Studies

Three Phase 1 human clinical trials evaluating an Army-developed Zika purified inactivated virus (ZPIV) vaccine have shown it was safe and well-tolerated in healthy adults and induced a robust immune response. Initial findings from the trials were published in The Lancet.

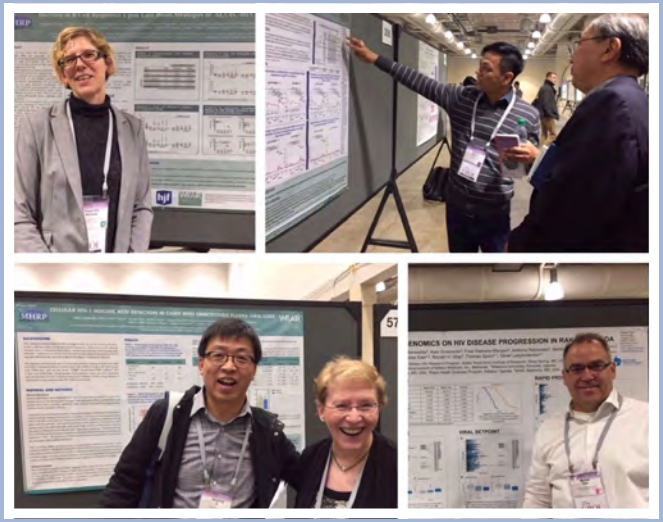
Each of the three studies included in the paper was designed to address a unique question about background immunity, vaccine dose or vaccination schedule.

Dr. Kayvon Modjarrad, WRAIR's Director for Emerging Infectious Diseases, the Zika program co-lead and the article's lead author said that "These results give us hope that a safe and effective vaccine will be achievable."

More than 90% of volunteers who received the vaccine developed an immune response against Zika. Research is ongoing, and next steps include evaluating how long vaccine-induced immunity lasts, and the impact of dose, schedule and background immunity.

CROI 2018

MHRP scientists and collaborators had an unprecedented 27 abstracts accepted at the 2018 Conference on Retroviruses and Opportunistic Infections. Research on acute HIV infection featured prominently at this year's conference, with 14 posters and presentations stemming from the RV254/SEARCH10 cohort and associated studies conducted in Thailand.



JWARG Activates Febrile Illness Study in Liberia

The Joint West Africa Research Group (JWARG) in March activated a study designed to identify and characterize cases of suspected severe infectious disease at medical centers in Liberia. The study opened in Nigeria late last year, and research activity will expand into Ghana in the coming months.

The study enrolls adult volunteers who present as severely ill with a suspected infectious source. In addition to receiving the usual care for their illness, they will be asked to provide samples for laboratory analysis and to complete a brief questionnaire that captures basic clinical, demographic and exposure data. By identifying and monitoring emerging cases, researchers will be able to characterize and compare patterns of illness and describe epidemiological patterns of infection, associated exposures and patient outcomes.

The West Africa region has experienced outbreaks such as Ebola and Lassa, and several other infectious diseases are endemic to the area, including malaria, yellow fever and dengue.

Lassa Outbreak Assistance

JWARG is also coordinating with the CDC and USAID to respond to a request for outbreak assistance from JWARG partners in Nigeria.

At this time assistance includes the acquisition and dissemination of 12,000 sets of Personal Protective Equipment (PPE) to the Irrua Specialist Teaching Hospital and other clinical sites to cover estimated need through June. JWARG is providing laboratory reagents for diagnostics and viral genome sequencing to permit molecular epidemiologic investigations.

Global Emerging Infections Surveillance-funded JWARG partners from USAMRIID will provide additional support through Lassa diagnostic assays brought to the 68th Nigerian Army Reference Hospital. In addition to much needed supplies, CPT Mate from WRAIR and the USAMRIID Diagnostics team traveled to Lagos in March to deliver diagnostic training to the 68th.

Lassa fever is a viral hemorrhagic fever that is transmitted to humans via contact with food or household items contaminated with rodent waste. The World Health Organization (WHO) reports that 317 confirmed cases of Lassa fever have resulted in 72 deaths in Nigeria from January 1 to February 28. A national Lassa fever Emergency Operations Centre (EOC) was activated in Abuja and continues to coordinate response activities in collaboration with WHO and other partners.

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

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