MHRP EXCHANGE

SUMMER 2025

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

The Promise of Bispecific Antibodies to Mitigate HIV Risk to the Battlefield Blood Supply

MHRP and partners have completed enrollment in a Phase 1 human trial in Tanzania to evaluate the safety and antiviral activity of a long-acting bispecific antibody, alone and in combination with another potent monoclonal antibody, to combat HIV.

Bispecific antibodies are lab-engineered antibodies designed to target two distinct binding sites on immune cells or virus envelopes. These molecules can neutralize HIV with improved breadth and potency, and they can be used as both preventive and therapeutic countermeasures.

The trial is also exploring fixed dosing and the safety of intramuscular injection to deliver these mAbs, important advantages for future potential use in remote or military settings where medical infrastructure may be limited.

"We see these bi-specific antibodies as valuable potential tools for use in strategic geographies where HIV is highly endemic, especially in INDOPACOM and EUCOM areas of operation," explained MHRP director Col. Julie Ake.

WRAIR's long-time collaborator, Tanzania's National Institute for Medical Research - Mbeya Medical Research Center, is conducting the study, called RV584. WRAIR has been working in Tanzania on countermeasure development for infectious diseases since 2001 and its research is conducted in close collaboration with the Tanzanian government and the Mbeya Zonal Referral Hospital.

The products being used for the study include 10E8.4/iMab, a bispecific antibody developed by Dr. David Ho's lab at the Aaron Diamond AIDS Research Center. The bispecific antibody is very potent against a wide range of HIV virus variants. In one of the arms of RV584, it is being tested with the broadly neutralizing monoclonal antibody (mAb) VRC07-523LS, which was developed at the U.S. National Institutes of Health (NIH) Vaccine Research Center and has been shown to be active against 96% of diverse HIV strains. The trial reached full enrollment in April 2025.

HIV Sequencing Sheds Light on Rapidly Growing Philippines Epidemic

While HIV is declining globally, the Philippines stands in stark contrast, experiencing a 411% increase in daily incidence between 2012 and 2023, as reported to the HIV/AIDS and ART Registry of the Philippines. Now recognized as the fastest growing HIV epidemic in the Western Pacific region, the country is facing a mounting public health challenge with limited data on the virus' regional molecular epidemiology.

MHRP, in collaboration with the Armed Forces of the Philippines (AFP) and other partners, is conducting a study to characterize HIV-1 viruses that are currently circulating in the Philippines. Researchers analyzed recent samples (2022-2024) from 22 people living with HIV in the Philippines, revealing findings that could inform both prevention and treatment strategies in the region.

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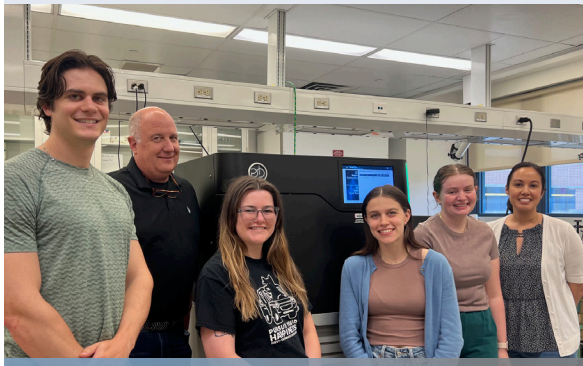

Pictured left to right: Matt Lind, Eric Sanders-Buell, Morgan Geniviva, Elizabeth Comeau, Kathleen Monahan, and Meera Bose, of MHRP's Viral Genomics Section.

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WRAIR
Walter Reed Army Institute of Research
MILITARY HIV RESEARCH PROGRAM

Second Annual Showcase Highlights MHRP's Early Career Investigators

The last week of May, MHRP hosted its second annual Early Career Investigators Showcase, an event designed to commemorate HIV Vaccine Awareness Day and develop the program's bench of up-and-coming scientists. Held at the Walter Reed Army Institute of Research (WRAIR), the showcase provided a platform for junior investigators to present their research to advance HIV countermeasures across a range of disciplines, from AI-assisted vaccine design and adjuvant optimization to global health program implementation and clinical research findings.

This event underscored MHRP's commitment to nurturing the next generation of scientific investigators, fostering a collaborative research environment and innovating across MHRP's global network. Prior to the event, participants worked closely with senior scientist mentors to develop their materials. They also had the opportunity to partake in presentation training and receive one-on-one feedback.

The day-long program featured a morning session with full-length oral abstract presentations as well as three-minute scientific elevator pitches that required distilling the purpose and context of a research project into a compelling, accessible bite-size presentation. Twenty-four participants presented posters in an afternoon session that facilitated formal and informal discussions around HIV research topics.

A panel of guest judges from WRAIR, the Uniformed Services University, HJF, and the NIH Division of AIDS scored the presentations. The showcase concluded with awards for outstanding presenters:

- **Best Scientific Elevator Pitch:** Elizabeth Comeau, "Rare drug resistance mutations in HIV-1 detected with deep sequencing in a Philippines cohort"
- **Best Poster Presentation:** Roger Ying, "Low HIV pre-exposure prophylaxis use despite high Interest among individuals with behavioral vulnerability to HIV in Uganda"
- **Best Oral Abstract Presentation:** Michelle Zemil McCrea, "Elucidating development pathways of broadly neutralizing antibodies from people who acquired multiple founder variants of HIV"

The Early Career Investigators Showcase also highlighted key messages from HIV Vaccine Awareness Day, which was May 18. HIV remains an ongoing global health challenge, with more than 1 million new cases per year, and about 340 new cases annually in the U.S. Department of Defense.

HIV Sequencing Sheds Light on Rapidly Growing Philippines Epidemic

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The majority of samples had virus of the CRF01_AE HIV subtype, which is commonly found in Southeast Asia. Full genome sequencing showed that these sequences formed a distinct clade among known CRF01_AE sequences, suggesting a single introduction and localized transmission. One participant was found to have a subtype B virus, which is most common in the U.S. and Europe.

Additionally, researchers identified drug mutation resistance in nine of the 22 participants. The deep sequencing technique was able to identify some rare drug resistance mutations and low-level drug resistance in an additional four participants. This insight into a growing epidemic in the INDOPACOM region is increasingly valuable for the U.S. and partner militaries given its strategic geographical location.

This analysis is part of a broader military-to-military HIV prevention, care and treatment initiative supported by the U.S. President's Emergency Plan for AIDS Relief (PEPFAR). This collaboration includes MHRP, the AFP, WRAIR-AFRIMS, and the Department of Defense HIV/AIDS Prevention Program (DHAPP).

The sequencing and sequence analysis were conducted by Kathleen Monahan, Bryce Weigartz, Elizabeth Comeau, Matthew Lind, Meera Bose, Eric Sanders-Buell, Phuc Pham, Yifan Li, Morgan Geniviva, and Morgane Rolland.

Celebrating a Study Milestone: 15 Years of the RV254 Acute HIV Cohort Study

This year MHRP celebrates the 15th anniversary of the RV254 acute HIV cohort study, a landmark collaboration between MHRP, WRAIR-AFRIMS and Thai research partners, including SEARCH and IHRI. Launched in 2009 and supported by the Division of AIDS at the U.S. National Institutes of Health, the study provided critical insights into the earliest stages of HIV infection and potential strategies to induce long term viral remission.

RV254 was designed to enroll individuals within days to weeks of initial infection, which is key for understanding early viral dynamics and immune response. Early treatment during this period is thought to limit the size of the viral reservoir, a major barrier to curing HIV. The cohort has produced more than 100 peer-reviewed publications, contributing to global conversations about cure strategies, immune interventions, and the importance of early diagnosis and treatment.

As of April 2025, the researchers have performed 589,145 real-time screenings of samples in Thailand. More than 1000 cases have been identified, with 752 participants enrolled into the cohort. Key milestones from the past 15 years include the identification of biomarkers associated with post-treatment control, breakthroughs in understanding the HIV reservoir, and testing novel cure strategies. It has also supported investigations into the impacts of HIV on the brain, nervous system, and gut, offering a holistic view of the virus' effects.

RV254 is the result of a long-time collaboration between U.S. and Thai militaries, clinicians and researchers, but the key to the study's success is a dedicated community of study participants. Many participants have remained engaged in the study for years, contributing to longitudinal research that helps researchers understand how the virus changes over time. MHRP and its partners would like to take this opportunity to express sincere thanks to the study participants and our many collaborators who have contributed so generously to this endeavor over the past 15 years.

DHAPP and MHRP Launch Mil-Mil HIV Epidemiology Study in Republic of Georgia

The HIV response in Eastern Europe has faced service delivery challenges and epidemiology shifts since the onset of hostilities in Ukraine. MHRP is supporting the Department of Defense HIV/AIDS Prevention Program (DHAPP) and the Georgia Defence Force (GDF) to characterize HIV prevalence, demographics, risk factors for HIV acquisition, and other STIs among GDF personnel. In April, researchers launched a similar epidemiologic study within the civilian population to understand HIV subtype distribution in the country and drug resistance patterns. MHRP is working closely with WRAIR's forward directorate in Tbilisi, WRAIR-Europe-Middle East on both studies.

DELIVER-01 HIV Combination Cure Trial Starts in Thailand

MHRP's Phase 1 clinical trial RV630, or DELIVER-01, has launched in Thailand to test a combination of experimental antibodies and vaccines to assess their safety and potential to control HIV without antiretroviral therapy (ART) in people living with the virus.

This study is enrolling participants from the RV254 cohort in Thailand, which is made up of individuals diagnosed during the early acute stages of HIV and have maintained undetectable viral loads on ART. Researchers will evaluate the safety of two long-acting antibodies, VRC07-523LS and PGDM1400LS, used alongside a series of HIV vaccine candidates including ChAdOx1 and MVA vaccine platforms and a gp120 protein vaccine. The study design includes an analytical treatment interruption, when participants will stop ART to see whether, under close monitoring, the combination of study products continues to suppress viral load.

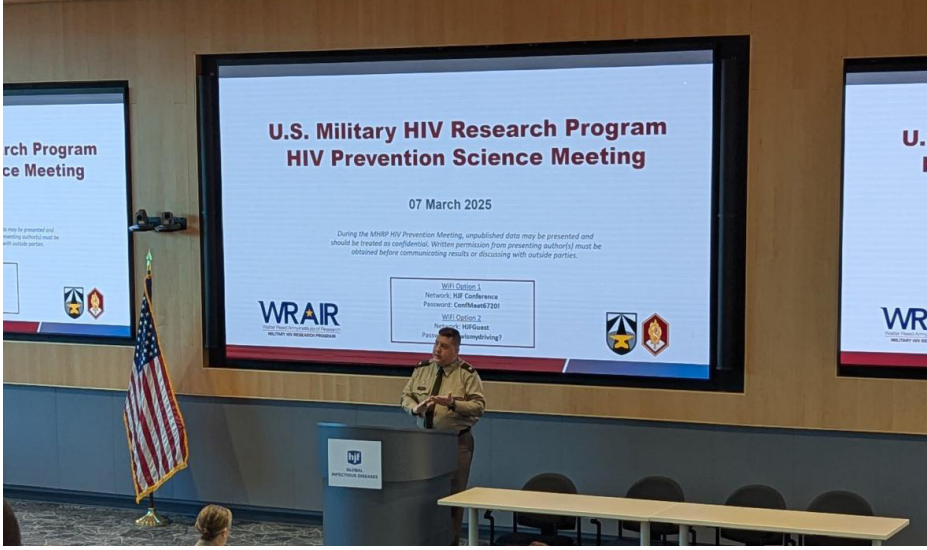
This study is the first to come out of MHRP's DELIVER initiative, which stands for Developing Leadership and Innovation in Viral Eradication Research. This collaborative project aims to enhance HIV cure research capabilities in regions most affected by the virus, focusing on building infrastructure and expertise, thereby enabling accelerated research results. Primary objectives are to develop laboratory and clinical research capacity, transfer research technology, foster collaboration between international and local experts, and to share best practices across the partners. The initiative also emphasizes community engagement. To implement DELIVER, MHRP is partnering with existing and new collaborators in Brazil, Kenya, Mozambique, Nigeria, the Philippines, Tanzania, Thailand and Uganda.

MHRP at CROI

Conference on Retroviruses and Opportunistic Infections (CROI) in San Francisco, presenting more than 10 posters and featuring oral presentations from MHRP researchers.

Dr. Lydie Trautmann, MHRP's Director of Translational Research, presented at the symposium Pathogenesis of HIV in the Brain: The Final Frontier. She discussed how T cells and specific T cell subsets are revealing new insights in neuroHIV pathogenesis, specifically in HIV neuroinvasion, persistence, and neuroprotection.

WRAIR-AFRIMS researcher Dr. Matthew Parsons presented at the Immunology and Vaccines session about the ability of the VRC07/PGT121 bispecific anti-HIV-1 broadly neutralizing antibody to protect against high-dose intravenous viral challenge in a nonhuman primate model.



MHRP Hosts Annual HIV Remission and Prevention Science Meetings

MHRP hosted its annual HIV prevention and remission science meetings in Bethesda, Md., on March 6 and 7. The meetings brought together collaborators from around the world to share findings from MHRP's ongoing cohort and clinical trials, and to discuss new strategies in the field. More than 150 people attended each day of meetings in person, and nearly 200 joined online.

Creating a Lifeline: Community Volunteers Bring HIV Services to Fishing Village

By Owen Mwandumbya and Dr. Juma Liwanje

In the remote fishing hamlet of Ilanga Village Camp, nestled along the shores of Lake Rukwa in southwestern Tanzania, people living with HIV (PLHIV) have long faced significant barriers to consistent treatment. The realities of fishing life—frequent travel, unpredictable schedules, and long distances to health facilities—often led to missed appointments and treatment interruptions.

But change came through Lucia Chitto, a resilient woman living with HIV who turned her personal journey into a mission of service. As a community volunteer, Lucia—known affectionately as Lucy—became a trusted lifeline for her fellow villagers, especially those too isolated, mobile, or hesitant to seek care.

Lucy receives training and support from MHRP and the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) to bring HIV care and treatment services directly to the community. MHRP implements PEPFAR-supported HIV programs in partnership with the Tanzanian Ministry of Health, the President's Office of Regional Administration and Local Government (PORALG), and HJFMRI. These efforts support underserved regions in the Southern Highlands, including Mbeya, Songwe, Rukwa, and Katavi.

Under a village-based community volunteer model, Lucy became a vital link between Muze Dispensary and 40 PLHIV in Ilanga. With patient consent, and using clinic cards and unique identification numbers, she discreetly collects antiretroviral therapy (ART) refills on their behalf and confidentially distributes the medications from her home. This innovative approach removed the burden of long, costly clinic visits and helped preserve the privacy and dignity of her recipients of care.

The results were remarkable: All 40 recipients of care received their medications on time, and 100% achieved viral load suppression, a key indicator of treatment success and a major milestone toward epidemic control.

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