

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

### Multinational Observational Cohort of HIV and Other Infections Expands into the Philippines

MHRP's multi-site prospective observational study of HIV and other STIs (MOCHI), already ongoing in Uganda and Kenya, is set to open a new site in the Philippines in the spring of 2024. This study provides one unified protocol and set of data collection instruments for deployment across multiple sites in diverse regions of world.

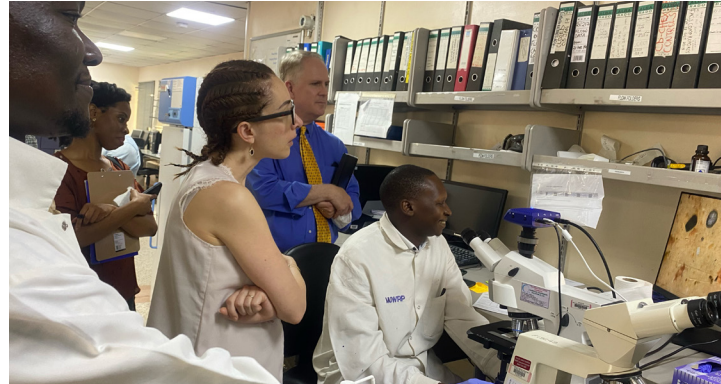
MOCHI prepares for future HIV and STI prevention studies by estimating HIV and STI incidence in high-risk populations, tracking the evolution of risk and healthcare-seeking behaviors, building site capacity, and maintaining relationships with communities affected by HIV and other STIs. The study will also help further characterize acute HIV infection, response to therapy, and long-term outcomes.

The MOCHI study launched at the Walter Reed Project-Kenya in late 2021, and at the Makerere University Walter Reed Project (MUWRP) in Uganda in late 2022. Initial data is already providing insight into cross-sectional assessments of PrEP uptake and prevalence of HIV and other STIs.

Research partners in the Philippines include the service delivery organization Love Yourself, the Armed Forces of the Philippines and the Philippines AFRIMS Virology Research Unit (PAVRU). The study is funded by the Division of AIDS, NIAID, U.S. National Institutes of Health.



*The MOCHI study team met with staff from the Philippines AFRIMS Virology Research Unit (PAVRU) in Manila. PAVRU, an arm of the Virology Department at AFRIMS, will provide laboratory support for the study.*



### New "RapidVax" Clinical Trial in Uganda

MHRP is partnering with the Makerere University Walter Reed Project (MUWRP) in Uganda to conduct a novel HIV vaccine study called "RapidVax," which will begin in late 2023. This study (RV591) combines experimental HIV vaccines with a novel dose escalation strategy with the goal of improving the body's immune response.

When an HIV infection occurs, the virus rapidly makes copies of itself and spreads throughout the body, making it difficult for the body to mount an effective immune response. This rapid vaccination strategy mimics those early-stage viral dynamics by administering vaccines more frequently than the traditional vaccine schedule. Researchers hypothesize that with RapidVax's repeated immune system stimulation the body can better defend itself against infection.

The experimental vaccines are Ad26.Mos4.HIV and CH505 TF chTrimer, which will be mixed with the Army Liposomal Formulation (ALFQ) adjuvant. The candidate vaccines are provided by Janssen and Duke University, respectively, and ALFQ was developed at WRAIR. The Rapidvax study is funded by the Division of AIDS, NIAID, U.S. National Institutes of Health and sponsored by the U.S. Army.

The principal investigator, Dr. Grace Mirembe, applauds the collaborative partnership. "Working together, we are pushing the science forward in HIV vaccine development in Africa" she said.

- 2 HIV Acute Infection Multiple Founder Variants as Vaccine Candidates
- 3 Novel Antibody Clinical Study to Inform Development of HIV Immunoprophylaxis
- 4 PEPFAR Celebrates 20 Years

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## MPOX Diagnostics Training

WRAIR held mpox diagnostics training in March 2023 for colleagues from partner research sites in Nigeria and Uganda. The Diagnostics and Countermeasures Branch (DCB) conducted the trainings with support from the HJF International Laboratory Program (INLAP). This training supports studies to determine mpox prevalence among WRAIR cohorts in Nigeria, Tanzania, Uganda and Kenya. Training sessions included data analysis, presentations, and a visit by a representative of Meso Scale Diagnostics (MSD), who provided hands-on demonstrations of their diagnostic machines. Currently, there is no FDA approved diagnostic assay for mpox, and DCB is working with the CDC, NIH and MSD to develop standardized assays and algorithms.



## MHRP Annual Science Meetings

In February, MHRP hosted collaborators and colleagues at its annual Acute HIV and Vaccine Science meetings to discuss MHRP's ongoing and planned research. MHRP scientists and collaborators shared data on acute infection and cure studies; the vaccine sessions focused on adjuvants, ongoing clinical trials for HIV prevention, novel HIV antigens and plans for future studies. Approximately 200 attendees joined each day of the meetings both in-person in Bethesda, Md., and via webinar.



## MHRP Develops Novel Vaccine Strategy based on Multiple Founder Variants

MHRP is developing an innovative HIV vaccine candidate that aims to elicit the broadly neutralizing antibodies needed to block viral transmission.

This vaccine strategy leverages MHRP's landmark RV217 acute infection study, which enrolled individuals prior to acquiring HIV and followed them during the earliest stages of HIV. This data enabled our viral genetics group, led by Dr. Morgane Rolland, to finely interrogate the earliest viral determinants of broadly neutralizing antibody (bNAbs) development.

By comparing sequences sampled in acute HIV infection in people living with HIV in the RV217 cohort to the subsequent breadth of immune responses in these participants, MHRP scientists showed that the quarter of individuals who were infected with multiple founder variants (MFV) were more likely to develop broad neutralizing responses three years later.

Based on these findings, investigators are designing vaccine candidates that would mimic the minimal diversity found in acute HIV-1 infections with multiple founder variants. According to Rolland, "we are working on novel immunogen designs that will include a cocktail of minimally distant multiple founder variant-like sequences." MHRP's vaccine development team is planning to deliver these immunogens as mRNA and stabilized HIV Env proteins with the ALFQ adjuvant to best elicit protective immune responses.

Alongside many external collaborators, MHRP's multi-disciplinary scientific team is working closely together to develop this innovative vaccine candidate, each leading a distinct but complementary function: Dr. Rolland for computational studies and antigen design; Dr. Gordon Joyce for antigen design, structural studies, and protein expression/purification; Dr. Shelly Krebs for humoral and B cell analyses; Dr. Mangala Rao for liposomal/adjuvant synthesis and small animal studies; and Dr. Diane Bolton for non-human primate studies.

"Our goal is to develop an HIV vaccine candidate capable of eliciting neutralization breadth for future manufacturing and clinical development," said Dr. Sandhya Vasan, the principal investigator of a new NIH RO1 award to pursue this strategy. "We are very excited to work with our long-term private, public and international research partners to create and develop this novel vaccine candidate."



## Novel Antibody Clinical Study to Inform Development of HIV Immunoprophylaxis



MHRP, through an international collaboration, is launching a new study (RV584) in Tanzania to test novel long-acting bispecific antibody alone and in combination with another potent monoclonal antibody (mAb) to determine and compare safety and antiviral effects, or how effective these drugs are at reducing the amount of HIV in people living with HIV, both alone and in combination.

“This study will inform countermeasures that can potentially be used to mitigate HIV risk to the battlefield blood supply in pre- and post-exposure prophylaxis settings,” according to MHRP director COL Julie Ake.

The bispecific antibody 10E8.4/iMab will be tested alone as an infusion at different doses and as an injection into muscle, or in combination with the mAb VRC07-523LS as an infusion.

This study will not only help researchers understand how these drugs might be useful for preventing or treating HIV, but will also explore the safety of intramuscular injections of mAbs, which if found to be safe, would greatly expand the feasibility of using them to prevent and possibly treat HIV.

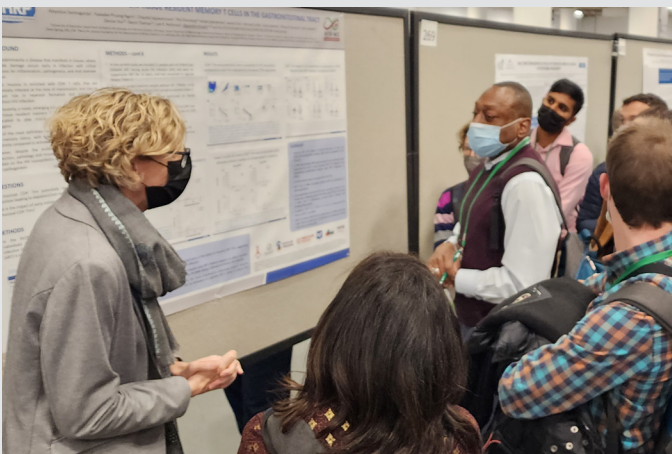
The products being used, 10E8.4/iMab and VRC07-523LS, are designed to synergistically target the HIV virus and its binding site on human CD4 lymphocytes. The bispecific antibody (10E8.4/iMab) was developed by the lab of Dr. David Ho, the director of the Aaron Diamond AIDS Research Center at Columbia University in New York City. Bispecific antibodies (bsAbs) are engineered antibodies that contain two different antigen-binding sites in one molecule. The two components of 10E8.4/iMab include Ibalizumab, which is specific to CD4 and is already approved for treatment-resistant HIV, and 10E8.4, a very broad monoclonal antibody that targets the membrane proximal external region of the HIV envelope. The bispecific antibody is very potent and active against a wide range of HIV virus variants because it is designed to focus the activity of the antibody at the precise location where it is needed. Dr. Ho is also serving as the RV584 study sponsor.

VRC07-523LS, a highly potent and broadly neutralizing monoclonal antibody that targets the HIV-1 CD4 binding site, was developed at the U.S. National Institutes of Health (NIH) Vaccine Research Center. It has been shown to be active against 96% of diverse HIV-1 strains. MHRP is testing both drugs in this research study to see if this combination is safe and more effective at reducing volunteers' viral load.

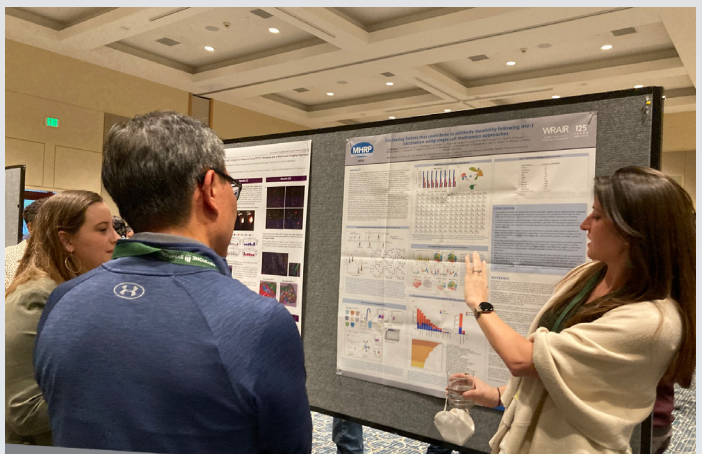
COL Ake added that “the research team plans to leverage our existing partnerships and international network to recruit volunteers from health care facilities with very high patient populations in Mbeya which are supported by MHRP's PEPFAR program.”

RV584 will enroll participants from the Mbeya Regional and Zonal Referral Hospitals with local research leadership provided by Tanzania's National Institute of Medical Research - Mbeya Medical Research Center. Dr. Marco Missanga is the principal investigator of the study, which is funded by the DoD through MHRP.

## MHRP at CROI and Keystone



Alexandra Schuetz answers questions about her research at the Conference on Retroviruses and Opportunistic Infections (CROI).



MHRP's Samantha Townsley presenting at Keystone HIV Vaccines, Immunoprophylaxis and Drugs in Colorado.

## PEPFAR Celebrates 20 Years



The U.S. President's Emergency Plan for AIDS Relief (PEPFAR) is celebrating its 20th anniversary this year. PEPFAR was established on January 28, 2003, by President George W. Bush with bipartisan support from Congress. PEPFAR leveraged years of HIV/AIDS research, collaboration with partner governments and engagement with community and faith-based organizations to create an unprecedented response to a global health crisis.

PEPFAR supports 65 million people with HIV services, provides more than 20 million people with life-saving antiretroviral treatment (ART) and has saved more than 25 million lives worldwide.

MHRP at WRAIR has been a leader in implementing cutting-edge HIV programming since PEPFAR began. In fact, MHRP provided treatment to some of the first recorded patients under PEPFAR at its partner site in Kericho, Kenya in 2004.

Currently, the Program supports HIV prevention, care and treatment in Kenya, Tanzania, Uganda, Nigeria and the Philippines. In 2022, MHRP at WRAIR supported 381,828 people on antiretroviral treatment, performed 165,0229 voluntary medical male circumcisions and provided 1+ million people with HIV counseling and testing.

Working in collaboration with the Department of Defense HIV/AIDS Prevention Program (DHAPP), MHRP is committed to providing equitable access to quality HIV prevention, care and treatment services for all with a goal of ending AIDS as a public health threat by 2030.

## Learning Visit for PEPFAR Philippines Team at AFRIMS

The U.S. Army Medical Directorate - Armed Forces Research Institute of Medical Sciences (USAMD-AFRIMS) team in Bangkok, Thailand, welcomed key medical personnel from the Armed Forces of the Philippines (AFP) who lead units with vital roles in HIV program implementation for the AFP.

This educational visit provided a platform for regional mil-mil information sharing. AFP delegates gained insights into the Royal Thai Army (Phramongkutklao Hospital), Royal Thai Air Force (Bhumibol Adulyadej Hospital), public and private sector systems, and their innovations in PEPFAR prevention, care and treatment initiatives, as well as research programming, challenges, and lessons learned.



## Empowering Healthcare Providers in Fight against Cervical Cancer

MHRP PEPFAR in Nigeria, in partnership with the Nigeria Ministry of Defence Health Implementation Programme (NMODHIP), conducted a 3-day cervical cancer screening training for 28 healthcare professionals in April. The training was funded by PEPFAR.

Participants at the training were a mix of military and civilian nurses and doctors selected from some of the comprehensive military and Accelerating Progress in Pediatrics and PMTCT (AP3) sites supported by Walter Reed Program - Nigeria..

The Director General of NMODHIP, Brig. Gen. NAE Okeji (rtd) and the Country Director of the U.S. Army Medical Research Directorate-Africa/ Nigeria (USAMRD-A/N), Ms. Helina Meri, opened the training. During her remarks, Ms. Meri expressed her gratitude to the participants for their commitment to delivering quality healthcare services.

The training covered various aspects of cervical cancer screening, with a special focus on a practical demonstration of the use of a thermal coagulator device, a treatment approach used for precancerous lesions. The capacity-building activity also featured clinical observation and practice at the Defence Headquarters Medical Centre Abuja, where participants witnessed live demonstrations of what they learned. The training also featured the supply and distribution of 26 thermal coagulator devices to the various sites represented.





## A life saved by PEPFAR: Edna's Story of Resilience and Hope



Edna is one of the oldest stories of PEPFAR's impact in Kenya and is a true testament to the purpose and mission of PEPFAR. More than 20 years ago, Edna was diagnosed with HIV. She says, "I stayed home for a long time, thinking that I wished the earth could open up and swallow me."

In 2003, MHRP began implementing PEPFAR's prevention, care and treatment program in Kenya and Edna became the second PEPFAR patient to be put on PEPFAR-funded lifesaving antiretroviral treatment (ART).

Out of desire to 'pay it forward,' Edna then mentored HIV positive children and their families, seeking out children not taking antiretrovirals (ARVs) and urging their families to get them back on the treatment that saved her own life. "I went to neighborhoods, schools, churches, hospitals - everywhere; I was free talking to people; I didn't hide [my status]; I wanted to help people."

Edna has encouraged countless pregnant women with HIV to seek out prevention of mother-to-child transmission (PMTCT) services, sharing her own impactful experience.

In 2013, MHRP initiated the African Cohort Study (AFRICOS), a large, long-term cohort study to evaluate the HIV prevention, care and treatment services it supports through local facilities, funded by PEPFAR. Edna was also the first volunteer to enroll in AFRICOS in Kenya. After enrollment, Edna was screened and treated for cervical cancer.

*“ If it was not for AFRICOS, I wouldn't have known that I had cervical cancer. They saved my life. ”*

Today, Edna teaches tailoring skills to those who are vulnerable to or affected by HIV. She is one of millions of Kenyans who is able to live with hope, thanks to PEPFAR's long-term, multi-layered support. In her own words: "I am proud of myself, because I don't think about whether I am HIV positive now... we used to be stigmatized, but since starting ARVs, I am free, I can do anything that I want to do, and I am seeing that I am somebody."

Edna not only is somebody special, but she has made it possible for her daughters to be somebody too, and she has raised, strong, empowered women, just like herself - but with even greater levels of education and opportunity than she has had herself. "I am proud of them and myself for what we have accomplished."



Sarah Day Smith / PEPFAR



## MHRP Tanzania, Kenya and Uganda Gather for South-to-South Learning Visit

MHRP's PEPFAR teams from Uganda (Makerere University Walter Reed Project/ MUWRP) and Kenya gathered in Tanzania this Spring for a four-day knowledge transfer meeting, providing an opportunity to share lessons learned and new approaches to enhance HIV service delivery.

The participants visited three prominent health facilities in Mbeya and attended a government-to-government learning session where the Mbeya Regional Commissioner, Hon. Juma Homera, welcomed the team and said that "Our strong collaboration with HJFMRI, PEPFAR and the Walter Reed Army Institute of Research has impacted our achievements addressing HIV challenges through innovative HIV interventions. As a region we feel proud that we are serving our people with quality HIV services."

Dr. Muthon Karanja from Kenya said his delegation gained valuable insights on how Tanzania advanced HIV testing services, with a focus on screening and testing at the Outpatient Department and HIV verification including index testing. He added, "We are happy that my team has explored in detail how to effectively maximize our approaches to HIV testing services delivery for highly mobile and at-risk populations and learned about successful index testing and linkage to treatment within such populations including Pre-Exposure Prophylaxis (PreP) services, and Adolescent and Youth services."

Speaking for his Uganda colleagues, MUWRP's Dr. Magala said the visit empowered the MUWRP team on the implementation of comprehensive HIV services including ensuring PrEP services are available particularly for pregnant and breastfeeding women and address the challenge of low uptake despite high demand.

## TDPF Data Center Inaugurated

MHRP recently celebrated the inauguration of a new Tanzania People's Defence Force (TPDF) Data Centre at Lugalo Military College of Medical Science in Dar es Salaam. The hardware and software installation at the TPDF Data Centre was funded by PEPFAR through MHRP at WRAIR to support HIV data analysis capabilities in TPDF health facilities.

The establishment of this Data Center will strengthen the TPDF-WRAIR collaboration and enhance the program's ability to quickly pivot and identify technical areas that may require further attention. This rapid response capability will help data reporting and analysis, and support research and operations.



## Improving TB Outcomes

MHRP in Tanzania, with support from PEPFAR, empowers volunteers like Christina Fifi (right) to provide tuberculosis (TB) screening, counseling and education sessions to people living with HIV at health facilities in the Mbeya Region to limit the spread of TB.



## Dr. Fred Sawe Recognized



The AIDS Clinical Trial Group (ACTG) awarded the 2023 James Hakim International Investigator Mentor Award to Dr. Fred Sawe, who directs WRAIR's HIV research and PEPFAR efforts with HJFMRI in Kericho, Kenya.

Dr. Sawe is the Director of the Kenya Medical Research Institute, United States Army Medical Research Directorate-Africa Kenya Program in Kenya, which is part of MHRP's international research network. Dr Sawe is a Specialist Obstetrician and Gynecologist who has worked in the Kericho area for more than 30 years.

Dr. Sawe has played a key role in the execution of several HIV vaccine and therapeutic clinical trials and related HIV cohort studies in Kericho, along with many studies on other infectious diseases. Dr. Sawe is the Clinical Research Site leader for National Institutes of Health (NIH) funded networks for HIV research and has been a Chair or Principal Investigator on a number the protocols, including studies sponsored by the U.S. Army and the U.S. National Institutes of Health. In addition to the ACTG, the site participates in the International Maternal, Pediatric, Adolescent, AIDS Clinical Trials (IMPAACT); HIV Vaccine Trials Network (HVTN); and Corona Vaccine and Prevention Network (COVPN) studies.

## PEPFAR DREAMS Participants Engage in UN Women's Leadership Program

5 young women in the MHRP PEPFAR Determined, Resilient, Empowered, AIDS-free, Mentored and Safe (DREAMS) program are participating in a year-long program, "Investing in Adolescent Girls and Young Women's Leadership and Voice in the HIV Response." The program is a partnership with UN Women and PEPFAR.

The partnership provides adolescent girls and young women (AGYW) support to strengthen their leadership and advocacy skills. It aims to empower women to demand non-discriminatory access to HIV services, while also creating conducive environments for AGYW to realize their rights.



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