MHRP EXCHANGE

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

MHRP
U.S. MILITARY HIV RESEARCH PROGRAM

Spring 2021

MHRP Evaluating IL-15 Agonist as Therapy to Reduce Establishment of HIV Reservoir

MHRP recently launched a Phase 2 clinical trial in Thailand to evaluate an interleukin-15 (IL-15) superagonist, ImmunityBio's Anktiva® (also called N-803), administered during acute HIV infection as an experimental therapy to target establishment of the HIV reservoir at a very early stage.

A critical barrier to curing HIV is the reservoir of latent virus that remains hidden and infects cells throughout the body, and previous studies have shown that the reservoir is established very early in HIV infection.

Researchers hope that administering an IL-15 agonist alongside traditional ART will reduce the HIV reservoir in lymphoid tissues and help inform a strategy towards inducing long-term HIV remission.

The trial's participants are enrolled through MHRP's RV254 acute HIV infection cohort, which identifies and treats individuals in the earliest post-infection stages. Volunteers will receive their first dose of IL-15 agonist and initiate antiretroviral therapy (ART) within days of the diagnosis of acute HIV infection.

Read more: https://www.hivresearch.org/news/press-release/mhrp-phase-2-clinical-trial-launches-evaluate-il-15-agonist-therapy-reduce

HIV VACCINE AWARENESS DAY
MAY 18th

View MHRP's HIV Vaccine Awareness Day video: [URL]

Marking 35 Years of Mission-Driven Science

A Message from MHRP Director Col. Julie Ake

Congress established the Military HIV Research Program (MHRP) in 1986 with the primary mission to develop a safe, effective vaccine. Fast forward to 2009, when we announced the results of the RV144 Thai study, the first HIV vaccine trial to show modest ability to protect people against this disease, demonstrating that such a feat is possible.

2021 marks MHRP's 35th anniversary. This year we will launch three strategic vaccine studies to test novel vaccine antigens and adjuvants, as well as to optimize dosing of vaccine components. These studies play to the strengths of our program and approach HIV vaccine research and development from new angles.

Although we haven't yet achieved our ultimate goal of an HIV vaccine, the last year has proven that a spirit of perseverance and collaboration can yield results beyond what previous experience has shown us is possible. MHRP will continue to work towards its mission to protect service members and reduce global impact of HIV until together with partners around the world we can end this continuing pandemic.

MHRP | 35 YEARS 1986-2021

WRAIR
Walter Reed Army Institute of Research
Soldier Health • World Health

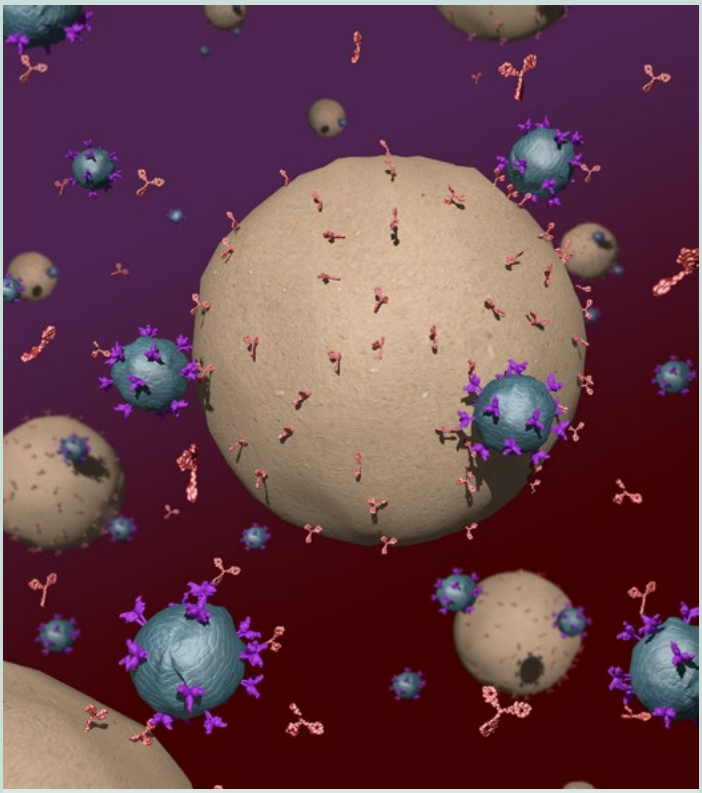
B Cells, HIV-1 Founder Viruses and Broadly Neutralizing Antibodies

A recent study led by MHRP researchers showed elevated B cell immune interactions with the envelope glycoprotein (Env) on the surface of HIV during the first month of HIV infection predict the development of broadly neutralizing antibodies (bNAbs) years later. Findings were published in *Cell Host & Microbe* in April.

Gathering information from people living with HIV who produce bNAbs can provide valuable insight into mechanistic aspects of the immune system that initiate or guide bNAb development. Using samples from MHRP's RV217 East African acute HIV infection cohort, researchers investigated factors that were found to be important in the development of neutralization breadth. They found three key B cell determinants are associated with the development of bNAbs:

- A reduction in total peripheral B cells associates with HIV neutralization breadth.
- The initial interaction of founder virus Env with naive B cells predicts bNAb development.
- Increased B cell engagement with founder Env increases activation and differentiation.

These data demonstrate that the initial B cell interaction with the founder HIV Env is important for the development of bNAbs and provide evidence that events within HIV acute infection impact outcomes.



A major goal for HIV vaccine design is the generation of broadly neutralizing antibodies that target the envelope glycoprotein. This illustration shows the binding of HIV envelope glycoprotein (purple) by antibodies (red) expressed on a B cell (brown). Image credit: Samantha Townsley and David Arthur

Pre-clinical SHIV Remission Study Shows Progress in Delaying Viral Load Rebound

A recent preclinical study by MHRP researchers showed that an experimental therapy combining a TLR7 agonist and two broadly neutralizing antibodies (bnAbs) delayed viral rebound in SHIV-infected macaques after antiretroviral therapy (ART) interruption.

The experimental combination therapy consisted of TLR7 agonist GS-986 and two bnAbs, N6-LS and PGT121, targeting different regions of the HIV envelope. The hypothesis behind this strategy is that an agent such as the TLR7 agonist, bolstered by therapeutic bnAbs, can stimulate the immune system to clear latent HIV. The paper was published in *PLOS Pathogens*.

"This study demonstrated that the combination of TLR7 agonist and dual bnAbs delayed viral rebound after ART interruption by two-fold," said Dr. Denise Hsu, MHRP Associate Director of Therapeutics. "This approach may represent a potential strategy to target the HIV reservoir in HIV-infected individuals."

Read more: https://www.hivresearch.org/news/press-release/new-mhrp-pre-clinical-shiv-remission-study-shows-progress-delaying-viral-load

AFRIMS Expands Mil-Mil PEPFAR Program in the Philippines

New PEPFAR activities will be coordinated in the Philippines through the Armed Forces Research Institute for Medical Sciences (AFRIMS) under the auspices of the DoD HIV/AIDS Prevention Program (DHAPP). AFRIMS, a Special Foreign Activity of WRAIR, is a long-time partner and helped lead the RV144 HIV vaccine study in the 2000's.

The new PEPFAR initiative will support lab strengthening, clinical training and diagnostic capabilities. The primary focus will be HIV, but these capabilities can combat other health threats and reinforce existing partnerships.

Headquartered in Bangkok, AFRIMS is a joint undertaking between the U.S. and Thai militaries with satellite surveillance and research sites across Southeast Asia. Through the Philippines-AFRIMS Virology Research Unit (PAVRU), AFRIMS has a longstanding partnership with the Armed Forces of the Philippines in Manila in the evaluation and surveillance of infectious diseases threats.

The new program will leverage AFRIMS' relationships and existing infrastructure, and MHRP will provide technical and programmatic assistance.

MHRP Expands STI Research

Sexually transmitted infections (STIs) impact both short and long-term reproductive health and contribute to increasing HIV transmission. MHRP is working around the world to better understand common and uncommon STIs and develop prevention tools.

In Thailand, two MHRP partner sites have launched a Phase 2 study to assess the efficacy of meningococcal Group B vaccine (Bexsero) in preventing gonococcal infection. This study is a collaboration with the Uniformed Services University's Infectious Disease Clinical Research Program and is supported by the Division of Microbiology and Infectious Diseases of the National National Institute of Allergy and Infectious Diseases.

MHRP and collaborators at the Institute for HIV Research at the University of Bonn recently concluded their longitudinal cohort study in Germany called BRAHMS. This was the largest systemic epidemiological study for STD's and STI's in German and MHRP's first study in Europe.

MHRP is also conducting a study to evaluate an STI behavioral intervention at military medical treatment facilities. The KISS study, which stands for Knocking out Infections through Safer sex and Screening, is now open at Fort Bragg and Joint Base LewisMcChord.

Comparative Adjuvant Trial is Underway in Kenya

RV460, a comparative adjuvant trial, launched in Kericho, Kenya, in March and has completed enrollment of its first group. The Phase 1 vaccine study is evaluating experimental DNA prime protein boost HIV-1 vaccine regimens formulated with combinations of different adjuvants, including one from the Army Liposome Formulation (ALF) family of adjuvants developed by scientists with MHRP.

MHRP Provides Cervical Cancer Screening Equipment in Tanzania

Earlier this year, MHRP provided cervical cancer screening and treatment equipment as part of PEPFAR initiatives in Tanzania. More than one hundred health care facilities across Tanzania, including the Katavi, Mbeya, Rukwa and Songwe regions, received cryotherapy units.

Every year in Tanzania, 51 of 100,000 women die from cervical cancer. Additionally, only 20 percent of diagnosed women will survive after 5 years of diagnosis, due to limited access to cervical cancer screenings and treatment services. Women living with HIV are at a higher risk for cervical cancer and severe illness.

MHRP Leadership Update

CAPT Joseph (Sean) Cavanaugh MD (USPHS) is a public health physician who recently joined MHRP as the Senior Associate Director of Health Services. Sean comes to MHRP from the Office of the Global AIDS Coordinator (OGAC), where he was Director of HIV Care and Treatment for the past two years and Senior Technical Advisor for Tuberculosis for the two years before that. Over the past four months, he has worked on the White House COVID-19 Task Force as part of the Data Strategy and Execution team. At MHRP, Sean will focus on PEPFAR programming across Tanzania, Uganda, Nigeria and Kenya and contribute to relevant research in these countries.

Career Opportunities:
Looking for your next career? MHRP has many job opportunities available.
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Please submit your questions and comments via email to communications@hivresearch.org.