2015-2016
Annual Report
EMERGING INFECTIONS RESEARCH TO IMPROVE GLOBAL HEALTH

Duke Human Vaccine Institute
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The Duke Human Vaccine Institute was formed to support interdisciplinary efforts across Duke to develop vaccines and therapeutics for HIV and other emerging infections that threaten the health of our nation and our world. Since 1990, DHVI investigators have been at the forefront in the battle against AIDS and specifically in the quest for an HIV vaccine.

By focusing on the scientific "bottlenecks" for the development of HIV, TB, and other vaccines, DHVI investigators continue to make significant contributions to overcome global health challenges.
Director’s Message

The Duke Human Vaccine Institute (DHVI) continues to lead with cutting edge vaccine research against infectious diseases that impact global health. The investigators at DHVI conduct basic and translational research to develop novel vaccines, therapeutics and diagnostics for diseases such as HIV-1, tuberculosis, influenza, malaria, ebola, cytomegalovirus and now the zika flavivirus. Several DHVI investigator led basic science discoveries are currently being produced in Good Manufacturing Practice (CGMP) facilities for early phase vaccine trials.

Over the past year, the DHVI has made innovative discoveries in the field of HIV-1 vaccine development. One challenge is that current HIV-1 vaccine candidates have been unable to induce adequate amounts of broadly neutralizing antibodies.

DHVI investigators have led efforts for driving subdominant broad neutralizing antibody lineages for vaccine strategies using the membrane bound trimer, as well as intermediate and minimal immunogens. Additionally, DHVI investigators are using novel approaches to expand the induction of bnAbs.

Supporting our state of the art vaccine development efforts is the DHVI’s unique experience managing large, complex programs such as the Duke Center for HIV/AIDS Vaccine Immunology (CHAVI-ID) where we celebrated our 10th anniversary this year, the External Quality Assurance Program Oversight Laboratory (EQAPOL), and the Immunology Virology Quality Assessment Center (IVQAC).

We are excited to share that we have completed construction of the DHVI’s own CGMP Facility unit to produce our own experimental vaccines for early phase clinical trials. Making our own vaccine for human clinical trials will speed the pace by which new vaccines are tested and allow for rapid progress. We anticipate commissioning the facility in the first quarter of 2016. This is another way that DHVI is leading in efforts to develop new vaccines for difficult to treat diseases.

Please enjoy this review of the programs and the accomplishments of DHVI. I hope that you will consider supporting in our effort to protect and improve global health.

Barton Haynes, MD

Frederic M. Hanes Professor, Medicine and Immunology and Global Health
Director, Duke Human Vaccine Institute
Director, Duke Center for HIV/AIDS Vaccine Immunology and Immunogen Discovery
Leadership

Mr. Denny oversees the daily operations of the DHVI and its programs and helps to develop long term strategic initiatives to assure that the DHVI remains scientifically competitive. He works with the leadership team to develop and implement best practices for each area of responsibility and to assure that the DHVI maintains the highest regulatory and financial compliance performance.

Dr. Tomaras is the Director of Research for the DHVI and is responsible for facilitating cutting-edge, collaborative and interdisciplinary research consistent with the goals and mission of the Institute. She serves as the primary liaison between the research staff and the administration and contributes to both short-term and long-term strategic planning. Additionally, in 2015, Dr. Tomaras together, with Dr. Thielman, in Duke University’s Division of Infectious Diseases, wrote and were awarded a 2.1 million dollar T32 training grant from the National Institutes of Health for postdoctoral research training.

Dr. Saunders is the Associate Director of Research and leads DHVI’s pre-production protein research effort. Dr. Saunders oversees the design, expression, and purification of a variety of human and pathogen-derived proteins. In addition to the protein design and production effort, he also leads the Institute’s antibody isolation endeavors to characterize adaptive immune responses in rhesus monkeys and humans.

Dr. Tony Moody is the Chief Medical Officer and Director of the DHVI Repository. In these roles, he provides support for the collaborative work occurring at the DHVI and with its many collaborators around the world. He is also the Principal Investigator of the Laboratory of B Cell Immunotechnology, which focuses on developing techniques to understand the development of antibodies in infection, after vaccination, or in other human disease states.

From Thomas Denny, COO

The DHVI offers a highly collaborative environment in which its resources enable research teams to focus on complex scientific questions. Core laboratories house advanced equipment and highly skilled technical teams to support projects in a manner that helps to efficiently advance the science. Administrative management teams at the institute bring extensive financial and grants management, project management and compliance support to faculty, students and staff engaged in our research endeavors. These have helped to develop best practices for the administration of large research programs.

The DHVI continues to look for new innovative approaches to advance our work and to be prepared to respond to global public health threats as they emerge. One example of this is the recently designed and constructed CGMP facility. Becoming fully operational in 2016, this facility will enable the DHVI to develop pilot material for early Phase I clinical trials quicker than has been previously possible. By doing so, we hope to be able to quickly assess new vaccines in humans and determine which should move forward in an expanded clinical assessment.

We hope that you will enjoy reading this report and learning more about the institute and its programs. We also look forward to hearing from those who have an interest in helping to support the mission of The Duke Human Vaccine Institute.
Dr. Richard Frothingham directs the Regional Biocontainment Laboratory (RBL) at Duke. The RBL supports research to develop treatments and vaccines against hazardous microbes including tuberculosis, plague, and influenza. Under the direction of Dr. Frothingham, during the recent Ebola outbreak, Duke clinicians received advanced training in the proper use of personal protective equipment.

Richard Frothingham, MD  
Director, Regional Biocontainment Laboratory

Dr. Sempowski is the scientific Director of the DHVI Shared Resources. Dr. Sempowski is highly collaborative and works closely with investigators from Duke, UNC Chapel Hill, Wake Forest, Boston University, Memorial Sloan Kettering, University of Georgia, University of Arizona and the Radiation Effect Research Foundation (Hiroshima, Japan). Additionally, Dr. Sempowski has developed an independent research program studying immunosenescence associated with aging and host response to infectious diseases.

Gregory Sempowski, PhD  
Scientific Director, DHVI Shared Resources

Dr. Kelly Soderberg oversees all efforts put forth by the DHVI program management team. Continuing to support the scientific advancements at the DHVI, the program team has been an integral part of the success of our large efforts in vaccine research. Program management is expected to grow as the DHVI moves even further down the translational pathway and expands into additional infectious disease vaccine research.

Kelly Soderberg, PhD  
Director of Program Management

Cherie Lahti is primarily responsible for the financial management and grants administration of all projects awarded to the institute. Under Cherie’s leadership, the DHVI finance team works with Principal Investigators in managing grant expenditures, effort allocation, budgets, subcontracts, grant applications and non-competitive renewals. In addition, the group provides senior leadership with financial analysis and recommendations for short-term and long-term planning.

Cherie Lahti, MBA  
Director of Finance

Working in collaboration with investigators worldwide, we are committed to performing the translational research necessary to take products from “bench to bedside.”

Barton Haynes | Director
Investigators

Munir Alam, PhD
Director, Laboratory of Immune Recognition

Mattia Bonsignori, MD
Director, Laboratory of B cell Repertoire Analysis

Thomas Denny, MSc, MPhil
Director, Immunology Virology Quality Assessment Center

Guido Ferrari, MD
Associate Professor of Surgery

Genevieve Fouda, MD, PhD
Assistant Professor

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Director, Laboratory of Plague Pathogenesis

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Director, Laboratory of Molecular Virology

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Professor, Department of Pathology

Barton Haynes, MD, PhD
Director, Laboratory of Host Defense Research

Kwan-Ki Hwang, PhD
Monoclonal Antibody Facility

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Garnett Kelsoe, DSc, MS, MS
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Director, Laboratory of Protein Expression

Sunhee Lee, PhD
Director, Laboratory of Mycobacteriology

David Montefiori, PhD
Director, Laboratory for AIDS Vaccine Research & Development

Tony Moody, MD
Director, Laboratory of B cell Immunotechnology

Nathan Nicely, PhD
Director, Duke University X-ray Crystallography Shared Resource

Sallie Permar, MD, PhD
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Kevin Saunders, PhD
Medical Instructor
Associate Director of Research, DHVI

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Georgia Tomaras, PhD
Director, Laboratory of Immune Responses and Virology
Professor, Departments of Surgery, Immunology, Molecular Genetics and Microbiology
Director of Research, DHVI

Nathan Vandergrift, PhD
Director, Biostatistics and Bioinformatics Center

Laurent Verkoczy, PhD
Director, Laboratory of B cell Immunoregulation

Emmanuel (Chip) Walter
Director, Duke Translational Medicine Institute Clinical Vaccine Unit
Associate Director, Primary Care Research Consortium, Duke Clinical Research Institute

Kent Weinhold, PhD
Professor, Departments of Immunology and Surgery, Duke University School of Medicine

John Whitesides, PhD
Director, Cytometry Innovation and Engineering

Jae-Sung Yu, PhD
Laboratory of Protein Expression
DHVI has an annual budget of about $45,000,000 and has maintained this level of funding for ten years.

A primary goal for the immediate future is to acquire the resources that will allow us to continue to be an intellectual and financial resource as well as a research-training powerhouse for Duke University, while making major breakthroughs in the prevention of infectious diseases. With additional resources, DHVI can begin to export the DHVI model of success to other Duke groups.

Private philanthropy, from both individuals and foundations, is absolutely essential to our ability to conduct the kind of innovative exploration that leads to new cures, more effective therapies, and improved diagnosis against the most complex and devastating diseases of our time. Your gift to the DHVI will help us achieve our mission of developing innovative diagnostics, vaccines and therapeutics to prevent and treat diseases of global importance, while working to eliminate health disparities, and train the next generation of scientists.

If you would like information on the many different ways you can help, please contact Sarah Nicholson.

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Scientific Breakthroughs

HIV
Influenza
Malaria
Ebola
Tuberculosis
CMV
Zika
The finding by a Duke Medicine-led research team suggests that a successful vaccine approach would need to somehow mask this easily induced, but ineffective antibody response, or stimulate a different antibody response altogether.

“With this study, we wanted to know whether a vaccine induced the same diverted, ineffective antibody response that occurs with acute HIV infection,” said Barton F. Haynes, M.D., director of the DHVI and senior author of the study appearing online in Science Magazine on July 30.

“We know that the intestinal microbiome can influence the types of antibodies that develop after birth when the microbiome is established,” Haynes said. “Our study raises the hypothesis that the microbiome imprinted the immune system to make these cross-reactive antibodies. It suggested that one way to improve the antibody response may be to block the undesired HIV sites during vaccination, or to vaccinate earlier in life to imprint the immune system on desired HIV regions.”
Haynes said the experimental vaccine induced antibodies that targeted a region of the HIV virus called gp41, which is part of the virus’s outer envelope. But these antibodies were non-neutralizing and were not able to stop the virus from infecting CD4 T cells.

What’s more, the gp41 region is a molecular mimic of some intestinal microbiome bacterial and self antigens that the body’s B cells are trained on, raising the hypothesis that the vaccine essentially stimulated a diversion that kept the immune system busy, allowing the virus to flourish.

“It’s another way that the virus evades the immune system,” Haynes said. “It gives the virus a leg up in escaping the early antibody response, by primarily inducing antibodies that cannot neutralize HIV.”

“The keys to inducing a successful HIV antibody response may be to mitigate or get around the virus’s ability to divert preexisting B cells that are cross-reactive with intestinal microbiota,” Said Dr. Wilton Williams, lead author of the study. “We are currently exploring early vaccination strategies and exploring new designs of the HIV viral envelope to induce the correct antibodies.”

Because the microbiome serves as a training ground to teach the immune system how to fight pathogens, HIV’s ability to mimic common microbiota suggests that a successful HIV vaccine approach might also include early childhood immunizations. This could provide a way to prime the immune system to better identify and attack HIV.

The study received funding from the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health, Center for HIV/AIDS Vaccine Immunology-Immunogen Discovery (UM1 AI100645); the Duke University Center for AIDS Research; and the Vaccine Research Center at NIAID.

Article credit: Duke Medicine News and Communications 2015
Antibody Response Linked To Lower Mother-to-Child HIV Transmission

How most babies are protected from acquiring HIV from their infected mothers has been a matter of scientific controversy. Now researchers at Duke Medicine provide new data identifying an effective antibody response that had long been discounted as inadequate to confer protection.

Mother-to-child transmissions account for about 250,000 HIV infections per year worldwide, despite greatly expanded access to antiretroviral drug regimens that can interrupt transmission into low-resource settings. Ongoing problems with access to the drugs, late initiation of the drug regimens during pregnancy, and acute maternal infection during pregnancy and breastfeeding all contribute to the ongoing infant transmission.

Even in the absence of antiretroviral drug regimens, however, the majority of newborns are naturally protected against HIV, despite chronic virus exposure. The Duke research team sought to define what is different in the babies who become infected compared to those who don’t.

We know that mothers pass antibodies to fetuses in-utero, but a true understanding of how maternal antibodies were contributing to protection had never been established.

Sallie Permar, MD, MSH | Lead author, Principal Investigator

Permar and colleagues at the DHVI and the Fred Hutchison Cancer Research Center analyzed data from a U.S. study in the 1990s that predated therapies such as AZT. The study included mothers and babies, yielding information about risk factors and transmissions in a pre-treatment environment.
By profiling the immune responses of mothers in this early study, the researchers were able to pinpoint the differences between those who transmitted the virus to their infants, and those who did not. Among mothers whose babies were shielded from infection, they found a strong antibody response to a particular region on the HIV virus envelope (the HIV envelope third variable or V3 loop) that has been considered too variable and too inaccessible to be a relevant target for a neutralizing antibody.

“That was very surprising,” Permar said, “because this type of weak neutralizing antibody response, which had previously been thought to be inconsequential for HIV transmission, could potentially be effective in preventing mother-to-child transmission. And there are current HIV vaccine candidates, such as recombinant HIV envelope protein immunization, in early-stage clinical testing that can elicit this type of response.” Permar said the team’s study raises a compelling question about why the V3 neutralizing antibody response seems to be enough to reduce mother-to-child transmission, yet is not protective in other modes of HIV transmission.

“The difference in mother-to-infant transmission might be that the infant is only being exposed to the mother’s virus, and the infant is born with antibodies that are transferred from the mother,” Permar said. “The presence of antibodies that were raised against the mother’s virus prior to exposure to the same virus makes the infant transmission setting very different from that of other modes of HIV transmission. So how well the mother’s antibody can neutralize her own virus could be the key to whether the baby is infected.”

Permar said additional research at Duke will focus on testing newer experimental HIV vaccines to raise this potentially protective antibody response in mothers to neutralize her virus and thereby protect the baby. “We hope this will be a major clue to making a vaccine to effectively prevent all mother-to-child HIV transmission, since these antibodies are the type that our current experimental HIV vaccines can boost,” said Tony Moody, MD, a co-author and DHVI chief medical officer.

Funding included grants from the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health (5-UM1-AI100645, 5-P30-AI064518) and HIV Vaccine Trials Network.

The study was published online June 8, 2015, in the Journal of Clinical Investigation.
Duke Research Teams Win Large Federal Grants for HIV Vaccine Studies

Two research teams at Duke Medicine have received large, multi-year grants from the National Institutes of Health to pursue projects on HIV vaccine development.

The National Institute of Allergy and Infectious Diseases (NIAID) awarded a five-year grant totaling more than $9 million to a team led by Mary Klotman, MD, chair of the Department of Medicine at the Duke University School of Medicine.

This grant represents an exciting collaborative effort. It combines our long-standing interest in developing integrase defective lentiviral vectors as a safe approach to persistent immunogen expression along with expertise within the Duke Human Vaccine Institute that is focused on innovative envelope immunogen design and B cells.

The NIAID presented a second grant of more than $11 million over five years to a collaborative effort led by Sallie Permar, M.D., Ph.D., associate professor in the Department of Pediatrics at Duke, and involving researchers at the University of North Carolina and the University of California, Davis.

Klotman’s grant will support two research projects and two core facilities that together will aim to develop a safe, effective HIV vaccine using a vector delivery strategy to drive a successful immune response.

Klotman’s collaborators include Andrea Cara, Ph.D., a Duke visiting scholar; Tony Moody, MD, associate professor of pediatrics and director of the Laboratory of B cell Immunotechnology in the DHVI; and Sampa Santra, Ph.D., assistant professor of medicine at Harvard University and a member of the Center for Virology and Vaccine Research at Beth Israel Deaconess Medical Center.

Both grants draw on the longstanding expertise in the Duke Center for HIV/AIDS Vaccine Development led by Barton Haynes, MD. Permar’s grant funds two projects and three core facilities to develop a maternal and infant vaccine approach to eliminate pediatric HIV-1 infections.
Influenza

Influenza is one of the most common infections worldwide. Each year, new influenza vaccines are needed that incorporate currently circulating strains because influenza viruses mutate and change every year. These new strains can emerge in either epidemic or pandemic waves. Influenza vaccination has been shown to be effective in reducing influenza disease and this has led to recommendations for near universal vaccination in the US.

The annual changes that occur in influenza viruses usually make the previous year’s vaccine ineffective in providing long-lasting protection. Furthermore, it is possible that a new influenza strain, such as those that circulate in birds, could infect the human population resulting in a new global lethal pandemic. Finding a vaccine strategy that results in long-lasting protection against multiple influenza strains is a goal of the DHVI Influenza Vaccine Program.

Influenza receptor binding site antibodies

Protection against influenza infection is primarily due to antibodies made by the body in response to vaccination or infection. Most of these antibodies are highly specific, reacting primarily with the influenza strains in the vaccine or the one causing infection. In recent years, antibodies that have the ability to neutralize many strains of influenza have been discovered, and one group of these antibodies block influenza viruses by interfering with the ability of a virus protein called hemagglutinin to bind to its target on human cells. If a vaccine could elicit these antibodies, called receptor binding site antibodies, the vaccine might be able to prevent infection with many strains of influenza viruses. DHVI is actively pursuing vaccine strategies to elicit this class of antibodies with the hope of creating a universal influenza vaccine.

New tools for studying influenza antibodies

The DHVI is actively working to understand how receptor binding site antibodies, and other broadly protective antibodies, arise in humans. To do this, we have partnered with Stephen Harrison at Boston Children’s Hospital to study the structural basis for the activity of these antibodies, to develop new tools for their study, and to design vaccine candidates for testing. As part of this collaboration, we recently reported that receptor binding site antibodies in humans could arise from multiple different starting points, suggesting that this class of antibodies might be easier to induce than similar antibodies against HIV-1.

Original Antigenic Sin / Immune Memory

In some cases, exposure to new strains of influenza may produce a response that is directed toward strains seen in prior years of infection or vaccination rather than to that being seen in the present infection or vaccination. This phenomenon has been called original antigenic sin (OAS) and has been described not just for influenza but has been observed for many kinds of pathogens. Work at DHVI previously showed that for influenza, OAS was more likely to occur following infection compared with vaccination. Using that knowledge, we are developing strategies to leverage the OAS phenomenon with the goal of eliciting receptor binding site antibodies that can provide long-lasting protection against many influenza strains.
Malaria, which is caused by infection with parasites of the genus Plasmodium, predominantly by P. falciparum, remains a significant public health problem worldwide and a leading cause of morbidity and mortality in tropical and sub-tropical regions. P. falciparum is transmitted to humans from mosquitoes of the genus Anopheles, the non-human carrier of the parasite, through bites. Half of world’s population is at risk of malaria, with an estimated 198 million cases occurred globally and more than 584,000 deaths annually, mostly in the African region and among children under the age of 5 years (World Health Organization. World Malaria Report 2014).

Despite extensive efforts to control and treat malaria, including public health measures and widespread usage of anti-malaria drugs, the most cost-effective solution to prevent infection and control the malaria endemic is to develop a vaccine.

Dr. Tomaras leads a team that is actively working on developing methods to enable identification of correlates of protection for malaria vaccines. Technical and conceptual advances from DHVI’s work on the relationship between antibody specificity, subclass and HIV-1 protective efficacy are being applied to the evaluation of candidate malaria vaccines to identify potential correlates. Her work, in collaboration with Dr. Munir Alam, focuses on the evaluation of the biophysical interactions between antibodies and antigenic determinants exposed during the pre-erythrocytic stages of P. falciparum.

Dr. Bonsignori leads a team committed to isolate and characterize malaria-specific monoclonal antibodies from B and plasma cells of vaccine recipients and infected individuals. By leveraging the established platform for B cell repertoire analysis and antibody production developed at the DHVI, his work focuses on characterizing the functional repertoire of vaccine-induced malaria-specific monoclonal antibodies with diverse specificities and evaluating clonal persistence and evolution, as well as differences between naturally occurring and vaccine-induced antibodies.

Detailed analysis of vaccines can reveal potential immune correlates of protection and lead to testable hypotheses about the mechanism of action critical to further vaccine improvement.
Ebola

In addition to immunizing non-human primates with proteins and extracting antibodies, investigators at The DHVI are working with investigators at Los Alamos National Laboratory as well as The University of Oxford to generate two different structural mosaic Ebola envelope proteins to use as potential vaccine antigens for vaccination against Ebola.

Because Ebola has an extremely variable envelope protein, the idea is that the vaccine antigen would raise T-cell responses that are cross-reactive to several common variants of the Ebola viral envelope. The structural envelope mosaics are made from combinations of 3 artificial proteins that a group led by Dr. Korber, at LANL, designed using computational methods. The artificial proteins mimic several different envelope epitopes so that T-cells that are generated would recognize several different Ebola virus variants.

In this particular work, the DHVI, as well as others, will test the effectiveness of two different structural mosaics for generating T-cell responses in mice. If mice vaccinated with the mosaics produce T-cell responses to Ebola, then future studies might include vaccination in non-human primates to confirm that the immune response to the vaccines is similar in those animals. The long-term goal is to develop vaccine antigens for human immunization trials and effective human vaccines against Ebola.

This work is a collaboration between Bette Korber, PhD (Los Alamos National Laboratory), Tom Hanke, MSc, BSc, PhD (University of Oxford), and Barton Haynes (The DHVI).

Ebola is a rare and deadly disease caused by infection with a strain of Ebola virus. The 2014 Ebola epidemic is the largest in history, affecting multiple countries in West Africa. The risk of an Ebola outbreak affecting multiple people in the U.S. is very low. The disease is spread through direct contact with blood and body fluids of a person already showing symptoms of Ebola. Ebola is not spread through the air, water, food, or mosquitoes.

Following on what we have been doing with a conserved region T cell vaccine for HIV, we are applying the same kind of strategy to the Ebola virus.

Bette Korber, PhD | Collaborator
**Tuberculosis**

TB is a disease caused by a bacterium called *Mycobacterium tuberculosis*. The bacteria usually attack the lungs, but TB bacteria can attack any part of the body such as the kidney, spine, and brain. If not treated properly, TB disease can be fatal. TB disease was once the leading cause of death in the United States.

**Tuberculosis Vaccine Improvement**

Tuberculosis remains a major global health problem, despite the widespread use of the *Mycobacterium bovis* bacillus Calmette-Guerin (BCG) vaccine and drug therapies. Coinfection with *Mycobacterium tuberculosis* and HIV, as well as multidrug-resistant (MDR) and extensively drug-resistant (XDR) tuberculosis, makes TB control difficult, complex and challenging.

*M. tuberculosis* is an extraordinarily successful pathogen that has managed to latently infect nearly one third of humanity and is responsible for an estimated two million deaths annually. The success of this pathogen is linked to its ability to manipulate the intracellular environment of phagocytic cells in the host. Many lines of evidence indicate that *M. tuberculosis* has evolved mechanisms to evade host immunity, in some cases by inhibiting the priming and effector functions of these T cell subsets. For example, the manipulation of cell death (apoptosis) by virulent mycobacteria is a well-known survival and immune-modulating strategy. By blocking apoptosis of cells early after infection, *M. tuberculosis* prevents or delays presentation of its antigens and thus fails to stimulate effective T cell responses.

The Lee lab is currently studying these immune evasion strategies of *M. tuberculosis* and is researching novel approaches for improving mycobacterial vaccines by manipulating mycobacterial proteins responsible for evasion of host immune responses. In particular, studies of mycobacterial modulation of apoptosis and autophagy, as innate and adaptive immunity defense against intracellular pathogens, are main focuses of the lab. We have screened *M. tuberculosis* transposon mutant library and isolated 23 pro-apoptotic and 12 pro-autophagic mutants that are not able to inhibit infection-induced host innate responses.

Some of these *M. tuberculosis* mutant strains demonstrated enhanced immune responses in mice and thus could be important targets incorporated into TB vaccine candidates. The major long-term goal of our laboratory is to engineer safe and more effective live TB vaccines that will contribute to the global control of tuberculosis and also reduce the emergence of drug resistant strains.
Surface Binding Human M. tuberculosis Monoclonal Antibodies

Cell-mediated immunity is a major component of host defense against M. tuberculosis (Mtb) infection. The predominant Th1 CD4+ cell response reduces progression of Mtb infection, but does not prevent establishment of infection or clear established infection. Mtb antibodies can play a significant role in protection as demonstrated by vaccination studies and by administration of either polyclonal or monoclonal antibodies. However, the mechanisms underlying antibody-mediated protection from Mtb infection remain unclear.

Our long-term goal is to develop an efficacious TB vaccine that induces antibodies capable of preventing Mtb infection. Critical to achieving this goal is a clear understanding of the contribution of B cells and the humoral response to the control of MTB in infected hosts. We have identified three murine Mtb surface binding monoclonal antibodies (mAbs) that reduce Mtb burden in lung at early time points after experimental Mtb aerosol infection in mice. The mAbs block entry of the bacterium into lung cells and also divert the bacteria from alveolar macrophages toward other phagocytic cells.

Most humans with Mtb infection generate poor responses to the surface of the Mtb bacterium, but we have identified a small subset of humans (about 7%) who produce high-titer high-avidity antibodies to the Mtb surface. We are isolating monoclonal antibodies from these individuals in order to identify the targets of these antibodies. These targets may serve as the basis for a preventive vaccine to be administered prior to Mtb infection. We also evaluating human surface binding antibodies as potential therapeutic agents for humans infected with extensively drug-resistant Mtb (XDR-TB).

Dr. Richard Frothingham and coworkers have developed a murine model of latent M. avium infection that mimics many aspects of latent human infection with environmental mycobacteria.
Tuberculosis

Buruli Ulcer Vaccine Development

At the Laboratory of Mycobacteriology, we have developed safe and effective vaccines for Buruli ulcer caused by M. ulcerans. Buruli ulcer is an emerging ulcerative skin disease caused by infection with Mycobacterium ulcerans (MU). It is one of the 17 Neglected Tropical Diseases (NTDs) prioritized by World Health Organization. The extensive cutaneous and subcutaneous lesions provoked by BU often lead to grotesque deformities and permanent disability of the human host. Often young children succumb to the infection.

Despite the progress made in early detection and treatment of BU, surgical excision of the lesions with skin grafting remains the only treatment for advanced ulcers. Thus, a vaccine against MU is imperative to protect at-risk populations in hyper-endemic areas. Currently, there are no specific vaccines against BU.

Similar to the responses of the two best-understood mycobacteria of clinical interest, M. tuberculosis (Mtb) and M. leprae, Th1-type cellular immune responses are essential for control of MU. However, despite early development of T cell immunity in experimental mouse infections, the host response is not sufficient to inhibit the proliferation of highly virulent MU strains. To test if vaccination triggering heightened MU specific cell mediated immunity will elicit a more effective and prolonged protective immunity against virulent MU infection, we constructed recombinant mycobacterial strains overexpressing the MU antigen 85A (Ag85A). This recombinant BCG showed significantly improved antigen-specific T cell responses, correlating with the protection against virulent MU in the mouse footpad model. This result warrants the development of an attenuated, live, BU vaccine that can induce strong immune responses against species-specific antigens, which we are currently working on.

Laboratory of Mycobacteriology focuses its research on: the development of safe and effective vaccines and immunotherapeutics for tuberculosis via novel strategies and approaches; evaluation of alternative methods to enhance the efficacy of current mycobacterial vaccines; development of recombinant mycobacterial vehicles capable of eliciting strong immune responses to HIV and other foreign antigens; and study of the virulence and immunogenicity of drug-resistant strains of MTB.

Sunhee Lee, PhD | Director
Stable Expression of Lentiviral Antigens by Quality-Controlled Recombinant Mycobacterium bovis BCG Vectors

The well-established safety profile of the tuberculosis vaccine strain, Mycobacterium bovis bacille Calmette-Guérin (BCG), makes it an attractive vehicle for heterologous expression of antigens from clinically relevant pathogens.

However, successful generation of recombinant BCG strains possessing consistent insert expression has encountered challenges in stability. At the Laboratory of Plague Pathogenesis, we developed a method for the development of large recombinant BCG accession lots which stably express the lentiviral antigens, human immunodeficiency virus (HIV) gp120 and simian immunodeficiency virus (SIV) Gag, using selectable leucine auxotrophic complementation. Successful establishment of vaccine stability stems from stringent quality control criteria which not only screen for highly stable complemented BCG ΔleuCD transformants but also thoroughly characterize postproduction quality.

Importantly, these quality assurance procedures were indicative of overall vaccine stability, were predictive for successful antigen expression in subsequent passaging both in vitro and in vivo, and correlated with induction of immune responses in murine models. Production of large, well-defined recombinant BCG ΔleuCD lots can allow confidence that vaccine materials for immunogenicity and protection studies are not negatively affected by instability or differences between freshly grown production batches.

Laboratory of Plague Pathogenesis focuses on Yersinia pestis, the bacterial cause of bubonic and pneumonic plague. The goals of the Frothingham laboratory are to define specific protective mechanisms that are a part of the host response to plague and to use this information to develop better drugs and vaccines against plague infection.

Richard Frothingham, MD, FACP, CBSP | Director
Cytomegalovirus

Cytomegalovirus (CMV) complicates 1% of all pregnancies and results in 8,000 severe infections in U.S. children annually, resulting in hepatitis, neutropenia, brain damage, seizures, and vision and hearing loss. It is the leading nongenetic cause of infant hearing loss, accounting for 25% of all hearing loss, and causes more permanent disabilities in U.S. children then spina bifida or Down syndrome. Much like the rubella vaccine eliminated congenital rubella syndrome in this country, a vaccine that induces protection maternal immune responses in needed to protect against congenital CMV. Thus, a team of DHVI researchers, led by Sallie Permar, MD, PhD, are working to identify the maternal immune responses that are required to protect against placental transmission of CMV in mother-infant cohort studies.

Monkey Model Discovery Could Spur CMV Vaccine Development

Cytomegalovirus (CMV) is the leading infectious cause of birth defects worldwide, but scientists have been frustrated in their efforts to develop a vaccine to protect against infections. Among the most confounding problems is the lack of animal models that aptly mimic CMV passing from mother to unborn child, as it does in humans. Aside from guinea pigs, which have limited similarities to humans, no other mammals were known to pass the virus to their fetuses.

Or so it has seemed.

Now researchers have discovered that rhesus monkeys can, in fact, transmit the virus across the placenta to their unborn offspring. This finding, reported online during the week of October 19 in the Proceedings of the National Academy of Sciences, establishes the first primate model that researchers can use to study mother-to-fetus CMV infections and spur development of potential vaccine approaches.

CMV is related to the herpes viruses that cause chicken pox and mononucleosis, and in most people, it results in mild to no symptoms of disease when they acquire an infection. However, in about a third of instances when women who have never been exposed to CMV contract the virus during pregnancy, they can pass an infection to the fetus. About a quarter of those infants will go on to have neurologic impairment. The Centers for Disease Control and Prevention reports that about 5,000 children a year in the U.S. are born with permanent problems resulting from CMV infections, including deafness, blindness, seizures and cognitive delays.

"A huge impediment to CMV vaccine development has been our lack of ability to determine what immune responses would be needed to protect against mother-to-fetus transmission. This requires good animal models, where we can manipulate each arm of the immune system to evaluate its role in congenital infection."

Sallie Permar, MD, PhD

“This is a situation of great concern and we need to work to prevent it,” Permar said. “After the rubella vaccine was developed in the 1960s, schools for the deaf and blind had to close their doors because there were far fewer children who had suffered congenital rubella infections and needed the services. That’s the kind of impact a CMV vaccine could have.”
Using macaques at the New England Primate Research Center, Harvard Medical School, that were specially bred to be free of CMV and all herpes viruses, they depleted the CD4 “helper” T cells that play an important role in antibody responses. When infected with CMV a week later, all the animals passed the virus through the placenta, resulting in miscarriage in three of the four animals. “This told us not only that the virus could be transmitted through the placenta, but that the mother’s immune system was playing an important role in the severity of the infection,” Permar said.

In a second experiment, Permar and Kaur infected CMV-negative animals with the virus, and left their immune systems intact. Among this group, CMV was transmitted to two of three offspring in utero, but the animals were born with no major neurological deficits – mimicking what often occurs in humans.

In a third control group of animals, the researchers studied females that had naturally been infected with CMV earlier in their lives, and depleted their CD4 helper T cells during pregnancy. The mothers had little to no circulating virus and the offspring appeared to be unaffected by the CD4 helper T cell depletion.

Permar said simple approaches to vaccine development, such as creating a weakened virus to trigger immunity, have failed, because the virus has evolved alongside humans to elude the immune system. So having a non-human primate model — something of a higher order than guinea pigs — became imperative. Permar said finding the mother-to-fetus transmission in the rhesus macaques became a hunt. She enlisted the help of co-senior author Amitinder Kaur of Tulane National Primate Research Center, an expert in CMV-specific immunity in rhesus macaques.

Most macaques are infected with the rhesus version of CMV before adulthood, yet their young are born without the hearing loss or neurological problems that human babies can acquire in utero. In an earlier study, coauthor Peter Barry of the University California at Davis found that infection of a macaque fetus directly through the abdomen resulted in a similar disease to that in humans. Permar and Kaur wanted know if the infection could pass through the placenta.

In addition to establishing a primate model for congenital infection, we gained new information about the importance of the maternal immune system in protecting the fetus. Whereas CMV transmission among immune-competent mothers did not result in fetal disease, transmission in mothers with compromised T cell immunity led to severe fetal outcome.

Permar said the next stage of research will be to determine whether neutralizing antibody responses would be enough to protect against transmission of severe disease, or whether a T-cell vaccine would be the better approach. In addition to Permar and Bialas, study authors at Duke included Eduardo Cisneros De La Rosa; Erika L Kunz; Jennifer Kirchherr; Qihua Fan; and Allison Hall.
The recent, rapid spread of Zika Virus (ZKV) from a locally-harbored epizootic arbovirus has been a public health wake up call. Carried and transmitted by the Aedes species of mosquitoes, this epidemic follows a now familiar pattern of spread to that of Chikengunya, and West Nile Virus, which were both newly spread from primarily tropical zones to the western hemisphere within the last two decades.

Yet, unlike these other two globally mobile arboviruses, the ZKV epidemic in the Americas stands out as particularly alarming due to its association with poor pregnancy outcomes, including fetal demise, infant death, and severe fetal neurologic damage.

An epidemic of this proportion will result in a generation of disabled children in areas of the world that suffer from limited health care resources, leaving a costly societal burden in its wake.

An effective maternal vaccine is the only intervention that will protect all infants against ZKV-associated permanent brain damage and birth defects. The success of a maternal vaccine has been demonstrated by the elimination of congenital rubella syndrome in the Americas through the introduction of a rubella vaccine. Yet a considerable gap exists in our understanding of the natural immune responses that develop to infection and its impact on virus transmission and disease, impeding the way forward for development of an effective vaccine.

Researchers at the DHVI, along with researchers at Universidade Federal do Espirito Santo (UFES) in Victoria, Brazil, hypothesize that a prime-boost immunization strategy of the ZKV Env protein expressed in a Yellow Fever vector and/or a TLR-adjuvanted envelope purified protein will elicit high magnitude and specific binding and neutralizing antibody responses against Zika virus.

The team of researchers plan to identify ZKV infection in women in the early phases of pregnancy, perform a detailed characterization of the ZKV binding and neutralizing antibody assays, as well as the cross reactivity to endemic serotypes of dengue virus, and then relate these antibody responses to fetal outcome.

The first step towards developing an effective vaccine is to understand the natural immune responses against the virus, particularly in pregnant women, and their impact on fetal outcome.
2015 marked the 10th anniversary for the Duke Center for HIV/AIDS Vaccine Immunology (CHAVI). The current CHAVI-ID is a consortium that was established by the National Institute for Allergy and Infectious Diseases (NIAID) to undertake the immunologic research that will tackle the major scientific obstacles in the development of an effective HIV-1 vaccine.

The vaccine strategy of the Duke CHAVI-ID is based on identifying and targeting novel HIV-1 vulnerabilities to B, T and NK cell immune responses and using this information to design vaccines that will induce protective immunity at the time and location of HIV-1 transmission.

The CHAVI-ID consortium has continued to conduct “big science” that is both qualitatively and quantitatively different than what can be accomplished by individuals alone. Additionally, the Duke CHAVI-ID has succeeded in speeding up the tempo of the work, sharpening the focus, and answering questions that have been intractable for the field for many years.

Finally, the work in the CHAVI-ID has defined the host-HIV interaction that has justified HIV development to date and, on this work, charted a course for successful HIV vaccine development.

The goal of the HIV Vaccine Trials Network laboratory program, NIH/NIAID is to provide cutting edge immune monitoring of HIV-1 vaccine clinical trials.

The laboratory program at Duke is led by Georgia Tomaras, PhD, and is comprised of three laboratories (David Montefiori, Guido Ferrari, Georgia Tomaras) working together to comprehensively evaluate vaccines, including vaccine immunogens designed by Dr. Haynes, Director of DHVI. The Duke laboratory works in partnership with the Fred Hutchinson Cancer Research Center, Seattle, WA.
The goal of the EQAPOL program is to support the development, implementation and oversight of external quality assurance (EQA) programs that monitor laboratories involved in HIV/AIDS research and vaccine trials around the world. In addition to EQA programs, the EQAPOL program has established and continues to add to an HIV Viral Diversity Panel that represents the current genetic and geographic diversity of HIV.

The EQAPOL program currently administers five EQA programs with over 70 participating sites worldwide to assess proficiency in the following assays: interferon-gamma (IFN-y), Enzyme-linked Immunosorbent Spot (ELISpot) assay, Intracellular Cytokine Staining by Flow Cytometry, Luminex bead-based assay, A3R5 HIV neutralizing antibody assay, and HIV incidence assay (ICS) testing (newly added in late 2015).

The goal of the EQAPOL Viral Diversity program is to establish a panel of fully characterized viruses from acute/early and chronic HIV infections. The panel of viruses can be used for various applications, including:

- Impact of genetic diversity on assay performance
- Developing/validating new assays
- Assisting regulators to evaluate test kits
- Monitoring HIV drug resistance
- Informing vaccine development

In support of these programs, the Immunology and Virology Quality Assessment Center (IVQAC) maintains a College of American Pathologists (CAP)-accredited biorepository, which contains well-characterized cryopreserved peripheral blood mononuclear cells (PBMCs) for use in EQA testing and viral culture. The IFN-y ELISpot, Flow Cytometry and Luminex EQA programs are ISO/IEC 17043 accredited by the American Association for Laboratory Accreditation (A2LA) as a Proficiency Testing provider (A2LA Cert. 3614.01).

The Immunology and Virology Quality Assessment Center (IVQAC) is the home of the NIAID DAIDS Immunology Quality Assessment (IQA) program. Thomas Denny, MSc, MPhil, has led the IQA program since 1999.

The IQA is a resource designed to help domestic and international immunologists evaluate and enhance the integrity and comparability of immunological laboratory determinations performed on patients enrolled in multi-site HIV/AIDS therapeutic, vaccine and prevention investigations.

As part of the IQA program, two Proficiency Testing (PT) efforts are administered: a PT for Peripheral Blood Monoclonal Cell (PBMC) cryopreservation and a PT program for CD4 and CD8 immunophenotyping via flow cytometry. In addition, the IQA program assists the current and future NIAID-sponsored clinical trial networks and collaborating study groups, including the AIDS Clinical Trials Group (ACTG), the International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT), the HIV Vaccine Trials Network (HVTN), the HIV Prevention Trials Network (HPTN), and the Microbicide Trials Network (MTN), in a variety of capacities.
Through the IQA proficiency testing programs, over 200 sites worldwide are served helping to ensure quality and consistency in data generated from these sites. The PBMC cryopreservation program currently includes 86 domestic and international sites. The domestic immunophenotyping PT program currently services 60 laboratories across the United States, Canada and Puerto Rico. The IQA domestic immunophenotyping program is accredited by the American Association for Laboratory Accreditation (A2LA) as a Proficiency Testing provider (A2LA Cert. 3614.01).

In addition, the IQA reviews the performance and offers remediation to the international DAIDS laboratories participating in the UK NEQAS Immune Monitoring program. Currently, there are 63 laboratories from 18 countries participating in the UK NEQAS/IQA review and monitoring program for CD4 enumeration.

The Duke Clinical Vaccine Unit (DCVU), led by Emmanuel “Chip” Walter, MD, MPH, is a consortium of investigators across multiple disciplines committed to conducting clinical investigations related to the control and prevention of infectious disease with an overarching goal of furthering our understanding of vaccine immune responses and correlates of protection from infection.

The DCVU conducts clinical investigations through funding provided by government (NIAID DMID and CDC) and industry. Two major projects of the DCVU are the NIAID DMID Vaccine and Treatment Evaluation Unit (VTEU) and the Clinical Immunization Safety Assessment (CISA) Project. Both projects rely on the extensive scientific and research expertise afforded by the Duke Human Vaccine Institute (DHVI) and the Duke Clinical Research Institute (DCRI).

During this year, Dr. Walter was appointed to the Advisory Committee on Immunization Practices (ACIP). The ACIP consists of medical and public health experts that develop recommendations on how to use vaccines to control diseases in the United States. Dr. Swamy was appointed to the National Vaccine Program Office’s National Vaccine Advisory Committee (NVAC) Maternal Immunization Working Group.

The working group is charged to identify barriers to and opportunities for developing vaccines for pregnant women and make recommendations to the Assistant Secretary of Health to overcome these barriers. Dr. Swamy was also appointed to the American College of Ob/Gyn’s (ACOG) Immunization Expert Work Group. The work group serves in an advisory capacity to many ACOG standing committees such as the Committees on Obstetric Practice, Gynecologic Practice, Adolescent Health, and Health Care for Underserved Women as they develop clinical guidelines and patient resources.
In September 2013, the Duke Clinical Vaccine Unit was named a NIH Vaccine Trial Evaluation Unit (VTEU) with Dr. Chip Walter and Dr. Geeta Swamy as the Co-Principal Investigators. The Duke VTEU joins eight other VTEU units around the country. VTEUs play a key role in the development of new and improved vaccines and therapies against infectious diseases.

The VTEU funding mechanism enables VTEU sites to compete for projects including study concept generation, protocol development, protocol implementation, and laboratory endpoint analysis.

Successful project bids:

1. Conducted influenza vaccination studies in pediatric populations against variant H3N2 and geriatric populations against H7N9 influenza strains. The later investigation included the use of MF59 adjuvant
2. Drafted a protocol and initiated implementation for a Phase I study to examine the pharmacokinetics of a therapeutic drug for tuberculosis (PA-824) in patients with known hepatic impairment
3. Drafted a protocol and initiated implementation and endpoint laboratory analysis for a study to examine early anti-fungal treatment of patients with community acquired pneumonia (CAP) in Valley Fever-endemic areas and received funding to better elucidate genomic signatures associated with coccidioides infection with an overarching goal of developing improved diagnostic tests
4. Initiated and completed enrollment in a Phase I study to examine the safety and immunogenicity of an inactivated West Nile Virus vaccine
5. Begun work on developing and implementing a protocol to examine short versus long-course antibiotic treatment of CAP in pediatric populations
6. Received funding to conduct a clinical trial and endpoint laboratory analyses testing a new anti-botulism toxin monoclonal antibody cocktail
7. Became a core site to conduct immunology assays for T and B cell activation using clinical samples collected as part of VTEU studies

The Duke Clinical Vaccine Unit is a member of the CDC-sponsored Clinical Immunization Safety Assessment (CISA) Project to assist safety experts from the CDC’s Immunization Safety Office (ISO) in providing a comprehensive vaccine safety public health service to the nation.

Led by Drs. Walter and Swamy, Duke joined a network of six other sites from across the country to address vaccine safety issues and help prevent adverse events following immunization. Since becoming a CISA site in 2012, Duke has participated in numerous vaccine safety studies:

1. Examining whether providing young children with antipyretics immediately following inactivated influenza vaccine (IIV) affects the immune response and rates of fever following vaccination
2. Examining the safety of administering Tdap vaccine to pregnant women
3. Conducting a clinical trial in adolescents and young adults assessing pre-vaccination hydration as a strategy to prevent presyncope and/or syncope following receipt of an intramuscular vaccine

Duke was selected as one of three sites to assess the safety of live-attenuated intranasally administered influenza vaccine in asthmatic children. Additionally, Duke was awarded a study to assess the safety of simultaneous vs. sequential administration of IIV and Tdap vaccines in pregnancy.
Since its inception in 2012, the DHVI protein production facility (PPF) has been funded by the Bill & Melinda Gates Foundation and has produced more than 120 proteins for the Gates Collaboration for AIDS Vaccine Development grantees, and currently makes approximately 150mg of purified protein per month. The PPF operates using a set of standards embracing applicable elements of Good Laboratory Practices (GLP) and Current Good Manufacturing Practice Facility (CGMP) regulations for the production of proteins used for research.

In 2015, the DHVI embarked on an ambitious mission to plan, design and build a CGMP facility that would enable DHVI research teams to manufacture new vaccines for use in “proof of concept” experimental medicine Phase I clinical trials.

The new facility will utilize both Quality Assurance (QA) and Quality Control (QC) protocols and audits to ensure that all CGMP requirements are met for the manufacture and release of immunogens. QC will be managed by the Quality Assurance for Duke Vaccine Immunogenicity Programs (QADVIP), which currently oversees all DHVI clinical trials materials Env production by KBI, Biopharma, and a gp41 peptide vaccine by CPC, Inc, and Infectious Disease Research Institute (IDRI).

Construction has now been completed and we are in the process of performing the commissioning and certification activities. We expect the CGMP facility to be fully operational in the first quarter of 2016.

"Having a CGMP facility as part of the DHVI makes us one of the most globally advanced vaccine institutes in the country. It positions the DHVI teams to advance our HIV vaccine development efforts, while having an infrastructure to respond to emerging public health threats.

Thomas Denny | Chief Operating Officer, DHVI
Comprehensive Shared Resources or Cores are available to the DHVI and overall Duke community and their collaborators. The DHVI has assembled a group of state-of-the-art instruments, techniques and services to support basic and translational research initiatives in vaccine immunology, immune reconstruction, host-pathogen interactions, emerging infectious diseases and biodefense.

Regional Biocontainment Laboratory and Research Support Units
Gregory Sempowski, PhD | Thomas Alderman | Richard Frothingham, MD

The Regional Biocontainment Laboratory (RBL) at Duke was built with funding from NIH to support basic research to develop drugs, diagnostics, and vaccines for emerging and reemerging infections and biodefense.

The RBL has a comprehensive safety and operations program to provide state-of-the-art biocontainment facilities for BSL2, BSL3, and Select Agent research. The RBL was fully-commissioned in late 2007 and is divided into three research support units (Immunology, Virology and Bacteriology).

The RBL Immunology team has a long track record of performing single-plex high-throughput antigen-specific antibody binding titer assessment for multiple species including mice, humans and NHPs and runs an international proficiency testing program for multiplex luminex bead-based cytokine profining assays for NIAID (EQAPOL). The Immunology unit also performs TCR sequencing, and immune reconstitution monitoring with the Duke patented sjTREC assay.

The RBL Virology unit has extensive experience with a wide-range of viruses and has a particular focus on influenza viruses and neutralization assays. The RBL has mouse, rabbit and ferret challenge models to support DHVI/Duke investigators and their collaborators.

Clinical Support
Tony Moody, MD

The DHVI Accessioning Unit (AU) provides support for procurement, processing and storage of samples derived from human and animal studies/trials. The AU provides IRB and IACUC protocol submission and oversight support to DHVI investigators.
Flow Cytometry and Cell Sorting
Gregory Sempowski, PhD

The DHVI Research Flow Cytometry Facility serves the polychromatic analytical and cell sorting needs of the DHVI and Duke Community. The Flow Facility offers state-of-the-art cytometric support to investigators in basic, developmental, and clinical research at BSL2 and 3 on six instruments.

Sequencing
Feng Gao

The DHVI Viral Genetic Analysis Facility (VGAF) offers large-scale fluorescent DNA sequencing, sequence analysis, PCR purification, and a variety of other genetic analysis assays. The state-of-the-art DNA sequencing technology yields high quality sequences of up to 1000 bases per read. The VGAF is well-equipped to handle large volumes of sequencing orders and is committed to meet the need of researchers at the DHVI and the Duke community.

X-ray Crystallography
Nathan Nicely

The DHVI Macromolecular X-ray Crystallography Facility offers services to all research laboratories on the Duke campus in solving and publishing macromolecular crystal structures. Facility staff assist with crystallization trials, data collection, phasing, refinement, and analysis. This facility offers automated crystallization systems and high-resolution X-ray diffraction image collection.

Surface Plasmon Resonance
S. Munir Alam

The DHVI Biomolecular Interaction Analysis (BIA) Facility provides specialized applications and support in Surface Plasmon Resonance (SPR) based biomolecular interaction analyses to basic and clinical researchers within the DHVI/Duke Community. The facility offers state-of-the-art SPR BIAcore and ForteBio Biolayer interferometry (BLI) instruments for monitoring real time interactions and diverse sets of measurements that include binding affinity, kinetics, resolution of binding mechanism.
Recent Publications

Published between July 2014 - 2015
Author names listed in a blue font indicate the author's affiliation with The DHVI


Get Involved

To achieve our goals, we have assembled a talented group of investigators and staff, each committed to teamwork and synergy to solve critical problems that stand in the way of difficult scientific problems. To learn more about DVHI and support our work, engage with us via social media and directly by email.

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Meagan Daly is responsible for implementing the strategic communications plan at the DHVI by designing and developing content for effective and innovative communications, including annual reports, newsletters, websites, and social media.

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Meagan Daly, MA
The Duke Human Vaccine Institute continues to lead the scientific field with cutting edge vaccine research against infectious diseases that impact global health.

Barton Haynes, MD | Director, Duke Human Vaccine Institute

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