Progress Through the Pandemic

HJF Fights COVID-19

Diagnostics + Testing

Epidemiology

Prevention

Treatment

This section contains selected stories from our full FY20 Annual Report website found at https://www.hjf.org/ar-20.

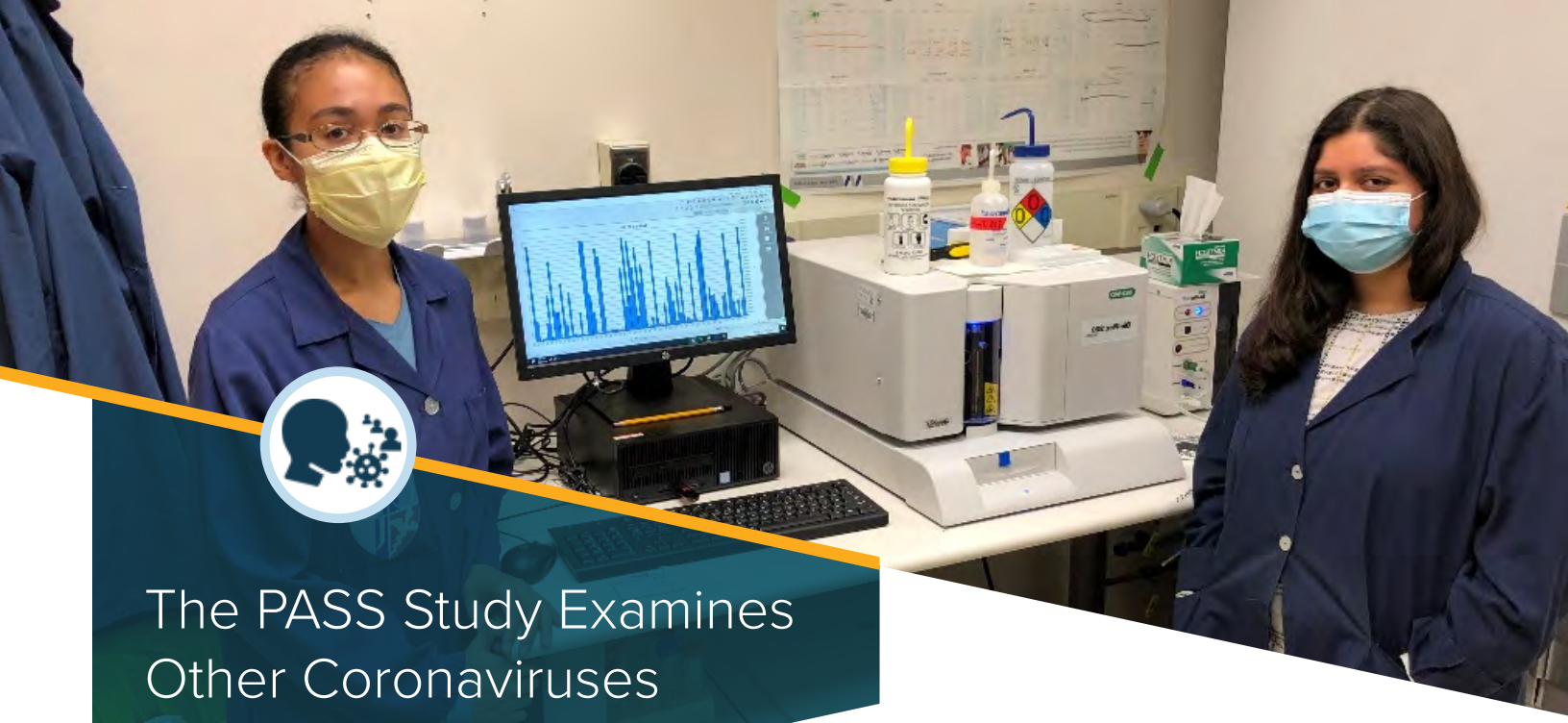
The Imperatives of Biological Defense

HJF supports the Molecular Diagnostics Department at the Biological Defense Research Directorate, which serves as a national resource providing testing and analysis for the presence of potential biological hazards. Part of the Naval Medical Research Center, the Directorate focuses on how to defend against the threat of biological and chemical warfare by conducting health and medical research, development, testing, evaluation, and surveillance to enhance deployment readiness of Department of Defense personnel worldwide.

The Molecular Diagnostics Department serves as a subject matter expert on biological warfare widely regarded throughout the DoD and other U.S. government agencies. As part of the U.S. government's response to the COVID-19 pandemic, it was approached by the Defense Biological Product Assurance Office, which is part of the Joint Program Executive Office for Chemical and Biological Defense and whose mission is to develop medical and physical countermeasures to protect the warfighter from chemical and biological threats.

The Directorate also focused on production of the CDC assays and evaluation of the logistics required, including providing sample extraction kits, viral transport medium production, and ancillary Taq Polymerase kits. Emphasis was changed to adapting the primer/probe sets of the Centers for Disease Control and Prevention to the standard formulation currently produced by the facility reducing the logistical burden and providing reagents in a format more familiar to current customers of the Defense Biological Product Assurance Office.

The Directorate is the sole DoD real time reagent production facility for PCR (polymerase chain reaction), which is a key component of COVID-19 detection kits. Its production facility has functioned since 2006. The reagents are used daily by the DoD (Pentagon Force Protection Agency, National Guard units, the U.S. Army Medical Research Institute of Infectious Diseases, National Guard units, and other DoD organizations), the National Institute of Allergy and Infectious Diseases at the National Institutes of Health, and DHS BioWatch. Annually, the Molecular Diagnostics Department produces in excess of 3.5 million reactions resulting in cost savings to the U.S. government of at least $44 million versus commercial vendors. The reagents support research and development activities in addition daily monitoring programs to detect the presence of biological warfare agents in environmental aerosol samples.



The PASS Study Examines Other Coronaviruses

While SARS-CoV-2 is a new virus in humans, there are other coronaviruses that have been present for a long time that commonly cause respiratory tract infections. Indeed, the human coronaviruses OC43, HKU1, 229E, and NL63 are the second most frequent cause of the common cold and are responsible for over 10 percent of all respiratory infections in adults and children during winter months.

The PASS (Prospective Assessment of SARS-CoV-2 Seroconversion) Study seeks to improve our understanding of the clinical manifestations and immune responses that occur after infection with SARS-CoV-2, the virus that causes COVID-19. The central question being asked by the study is: Does the presence of pre-existing antibody or T-cell responses to these common coronaviruses affect immune responses and/or disease severity during SARS-CoV-2 infection?

The PASS study, which started in August 2020, is a collaborative project being conducted by HJF, the Naval Medical Research Center Clinical Trials Center, the Infectious Diseases Clinical Research Program, and Department of Microbiology and Immunology at the Uniformed Services University of the Health Sciences. Other questions being addressed by the study include: How often do healthcare staff at Walter Reed National Military Medical Center acquire asymptomatic SARS-CoV-2 infection? What is the baseline prevalence and magnitude of antibody responses to the common coronaviruses? And are immune responses to SARS-CoV-2 altered by the presence of pre-existing antibody or T-cell responses to other coronaviruses?

To conduct the study, investigators are recruiting up to 300 staff who work at Walter Reed National Military Medical Center. Study subjects are being followed over the course of one year with monthly antibody testing, frequent symptom questionnaires, and testing for COVID-19 whenever a subject is symptomatic. Laboratory assays to be done on blood samples include measurement of pre-existing antibodies to the common coronaviruses and assessment of cross-reactive T-cell responses to SARS-CoV-2 proteins. The study is using a novel multiplex coronavirus antibody test developed by Dr. Eric Laing and Dr. Christopher Broder that simultaneously measures antibodies specific for SARS-CoV-2, SARS-CoV-1 (the virus that causes Severe Acute Respiratory Syndrome), MERS (the virus that causes Middle East Respiratory Syndrome), and the four common coronaviruses that routinely circulate in the United States.

The investigators hope that results obtained from this study will inform strategies for diagnostic testing, risk stratification, vaccine design, and antibody-based therapies for SARS-CoV-2 as well as for future novel coronaviruses.

3-D Printing to Create PPE

In the early weeks of the COVID-19 pandemic, HJF employee Betsy Weissbrod, a Medical Illustrator at the Val G. Hemming Simulation Center, designed and developed personal protective equipment (PPE) using 3-D printing. With this equipment in short supply and high demand, Weissbrod created a design that could be used by healthcare providers and researchers.

The Val G. Hemming Simulation Center is part of the Uniformed Services University of the Health Sciences and is recognized as the nation's premier simulation center for the development and application of medical simulation programs. The simulations allow health care personnel to develop and maintain the skills necessary to perform medical tasks that are high-risk or high consequence for patient safety and therefore, are done in simulated medical procedures.

Check out the video describing the 3-D Printing at https://www.hjf.org/ar-20.

Vaccine for a Deadly Spike Protein

HJF scientist Dr. Gordon Joyce spent much of 2020 focused on understanding and documenting the structural biology of the novel coronavirus, SARS-CoV-2. As the head of the Structural Biology Lab at the Walter Reed Army Institute of Research, he successfully produced the most detailed atomic level view of the structure of the SARS-CoV-2 spike protein receptor binding domain, which is the part of the virus that binds to the lungs. This detailed understanding of the structure has been critical to vaccine discovery and development efforts.

In related work, Dr. Morgane Rolland, an HJF viral geneticist with the U.S. Military HIV Research Program, conducted genetic analysis of sequences from more than 27,000 individuals infected with SARS-CoV-2 and found that the virus has mutated minimally since its initial outbreak. Her work suggests that one vaccine would be sufficient to combat global infections.

Their research is part of the coronavirus vaccine development at the Emerging Infectious Diseases Branch of the Walter Reed Army Institute of Research. Led by Army researcher Dr. Kayvon Modjarrad, these efforts have developed a vaccine candidate known as SpFN (Spike Ferritin Nanoparticle). The SpFN vaccine is unique among other COVID-19 vaccines in development because the nanoparticle's multifaceted surface has been engineered to present specific pieces of the coronavirus spike protein (the part of the virus that attaches to the lungs) to the immune system many times over to elicit a strong immune response.

"The emergence of coronaviruses in human populations is accelerating and we need to be prepared for the eventuality that the current coronavirus mutates or other coronaviruses arise," said Dr. Modjarrad. "That's why we need a vaccine, like the one we're developing, that can be used to protect broadly against all coronaviruses."

The researchers are taking a strategic long-term approach to vaccine development. In the future, the vaccine might be adapted so that different faces of the nanoparticle present different coronaviruses to the immune system at the same time. In addition, the vaccine platform could pave the way for a universal vaccine to protect against not only the current virus, but also other known and unknown coronaviruses that could arise.

HJFMRI Receives Grant from the Bill & Melinda Gates Foundation

HJF Medical Research International (HJFMRI), a wholly owned subsidiary of HJF, was awarded $1.3 million by the Bill & Melinda Gates Foundation to support antenatal, intrapartum and postnatal care in the Kenya Child Health and Mortality Surveillance (CHAMPS) and Antenatal/Postnatal Research Collective (ARC) network. This cutting-edge research will address current antenatal and postnatal COVID-19 research gaps in understanding the burden of COVID-19 in pregnant women and newborns, associated risk factors, and associated maternal morbidity and mortality in Western Kenya.

"Determining the likelihood of adverse pregnancy outcomes associated with maternal COVID-19 is an essential and urgent matter at this time, and HJFMRI is proud to support the study in the CHAMPS and ARC platforms to determine this likelihood," said HJF President and CEO Joseph Caravalho, M.D. "The research will help medical communities understand the risks—and potential methods to mitigate those risks—for infected mothers and their newborns."

This study precedes the ARC (Antenatal/Postnatal Research Collective) Study, a new four-year initiative aimed at improving antenatal care and postnatal care through risk stratification and reducing maternal and infant mortality. The study is also funded by the Gates Foundation through a collaborative effort between multiple governmental and non-governmental organizations. COVID-19 surveillance will be implemented as a precursor to the full implementation of the ARC study. It will monitor the impact of COVID-19 on pregnancy and newborns' outcomes, with additional considerations of maternal anemia and co-infection with HIV, tuberculosis or malaria. The study will also look at the birth outcomes and the health of infants born to individuals who tested positive for COVID-19 and the rate, or possibility, of transmission from mother to child.

The CHAMPS Network was established with the aim to develop a long-term network of high-quality sites to collect robust and standardized longitudinal data with the overarching objective of understanding and tracking the preventable causes of childhood death globally. The CHAMPS Network's objective—to provide accurate and timely data for decision-making on the causes of stillbirths and deaths among children under age five—will help provide answers needed to support the goal of significantly reducing child deaths in lower-resource countries. This new research will enable CHAMPS to investigate risks to women and children in relation to the COVID-19 disease.

An Urgent Need for Ventilators

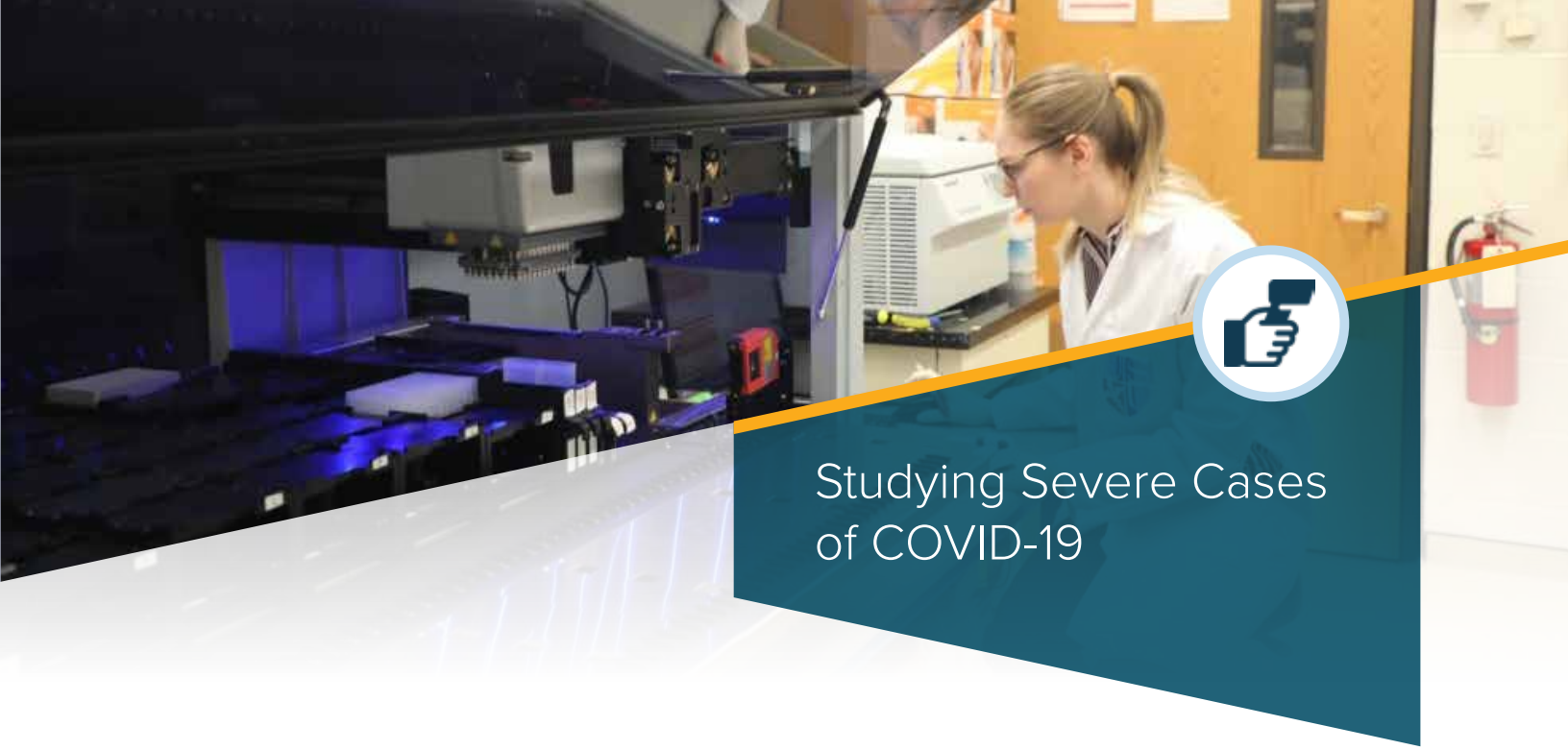
The COVID-19 pandemic ushered in a grim reality that hospitals all over the globe may not have sufficient numbers of ventilators to care for the onslaught of critically ill patients. Moreover, manufacturers were not expected to be able to meet the demand for traditional ventilators in the timely manner required to save lives.

In response to this global health crisis, the Defense Health Agency in the Department of Defense, created the "Vulcan Innovator Challenge" to develop easily manufactured, low cost ventilators. Over the course of seven days, 172 innovative ideas were submitted by industry, universities, government agencies, and individuals, all with the singular focus to design a ventilator to fill the impending gap in capacity and save lives.

Two panels of experts in the fields of engineering and critical care anesthesiology, medicine, and surgery selected five of the most promising designs for further evaluation. Following selection and prototype development, we aimed to evaluate the frontrunning limited performance ventilators in an *in vivo* system, including a clinically relevant model of acute respiratory distress syndrome.

The Uniformed Services University of the Health Sciences, including its Department of Anesthesiology and the Defense and Veterans Center for Integrative Pain Management, with the support of HJF and the Department of Defense Joint Acquisition Task Force, provided opportunity for five prototypes selected by the Vulcan Innovator Challenge to be evaluated in a large animal lab. The testing consisted of four parts. Parts one and two evaluated, selected and measured ventilator parameters in a mechanical test lung and in healthy 70-100 kg swine, respectively. The ventilator parameters evaluated included positive end-expiratory pressure, peak inspiratory pressure, tidal volume, respiratory rate, and fraction of inspired oxygen. Part three evaluated the ventilator's ability to adjust minute ventilation to control hyper or hypoventilation in a healthy animal. Part four evaluated the ventilator's ability to maintain adequate controlled ventilation in a 70-100 kg swine with induced acute respiratory distress syndrome.

In response to the global crisis, many well-intentioned innovators developed new designs or fabricated ventilators out of other devices. The media and general public celebrated the innovations as solutions to fill the gap, yet it also revealed how difficult it is to develop safe, low cost, easily manufactured ventilators. Preliminary results revealed several design flaws in the prototypes, which required refinement of the devices. While the prototypes developed and evaluated through the Vulcan Innovator Challenge may be viable last-resort alternatives in severely resource-strained environments, rigorous monitoring and well-trained operators are even more important than with conventional ventilators.



Studying Severe Cases of COVID-19

HJF supported immunological COVID-19 research led by scientists from The American Genome Center and the Precision Medicine Initiative for Military Medical Education and Research, which are both part of the Uniformed Services University of the Health Sciences. Their work was part of the COVID Human Genetics Effort, which is a global consortium combining the efforts of more than 50 sequencing hubs and hundreds of hospitals and scientists.

Participating centers from the United States and around the globe provided samples to study genetic determinants of susceptibility to severe COVID-19 infection. Dr. Clifton Dalgard and his team from The American Genome Center rapidly performed human genomic DNA isolation from residual clinical tissue material and high-throughput, whole genome sequencing to study the genetic influences to COVID-19 disease. In addition to genomic profiling, the team generated DNA templates for T and B lymphocyte repertoire analysis to investigate T cell receptor repertoires for SARS-CoV-2 specific antigens and monitor immunologic response to SARS-CoV-2 infection or vaccine.

Following sequencing, Dr. Matthew Wilkerson and his team from the Precision Medicine Initiative for Military Medical Education and Research conducted primary genome data analysis, which involved sequence alignment, variant calling, and integrated quality analysis to ensure high, uniform sequencing data performance across the cohort and concordance with expected sample properties. These genome data analysis workflows were conducted with high urgency on its on-premise High-Performance Compute platform to meet the immediacy of the project and public health need.

The researchers published two papers in the journal Science ("Inborn errors of type 1 IFN immunity in patients with life-threatening COVID-19" and "Autoantibodies against type 1 IFNs in patients with life-threatening COVID-19"), which reported that individuals with severe forms of COVID-19 disease can present with compromised type 1 interferon (IFN) responses based on their genetics. Type 1 IFN responses are critical for protecting cells and the body from more severe disease after acute viral infection. These findings help to explain why some people with no underlying conditions develop a disease more severe than others in their age group and may also provide a molecular explanation for why more men die from the disease than women.

In addition to Dr. Dalgard and Dr. Andrew Snow from the Uniformed Services University of the Health Sciences, who are co-authors on both papers, HJF employees Miranda Tompkins, Camille Alba, Christopher Luthers, Daniel Hupalo, John Rosenberger, Gauthaman Sukumar, Matthew Wilkerson, and Xijun Zhang, along with graduate student Bradly Bauman in Dr. Snow's lab, also participated in the research and served as co-authors.

On the Frontlines of COVID-19 with HJF Employees

Brian Agan, Ph.D.

Deputy Director; Infectious Disease Clinical Research Program at the Uniformed Services University of the Health Sciences
HJF employee since 2005

As an HJF employee and Deputy Director of the Infectious Disease Clinical Research Program at the Uniformed Services University of the Health Sciences, Brian Agan oversees a team of 120 that is highly focused on COVID-19.

"My role is to help direct our efforts in response to COVID-19 and support the leadership team, investigators, clinical research managers, site teams, data center, analysts, and other staff as they engage with several COVID-19 studies," he said.

In response to the COVID-19 pandemic, these researchers activated an observational, longitudinal cohort study ("Epidemiology, Immunology and Clinical Characteristics of Emerging Infectious Diseases with Pandemic Potential") at six military treatment facilities within the United States and will be expanding to others.

"This study is capturing longitudinal clinical and laboratory data, as well as specimens, from patients with suspected or confirmed COVID-19, as well as those with high risk exposure to better understand the natural history of SARS-CoV-2 infection, including the clinical, virologic, and immunologic determinants of severe disease," said Agan, who now serves as study principal investigator.

Gordon Joyce, Ph.D.

Chief of Structural Biology; Walter Reed Army Institute of Research
HJF employee since 2016

Gordon Joyce, Ph.D., who is an HJF employee and Chief of Structural Biology at the Walter Reed Army Institute of Research (WRAIR), has been working diligently to advance research efforts to prevent and treat COVID-19. Early in the pandemic, he produced the most detailed atomic level view of the structure of the SARS-CoV-2 spike protein receptor binding domain—the part of the virus that binds to the lungs.

"This detailed understanding of the structure has been critical to vaccine discovery and small molecule development efforts," said Joyce.

Along with the WRAIR team, which is led by Dr. Kayvon Modjarrad, the Director of its Emerging Infectious Diseases Branch, Joyce and his colleagues have developed a vaccine candidate which is built on a Spike Ferritin Nanoparticle (SpFN) platform. WRAIR's scientists are taking a strategic long-term approach to their vaccine development efforts. They expect the ferritin vaccine platform to pave the way for a universal vaccine to protect against all known and unknown coronaviruses that could arise in the future.

Joyce is also working on a collaboration with the University of Maryland to investigate nano-bodies generated by sharks after vaccinations. He and other scientists are exploring these antibodies' potential to neutralize the virus. The structural biology group is also supporting efforts at WRAIR to identify novel therapeutics for COVID-19. They have also determined the structures of multiple neutralizing monoclonal antibodies in complex with the SARS-CoV-2 spike protein receptor binding domain. This information serves to define novel sites of vulnerability that can be exploited to treat COVID-19.

Ines Elakhal Naouar, Ph.D.

Associate Lab Director;
Walter Reed Army Institute of Research
HJF employee since 2013

Dr. Ines Elakhal Naouar has been helping prepare the diagnostics laboratories at the Walter Reed Army Institute of Research to support COVID-19 surge testing for the Military and the national capital area. The institute's Diagnostics and Countermeasures Branch, which is led by Dr. Sheila Peel, is supported by HJF.

In January 2020, there were very few assays or tests available for SARS-CoV-2 diagnosis. A rapid response team, including Dr. Elakhal Naouar, immediately sought to develop an algorithm-based approach to correctly classify individuals currently infected with COVID-19 and those with prior exposure. First, they identified and deployed an assay under Emergency Use Authorization for clinical testing in April 2020.

In parallel, Dr. Elakhal Naouar leads development of a high throughput assay and other molecular assays to assess viral clearance and to use in vaccine studies. The multiplex assay they developed has shown to be sensitive and specific for SARS-CoV-2 with good clinical performance. She and her team are working to transition and validate the assay on a commercially available platform, which will automate extraction and amplification for quicker, high-throughput results.

Michele Tisdale

Research Associate;
Infectious Disease Clinical Research Program
HJF employee since 2009

Last spring the USNS Comfort was stationed in New York City for approximately one month to help the city cope with the coronavirus pandemic. A Mercy-class hospital ship of the U.S. Navy, the Comfort initially treated non-coronavirus patients and later began accepting patients who had contracted the COVID-19 disease.

Among those assisting with the operations for the USNS Comfort was Michele Tisdale, a Research Associate with the Infectious Disease Clinical Research Program and an HJF employee. Tisdale helped obtain more than 400 specimens from the ship in a secure lab.

"I was able to assist in collection as well as train and assist in processing and storage of the lab specimens," Tisdale said.

Tisdale also supports a clinical trial known as Protocol 124 that is focused on Remdesivir, an antiviral medication being used as a treatment for COVID-19. Tisdale collects laboratory specimens and helps manage the storage of plasma, serum and swabs in a controlled environment.

"The hope is that this clinical trial will lead to more patients receiving an effective treatment that shortens the length of their hospital stay," she said.

Susan Banks, RN

Registered Nurse;
Infectious Disease Clinical Research Program
HJF employee since 1998

Susan Banks, RN, is one of HJF's programmatic support teammates working with the Infectious Disease Clinical Research Program on COVID-19 research. Her worksite is one of many enrolling subjects in the Adaptive COVID-19 Treatment Trial (ACTT). Nine subjects have been enrolled and five subjects have completed the trial. In addition to ACTT, Banks participated in a study looking at the seroprevalence of novel coronavirus antibodies among personnel deployed on the USNS Mercy and her sister ship the USNS Comfort during early months of the pandemic.

One of the biggest challenges around COVID-19 has been safely interacting with patients and participants, while still providing them with the best care possible. Banks strives to maintain the human aspect of being a nurse, while at the same time adhering to all the restrictions and safety guidelines to protect the patients and herself.

Ultimately, Banks hopes her efforts on the front lines of the COVID-19 research leads to identifying the ways this virus presents itself as well as to identify the most effective treatments. The goal of the second study is to aid in finding the best ways to test for this virus, which in turn will help the DoD better screen active-duty service members.