BRIghtLights
Shining a light on research and discovery

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versiti™
Blood Research Institute

Message from Versiti President and CEO Chris Miskel

Since the beginning of the COVID-19 pandemic, we have seen communities band together to help those in need. From blood donors answering the call for donations to convalescent COVID-19 patients donating plasma to aid in the recovery of those suffering from the virus, the response has been remarkable.

Versiti Blood Research Institute investigators are also doing their part to better understand COVID-19 and search for more effective treatments—and even a cure—for the deadly virus. Versiti Executive Vice President for Research and Chief Science Officer Gilbert C. White, II, MD, has established a research study with Froedtert Hospital and the Medical College of Wisconsin, and was recently awarded nearly $400,000 from the Advancing a Healthier Wisconsin Endowment to research convalescent plasma to treat patients with COVID-19.

Grants like this help to propel our research, but our investigators also rely on donations to the Versiti Blood Research Institute Foundation to make their lifesaving discoveries possible. A gift to the Foundation is a gift both to patients in the communities we serve as well as to those around the world.

Versiti investigators join in the fight against COVID-19

Tragically, COVID-19 has killed more than 1,000,000 people worldwide and more than 200,000 in the U.S. Many more have been infected and recovered, and even more have been infected and don't know it. The cause of this deadly virus is a highly contagious member of the SARS virus family called SARS-coronavirus (CoV)2, or SARS-CoV2; though it has been present in animals like bats for at least five years, it is a new virus to humans and more work is needed to understand it.

Respiratory viruses like SARS-CoV2 need hosts in order to reproduce and spread. Once infected, the virus sheds and multiplies within the cells of its host, spreading to others when it's coughed or sneezed out. As blood health innovators with more than 70 years of experience researching complex topics like this, Versiti Blood Research Institute is uniquely positioned to take on this challenge.

Solving COVID-19 Mysteries Today

Decoding the immune system's response to COVID-19

As soon as the virus enters the body, immune cells see SARS-CoV2 as foreign and begin to mount a response. In most COVID-19 cases, patients produce antibodies that take care of the virus and get rid of it. But when there is a large inoculation of the active virus, it may overwhelm the immune system. These patients are the ones who are most often moved into the intensive care unit or are put on ventilators. One of the biggest mysteries that today's COVID investigators are working to solve is what factors cause a mild reaction in some patients but prove fatal for others.

Subramaniam Malarkannan, PhD

Subramaniam Malarkannan, PhD

Infection with SARS-CoV-2 results in severe inflammatory responses in patients. Specifically, children infected with SARS-CoV-2 develop a condition known as multi-system inflammatory response (MSIS). MSIS is highly prevalent in children, with 80% requiring intensive care and 20% requiring mechanical ventilation. These conditions lead to a nearly 2% fatality rate.

The long-term effect of MSIS in recovered children is unknown, with prediction ranging from neurological impairment and predisposition to cardiac diseases. Work in the lab of Senior Investigator Subramaniam Malarkannan, PhD, has identified a unique molecular mechanism that is responsible for controlling inflammation caused by multiple immune cells, including two important types of white blood cells known as natural killer (NK) cells and T (thymus derived) cells.

By specifically targeting a single protein called ADAP within the NK and T cells, Dr. Malarkannan and his colleagues were able to significantly reduce the production of inflammatory factors and thereby contain the severe inflammation in cells. Their current work focuses on identifying synthetic drugs that can be administered to patients to control severe inflammation, including MSIS.

Weiguo Cui, MD, PhD

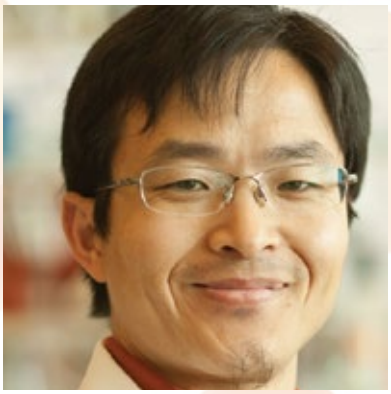
Weiguo Cui, MD, PhD

The generation of the immune system's memory to the SARS-CoV-2 virus critically depends on responses by T cells, a type of white cell that responds to a viral infection by either orchestrating a robust antiviral immune response or enhancing antibody production. Another subset of T cells clonally expands and acquires the ability to directly kill cells infected with a virus. After the virus is cleared, most of these T cells die and only a small portion develop into memory T cells that provide long-lasting immunological protection. Similarly, B cells develop into memory B cells and long-lived plasma cells that produce neutralizing antibodies.

Understanding how memory cells are developed in COVID-19 patients will help researchers like Investigator Weiguo Cui, MD, PhD, generate effective vaccines to fight the pandemic. Dr. Cui's lab is using newly developed, single-cell RNA sequencing technology to directly trace the developmental lineage of each patient's SARS-CoV-2 specific T cell response and memory formation at the single-cell level throughout the course of natural infection. They will also measure T cell clonal diversity and the quality of T cell memory from COVID-19 patients, as well as healthy human controls. The latter will be used to gauge the possible presence of pre-existing immunity in the form of memory T cells derived from cross-reactivity to common coronaviruses.

Finally, successful vaccine development relies on an advanced understanding of the types of T cells that are generated during natural infection and how they react with B cells, as well as T regulatory cells, for anti-SARS-CoV-2 antibody production in humans. To this end, Dr. Cui's lab will monitor circulating T cells in both SARS-CoV-2 infected and healthy human control subjects. Additionally, they will perform T cell-B cell coculture assays to dissect the functional contributions of each subset of T cells and how the different types of T cells interact in regulating anti-SARS-CoV-2 neutralizing antibody responses.

Understanding the protein responsible for COVID-19



Jieqing Zhu, PhD

In the case of SARS-CoV2, a protein on the outer surface of cells called the S protein (or spike protein) attaches to a protein on cells in the human respiratory tract called ACE2. This attachment occurs through very specific parts of both the S protein and ACE2. These parts of the S protein are the target for vaccines and understanding the molecular architecture of their attachments will enable the design of better vaccines. Versiti Blood Research Institute Investigator Jieqing Zhu, PhD, is using highly sophisticated X-ray crystallography to identify the specific part of the S protein involved in binding to ACE2 to aid in COVID-19 vaccine development. This work will be critical to ensuring the solutions created will have long-term impact for tackling this virus.

Lisa Baumann Kreuziger, MD, MS

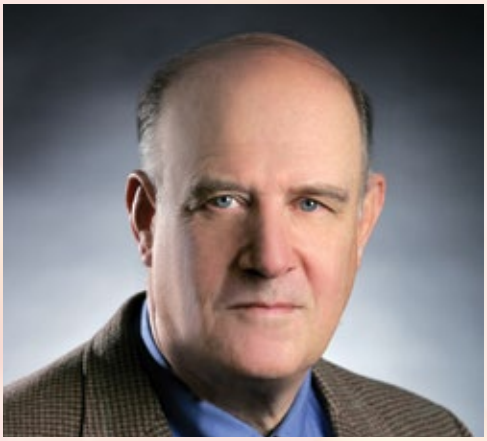
Lisa Baumann Kreuziger, MD, MS

A recent but potentially devastating complication of COVID-19 is the development of blood clots; however, the best way to prevent clots in COVID-19 patients is unknown. Associate Investigator Lisa Baumann Kreuziger, MD, MS, leads the Venous thromboEmbolism Network US (VENUS), a research network focused on studying blood clots, and recently published an international survey asking doctors how they are treating patients with COVID-19, given the limited data.

Dr. Baumann also recently received the International Network of Venous Thromboembolism Clinical Research Networks Kickstarter Award for her efforts to open and coordinate sites for a multi-center clinical trial to determine the effects of therapeutic anticoagulation compared to standard care in patients hospitalized with COVID-19.

Finally, Dr. Baumann is working with the National Institutes of Health's Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) partnership as they develop three master protocols for evaluating the effectiveness of blood thinners to prevent blood clots and worsening of organ damage due to COVID-19. These studies will involve patients with COVID-19 at diagnosis, hospitalization and discharge from the hospital.

Investing in the future: Versiti and Medical College of Wisconsin awarded $400,000 to study convalescent plasma



Gilbert C. White, II, MD

Versiti Blood Research Institute takes pride in the collaborative environment among our own research team and the partnerships we have cultivated across the country and around the world. Executive Vice President for Research Gilbert C. White, II, MD, and a team at Versiti are working with Mary Beth Graham and her team in the Department of Medicine and Division of Infectious Diseases at the Medical College of Wisconsin to perform a clinical trial of recovered or convalescent plasma in the treatment of active COVID-19. Plasma obtained from Versiti donors who have recovered from the coronavirus is given to individuals who are actively infected to determine the plasma's effect on the course of the disease.

Karin Hoffmeister, MD

Karin Hoffmeister, MD

Emerging studies have shown that altered sugars (carbohydrates or glycans) are central but overlooked contributors to COVID-19 in a few different ways:

1. The ABO blood group system consists of small sugars expressed on blood cells and lung cells. COVID-19 patients with type A blood experience worse outcomes than patients with type O blood, suggesting that sugars may contribute to disease progression.
2. COVID-19 displays unique sugars, specifically TF and Tn antigens, which are sugars usually found in cancer cells but not normal cells; they are thought to be a mechanism by which cancers evade the immune system. Senior Investigator Karin Hoffmeister, MD, believes that the expression of sugars on SARS-CoV-2 may also work to help the virus evade the immune system.
3. Preliminary data indicates the presence of unexpected antibodies and unusual sugars in plasma from patients who have recovered from COVID-19. These antibodies may promote platelet activation and blood clots and increase the consumption of platelets by bound aberrant antibodies.

Based on preliminary data, Dr. Hoffmeister and her colleagues currently investigate how aberrant glycosylation associated with COVID-19 infection affects the immune response, ultimately impacting the function of platelets and blood cells. Data gathered through further studies may identify markers for patients at risk for the development or progression of COVID-19 and may apply to other hematologic cancers.

Developing groundbreaking vaccines to fight COVID-19

Demin Wang, PhD

The patients who survive COVID-19 develop antibodies to the virus. These antibodies are highly specific and thought to protect against reinfection with the virus. Traditional vaccines like the polio vaccine or mumps use live attenuated or dead virus to stimulate the formation of these antibodies. Senior Investigator Demin Wang, PhD, is attempting to bypass traditional vaccine development by cloning the antibodies to COVID-19 from individuals who have recovered from the virus. Those antibodies could be used to help treat people with active COVID-19 infection or to protect frontline workers. While the cloned antibodies would last only a month or two, compared to a vaccine, which would last many years, the antibodies would constitute an important frontline treatment alone or in combination with anti-viral drugs.

Together, Versiti Blood Research Institute investigators are responding to the COVID-19 outbreak with both cutting-edge laboratory research and important clinical trials that will contribute to knowledge about how to treat and prevent this virus.

Shawn Jobe, MD, PhD

Shawn Jobe, MD, PhD

Associate Investigator Shawn Jobe, MD, PhD, is working closely with investigators Renren Wen, PhD, Weiguo Cui, MD, PhD, and Demin Wang, PhD, to understand how immune cells react when confronted with the COVID-19 virus.

Dr. Jobe and his colleagues believe that understanding the body's immune response to the virus is of utmost importance. Instead of the immune system reacting normally to a virus, like it would a cold or the flu, it produces an overly exuberant reaction in an effort to protect itself—something that can have dangerous side effects, including blood clots. Understanding this immune response may be the key to finding ways to treat—or even prevent—COVID-19.

One such treatment is convalescent plasma, or plasma from donors who have recovered from COVID-19. Currently, researchers know that recovered patients have developed antibodies to the virus that are useful in treating patients who are critically ill. But they are still trying to understand what, exactly, the antibodies are and how they are developed; understanding this may help inform a more effective convalescent plasma therapy.

To accomplish this, Dr. Jobe and his colleagues at Versiti and the Medical College of Wisconsin, including Parmeswaran Hari, MD, and Mary Beth Graham, MD, are collecting samples from COVID-19 convalescent plasma donors and recipients that they hope will help them better understand the virus. "We are intensely proud of our efforts and think that we will provide fundamental insights to COVID-19," he said.

He likens the process to solving a problem in reverse. We know what the answer is—but what is the question and what are the steps to arrive at that answer? "We need to understand this," he said. "Hopefully, COVID just goes away, but we're not making that assumption. We need to understand the fundamental mechanisms behind this and what's going on."

Identifying each step in the process will also provide investigators insight into how the immune system responds to other viruses and diseases, including cancer, and give them the knowledge they need to improve existing therapies and develop new ones to better treat patients. "These fundamental mechanisms pave the groundwork for everything," Dr. Jobe said.

Community Beacon of Hope

Spotlighting organizations and individuals in our community who go above and beyond in their support of Versiti Blood Research Institute.

Dave Lal, MD

Dave Lal, MD, a pediatric oncologist at Children's Wisconsin and professor of pediatric surgery at the Medical College of Wisconsin, became the first to donate as part of Versiti's COVID-19 convalescent plasma program. "I have a unique opportunity to help others," Dr. Lal said. "Even in my own community, I know people who are really struggling and who are critically sick. So, if I can help any one of those people, it would give me much joy."

Dr. Lal tested positive for coronavirus in March after being exposed to an individual with COVID-19. He suffered mild symptoms like fatigue and muscle aches before making a full recovery. Individuals like Dr. Lal who have contracted COVID-19 and have fully recovered have developed antibodies to the virus, which may help patients seriously ill with the virus in their recovery.

The convalescent plasma treatment—approved by the FDA as an Emergency Investigational New Drug (EIND)—could offer hope to the hundreds of patients who continue to be diagnosed, and many of Versiti's partner hospitals have already begun using it to treat patients with COVID-19.

Planned Giving: Leaving a Legacy

The Versiti Legacy Society celebrates our most dedicated and generous supporters who invest in supporting our research and improving patient health and outcomes. By making a planned gift to the Versiti Legacy Society, you will help Versiti Blood Research Institute continue to invest in innovation and discovery through research.

Versiti Legacy Society accepts gifts from a will or trust, beneficiary designations, life insurance, appreciated securities and real estate, personal property, and even the gift of your home.

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