The Fight Against COVID-19

Illustration of the SARS-CoV-2 virus that causes COVID-19. Source: CDC

Nanovaccine Institute researchers are pushing multiple frontiers in the complex fight against COVID-19: diagnostics, therapeutics, and of course, vaccines. Institute researchers are developing a next-generation COVID-19 vaccine, encapsulated in tiny nanoparticles, that will be needle-free, stored at room temperature, and capable of simple self-administration via a nasal inhaler. This coronavirus vaccine builds on years of Nanovaccine Institute research with influenza vaccines, which have progressed through safety and efficacy testing in FDA-required animal models and are moving toward human clinical trials. The biodegradable nanoparticles being tested for flu vaccines are a versatile “platform technology” that can be easily adapted for coronavirus vaccines by switching out the antigenic protein payload encapsulated in the particles.

The Nanovaccine Institute’s COVID-19 research is underway on several fronts simultaneously. A fast-track project involving Iowa State, the University of Iowa, Southwest Research Institute, Skroot Labotory, and Zeto Biomedical is developing antigen synthesis, immunity and efficacy testing, nasal applicator devices, and FDA-compliant mass-production methods.

Nanovaccine Institute members at Southwest Research Institute are using its drug discovery software to screen millions of drug compounds for efficacy against the coronavirus. Nigel Reuel is developing a printed paper sensor to serve as a low-cost, mail-safe, fast-scan diagnostic platform for widespread monitoring of infection during pandemics. And Imbed Biosciences is reformulating a silver nanoparticle wound therapy product as an antiviral nasal spray to prevent the spread of Covid-19.

Nanovaccine Institute

Received $2 Million CARES Act Grant for COVID-19 Nanovaccine

A $2 million grant of federal CARES Act funding distributed by the state of Iowa will support university research of a nanovaccine to protect against COVID-19 infections.

The project will build on previous research and existing patents by Iowa State University and University of Iowa researchers affiliated with the Nanovaccine Institute based at Iowa State. The fast-track project will be largely completed by the end of the year.

Iowa Gov. Kim Reynolds announced the grant October 29. It will be administered though the Iowa Economic Development Authority.

“This is an exemplar of the value of Iowa State University’s land-grant mission – having world-class faculty and scientists with the expertise and innovation to tackle an urgent, complex problem to benefit Iowans and the world,” said Iowa State President Wendy Wintersteen. “Development of a COVID-19 nanovaccine will be a game-changer for the pandemic response, and we are proud to have Dr. Narasimhan and his team at the forefront of this critically important project.”

Nanovaccine Institute director Balaji Narasimhan will lead research to develop a nanovaccine against COVID-19 infections.

Development of a next-generation nanovaccine is expected to address some of the limitations of current vaccine candidates, according to a project summary. Unlike many of the more than 100 coronavirus vaccines under development, a nanovaccine will be needle-free, single-dose and won’t require refrigeration. It is expected to provide long-term protection against SARS-CoV-2, the novel coronavirus that causes COVID-19.

“This approach exploits ISU’s strengths in nanovaccine platform technology and UI’s expertise in SARS virology, immunity, and unique animal models,” said Iowa State’s Balaji Narasimhan, the project leader and director of the Nanovaccine Institute.

Additional leaders of the project include Iowa State’s Michael
Wannemuehler, associate director of the Nanovaccine Institute and a professor of veterinary microbiology and preventive medicine; and the University of Iowa’s Kevin Legge, a professor in the departments of pathology and microbiology and immunology.

The researchers will also collaborate with several industry partners: Skroot Laboratory Inc., a wireless sensor startup based in Ames; Zeteo Biomedical, a drug delivery device startup based in Austin, Texas; and Southwest Research Institute, a manufacturing-support nonprofit based in San Antonio, Texas. The project will also share equipment and expertise with vaccine companies with operations in Iowa.

Nanovaccines against a virus work by loading viral proteins into nanoparticles. Those nanoparticles are about 300 billionths of a meter across and are made from biodegradable polymers. The nanoparticles are incorporated into a nasal spray and delivered with a sniff. Exposure to the nanovaccine triggers the immune system to attack the virus.

“Our approach will result in the development and pre-clinical testing of a novel SARS-CoV-2 nanovaccine that will overcome current shortcomings and be ready for clinical trials with multiple partners,” the researchers wrote. “This work has the potential to address an urgent public health need and jumpstart Iowa’s economy.”

**Nanovaccine Institute Headquarters and Labs Moved to New Building at Iowa State**

In August, seven Nanovaccine Institute researchers at Iowa State moved and consolidated their laboratories into 8,850 square feet of shared lab space at the Institute’s new home in the new Advanced Teaching and Research Building on the Iowa State campus. The fifth floor of the Advanced Teaching and Research Building provides contemporary research laboratories, common and specialized research support space, shared formal and informal collaboration areas, and offices for graduate students, staff, scientists, and faculty to support the efforts of the Nanovaccine Institute.

The research space is comprised of five new research lab spaces, 1,225 square feet each, parallel to each other in an open floor plan. 14 core facility rooms, such as microscopy, immunology, nano, and others, are located around the labs’ perimeter.

Core Facility Manager Kathleen Ross resorted to scaled drawings and color-coding to plan how to organize equipment from seven labs across campus into the new shared space.

**Nanovaccine Institute Members Honored and Recognized**

Amy Vincent was elected as a member of the National Academy of Medicine for her groundbreaking research that led to improved vaccines and surveillance for swine influenza, characterization of vaccine-associated enhanced disease in a swine influenza model, and characterization of pandemic potential for swine influenza viruses. Dr. Vincent is a Research Veterinary Medical Officer and Lead Scientist at the National Animal Disease Center, Agriculture Research Service, U.S. Department of Agriculture. The National Academy of Medicine announced the election of 90 members and 10 international members October 19 during its annual meeting. Election to the Academy is considered one of the highest honors in the fields of health and medicine and recognizes researchers who have demonstrated outstanding professional achievement and commitment to service.

Nigel Reuel, an Assistant Professor of Chemical & Biological Engineering at Iowa State, received a Maximizing Investigators’ Research Award for Early Stage Investigators from the National Institutes of Health on September 2.
Reuel received five years of research funding for his project “Unsupervised optimization of protein therapeutics using closed-loop in vitro synthesis, nanosensing, and deep learning”, which will develop advanced tools to enable faster discovery and design of protein-based drugs for new disease targets.

Nicola Pohl of Indiana University was elected a Fellow of the American Association for the Advancement of Science on November 24, an honor that recognizes her outstanding contributions to the progress of science and research. Her citation of merit said: Nicola Pohl, a professor, the Joan and Marvin Carmack Chair in Bioorganic Chemistry, and associate dean of natural and mathematical sciences in the IU Bloomington College of Arts and Sciences’ Department of Chemistry, for distinguished contributions to the automation of oligosaccharide synthesis, production of noncovalent fluoros-interaction-based microarrays and de novo mass spectrometry analysis of isobaric sugars. Pohl, a chemist, focuses her research on developing synthetic, analytical, and automated methods to understand and exploit the differential reactivity and shapes of carbohydrates. She also leads a group of researchers in finding new ways to make and analyze sugars to dissects their important roles in plant, animal, and human biology. One of the long-term goals of her research group is to rationally design therapeutic interventions, such as vaccines and glyco-proteins, based on a deeper knowledge of the role of carbohydrates.

Alisger Salem of the University of Iowa was awarded the university’s Hancher-Finkbine Faculty medallion, which recognizes leadership, learning, and loyalty, on April 21. Salem is a professor in the Department of Pharmaceutical Sciences and Experimental Therapeutics in the College of Pharmacy. His research focuses on novel cancer therapies and regenerative medicine. He has pioneered the integration of nanotechnology in cancer therapies.

Salem has had an impact on the research done in his department. For the last seven years, he served as the head of his division and coordinated graduate programs, budgeting, and faculty mentoring. He has been a leader in promoting and supporting diversity, equity, and inclusion on campus. He is especially proud of the number of underrepresented students that he mentors. Salem exemplifies his commitment to educating and mentoring a wide spectrum of students by including PharmD researchers, undergraduates, postdoctoral fellows, research scientists, and high school students on his research team.

In 2020, Salem also received the Leadership in Research Award from the university’s Office of the Vice President for Research, and the Class of 2023 Teacher of the Year Award.

Narasimhan, a professor of chemical & biological engineering, for demonstrating “a highly prolific spirit of innovation in creating or facilitating outstanding inventions that have made a tangible impact on the quality of life, economic development, and welfare of society.” The academy’s announcement specifically cited Narasimhan’s work in nanomedicines and biomedical engineering.

Narasimhan said his work is at the intersection of materials science, nanotechnology and medicine. The latest projects in his lab include studies of a universal nanovaccine for flu, an immunotherapy treatment for pancreatic cancer, a new nanovaccine for respiratory syncytial virus, nanomedicine-based methods to overcome antimicrobial resistance by some pathogens and nanovaccines to treat older adults. Common to all the studies is use of nanoparticles as a platform for delivering vaccines and other treatments. Narasimhan said nanoparticle-based therapies have the advantages of being needle-free, available in single doses and stable at room temperature.

Researcher Spotlight: Rizia Bardhan

Nanovaccine Institute member Rizia Bardhan, Associate Professor of Chemical & Biological Engineering at Iowa State, recently received three awards totaling $2.25 million in August and September to support her innovative research program in engineered medicine. Bardhan has secured National Institute of Health (NIH) R01 and R21 awards, and an Idea Award from the Department of Defense Congressionally Directed Medical Research Program (CDMRP) to advance her core research in integrating nanoparticles and Raman spectroscopy to improve disease diagnostics and treatment. She also brought another half-million-dollar CDMRP Career Development Award for
immunomarker screening with her when she moved from Vanderbilt University to Iowa State in January 2020.

“Since joining Iowa State just months ago, Rizia has already made her mark as a forward-thinking researcher whose engineering discoveries will make a positive, lasting impact on human health,” said Andrew Hillier, Department Chair of Chemical & Biological Engineering. “These awards to Rizia’s efforts demonstrate just how creative and impactful her research program is—and how Iowa State engineering students have the opportunity to learn from and get hands-on research experience with the very best faculty.”

**Predicting immunotherapy success**

In one of the NIH awards, Bardhan will transform the way immunotherapies are performed in cancer patients. Immunotherapy is a ground-breaking new treatment for cancer and other immune system related diseases; however, right now only 20-25 percent of patients respond to immunotherapies. And no current diagnostic approach exists to help predict who will respond to treatment or to evaluate effectiveness during treatment, mostly because current clinical standard biopsy histopathology is not able to account for the immune biomarker PD-L1.

Bardhan will use an image-guided approach to solve this challenge by designing immunoactive gold nanostars, tiny particles that are about 500 times smaller than a strand of human hair. The gold nanostars will combine two medical imaging techniques, Positron Emission Tomography (PET) and Raman spectroscopy, that are widely used in guiding clinical therapies.

These nanostars will simultaneously detect both tumor cells expressing PD-L1 biomarker and also immune cytotoxic CD8 T cells directly in real time in vivo in animal models engrafted with breast cancer patient tumors.

“By tracking both cell types, our approach will help oncologists determine which patients are good candidates for immunotherapies and distinguish those who will not respond even before the start of treatment,” said Bardhan.

Bardhan will collaborate on this project with Dr. Anna Vlgelm at Ohio State Medical School and Dr. Thad Wadas at the University of Iowa. Bardhan recently published a paper in ACS Nano demonstrating these immunoactive nanoparticles.

**Tailored colorectal cancer treatment**

Leveraging the strengths of Raman spectroscopy as a cancer diagnostic, Bardhan’s DOD CDMRP Idea Award will study how colorectal cancer patients will respond to molecular therapies before treatment is administered in patients.

Metastatic colorectal cancer is highly lethal with limited treatment options and a 5-year survival of only about 11 percent. Early, accurate, and rapid diagnostic tools that can guide treatment choices are therefore necessary to ensure patients receive the most effective treatment at the earliest time point.

Bardhan is collaborating with Dr. Jonathan Mochel, Associate Professor of Biomedical Sciences at Iowa State’s College of Veterinary Medicine; Dr. Soumik Sarkar, Iowa State Associate Professor of Mechanical Engineering; and Dr. Bhuminder Singh at Vanderbilt University School of Medicine.

But how will they determine which is the best treatment for each patient? Bardhan’s answer is using “organoids,” which are 3D culture systems that closely capture the human tumor microenvironment and have revolutionized the drug development pipeline in multiple diseases.

“Drug discovery studies often use the ‘one mouse, one patient’ paradigm, where each mouse is engrafted with an individual patient tumor as an avatar for human tumor response. But such an approach is ineffective for timely clinical decisions because they are expensive, time-consuming, and inherently low-throughput,” said Bardhan.

Bardhan and her team will derive more than 100 organoids from each patient tumor and treat them with a panel of drugs, some of which are both standard of care in colorectal cancer patients and others in clinical trials. They will then perform high-throughput drug screening in these organoids with Raman spectroscopy, and apply machine learning to distinguish patients that will respond to drugs from the nonresponders.

Their approach will not only enable individualized treatment planning for each colorectal cancer patient, it will also decrease animal burden and read-out times, which are current challenges in drug efficacy studies. Bardhan’s team recently published a paper in Chemical Science demonstrating Raman spectroscopy-based screening in cancer cells.

**Early, accurate, affordable preterm labor screening**

Bardhan’s expertise in Raman spectroscopy and nanoparticles also extends far beyond cancer. Her NIH R21 award is focused on the development of a cutting-edge new technology in her lab, PRADA, or portable reusable accurate diagnoses with nanostar antennas, to detect biomarkers that lead to spontaneous preterm labor in pregnant patients.

Preterm labor occurring before 37 weeks gestation results in more than 1 million childhood deaths globally under the age of 5. The current clinical standard to identify women at high risk of preterm labor has not been successful in reducing neonatal deaths. Bardhan’s approach with PRADA will address this ongoing global clinical challenge.

The PRADA diagnostic platform consists of the same gold nanostars Bardhan’s team uses in other research efforts, but they are now labeled with targeting agents, such as peptides or antibodies, and Raman molecules to allow multiplexed detection of clinically relevant biomarkers with high sensitivity and specificity. PRADA is also reusable, allowing more than 15 uses of the same sensor chip, reducing the overall cost.

Bardhan has also teamed up with Dr. Mark Santillan at the University of Iowa Carver College of Medicine Department of Obstetrics & Gynecology and Dr. Jeff Reese at Vanderbilt University School of Medicine to generate a unique “PRADA maternal risk score” by studying patient serum both at risk of preterm labor and those with normal pregnancy.

PRADA can ultimately enable early, accurate and affordable bedside screening...
for pregnant patients, which is a game-changer compared to current clinical measures. Bardhan’s team recently published a paper on this work in Bioengineering and Translational Medicine demonstrating PRADA in patient samples.

Welcome New Members

Six researchers and two companies joined the Nanovaccine Institute in 2020:

Imbed Biosciences

Ankit Agrawal is President and CEO of Imbed Biosciences, a Madison, WI biotech company whose portfolio includes wound management products. They are collaborating with Iowa State University researchers on nanomedicines to treat respiratory infections.

Bailey Arruda is an Associate Professor of Veterinary Diagnostic & Production Animal Medicine at Iowa State. She is researching nanovaccines to prevent infectious diseases in swine.

Hua Bai is an Assistant Professor of Genetics, Development & Cell Biology at Iowa State. He uses fruit fly genetics to research the molecular and cellular mechanisms of cardiac aging.

Joshua Beck is an Associate Professor of Biomedical Sciences at Iowa State. He researches molecular parasitology, and how parasites such as malaria evade host immune mechanisms.

Paola Boggiatto is a Veterinary Medical Officer at the USDA National Animal Disease Center in Ames, IA. She is a veterinary immunologist with an interest in T cell immunology, intracellular pathogens, and the development of novel vaccine platforms that target persistent infections.

Anne Bronikowski is a Professor of Genetics, Evolution & Organismal Biology at Iowa State. She uses comparative genomics and physiology to research the mechanisms and evolution of aging using non-traditional models, especially reptiles.

Rohana Dassanayake is a Research Microbiologist at the USDA National Animal Disease Center in Ames, IA. His research focuses on viral and bacterial respiratory diseases in cattle. He is collaborating with Iowa State researchers on nanoparticle-encapsulated peptides to kill multi-drug resistant Salmonella.

Skroot Laboratory, Inc.

Skroot Laboratory, Inc. is a startup company in Ames, IA that is developing wireless sensors and process analytical technologies to speed up the production of cell and protein therapies and vaccines.

New Patent


Articles Published in High-Impact Journals

Nanovaccine Institute researchers published hundreds of articles in scientific journals in 2020, including these high-impact journals:

