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IOWA STATE UNIVERSITY FOUNDATION

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The *Nanovaccine Institute* at Iowa State

"Tomorrow's diseases will look very different from today's diseases and certainly from yesterday's diseases, so the ways we counter them must be very different. That's what we're working on."

Balaji Narasimhan,
Director, Nanovaccine Institute
Anson Marston Distinguished Professor and Vlasta Klima Balloun Faculty Chair, Chemical and Biological Engineering

A science of **billionths**, with potential for **billions**

FOR YEARS, MODERN MEDICINE HAS BEEN LOSING THE BATTLE AGAINST WHAT BALAJI NARASIMHAN CALLS "THE ENEMY." HE'S TALKING ABOUT DISEASE.

Story by
Susan Flansburg
Photos by
Dan McClanahan

He says it's an urgent matter, as some diseases are reemerging, such as whooping cough, some are new, such as SARS, and others, like bacterial infections, are gaining immunity to once-successful treatments.

"We must bring new tools to the fight," he says, "because the old ones are no longer working."

As director of the Nanovaccine Institute, headquartered at Iowa State University, Narasimhan is helping create the new tools. He and an interdisciplinary team of 65 researchers at 20 universities, research institutes, national laboratories, companies and healthcare coalitions from across the nation are working to deliver life-saving treatments and disease-preventing vaccines around the globe. The tools are based on particles so small you could line a thousand of them across the dot above this *i*.

For the researchers, these particles are their David against a towering Goliath. And if they can slay the giant, healthcare around the world will forever change.

"The motivation for the work we do is to make people's lives better," says Narasimhan, Anson Marston Distinguished Professor in chemical and biological engineering, and Vlasta Klima Balloun Faculty Chair. "To solve real-life problems. It's why we come to work every morning."

While the science of nanotechnology is complicated, the potential healthcare outcomes are breathtakingly straightforward: Dramatically improved treatments and preventions for everything from cancer to autoimmune diseases could be on the near horizon. And they will ride in on a tiny Trojan horse.

This metaphor, too, is popular among the institute's researchers. It perfectly describes how a microscopic nanoparticle, unique to each treatment, is designed to carry medications and vaccines into otherwise nearly impenetrable locations. Not only are these infinitesimal warriors able to slip past defense barriers, they also deliver their payload precisely and only where it needs to go, more effectively and with fewer side effects.

This has immense implications for human and animal health. Our immune systems are built to block intruders, whether good or ill. If needed medication can reach the appropriate target in the first place, many currently incurable diseases can be better treated or even cured. And if medication can arrive more precisely at the location it's needed – and not where it isn't – higher doses can be safely and tolerably administered.

"One approach to repairing damaged nerves is to engineer nerve cells that produce and secrete neurotrophic growth factors built within nanoparticles, so that one day, a neurosurgeon could simply pull a device off a shelf and implant it within an injury."

Donald Sakaguchi,
Morrill Professor, Genetics, Development and Cell Biology (opposite)

ALL SYSTEMS GO

In the bustling labs of the Nanovaccine Institute scattered across campus, Iowa State chemical and biological engineers collaborate with immunologists, neuroscientists, microbiologists and other experts from 14 different departments. This large-scale, interdisciplinary collaboration promotes seamless interaction among experts in the sciences, economics, social science, public policy and even the commercial sector. Such a systems-based approach allows concurrent and thorough investigation of questions from fundamental science to marketability and affordability.

It's one of the main reasons for basing the institute at Iowa State, long a leader in interdisciplinary collaboration. The marriage of life sciences and engineering first began at the university in the 1960s and yielded expertise in the core platform of nanotechnology. Other resources, from the veterinary college to the nearby USDA and animal vaccine manufacturers, bring significant value to the research process.

"Iowa State has the intellectual bandwidth and assets to support this initiative," Narasimhan says. "We know how to engage in the necessary systems-based approach. For example, social scientists help us understand how the new products will be perceived. Other experts help evaluate issues of adherence, cost, shipping and storage."

"The exciting thing about working in an interdisciplinary group is looking together at new approaches and challenges to be met and learning from each other."

Surya Mallapragada, Associate Vice President for Research, Distinguished Professor and Carol Vohs Johnson Chair in Chemical and Biological Engineering

IMMUTABLE IMMUNITY

Nanovaccine Institute researchers are designing nanoparticles for many uses: Some will sneak through the hard, fibrous surface of pancreatic cancer tumors to deliver chemotherapy. Others will cross the blood-brain barrier to treat diseases like Parkinson's. Others yet will help build powerful and long-lasting immunity to diseases like influenza and parasites that destroy the brains of children in Africa.

One research thrust is a universal influenza vaccine that is reliable, globally deployable and conveys full, lifelong immunity in one dose. Using a novel, non-egg-based manufacturing process, the nanovaccine likely won't require needles or refrigeration and will withstand variabilities during shipping. Surya Mallapragada, Distinguished Professor and Carol Vohs Johnson Chair in Chemical and Biological Engineering, calls it the Holy Grail of vaccines.

Nanoparticles will make it possible.

"We are taking the proteins H and N, which are antigens on the surface of the influenza virus, and putting them on the surface of the nanoparticle so the immune system will recognize it as an invader and attack," she explains.

As the nanoparticle erodes and delivers its payload, the immune system will discover proteins buried in the middle common to all strains of flu virus. These proteins can provoke a full immune response, and teach the immune system to respond more vigorously to influenza.

Successive formulations of this universal nanovaccine are being developed using outcomes of testing in mice. Marian Kohut, Barbara E. Forker Professor in Kinesiology, oversees this part of the institute's work.

"What we know about humans we first learn in mice," she says.

Marian Kohut,
Barbara E. Forker Professor in Kinesiology

"For example, we see greater immune response to vaccination in younger mice than we do in older mice. So one of the questions becomes, can we teach the aged immune cells to behave like young immune cells?"

Because she's working in tandem with researchers in other fields, Kohut can easily explore with them whether adding a metabolism-altering agent to the nanovaccine would enhance the immune response in older adults.

"Working in one lab like this enhances the interdisciplinary component of the institute," she says. "We can address all sides of the questions at the same time in our experiments."

When ready for human clinical trials, the institute's medical school partners, including the Mayo Clinic, the University of Iowa and the University of Nebraska Medical Center, will take over. Researchers expect that to happen yet this year.

Kohut studies how nanoparticles can be modified in different ways to elicit a type of immune response that may vary depending on host factors like age, stress or nutrition. It could mean a flu vaccine that is tailored for effectiveness in the very young to the very old.

HOME/TEAM ADVANTAGE

This spring, Iowa State begins construction on a much-needed centralized home and state-of-the-art research space for the institute on the fifth floor of the Advanced Teaching and Research Building. The $7 million project will be funded by the university and donor support, including recent alumni gifts of $2 million from Jim Balloun, $1 million from Mike and Jean Steffenson, and $300,000 from Bob Lane. Once completed, the fully-integrated, one-of-a-kind facility will position the institute to be more competitive in pursuing grants and to accelerate commercialization of its research. And it means invaluable synergy for faculty and students.

Morrill Professor and neuroscientist Donald Sakaguchi says being able to collaborate during his and his students' experiments on nerve regeneration not only leads to a more efficient use of time, it models the future of scientific investigation.

"Having students and trainees working in the lab alongside faculty means we are mentoring the next generation of scientists," he says.

Professor of veterinary microbiology and preventative medicine Gregory Phillips calls it team science.

(Continued on p.12)

"Genetically engineering bacteria to produce colored pigments allows for easy visual detection. These microbial biosensors act as small sentinels to provide early warning of infection and other diseases in both human and animal hosts. They are also being used to discover new compounds with antibacterial activity as a way to potentially combat antibiotic resistance of microorganisms."

Gregory Phillips,
Professor, Veterinary Microbiology and Preventive Medicine

Fighting the (new) good fight

Antibiotics are one of humankind's greatest life-saving discoveries. Not only are they important to human health, but antimicrobials are widely used for the prevention and control of animal diseases. In recent decades, however, the value of these "wonder drugs" has diminished due to the drastic increase in antimicrobial resistance, as more bacteria develop an ability to fight off the drugs that are used to stop them in their tracks. Illnesses that were once easily curable with antibiotics could soon become life-threatening, endangering public health and raising the specter of multi-billion dollar medical costs and economic losses.

But the solution is not as simple as just developing different, stronger types of antibiotics. Instead, antimicrobial resistance, or AMR, is a complicated challenge with both origins and impact in human health, animal health and our environment – and in the connections between all three systems. Solving such complex problems requires interdisciplinary research that brings together expertise from the molecular- to ecosystem-level.

That's why Iowa State has joined with the USDA Agricultural Research Service, Mayo Clinic, the University of Nebraska-Lincoln, University of Nebraska Medical Center and the University of Iowa in the new Institute for Antimicrobial Resistance Research and Education. The institute, based at Iowa State, involves a team of more than 100 researchers, educators, clinicians and extension personnel all dedicated to a "systems" approach that integrates better understanding of the biology of AMR organisms with our crop and animal agroecosystems, and social and environmental effects.

"Antimicrobial resistance touches each of us in our daily lives," said Paul Plummer, associate professor of veterinary diagnostic and production animal medicine at Iowa State, and executive director of the Institute for Antimicrobial Resistance Research and Education. "This new institute provides a great resource for the entire country as we work to build strong, collaborative research and educational programs to mitigate this risk."

(Continued from p.10)

"There's more to it than just having collaborative research projects," Phillips says. "In addition to a shared responsibility for using modern technologies and experimental methods in which each individual cannot be an expert, the Nanovaccine Institute includes a common vision to prevent and cure disease, and generate new approaches to understand complex systems related to human and animal health."

Phillips' research centers on the microbiome and antibacterial resistance, the latter of which is also the focus of a new national institute based at Iowa State. *(See sidebar p.11)*

Michael Wannemuehler, the institute's associate director and chair of the veterinary microbiology and preventative medicine department, focuses his research on vaccine work as well as the host-bacterial disorders that influence diseases such as Crohn's disease. He says students working within the institute's complex talent pool will have more than a leg up when they graduate.

"The interdisciplinary research approach these students are being trained in will solve the health problems of the century – flu, tetanus, plague, parasites, neurological conditions," he says.

Phillips says simply, "Our hope is that it will change the world for the better."

"Globally, millions of children die because they do not receive booster immunizations. Single-dose vaccines would protect these children. Another area single-dose vaccines would impact is food animal medicine – improved animal health as well as reducing costs associated with administrating booster immunizations to livestock species, especially pigs and cattle.

Michael Wannemuehler,,
Associate Director, Nanovaccine Institute
Professor and Chair, Veterinary Microbiology and Preventive Medicine

GIFTS at WORK

EXTENDING IOWA STATE'S IMPACT THROUGH PHILANTHROPIC GIVING

The place for blue sky thinking
Rising on the Iowa State campus is the Student Innovation Center, slated to open in 2020 and supported in part by donors like Boeing, Land O'Lakes and HNI, with a lead gift of $30 million from an anonymous alumni couple.

Photo: Chris Gannon