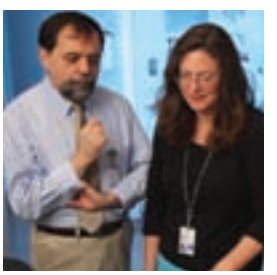
UNIVERSITY of VIRGINIA HEALTH SYSTEM

Closing In On the Cure

ACCELERATING DIABETES RESEARCH AT THE UNIVERSITY OF VIRGINIA



A Growing Epidemic

DIABETES CONTROLS EVERY aspect of your life.

As one mother of a recently diagnosed child put it, "As parents, we fight to keep the disease from defining her identity. Yet, every family interaction—every meal, every snack, every walk, every bike ride, every bedtime—has to involve an evaluation of blood sugar and insulin. Until we find a cure, she'll have to take over from us and practice this vigilance for the rest of her life. There's never a day off—even when a diabetic does everything right, they can still fail."

Once a disease of an unfortunate few, diabetes has become epidemic in recent years—both type 1 (juvenile) and type 2 (adult onset) diabetes are on the rise. More than 23 million Americans suffer from this chronic disorder that more than doubles their risk of premature death and imposes an almost certain risk of developing life-threatening complications that include heart attack, stroke, dementia, kidney failure, vision loss, and amputations. Treatment for diabetes and its complications costs Americans more than $174 billion annually.

Unraveling the complexities of this multifaceted disorder is a major research focus across the country. Here at UVA, our internationally-recognized researchers and pioneering clinicians have positively impacted the lives of our patients and their families. We are determined to not only find a cure, but also to develop innovative ways to prevent the disease, minimize complications, and make life easier for those who have it.

A Search for Answers

RESEARCHERS AT UVA'S Center for Public Health Genomics, headquarters for the National Institutes of Health Type 1 Diabetes Genetics Consortium, are making progress in the quest to identify who among us might develop diabetes. As co-directors of the largest group of researchers in the country devoted to teasing out the genetic factors associated with diabetes, the work of geneticists **Stephen Rich, PhD,** and **Patrick Concannon, PhD,** is directed toward understanding the disease and its complications and coming up with novel ways of preventing and treating it.

In the last three years, the number of locations on the human genome that are known to increase the risk for type 1 diabetes has jumped from a handful to over 50 potential genes that researchers are mining for insight into the disease. These discoveries represent fundamental changes in the understanding of the genetic basis for the disease, and researchers are exploring many of these genes as possible targets for drugs.

As head of UVA's Diabetes Research Center, endocrinologist **Eugene Barrett, MD, PhD,** is working to piece together another puzzle, that of why more and more people are developing type 2 diabetes.His lab has developed an innovative ultrasound imaging technique that enables researchers to study how blood vessels respond to insulin. Using this technology, they are developing a better understanding of how insulin is delivered to the tissues and the mechanism by which insulin passes from the blood vessels into the cells.

Unlocking the answers to the very building blocks of diabetes opens up vast new possibilities for treatment—and possibly one day a cure.

We know that at least half of the risk for developing type 1 diabetes is determined by environmental, not genetic factors. That's why it's important to identify the genetic factors so epidemiologists can identify the environmental factors that differentiate those who develop type 1 diabetes from those who don't. The genes alone won't do it.

—Geneticist Stephen Rich, PhD

Harnessing the Power of Technology

Freeing diabetics from daily insulin injections

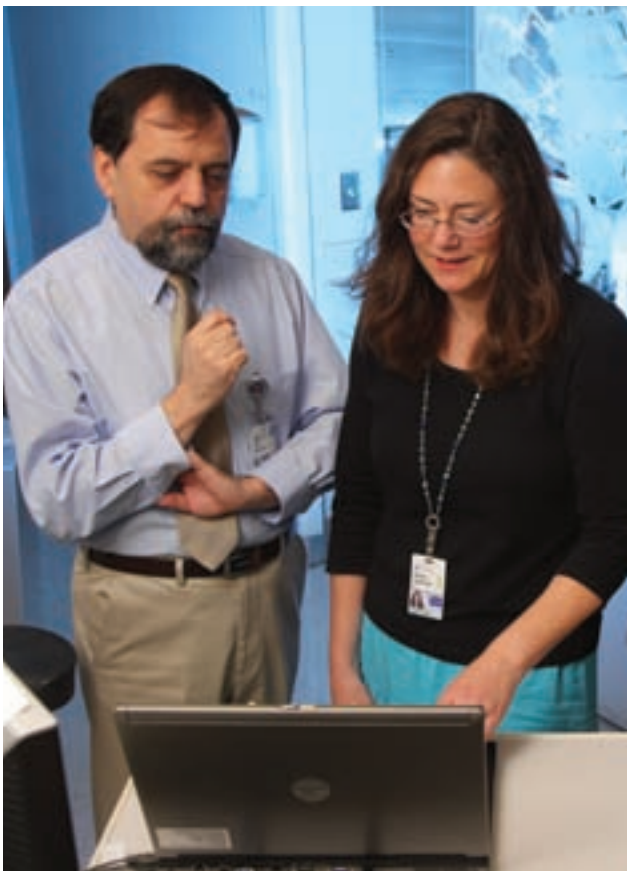
WHILE SOME SCIENTISTS try to understand why our immune system slows or stops the production of insulin, others at UVA are developing promising new technologies to intervene with the disease. Transplant surgeon **Kenneth Brayman, MD, PhD,** for example, is conducting clinical trials on islet cell transplantation. This procedure infuses insulin-producing islet cells from a donor into the liver of a patient with diabetes so his or her body can begin to make insulin again and maintain normal blood sugar levels without injections or constant monitoring.

For diabetics, this procedure is life-altering. While at this time none of the patients who received islet cell infusions have been able to give up insulin injections completely, all have experienced significant reduction in the amount of insulin they use on a daily basis. Even this small step allows them to live a more normal life.

Islet cell transplantation is made safer and more efficient at UVA because of Brayman's cell processing facility. The facility is one of only a handful of FDA-approved sites in the country with the capacity to process the fragile islet cells for transplantation. This facility also processes cells that are used by other scientists—researchers who are working to understand genetic abnormalities and inflammatory processes associated with diabetes-damaged islets and others who are creating innovative bioengineered structures that can enhance the survival and function of the transplanted cells.

The main thing I hear from the patients who participate in our clinical trials is that a system like the 'artificial pancreas' would allow them to be independent. They wouldn't have to think all the time about their disease.

—Mathematician & investigator Boris Kovatchev, PhD



A sophisticated computer with the power to save lives

UVA MATHEMATICIAN **Boris Kovatchev, PhD,** has put the University at the center of another major therapeutic innovation with the closed-loop diabetes control system or "artificial pancreas." As director of the University's Diabetes Technology Center, Kovatchev is the principal investigator for international clinical trials now underway for this biomedical interface that links a patient's continuous glucose monitor with his or her insulin pump. The complex algorithm he developed with colleagues in Italy promises to seamlessly coordinate these two existing technologies, allowing for calculation and administration of the correct dose of insulin without the patient's intervention.

The artificial pancreas team at UVA—where clinician **Stacey Anderson, MD,** manages clinical trials of the closed-loop system—has received funding from the NIH, the **Juvenile Diabetes Research Foundation (JDRF),** and industry. The project promises to be a breakthrough for those with type 1 diabetes who frequently may be unaware that their blood sugar is dipping to dangerous levels. With this automated system, patients will be able to go to bed at night confident that they will not experience this life-threatening condition.

UVA is the only institution in the world that has simultaneously developed research programs for both islet cell transplant and the artificial pancreas. Working in conjunction, these two approaches show unprecedented promise for improving blood sugar control with minimal or no intervention on the part of the patient.

It's not a one time 'I found it' kind of thing. Diabetes research is slow, plodding ... building one block after another of evidence. Now immunologists have a new focus that may be a much safer avenue for us to try to manipulate clinically.

—Researcher Marcia McDuffie, MD

Collaborating for a Cure

PEDIATRIC ENDOCRINOLOGIST **Marcia McDuffie, MD,** is at the leading edge of another avenue of research, working to piece together an understanding of the pathways involved in the autoimmune process that is at the heart of type 1 diabetes: the destruction of insulin-producing islet cells. Combining her work in immunology with information from the field of genetics, she is exploring the properties of a particular gene that is important to the immune response in the pancreas.

McDuffie's work has demonstrated exciting new information about the cells that initiate the immune response, which has implications for biochemical reactions along the entire autoimmune pathway. This promising finding has been a primary force in redirecting the focus of immunology's diabetic research, allowing a much broader view of other parts of the immune system as potential targets for treatment of type 1 diabetes.

Other collaborations between basic scientists, biomedical engineers, and clinically-focused researchers are exploring a wide variety of innovative approaches to solving problems with diabetes treatment. Biomedical engineers, for example, have teamed up with researchers in the islet transplant program. They're probing the potential of futuristic materials, such as nanotechnology and polymers, in applications that may overcome issues of transplant rejection and recurrent autoimmunity.

Similarly, basic scientists and clinicians have joined forces to address the problem of retinopathy, a common complication that currently has no effective treatment. This novel approach uses adult stem cells to repair damage that occurs in the tiny blood vessels in the retina. If successful, this treatment could eliminate a significant side effect that occurs in as many as 80% of people with diabetes and is a leading cause of blindness.

Building scientific partnerships across disciplines is a key strength at UVA, and one with the greatest potential to translate discoveries in the lab into new treatments for patients.

LaunchPad for Diabetes Innovations

THE ROAD TO A WORLD WHERE DIABETES is no longer a dreaded, life-threatening disease is still a long one. Progress in the search for treatments and a cure can only be achieved through close interaction among scientists and clinicians from a variety of disciplines working together toward that goal. The unique culture of collaboration that exists at the University of Virginia is perhaps the most valuable component in the push to advance diabetes understanding. In this cross-disciplinary, interactive environment, researchers have the advantage of immediate access to the University's wide range of scientific and bioengineering experts who can provide the creative impetus necessary to propel a project into higher levels of understanding.

It's this sort of pioneering leap that the LaunchPad for Diabetes Innovations program was designed to foster. Founded by philanthropists **Paul** and **Diane Manning,** LaunchPad is a novel initiative that provides seed funding for high-impact, collaborative projects that have the potential for revolutionizing the care and treatment of diabetes. For the Mannings, this fight is personal—the couple have two children with diabetes. Their support for diabetes research at UVA has dramatically impacted the program. Now, their LaunchPad initiative provides technical support to help scientists quickly move vital new technologies out of the realm of potential and into real-world application.

For the millions of patients who live daily with the dangers and difficulties of diabetes, this process can't move fast enough.

THE UNIVERSITY OF VIRGINIA, with a full range of nationally recognized, cutting-edge research programs, holds all the keys for unlocking vital new understanding that will lead to the prevention, treatment, and cure of diabetes. Now is the time to partner with us. Private philanthropy is our best hope to speed innovation and discovery. It is the best hope for our patients and their families.

A cure is within our reach.

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What we're trying to do with every resource at our disposal is to develop cross-disciplinary fertilization to move this collaborative research effort forward. We have everything it takes to develop a cure right here, right now at UVA.

– Physician scientist Kenneth Brayman, MD, PhD

THE UNIVERSITY OF VIRGINIA DIABETES PROGRAM is poised at a critical threshold in its development. UVA has attracted some of the foremost investigators, developed a series of specialized clinics for high-risk patients, and launched an innovative education program that trains expert physicians and helps people with diabetes manage their disease and avoid many of its complications. Now we are ready to accelerate the pace of research, and translate our findings into treatments that relieve suffering and save lives.

Call **(434) 924-8432** or **(800) 297-0102**—or e-mail **SupportDiabetesResearch@Virginia.Edu**—to help shape the future of diabetes care and research.