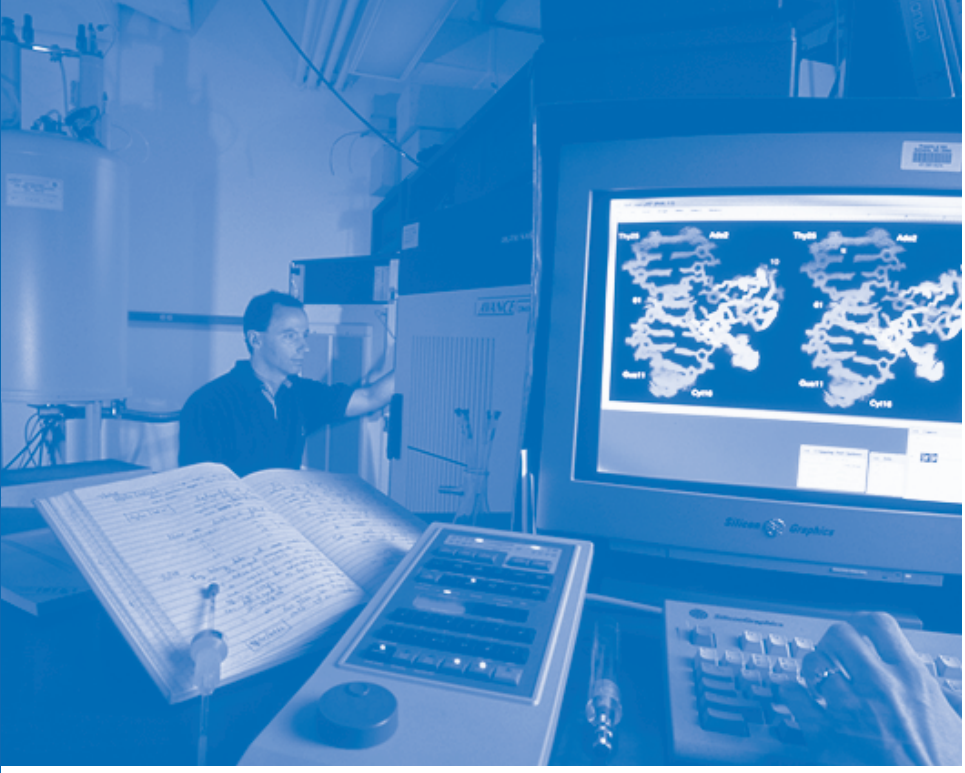


# GOAL VI:

# ATTRACT NEW TALENT AND APPLY NEW TECHNOLOGIES TO RESEARCH ON TYPE 1 DIABETES

## Why It Is Important To Attract New Talent and Apply New Technologies to Research

**Attracting New Talent To Tackle Research on Type 1 Diabetes**

- Recruit Experts in Diverse Fields and Train New Researchers
- Collaborative Research

**Applying New and Emerging Technologies to Type 1 Diabetes Research**

- Visualizing Islets in the Body
- Technology for Identifying Disease Genes
- Studying Proteins Involved in Disease Onset and Progression
- Application of Engineering Principles
- Animal Models To Study Type 1 Diabetes
- Gene Therapy Approaches
- Collection and Analysis of Scientific Data
- Communication Technology

**Moving the Research Agenda Forward**

## Investigator Profile

**Andrew Norris, M.D., Ph.D.—Research in Pediatric Endocrinology: Road to Independence**

# WHY IT IS IMPORTANT TO ATTRACT NEW TALENT AND APPLY NEW TECHNOLOGIES TO RESEARCH

**Type 1 diabetes patients and family members may ask: "How will research help me? Will someone invent instruments to test glucose levels without painful finger sticks? Are there tests that can catch diabetes complications at an early stage?" Simply put, research is the key to a cure for type 1 diabetes. It was through research efforts in the early 1900s that scientists discovered insulin and started using it to save the lives of type 1 diabetes patients. It was also through research that improvements in disease monitoring and treatment strategies have been achieved. These advances have contributed to significant improvements in patients' health and quality of life. Only through research efforts will a real cure for this disease be realized.**

## Attracting New Talent To Tackle Research on Type 1 Diabetes

Harnessing new and emerging technologies, as well as pursuing all of the future research directions described in this Strategic Plan, is dependent on the existence of a workforce of talented researchers with diverse expertise. The NIH has been proactive in developing research programs, supported by the *Special Statutory Funding Program for Type 1 Diabetes Research*, to attract creative, skilled scientists to study type 1 diabetes and its complications, and to empower them to conduct their research through access to cutting-edge tools and technologies. Research initiatives and mechanisms designed for type 1 diabetes should continue to serve as a model for NIH in exploring how to translate discovery research into health gains.

***Recruit Experts in Diverse Fields and Train New Researchers*:** Type 1 diabetes affects many different organ systems (e.g., pancreas, eyes, kidneys, heart, nervous system) and involves diverse areas of science (e.g., immunology, stem cell and developmental biology, bioengineering, behavioral research) and medicine (e.g., pediatrics, transplant surgery). Therefore, it is imperative to pursue research on all of these different areas to have the greatest impact on the health of patients. Experienced researchers with a particular expertise (e.g., immunology, heart disease, eye disease) should be recruited to apply their talents to research on type 1 diabetes. Researchers with expertise in many of the newest technologies should also be recruited to apply these sophisticated tools to further understanding of the disease. Moreover, it is important to train and retain new scientists and clinicians to sustain momentum in the field.

The NIH promotes the translation of fundamental discoveries from the laboratory bench of basic scientists (below) into investigations in the clinic (opposite), which promise to directly benefit type 1 diabetes patients.

*(Photo credit: Below—third photo from left: Richard Nowitz for NIDDK; other photos: Getty Images. Opposite—Richard Nowitz for NIDDK.)*

***Collaborative Research*:** Increasingly, multidisciplinary teams of investigators must pool their expertise to catalyze research progress. Because researchers in a particular technology or research area may not have expertise in type 1 diabetes, they must be encouraged to work with scientists who have knowledge of the disease. These types of partnerships can truly synergize research efforts and reap tremendous benefits for patients.

## Applying New and Emerging Technologies to Type 1 Diabetes Research

The tools of biomedical research have evolved rapidly due to the biotechnology revolution. Many technologies that were used 20 years ago have been replaced by new technologies that permit scientists to conduct research more efficiently and to ask and answer questions that were previously impossible to frame. Some new and emerging technologies hold real promise for advancing the type 1 diabetes research field.

***Visualizing Islets in the Body*:** When a person breaks a bone, an x-ray is used to see the injury. This technique makes it much easier for doctors to diagnose the break and effectively treat it. Likewise, it would be useful to "see" a person's islets. Why would this be important? Type 1 diabetes is usually diagnosed late in the disease process, when most of the insulin-producing beta cells have already been destroyed. If researchers could detect islet destruction by visualizing the islets before the onset of clinical symptoms, then they could intervene earlier to try to prevent further islet loss and the need for insulin administration. Furthermore, such a technological breakthrough would make it more efficient to conduct clinical trials, because scientists could actually "see" if a therapy was effective at either preventing or reversing islet loss. Another potentially beneficial application of this technology is to improve outcomes of islet transplantation. If doctors could see when transplanted islets are beginning to be rejected by the immune system, then they could intervene earlier, to prevent graft rejection and the need for patients to resume insulin administration. Recently, significant advances in visualizing islets using techniques such as magnetic resonance imaging (MRI) have been achieved in mouse models. More research in this area is needed to translate these results to humans, in order to overcome this major clinical and research barrier in type 1 diabetes.

***Technology for Identifying Disease Genes*:** With the completion of the Human Genome Project and with new "high-tech" laboratory methods, genetics experiments that once took months now take minutes. These advances will significantly speed the discovery of disease-causing genes, including those that play a role in type 1 diabetes disease onset or the development of complications. Identification of key genes will promote the development of novel prevention strategies.

***Studying Proteins Involved in Disease Onset and Progression*:** Recent research advances have improved scientists' ability to study proteins in the body. Fifteen years ago, researchers were only able to study relatively small numbers of proteins at one time to determine if or how they had a role in disease onset or progression. Because there are tens of thousands of proteins in the body, studying proteins a few at a time is an extremely time-consuming endeavor. However, novel "proteomics" technologies have been developed that now permit researchers to study thousands of proteins at once, as well as to determine how proteins may interact with each other. These technologies can be used, for example, to identify proteins that correlate with stage or rate of progression of type 1 diabetes and its complications. Furthermore, understanding the expression and function of proteins will enhance understanding of the genes by which the proteins are produced. These insights could directly translate into improved disease detection and prevention strategies.

***Application of Engineering Principles*:** There are several areas of type 1 diabetes research that could benefit from the application of engineering principles to disease (bioengineering). For example, identifying ways to measure blood glucose

levels without the need for a finger stick would dramatically improve the quality of life of type 1 diabetes patients. Even more beneficial would be linking such measures to insulin delivery devices to create an artificial pancreas. In the field of islet transplantation, if transplanted cells could be protected from the immune system by some material or device, then there would be a greater chance of transplant success with avoidance of toxic immunosuppressive drugs. To realize these and other advances, it is important to apply bioengineering approaches to type 1 diabetes research.

***Animal Models To Study Type 1 Diabetes*:** Animal models are an important scientific resource because they enable researchers to investigate underlying disease processes that cannot be studied in humans. These models also permit assessment of novel therapeutic interventions before they are tested in people. The use of animal models is a necessary early step to promote translation of research findings from the laboratory to human patients. It is crucial to develop and utilize animal models with greater fidelity to human type 1 diabetes and its complications to propel research progress.

***Gene Therapy Approaches*:** When genes in the body are defective, a plausible treatment strategy is to replace them with those that work properly. Researchers have been exploring novel ways to deliver genes to people or transplanted tissues, through a process called gene therapy. These approaches, once developed, could also be used to benefit type 1 diabetes patients. For example, islets transplanted into a type 1 diabetes patient undergo attack by the immune system, which treats them as foreign invaders. Gene therapy approaches could be used to protect islets from this attack or to deliver genes that enhance islet viability in the transplant site. With future research and scientific breakthroughs, gene therapy approaches could also be used to treat diabetic complications, as well as to replace the insulin that type 1 diabetes patients are no longer capable of producing. Gene delivery approaches are also being used to create animal models for the study of therapies for type 1 diabetes and its complications.

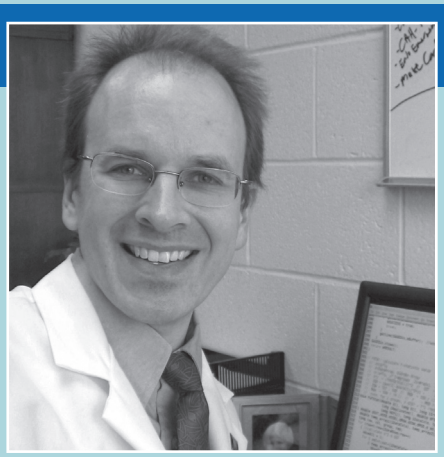
***Collection and Analysis of Scientific Data*:** Because scientists are now collecting more data than they ever thought possible, it has become increasingly important to find ways to assemble, organize, and analyze this valuable information. Furthermore, in order to achieve the greatest impact on the field, scientists must be able to share data with one another, so that they can compare results or combine their efforts to make novel discoveries that they cannot make individually. It is important for researchers to work together and coordinate their efforts in order to accelerate the pace of discovery.

***Communication Technology*:** Patients today have the ability to exchange information with their providers much more easily than ever before. Increased accessibility and improved usability of computers, the Internet, and cellular technology can potentially allow clinicians to be much more involved in frequent monitoring of their patients. Patients can also have access to information and suggested changes in management more quickly and efficiently. Improvements in monitoring technology, and its ability to communicate with a provider's office, can lead to new strategies of case management, higher patient satisfaction, and improved health outcomes.

## Moving the Research Agenda Forward

New and emerging technologies, coupled with a cadre of talented scientists, have the potential to bring about real breakthroughs in the understanding, prevention, treatment, and cure of type 1 diabetes. Under the auspices of the *Special Funding Program*, multiple research consortia have been created to tackle specific challenges that will impact the health of people with type 1 diabetes. These efforts bring together clinical and basic researchers, as well as link scientists investigating the pathogenesis and therapy of type 1 diabetes and its complications with new technologies needed to pursue evolving areas of opportunity. New therapies have already had a dramatic impact on extending life and retarding disability from type 1 diabetes. The pace of discovery is accelerating, and, as in the past, future research advances should directly translate into improvements in the health and quality of life of patients. Therefore, it is crucial to deploy new and emerging technologies and to engage experts from diverse fields in the battle to overcome type 1 diabetes and its complications.

This is a new and exciting era of scientific research. Scientists are now able to study biological processes in ways that were not possible even a few short years ago. It is essential to take full advantage of the new technologies and information that have emerged, in order to optimize progress. A talented workforce of researchers must be mobilized to apply their expertise to overcoming current barriers. Type 1 diabetes is a devastating illness for patients and their families, especially when it strikes in infancy, childhood, or adolescence. Pursuing novel research directions and attracting new research talent are key elements in conquering this disease.



# Andrew Norris, M.D., Ph.D.

## Research in Pediatric Endocrinology: Road to Independence

### A Lifelong Ambition

Dr. Andrew Norris always knew that he wanted to be a researcher. "Going into research was a lifelong ambition," recollects Dr. Norris, an Assistant Professor at the University of Iowa. "Beginning in second grade, I read every science book in the library of my elementary school."

Dr. Norris also developed an interest in medicine, so in order to pursue both medicine and research, he enrolled in a combined M.D. and Ph.D. training program at the Washington University School of Medicine in St. Louis. He entered the program intending to pursue medical research, with a particular interest in nutrition and the role that carbohydrates and lipids play in the development of human disease. He also enjoyed working with children. After receiving his degrees, he completed a pediatrics residency program. During that time, more and more children were being diagnosed with type 2 diabetes, and this sparked his interest in studying diabetes, an endocrine disease, in the pediatric population.

For further training as a sub-specialist in pediatric endocrinology, Dr. Norris applied to and was accepted into a combined fellowship program at the Children's Hospital Boston, and the Joslin Diabetes Center. "The fellowship program was an extremely wonderful experience for me," recalls Dr. Norris, "and I went there with the intention of doing diabetes research." During the first year of his fellowship, he worked directly with children with diabetes. "I found that I really enjoyed working with children with diabetes and their families. This positive experience also synergized with my interest in research," states Dr. Norris.

During the next two years of his fellowship, he pursued research in the laboratory of Dr. C. Ronald Kahn, a prominent diabetes researcher. Dr. Norris recalls, "While working in Dr. Kahn's lab, my goal was always to become an independent investigator studying pediatric diabetes." However, making the transition from being a research trainee to an independent investigator can be a daunting task.

### Transition to Independence

At the end of his fellowship, Dr. Norris would transition from being a "fellow" to a faculty member, at which time he would be expected to find his own source of funding to support his research program. In preparation for this transition, approximately 1 year before his fellowship ended, he applied for an NIH "Mentored Clinical Scientist Development Award" (K08) to support his research. Two months before becoming a faculty member, he found out that his application was, as he states, "good, but not good enough" to receive funding. Therefore, he was facing the prospect of having to put research on hold until he could find funding support.

Fortunately for Dr. Norris, the Children's Hospital Boston/Joslin Diabetes Center was one of seven sites participating in the NIH-supported "Pediatric Diabetes Research Training and Career Development Program."

Dr. Norris was familiar with this program because, earlier in his fellowship, he was supported by an institutional research training grant (T32) under this umbrella NIH-supported program. In addition to T32 training grants, the program also awards K12 grants (Clinical Scientist Career Development Program), which provide funding for investigators as they transition to independent faculty positions. "Fortunately," says Dr. Norris, "a K12 slot was available when I needed funding to bridge time between completing my fellowship and receiving my own grant. Without the K12 award, I would not have had professional time to pursue diabetes research, and might have instead had no choice but to spend the majority of my time in the clinic. This award mechanism allowed me to have 'protected time' so that I could resubmit my K08 grant application and still focus on diabetes research and building my own research program." While receiving support from the K12 training grant for 1 year, Dr. Norris resubmitted his K08 application and was awarded funding. Importantly, there was no disruption to his diabetes research endeavors.

Dr. Norris has recently joined the faculty at the University of Iowa, where he directs his own independent research program. His research focuses on how the events early in life affect later risk of diabetes and diabetic complications. As an example, a person's blood sugar level today has a strong effect on his or her risk of complications years down the line, even if the individual feels healthy in the interim. In other words, as Dr. Norris states, "The immediate effect is subtle and unnoticed, but over time can lead to significant problems." To this end, he is developing new mathematical models to better identify the early subtle effects of diabetes on gene expression. These tools will help determine how these barely noticeable effects eventually lead to such devastating complications. The hope is to develop improved strategies enabling doctors to better prevent or delay the development of complications, which affect patients with both type 1 and type 2 diabetes. Dr. Norris is also studying the ways that abnormal build-up of fat contributes to the complications of diabetes as well as the development of insulin resistance. This research could provide insights into additional means to prevent or delay certain diabetic complications.

Dr. Norris stresses that, "Because of the shortage of pediatric endocrinologists throughout the country, the pediatric endocrinology research training program is of incredible importance to attracting talented individuals to pursue research in this area." Furthermore, he notes, "It is difficult to secure funding for independent research by the end of a fellowship. The K12 grant mechanism is a necessary tool to bridge the gap between completing research training and pursuing independent research."

### Pediatric Diabetes Training Program

To enlarge the pool of pediatric endocrinologists conducting diabetes research, the NIH, in partnership with the ADA and the JDRF, awarded institution-wide research training and career development grants to seven medical centers with strong research programs in childhood diabetes: Children's Hospital Boston/Joslin Diabetes Center, where Dr. Norris received his training; Baylor College of Medicine; University of Colorado; University of Pennsylvania; University of Pittsburgh; Washington University; and Yale University. More information on the program can be found on the NIDDK Web site at: www.niddk.nih.gov/fund/diabetesspecialfunds/train_peddiab.htm.

The awards, through the T32 (institutional research training) and K12 (Clinical Scientist Career Development Program) grant mechanisms of the NIH, provide for 2-3 years of fellowship training, as well as 2-3 additional years of support for junior clinical investigators, for a total of 5-6 years of continuous, uninterrupted research training in diabetes. The funding supports up to five positions at each medical center; each center was free to decide how many of the five slots were to be reserved for pediatric endocrinology fellows or investigators who were transitioning from fellowship to independent scientist.

These T32/K12 awards now support 34 pediatric endocrinology fellows/junior clinical investigators each year, all of whom are receiving research training and career development in many aspects of diabetes research. At the time of this publication, nine pediatric endocrinologists supported by this program have received individual NIH or JDRF career development awards. Moreover, more than five of the trainees were recipients of an award through the NIH Loan Repayment Program that offsets some of the educational debt incurred by many graduates in the health professions. (See: www.lrp.nih.gov)