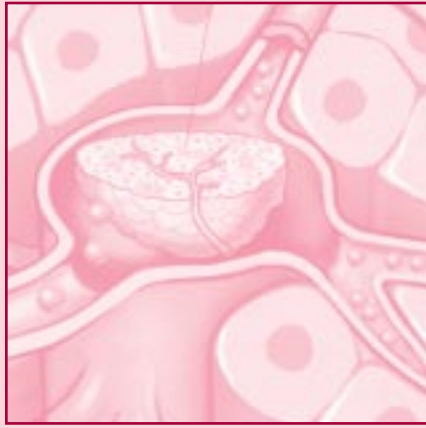


YOU ARE VIEWING A .PDF FILE FROM THE

OFFICE OF RESEARCH PUBLICATIONS

Please adjust your settings in
Acrobat to **Continuous Facing**
to properly view this file.
Thank You.



Doctor

MARK ATKINSON HAS EARNED A REPUTATION FOR PURSUING REAL-WORLD APPLICATIONS OF HIS INNOVATIVE BASIC RESEARCH ON DIABETES

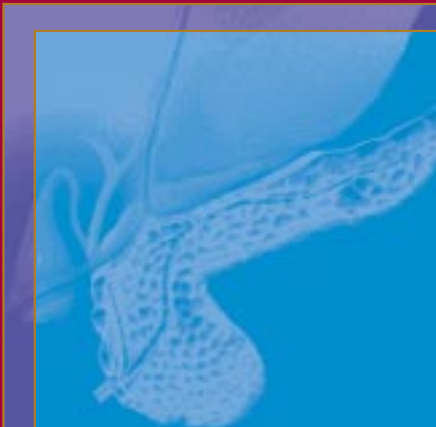
Diabetes



BY MELANIE FRIDL ROSS



Randy Barcisa



Mark Atkinson is a big-picture guy in a small-picture world.

Over the last 17 years, Atkinson has forged a reputation as one of the world's leading diabetes experts by conducting innovative basic research on the physiological changes that cause the debilitating disease.

At the same time, Atkinson has sought to pull back and understand how advances in his field and in related fields can be most effectively employed to serve patients and their families.

"Pathologists are thought by many to be individuals who focus on details. They hang around the microscope and try to look at smaller and smaller images," Atkinson says. "While there's a time for doing that, there are also times when it's better to take a step back and look at the whole picture."

It's a view that's not always shared by some of his basic science brethren, many of whom have chosen a life in the lab over a clinical career with its customary contact with patients.

But Atkinson, 43, has been heralded for his ability to bridge research interests with a commitment to directly serve patients and their families. He leads tours of his lab. He answers dozens of e-mails from people desperate for a cure. He gives generously of his time to national organizations such as the American Diabetes Association and the Juvenile Diabetes Research Foundation, regularly updating physicians and the public about the latest research developments.

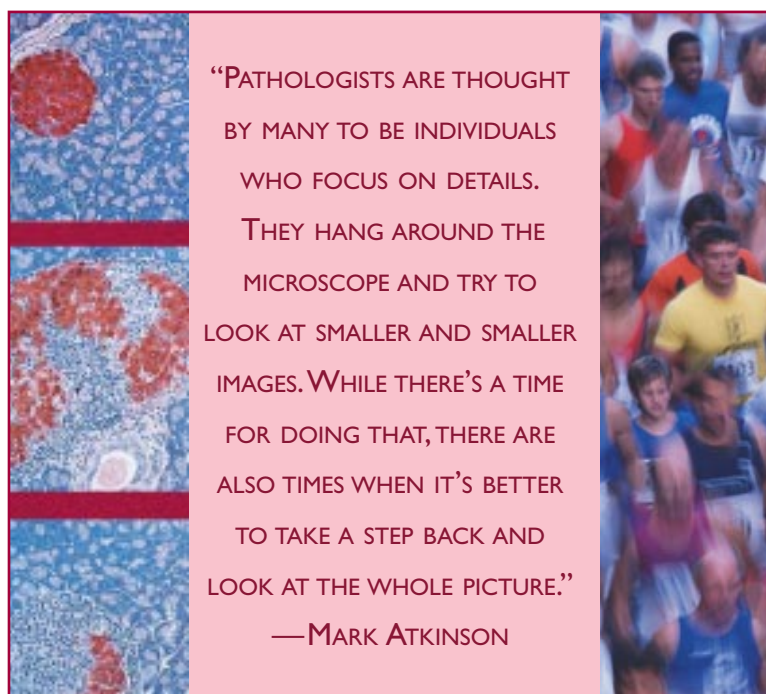
In fact, the ADA recently honored Atkinson with its 2004 Outstanding Scientific Achievement Award, sponsored by Eli Lilly and Company, calling him "one of the rare individuals who sees the big picture, from genetics and DNA to bench-side and clinical application. He has helped the cause of diabetes at many levels, working with equal passion in research, patient advocacy and in raising diabetes awareness."

The honor, presented at the ADA's annual meeting on June 8th in Orlando, is given to a scientist who has conducted outstanding research in diabetes and for creativity of thought.

Four days later, Atkinson was in Washington to receive the Mary Tyler Moore and S. Robert Levine, M.D., Excellence in Clinical Research Award, given by the Juvenile Diabetes Research Foundation International for contributions to the clinical translation of diabetes research.

"We've been trying to identify Ph.D. investigators who epitomize the translation of research to the bedside, and Mark exemplifies this beautifully; he is highly deserving of

this award," says physician Richard Insel, JDRF's executive vice president of research. "Mark has that unique ability to immediately think about the translation of basic science research, and he keeps his eyes on the big picture. I think he exemplifies exactly what you'd want to see in a Ph.D. who is conducting biomedical research. He goes beyond the day-to-day basic science results and thinks about the clinical applications. He's always focused on how he can apply his biomedical research to the bedside."



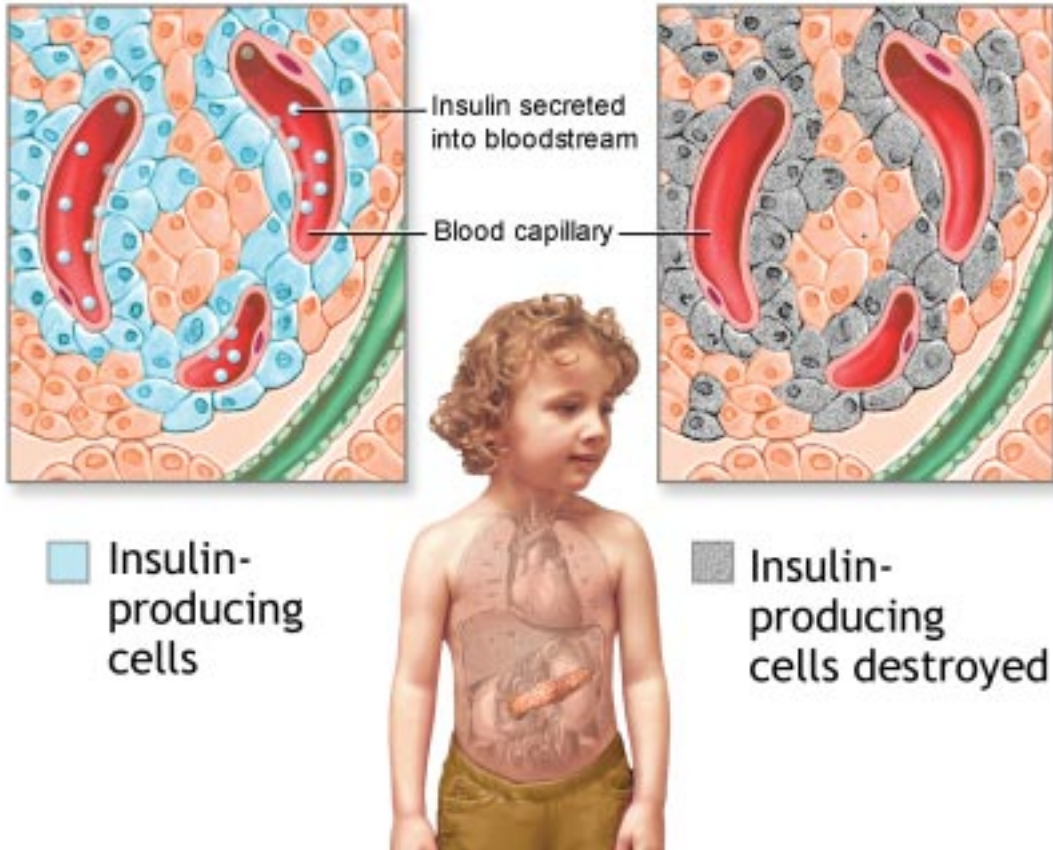
Ask Atkinson how he views his role, and he boils it down like this: Find what causes diabetes, predict who is at risk, then prevent the disease altogether.

Sometimes insights into how to achieve those lofty goals come from unexpected places.

Three miles outside Bar Harbor, Maine, the Jackson Laboratory, the world's largest mammalian genetic research facility, breeds more than 150 strains of mice for diabetes and obesity research. But it's one in particular that has Atkinson especially intrigued.

Last spring, in a colony of non-obese diabetic mice, Jackson researchers who routinely collaborate with Atkinson noticed something unusual, a true quirk of nature. The mice were supposed to be of normal weight and develop type 1

TYPE 1 DIABETES – AN AUTOIMMUNE ATTACK



TYPE 1

Insulin-dependent or “type 1” diabetes occurs when white blood cells vital to the body’s defenses against infectious diseases launch a self-directed or “autoimmune” attack on insulin-producing beta cells in the pancreas. The insulin these beta cells produce regulates how the body uses and stores sugar and other food nutrients for energy.

TYPE 2

Type 2 or non-insulin-dependent diabetes differs from its type 1 cousin in that it usually occurs in overweight individuals who typically fail to exercise regularly. These people develop a resistance to insulin, leading to symptoms of the disease. They account for 90 percent of the nation’s estimated 17 million diabetics.



THE CENTERS FOR DISEASE CONTROL AND PREVENTION RECENTLY REPORTED THAT ONE IN EVERY THREE CHILDREN BORN IN 2000 WILL EVENTUALLY DEVELOP DIABETES IN THEIR LIFETIME.

diabetes. But a single mouse was born that grew downright plump. Not only was the animal obese, it developed type 2 diabetes, not type 1 like its littermates.

The mouse has since been bred, and researchers are fascinated by what they're finding. In its entire genome it has a single mutation, in a DNA building block known as a nucleotide, that interferes with the ability of the hormone leptin to function after docking on the surface of cells where it would normally act.

Leptin has been in the news a lot because of its apparent weight-regulating mechanisms and its ties to type 2 diabetes. Atkinson says mice studies indicate it's likely involved in the development of type 1 diabetes as well.

"If you interrupt the immune system's ability to process leptin, the mice no longer develop autoimmunity and type 1 diabetes," Atkinson says. "If we can find an agent that would have the same effect, like a drug that would block leptin binding to its receptor on certain immune system cells, we could use a similar type agent to prevent type 1 diabetes in humans.

"Even though people have looked at it as a molecule associated with appetite and weight gain, leptin also has strong effects on the immune system and its production is related to the level of fat within an individual," he adds. "It could be that an individual's weight or the amount of fat they carry may modulate in some ways their immune response, and in the case of a person with type 1 diabetes, this may modulate their progression to diabetes. With increasing rates of obesity in children, this could explain, in part, why type 1 diabetes cases are occurring earlier and earlier in terms of age

at disease onset."

While many researchers devote their entire careers to solving one extremely specific piece of a puzzle, Atkinson is chasing many.

"I've known Mark for 20 years or so and he really is one of the most outstanding scientists I have ever met," says diabetes researcher Dale Greiner, a professor in the Department of Medicine at the University of Massachusetts Medical School. "He's one of very few individuals out there who are able to take findings in basic research and put them into clinically applicable protocols and approaches.

"Most technology that is created in the basic science realm has multiple applications," Greiner adds. "It really is just an individual having the foresight and the insight to be able to recognize what that can be translated into, and Mark is just exemplary in that."

When Atkinson began his career 17 years ago, the study of diabetes immunology was still in its infancy. Fresh out of a graduate program in pathology at UF's College of Medicine, Atkinson was among the first to show that administering insulin to mice genetically destined to develop diabetes could thwart the errant immune system's battle to destroy insulin-producing cells in the pancreas. His published findings helped pave the way for the massive National Institutes of Health Diabetes Prevention Trial, which tested the approach in humans.

He also was one of the earliest investigators of glutamic acid decarboxylase, or GAD, an enzyme generated by the insulin-producing islet cells of the pancreas. Patients with type 1 diabetes often develop autoantibodies to GAD as the immune system turns against the body's islet cells. Atkinson then helped develop a standardized way to use the presence of these GAD autoantibodies to predict diabetes.

GAD has since been licensed to a company that is developing an experimental drug designed to inhibit progression of type 1 diabetes in people. It's currently undergoing testing, but studies to date show the drug appears to improve insulin production.

Atkinson and his UF colleagues, most notably Desmond Schatz and Michael Clare-Salzler, have spent most of the past two decades building an internationally regarded research program on the immunology of type 1 diabetes.

They have extensively studied how to prevent and predict type 1 diabetes. They scrutinized the genetics of the disease. They launched newborn screening programs so treatment could be initiated earlier.

Then, about four years ago, they shifted focus, greatly expanding their research emphasis, buoyed in part by a \$10.4 million grant from the Juvenile Diabetes Research Foundation International to establish the JDRF Gene Therapy Center for the Prevention of Diabetes and Its Complications at the University of Florida and the University of Miami.

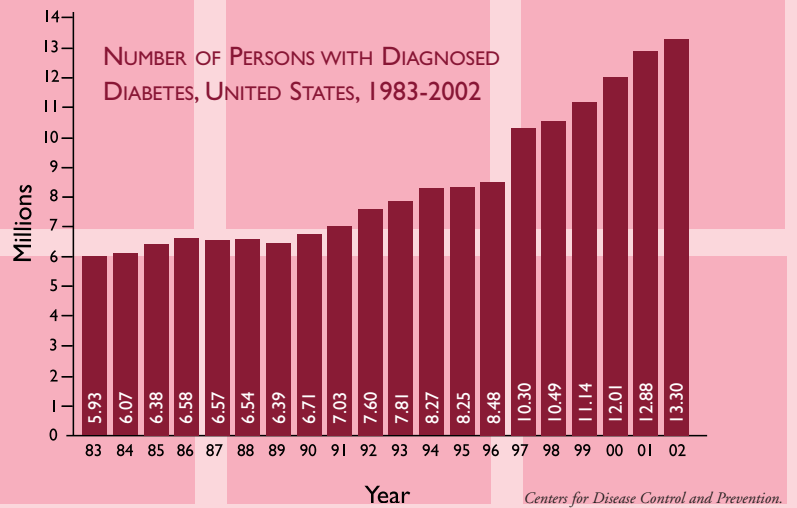
UF scientists affiliated with the center, which Atkinson directs, have been studying gene therapy's potential to deliver medicine in novel ways. They also are seeking to engineer rejection-proof tissues for islet and kidney transplant and expand existing efforts aimed at tackling diabetes-associated complications such as vision loss.

Today, as the Sebastian Family Eminent Scholar in UF's Department of Pathology, Immunology and Laboratory Medicine, Atkinson leads a team of researchers involved in many research pursuits, including:

- determining the role of environment in the increasing rates of type 1 diabetes in children.
- pinpointing which blood markers identify children at risk for type 2 diabetes.
- developing gene therapies for improving whole-body imaging of islet cells and kidneys.
- developing gene therapies to regenerate islet cells in the pancreas in those with type 1 diabetes.
- identifying the role of genetics in the formation and development of type 1 diabetes.
- exploring the use of pharmacologic agents that, on single application, would offer lifetime acceptance of transplanted organs.

Atkinson says UF scientists have made major advances in tests capable of predicting type 1 diabetes years before the onset of symptoms, with approaches that have commercial applicability, but they and the research community as a whole have been stymied in their efforts to prevent or reverse the disease.

“With increasing rates of complications, increasing rates of obesity and increasing rates of type 2 diabetes, we’re hav-



“WE ABSOLUTELY NEED TO RESPOND TO THIS EVER-GROWING THREAT OF OBESITY IN CHILDREN TO TRY TO FIND A WAY TO AVERT IT AND PREVENT IT. IN A WAY, WE’RE SETTING OURSELVES UP FOR A PERFECT STORM IN TERMS OF THE COMBINATION OF INCREASED FREQUENCY, NO EASY MEANS OF PREVENTION AND THE LACK OF PUBLIC UNDERSTANDING AND AWARENESS OF HOW BAD DIABETES IS.”

—MARK ATKINSON

ing to expand our efforts, because the scourge of diabetes is hitting us on all fronts,” Atkinson says.

Indeed, the Centers for Disease Control and Prevention recently reported that one in every three children born in 2000 will eventually develop diabetes in their lifetime. For minorities, the risk can be as high as one in two.

“We absolutely need to respond to this ever-growing threat of obesity in children to try to find a way to avert it and prevent it,” Atkinson says. “In a way, we’re setting ourselves up for a perfect storm in terms of the combination of increased frequency, no easy means of prevention and the lack of public understanding and awareness of how bad diabetes is.”

So Atkinson continues doing what he does best — traveling the world and preaching the gospel of diabetes prevention, treatment and cure.

Although he has logged well over half a million miles in the air and some weeks spends more time on an airplane than in his laboratory, Atkinson says his schedule offers him an opportunity to reflect in solitude on that big picture.

“I do see the value of getting that 35,000-foot perspective on things,” he says. ✕

Mark Atkinson

Sebastian Family Eminent Scholar, Department of Pathology, Immunology and Laboratory Medicine
(352) 392-0048
atkinson@ufl.edu

Related Web site:

<http://www.immunology.ufl.edu/jdfi/>