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Discoveries *in* Diabetes

A publication for those who support diabetes research at the University of Minnesota through the Minnesota Medical Foundation

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Two paths to a cure

Researchers use immunology and cell therapy to tackle type 1 diabetes

University of Minnesota researcher Pratima Pakala, Ph.D., knows the struggles of people living with diabetes. "My dad has been diabetic ever since I remember," she says. "I understand the hardships of patients and what families go through."

Pakala, who grew up in Varanasi, India, says that in her native culture people commonly believed that diabetes was the result of bad luck. When she learned in school that diabetes has a scientific basis, it changed her life's path. "It wasn't that he was unlucky or drew the short stick," she says of her father and his diabetes. "There were cells involved. We can do something about it," she recalls learning. "That was so fascinating."

That realization propelled Pakala into a career searching for a cure for type 1 diabetes—for her father and others. Her University colleague professor Brian Fife, Ph.D., also has a family connection to diabetes through uncles and cousins and is fascinated by the disease. "I've always been interested in how the body determines what is self and what is foreign," says Fife, an immunologist. In diabetes, he explains, the T-cells attack and destroy the body's own insulin-producing islet cells in the pancreas.

University researchers are focused on a number of promising ways to cure type 1 diabetes: through pig and stem cell islet transplantation and immune-cell regulation.

Despite their shared interest, however, Pakala and Fife are taking distinctly different approaches to preventing diabetes and finding a cure.

Pakala is seeking ways to make islet transplants safer for patients who already have diabetes, and Fife is working to "turn off" destructive immune cells that lead to type 1 diabetes to reverse or prevent the disease.

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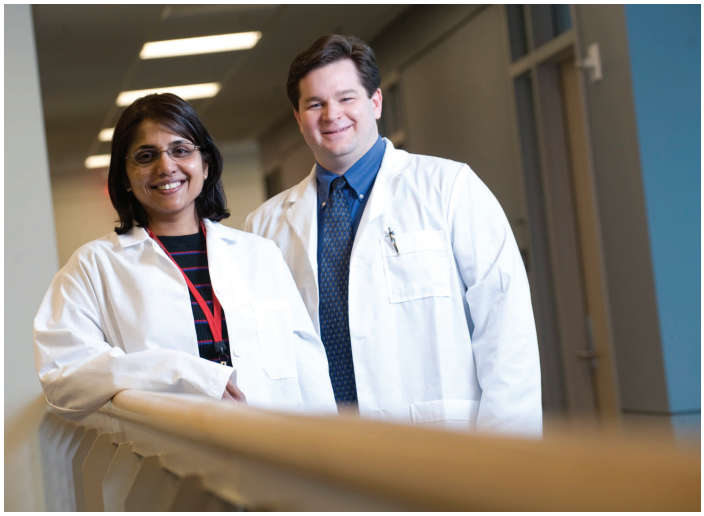


Photo by Scott Streble

University of Minnesota diabetes researchers Pratima Pakala, Ph.D., and Brian Fife, Ph.D.

University of Minnesota

Two paths to a cure continued from cover

Making immunosuppressives obsolete

Pakala, a member of the University's Schulze Diabetes Institute (SDI), is focused on therapies that would allow patients who have had islet transplants to avoid taking immunosuppressive drugs.

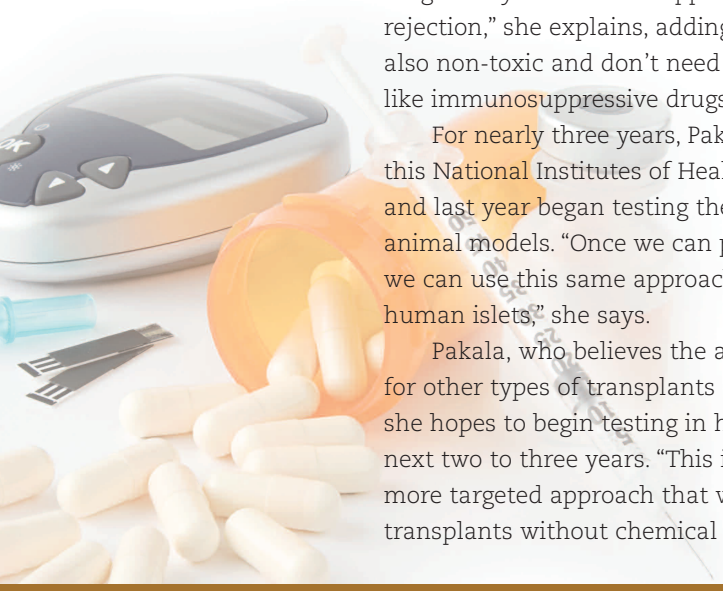
Such drugs are used post-transplant to stop the immune system's attack on transplanted islets, but they can cause serious side effects, and they are toxic to the body over time. Eventually, they attack islet cells.

"People are really afraid of immunosuppressive drugs. That's why [some] people who would benefit from transplants opt out," she says.

Pakala is developing a therapy that involves taking patients' blood, purifying the regulatory T cells, growing the cells in large quantities, and transplanting the new cells along with the islets. "Regulatory T-cells will suppress a transplant rejection," she explains, adding that they are also non-toxic and don't need to be taken daily like immunosuppressive drugs.

For nearly three years, Pakala has worked on this National Institutes of Health–funded project and last year began testing the treatment in animal models. "Once we can prove that it works, we can use this same approach for pig and human islets," she says.

Pakala, who believes the approach will work for other types of transplants as well, says that she hopes to begin testing in humans in the next two to three years. "This is a safer and more targeted approach that would allow islet transplants without chemical agents," she says.



Turning off diabetes

Fife's work also focuses on T-lymphocytes, but in a different way.

Since 2002, he has used diabetic mice to investigate aberrant T-cell activity in type 1 diabetes and better understand the mechanisms of the disease. Fife labels the T-cells red and then uses a powerful microscope to track their activity in the lymph nodes and pancreas. This monitoring helped him to develop a treatment to reverse diabetes in mice, with the goal of applying the technique to humans.

"We want to find these renegade T-cells that cause diabetes and turn them off. Using this approach, we can silence disease-causing cells, leaving the immune system intact—an enormous benefit over total immune suppression," says Fife, who is a new faculty member of the University's Department of Medicine and the Center for Immunology.

To cure diabetes, he believes researchers need to not only manage the immune response, but also replace the lost insulin-producing cells.

Fife is collaborating with Meri Firpo, Ph.D., a professor in the University's Stem Cell Institute and member of the SDI, to find a way to create new islet cells or replace those that have been destroyed.

Fife says that he and Pakala are working toward the same goal. "With a better understanding of how to regulate the immune response against islets," he says. "We'll be able to cure diabetes."

Noteworthy

The national American Diabetes Association elected **Elizabeth Seaquist, M.D.,** a University of Minnesota professor of medicine, to its board of directors for a three-year term. Seaquist holds the University's Pennock Family Chair in Diabetes Research, directs the University's Action to Control Cardiovascular Risk in Diabetes Trial, and is principal investigator on the National Institutes of Health training grant for endocrinology and diabetes fellows.

Bernhard Hering, M.D., scientific director of the University's Schulze Diabetes Institute, was appointed president-elect of the International Xenotransplantation Association from 2009 to 2011 and president from 2011 to 2013.

In addition, Hering will also be awarded the 2010 Health Care Hero award for Innovations in Health Care in June from the Community Health Charities Minnesota, a group of nonprofits dedicated to improving the lives of people with chronic illnesses.

A family affair

A mother's planned gift adds to her family's support of diabetes research at the U

Pat Lyon has frightening memories of diabetes from her youth and her work as a nurse decades ago. "It was an early death sentence when I was working," she says, adding that diabetes caused her aunt's husband to lose both of his legs.

In 1990, Pat's daughter, Cathy Myers-Korus, then 29, went to her doctor when she experienced blurred vision and extreme thirst. "She called me crying and said, 'Mom, I have diabetes,'" Pat recalls. "She was just devastated."

Nearly 10 years later, Cathy noticed symptoms of diabetes in her brother, Steve, who was subsequently diagnosed with diabetes.

"I worried a lot," Pat says of her children's battle with type 1 diabetes. "I was surprised, because we never had a family history of diabetes."

Choosing to turn her worry into action, in 2009 she pledged her retirement plan to support diabetes research at the University of Minnesota's Schulze Diabetes Institute (SDI), where researchers are focused on promising ways to cure type 1 diabetes.

In diabetes, the body's T-cells attack and destroy insulin-producing cells, causing the disease. SDI researchers are finding a way to create new islet cells or replace those that have been destroyed. "I want to do whatever I can to help," Pat says. "I have always had a lot of faith in the work done at the University."

But Pat's resolve to fight diabetes didn't stop with her expectancy gift.

She and Cathy are both active supporters of the University's Golf Classic "fore" Diabetes Research golf tournament, which takes place each June and has raised nearly $4 million for diabetes research at the University.

Photo by Scott Streble

From left to right, Steve, Jim, Cathy, and Pat

In December, Pat and three of her children—Cathy, Steve, and Jim—donated skin cells for diabetes research at the University. Meri Firpo, Ph.D., an SDI and Stem Cell Institute research scientist, is taking voluntarily donated skin cells and culturing them in the lab, wiping the cells clean, and reprogramming them back into unspecified stem cells, which she is able to turn into insulin-producing islet cells.

She is currently transplanting the reprogrammed skin cells into diabetic mice to see if the cells can function as insulin-producing islets. Next, she hopes to determine whether the treatment is a viable option for humans. "We want to see if we can transplant [the reprogrammed cells] into patients," Firpo says. "One of the goals is to use patients' own cells to cure their disease."

"It's amazing how far they have come in their research. It's really impressive," says Cathy. "I think a cure is on the horizon. And although it may not save your family member, it could save somebody in the future."

A gift that returns the favor

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Age 70	5.7% annual payout
Age 75	6.3% annual payout
Age 80	7.1% annual payout

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Stimulus-funded research takes aim at obesity and type 2 diabetes

University biochemist David Bernlohr, Ph.D., received $563,286 in federal stimulus grants for two projects aimed at studying mechanisms in the body that promote obesity and type 2 diabetes.

One grant supports a study of lipid binding—looking at how fats move from the bloodstream into the body. The second supports studies of insulin resistance, a condition that is a precursor to type 2 diabetes.

Bernlohr, head of the Department of Biochemistry, Molecular Biology, and Biophysics will use the funding to hire a new scientist, buy equipment, and continue his research.

Another federal grant for $146,373 will support the Obesity Prevention Center and the work of University epidemiologist Robert Jeffery, Ph.D., in a 14-year study called Look AHEAD. That study evaluates the effects of an intensive weight-loss intervention on heart disease in obese people who have type 2 diabetes.

A total of 5,145 overweight volunteers and 18 centers around the country are participating. Volunteers are either enrolled in a diabetes support and education program or assigned to weight-loss groups that are increasing physical activity and following a restricted diet.

Upcoming events

14th annual Golf Classic "fore" Diabetes Research
June 21, 2010, Town & Country Club
The tournament consists of morning and afternoon rounds and an exceptional live auction. To find out more about participating as a golfer or sponsor, contact Valerie Petermann at 612-624-4444 or v.petermann@mmf.umn.edu.

A special thank-you
Thank you to past supporters of Lightning Run for your commitment to diabetes research. Throughout the past 10 years, this event raised more than $1.7 million for diabetes research at the University of Minnesota. This event will not take place in 2010, but we hope to see you at a Lightning Run event in the future.

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