

A REPORT FROM
THE UNIVERSITY
OF WISCONSIN
FOUNDATION

SPRING 2009

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insights

With discretion

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deans seize opportunities

Lily's Fund

Girl inspires
epilepsy researchers

'Great people'

Gifts by the people,
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Lily's Fund inspires research

The lab and the everyday world meet in Lily Giroux, a dark-haired, blue-eyed seventh-grader who's tired of answering questions about seizures.

At 13, her world is filled with art, school and synchronized swimming. (Who would've guessed that the girls put Knox gelatin in their hair the night before a meet and sleep on it, so it's hard as a rock when they swim?)

When Lily was 18 months old, she'd try walking, then fall like a marionette with its strings cut. She'd pop back up though, and her parents, Anne Morgan and David Giroux, figured she was just having trouble learning to walk. When Lily was about 2, they saw behaviors they questioned more and asked for an electroencephalogram.

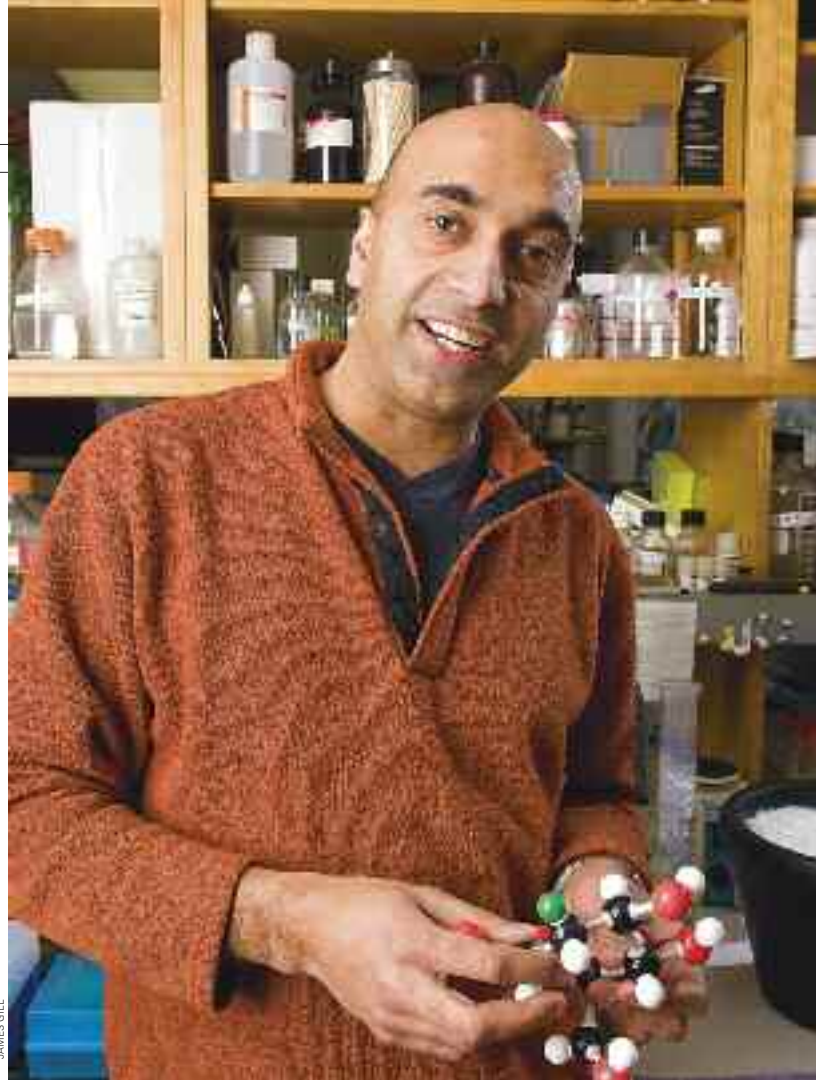
After days in a hospital with nodes glued to her head, Lily had a diagnosis: Epilepsy. The thumb sucking and hair twirling were coping mechanisms after small seizures.

Anne Morgan Giroux became what she called Internet possessed as she looked for information to help Lily. Years later, a newspaper story about Avtar Roopra's research into a new way to control epilepsy surprised her, especially when she learned his University of Wisconsin-Madison lab was just a mile from their home and across the street from David Giroux's new UW System office.

To meet Roopra is to understand that a basic researcher can be as exuberant as a child waiting for Christmas morning; a lab can be far from somber. "We have a blast," said the assistant neurology professor in the School of Medicine and Public Health. He and his lab team—in collaboration with Dr. Tom Sutula and Dr. Carl Stafstrom in the Department of Neurology—have shown how genes in the brain involved in epilepsy are controlled by metabolism.

Roopra's team also is showing how metabolism controls the same genes when they are found in breast cancer. The goal is to find ways to turn them off.

Roopra is a molecular biologist with a ready smile who was curious about how gene levels are controlled in the brain. "The genes tell you what the story's going to be," he said. "Then you see what they've been involved in."



JAMES GILL

Avtar Roopra

Epilepsy is a common condition that affects about 1 percent of the population and completely changes a patient's life. Seizures—from simple staring spells to violent convulsions—are the most widely recognized symptom. The disease can affect self-esteem, independence and quality of life as patients cope with its effects on everything from driving, swimming and sleeping to career choices, pregnancy and doing well in school. While there is no known cure for epilepsy, treatment can control the seizures.

In 2006, Roopra, his team, Sutula and Stafstrom co-authored a paper published in *Nature Neuroscience*, showing for the first time that the genes in rats could be controlled with 2-Deoxy-D-glucose (2DG), a compound

that prevents glucose from being used. The gene regulatory circuit stabilized and normalized and epilepsy progression was significantly slowed in rats fed 2DG.

A model of 2DG straddles the top of Roopra's computer monitor, and he pops off the extra hydrogen atom that makes it different from glucose. "It still tastes sweet," he said. "I know because I put it in my coffee and tasted it."

For 2,000 years, people have known that diet can control epilepsy, Roopra said. In the time of Hippocrates, patients who fasted had fewer seizures. In the early 1900s, ketogenic diets—think Atkins diet times 20—had the same effect. The diet has worked especially for children.

"When it works, it's like a miracle," Anne Morgan Giroux said. It didn't work for Lily, but David Giroux lost almost 20 pounds when he, too, eliminated all carbohydrates in his diet. The 2DG research, which may or may not help Lily, is on its way to clinical trials.

Once they found Roopra and the University neurology department, the Giroux family wanted more of a connection and established Lily's Fund for Epilepsy Research to provide an annual award to an epilepsy researcher in the neurology department. They hosted Lily's Luau in January and raised \$16,000 more for research. Along the way, they spent enough time with researchers to begin to feel like the department's adopted children.

Lily hasn't yet been treated at or participated in any clinical trials at the UW Hospital and Clinics, but David Giroux said, ultimately, the gift is selfish: "We want a cure for our daughter, and we want it here – at our university."

The wish is not unreasonable. Epilepsy has been a research strength in the neurology department since the 1950s, when Dr. Francis Forster, the neurology chair, made pioneering clinical observations about reflex epilepsy. The University's national reputation in epilepsy clinical care, research and training is considerable, said department Chair Tom Sutula, whose research looks at the long-term effects of epilepsy. The department's patient-based research also looks at the ketogenic diet and cognitive, neuropsychological and behavioral problems associated with epilepsy, he said.

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swimming and sleeping to career choices, pregnancy and doing well in school. While there is no known cure for epilepsy, treatment can control the seizures.

Roopra made a conscious decision to follow epilepsy and breast cancer instead of basic systems research. It's one thing to be excited by science, he said. "If it doesn't help people, it's just a chess game in your head."

Nothing motivates Roopra like an envelope from the German parents who enclose a photo of their child who has epilepsy, a family such as the Girouxes or a meeting with John Newton, from the Wisconsin Dual Sport Riders, who raises money for breast cancer. "It puts a human face on this stuff," Roopra said.

The way ordinary people give also is extraordinary to Roopra, who is from Great Britain. In the Midwest, especially, he's found "a philanthropic streak which you don't find in many other places in the world. ... Anne and David don't just sit around wishing someone would do something for them; they do something about it."

Roopra and his lab are far from done. They discovered in the fall that the same master regulator that fails to shut down genes in epilepsy is nonfunctional in aggressive, therapy-resistant breast cancers. "We're a bunch of gene jocks, and all of a sudden, 'BAM,' we found this thing," Roopra said. Rarely can researchers say, "That's it." This time, they could. Grad student Matt Wagner, who's driving the project, came to Roopra with the results at 10:30 that Tuesday morning. By 10:45, the lab team was at The Library, the bar across the street, celebrating.

By early winter, Roopra's team, led by Wyatt Potter and Ken O'Riordan in collaboration with Assistant Professor Corinna Burger, was chasing another metabolic sensor involved in epilepsy that could work even faster than the one involved with glucose—and already-approved drugs can turn it on and off. "It was flabbergasting," Roopra said, remembering the first time he saw the data. "When it's exciting science like that, it's art."

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FOR YOUR INFORMATION

For more information on Lily's Fund for Epilepsy Research, go to www.lilysfund.org. For more on Professor Roopra's research, go to molpharm.wisc.edu/faculty/roopra.html.