

STUDENT ROUNDS

External Support

UPSTATE MD/PHD STUDENTS RECEIVE PRESTIGIOUS FELLOWSHIPS TO FORWARD THEIR DOCTORAL RESEARCH.

In any academic environment, external grants are vital to funding research. For graduate students, the ability to secure their own funding—through a grant or fellowship—can signify a student’s promise as an independent scientist as well as the strength of their scholarship.

Upstate Medical University is no exception. Early in their doctoral program, MD/PhD students take a course in scientific writing steered by Leszek Kotula, MD, PhD, which includes writing a grant for submission. It’s not just an academic exercise, as evidenced by two prestigious awards recently received by Upstate students.

In June 2022, Akshay Patel was awarded a Ruth L. Kirschstein National Research Service Award (NRSA) Individual Fellowship from the National Institute of Diabetes and Digestive and Kidney Diseases. The fellowship funds Patel’s work examining the role of the enzyme Rab4A and its association with the onset and worsening of lupus.

Patel is a fourth-year PhD student in biochemistry, studying how the immune system, metabolism, and biochemistry work together in the body. At Upstate, MD/PhD students complete their first two years of medical school, followed by their doctoral work—generally four years—and then finish their two clinical years of medical school. Patel has conducted his doctoral research in the lab of Andras Perl, MD, PhD, Distinguished Professor of Medicine, and anticipates graduating with his dual degrees in 2025.

Patel has focused on the effect lupus has on the liver, which he calls “the most metabolically active organ in the body.” Rab4A is increased in lupus patients. Patel is looking at how Rab4A works within

cells to “turnover mitochondria that don’t work and adjust proteins on the surface of a cell,” he says.

Initially, Patel undertook an experiment to create model mice that don’t have the Rab4A enzyme within T cells, key parts of the body’s ability to fight disease, including cancer.

He theorized that removing the Rab4A from T cells would help reduce the prevalence of lupus and was surprised to find liver inflammation in the mice. “It had just the opposite effect,” says Patel.

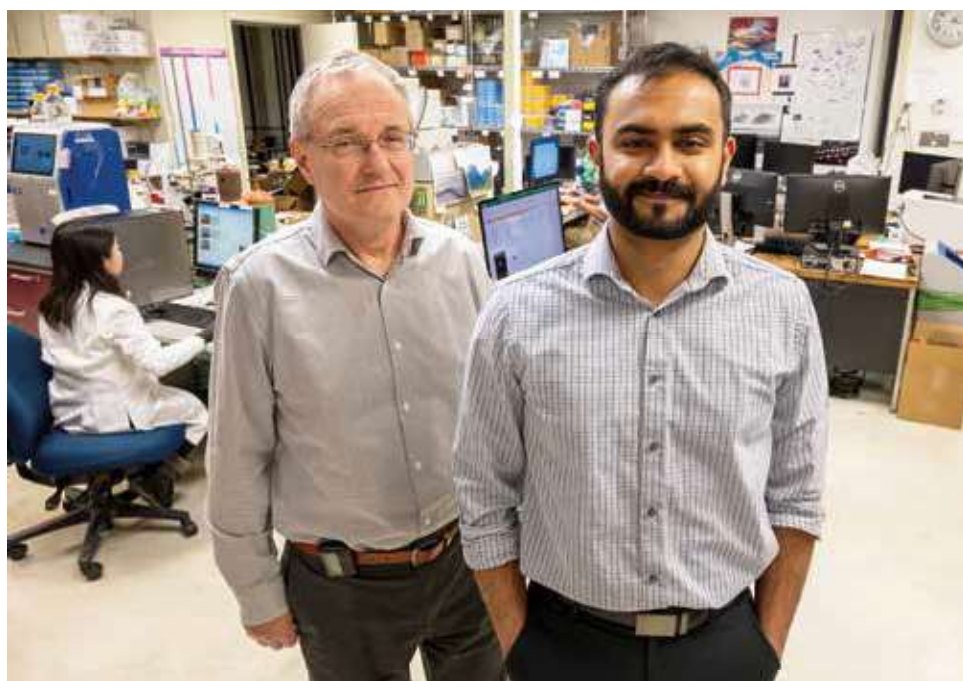
He applied for funding to support further investigation. While reviewers at the National Institutes of Health did not support his first application, they provided positive, specific feedback, resulting in success when he reapplied.

What Patel’s research has found is that the T cells without Rab4A are “overstim-

ulated,” as if the immune response that would normally shut off that reaction is dysfunctional because of the lacking enzyme. This overstimulation might be resulting in liver damage. “That’s the last bit we’re trying to solve,” he says.

Prior to Upstate, Patel attended a five-year program at Villanova University, which earned him both an undergraduate and master’s degree in microbiology. Planning on attending medical school, it was a summer research program at Drexel University that convinced him to pursue an MD/PhD. “It makes sense because my interest in becoming a physician was inspired by the things that were happening on the research side being applied clinically,” he says.

Patel was attracted to working with Dr. Perl, both for his expertise in immunology and his own reputation.



MD/PhD student Akshay Patel (right), with his advisor, Andras Perl, MD, PhD

"I'm his seventh MD/PhD student and he's an excellent mentor," Patel says. "The lab also has a lot of resources, with technicians, postdocs, and other graduate students."

Patel plans to apply to residency in internal medicine through the Physician Scientist Training Program, thinking he may ultimately pursue gastroenterology. Like his mentor Perl, he plans on an academic career, combining clinical practice with his own research lab.

"The possibilities are endless for what I'd like to study in 15 years, which is probably when I'll be setting up my lab," he says. "I have a lot of interests to delve deeper into what I want to study for a career."

When MD/PhD student Gargi Mishra joined the lab of Xin Jie Chen, PhD, Distinguished Professor of Biochemistry and Molecular Biology, her plan was to study mitochondrial function using a mouse model developed in a lab at the University of Connecticut. But the pandemic created issues generating the mouse model, forcing Mishra to switch to a more mechanistic basic science project using yeast.

The change in methodology brought unexpected benefits. "I found that I was able to do a lot more genetics and biochemistry and that I enjoyed exploring new biology in a way that I wouldn't have been able to in a mouse model," she says.

Mishra's research focuses on the dysfunction of mitochondria in cells and the possible contributions to heart

disease. In January, she was awarded a two-year American Heart Association (AHA) Predoctoral Fellowship to help fund her work.

Mishra's proposal was highly ranked by the AHA (0.14 percentile), which she views as an endorsement of the importance of basic science research. "Following the science can lead to discoveries of unexpected connections to real-world problems," she says.

Mitochondria are essentially hubs in a cell that help provide energy and other resources for the cell to function. "They're especially important in tissues that are undergoing high metabolic turnover and expending a lot of energy, which is why they're extremely relevant to the heart," she says. "You need healthy mitochondria for healthy heart cells."

Mitochondria require about 1,500 different proteins to function. "If import is halted, perhaps by a protein getting clogged in a transport channel, mitochondria cannot function properly," Mishra explains. She compares the phenomenon to food debris that accumulates in a clogged sink drain.

Mishra is using yeast to mimic the process to determine how mitochondria can either degrade or compartmentalize those accumulated proteins. She's hoping a better understanding of the basic science

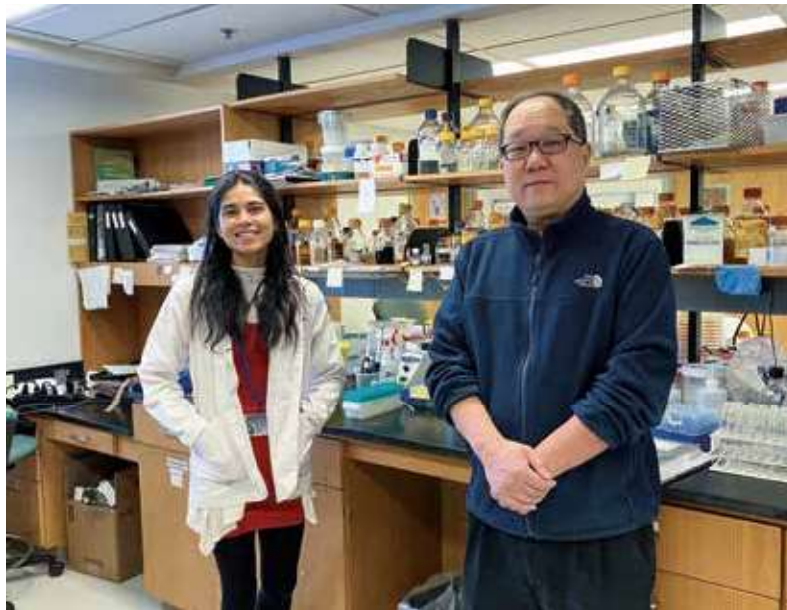
behind mitochondrial dysfunction can lead to future drug and therapeutic discoveries.

"While there are many drugs that treat heart disease, very few target mitochondrial function in the heart," she says.

An international student from India, Mishra studied biochemistry at Mount Holyoke College, then spent a year conducting research on cancer immunology at the Broad Institute of MIT and Harvard in Cambridge, Massachusetts, before coming to Upstate. Although she initially thought she would pursue cancer research, she chose a rotation in Dr. Chen's lab at the suggestion of MD/PhD student Liam Coyne '23.

"I could feel right away that this would be a good environment for me," she says. "There have been some curve balls, but the support and mentorship I have received have been invaluable. Developing this grant really was a team effort, and I am grateful to my advisor, Dr. Chen, for innumerable discussions, and my outside reader, Dr. Steven D. Hanes, emeritus professor of Biochemistry, who provided insightful critiques for my proposal."

Mishra is planning a career in academic medicine, with current interests focused on either neurology or physical medicine and rehabilitation. "I do want a significant portion of my career to be focused on research," she says. "I really enjoy basic biology, asking questions in the lab and trying to figure out mechanisms of disease, which can eventually lead to better health outcomes."



Gargi Mishra, an MD/PhD student in the lab with her adviser, Professor Xin Jie Chen, PhD