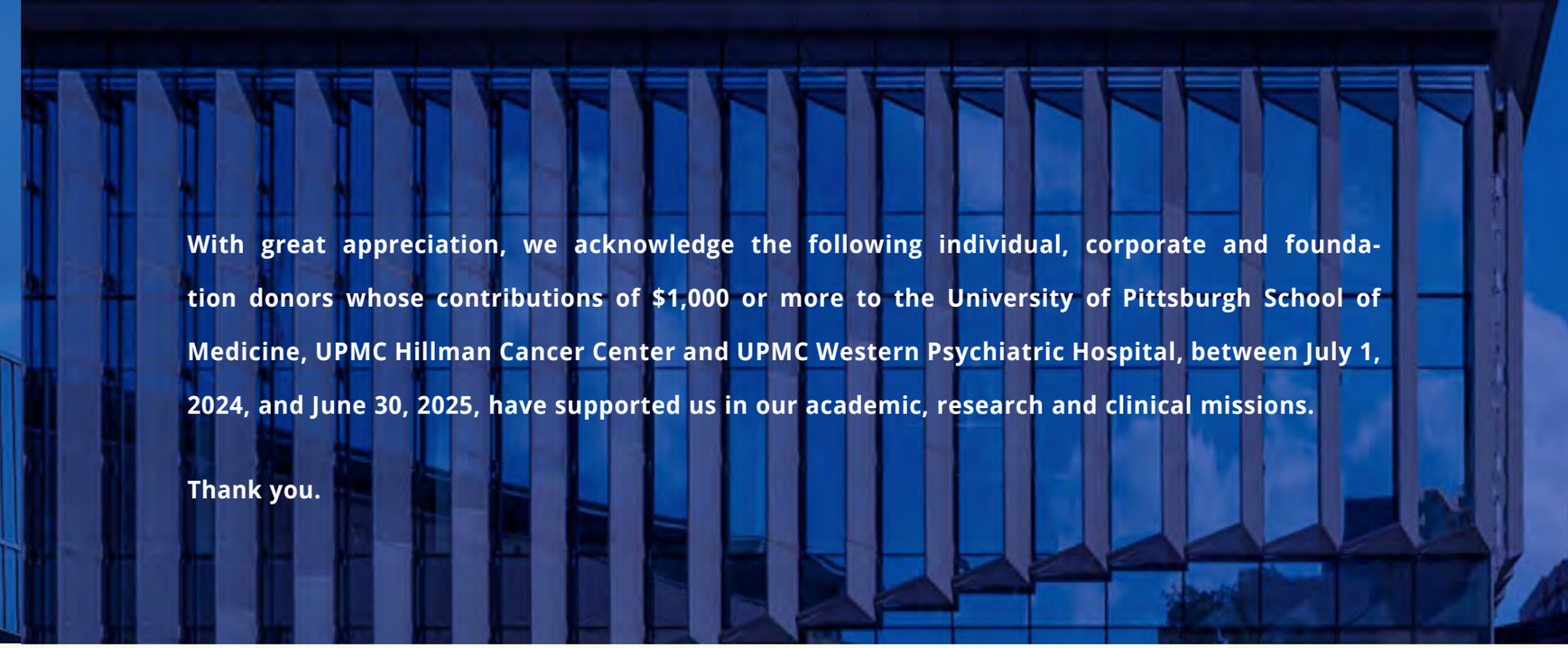


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THE PITTSBURGH FOUNDATION INVESTS IN UNDERSTANDING OF CHRONIC DISEASES



Gaffe

In Sarah Gaffe 's lab at the University of Pittsburgh, everything revolves around cytokine IL-17, which is secreted from various immune cells. The Gaffen lab focuses on how cytokines such as IL-17 coordinate host defense and autoimmunity. In the course of defining the molecular circuitry within the cell that allows responses to this cytokine, her team identified an unusual RNA-binding protein that amplifies the IL-17 signaling pathway. It appears to be a novel biomarker and molecular driver of autoimmune conditions, including inflammato y arthritis.

More than 18 million people live with autoimmune arthritis, including rheumatoid arthritis (RA). "My mother and grandmother both suffe ed from RA, and the goal of studying cytokines including IL-17 is to figu e out better ways to intervene clinically," says Gaffen, professor of medicine and immunology, who holds the Gerald P. Rodnan Chair and recently served as president of the International Cytokine and Interferon Society.

To explore the potential for targeting the IL-17 pathway to offer relief, Gaffen recently received support from The Pittsburgh Foundation. Michael Yonas, vice president for community partnerships and learning at the foundation, explained that the foundation manages about 26 medical research funds that provide $1.8 million to $2.1 million in research support per year. Gaffe 's work is supported by the Simeon M. Jones Jr. and Katharine Reed Jones Fund and the Frank L. Sprohar and Dolores M. Sprohar Trust.

Gaffen's is one of several Pitt labs supported this year by a total of $776,000 in grants from the foundation. Most of the foundation's grants to the School of Medicine focus on alleviating the burden of chronic diseases, particularly in underserved communities. The foundation has supported work at the School of Medicine since the early 1960s.

This year's funded projects include investigations in the lab of Matthew Steinhauser, associate professor of medicine, on a novel molecular signature for human resilience in aging; studies of equitable access and optimization of precision radiotherapy for breast cancer by Parul Barry, clinical assistant professor of radiation oncology; an exploration of the role of technology in achieving diabetes health by Margaret Zupa, assistant professor of medicine; and examinations on the role of DCAF7 in aging and brain health in the lab of Emily Rocha, assistant professor of neurology. The foundation also funded early career cranial research in the Department of Neurological Surgery.

"Rheumatoid arthritis is an incredibly painful condition afflictin millions of people, disproportionately affecting women. Given the . . . propensity for high impact for advancing scientific understanding of rheumatoid arthritis and more effecti e interventions, this request was an ideal study to receive support," Yonas says. "Dr. Gaffe 's personal motivation and professional commitment to addressing this condition is also truly inspiring."

—Keightley Amen

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LEFT: The Borzellino family (from left to right): Catherine, Erin, Nick, Giorgio and Emilia. ABOVE: Agnihotri

GIORGIO FOUNDATION CHAIR WILL FUND NF1 GENETIC RESEARCH

The relationship between the Giorgio Foundation and Sameer Agnihotri is a serendipitous one.

It traces to the beginning of the pandemic when the foundation wanted to expand its support for researchers investigating neurofib omatosis type 1 (NF1). A cold call to the University of Pittsburgh followed: Was there anyone at Pitt studying the condition?

Turns out there wasn't but that Agnihotri, a PhD and associate professor of neurological surgery, had just joined the University and had experience investigating NF1 before his arrival.

"When I started my program here in Pittsburgh, I always had NF1 in the back of my head," he says. "I just didn't have the resources or the time. I was a lab of one person at that point."

He and the foundation (www.endnf1.org) connected, though, and funding followed to get Agnihotri up and running on a genetic approach to curing the condition. Over the past few years, that funding has continued and now includes a gift to establish the Giorgio Foundation Chair in Neurological Surgery at Pitt, which Agnihotri will hold.

"Since the beginning of this journey, a significant part of our mission has been to create a legacy of truly groundbreaking NF1 research. Tha 's why 100% of the donations received by our foundation are used for medical research. We believe that Dr. Agnihotri and his lab are on an incredible path toward that goal, and we are excited to create an endowment that will help to continue NF1 research for decades to come," says Erin Borzellino, foundation cofounder.

NF1 is primarily a genetic condition that causes tumors to grow on nerves throughout the body. Most often those tumors are noncancerous but can create a host of problems for patients ranging from the external appearance of tumors to developmental delays, bone deformities and vision problems.

In NF1, a gene that regulates tumor growth has mutated and won't function properly. "Think of [that gene] as a brake system that keeps our cells and some cell signaling from running too fast," Agnihotri says. "It keeps everything in check."

About 1 in 3,000 people is born with NF1.

Agnihotri's approach to a cure includes diffe ent strategies:

The protein that the NF1 gene creates is a large one, so a first approach is to compartmentalize DNA to have it reassemble in the cell—a genetic engineering approach. "Because the protein is such a big thing, we can't just stuff it into a cell; but we can get small parts in and have [the protein] reassemble," Agnihotri says. It's akin to Lego-engineering a way to introduce the building blocks individually to construct the final product.

Another approach is to miniaturize the protein but maintain its functional power. "Think of it as how cellphones got smaller and the batteries got smaller but even in some cases got more powerful," Agnihotri says.

Like a pocketknife with diffe ent blades and tools (think small scissors, a corkscrew or even a toothpick), NF1 serves functions beyond regulating tumor growth, and those capabilities, Agnihotri says, could be engineered into new roles—"things we haven't thought about, namely in metabolism."

"What are some other things that have been reported but not really investigated? So we're considering new roles for NF1 that could produce additional therapies we haven't considered yet," he says.

Creating the endowed chair will perpetuate NF1 research at Pitt until a cure is found. The work is personal for Borzellino. Her son, Giorgio, who has NF1 but is thriving in college where he studies aerospace engineering, is the foundation's namesake. "It's so insidious," she says of the condition. "It affects every area of your life. And if we could change the gene and have it all go away for Giorgio and his kids and his grandkids . . . that's what we're focused on now." —*Michael Aubele*

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