Meet Mark Siracusa & Karen Edelblum

Up-and-Coming Research Leaders

No matter what path these scientific stars took into the world of medical research, their motivation looks very personal. Years of hard work, countless hours of study and training, as well as strong support systems have put them at the top of their games. But there is something else you'll detect when you read their stories: a youthful optimism so critical to the world of medicine. Both are Rutgers Biomedical and Health Sciences (RBHS) Chancellor's Scholars and both are among the best in their fields.

By Maryann Brinley

Mark Siracusa: The Power of Discovery

Ask Mark C. Siracusa, PhD, why he does experimental science. Go ahead. Lots of people ask, especially family members and friends back in Massachusetts where he grew up. No one in his circle is a scientist although his father is an engineer and his mother is a retired nurse. "I don't think anyone expected me to end up where I am."

So why did he choose his career path? To answer, this assistant professor in the NJMS Department of Medicine describes the thrill of discovery and the importance of advancing therapeutic strategies. "Essentially, clinicians have a toolbox of treatment options for their patients. When they exhaust all the tools, the options become very limited. In science you realize that it takes discoveries to advance that toolbox. It may not happen often but when it does, it's amazing."

The very first RBHS Chancellor's Scholar appointed, Siracusa is already well-known for his discoveries of the immunoregulatory role of innate immune cell populations during infectious disease. He has first-authored papers in *Nature* and *Immunity* and his own National Institutes of Health (NIH) funding but perhaps even more important is his passion for this science. "The immune system has multiple modules that it initiates. One is the type 1 response, basically pro-inflammatory, anti-bacterial or anti-viral. But another module and we know so little about it, is the type 2, an immune response originally meant to fight parasitic infections that might be triggering off randomly when it sees benign, really non-dangerous things like pollen." Think asthma, eczema, food allergies, hay fever, all sorts of allergic inflammation, and inflammatory disorders. "There has been a real increase in developed countries, where parasitic infections have been eliminated, and this type 2 immune system, kind of an artifact with nothing real to fight" might be to blame.

Siracusa earned his PhD in 2008 at Johns Hopkins University and then did post-doctoral work at the University of Pennsylvania, all the while following his fascination for biology and immunology. "I always come back to the aspect of discovery," he explains. "Once you start doing research at a high level, there is no more captivating feeling than discovering something that will work across animal model systems and into human patient populations," he says.

He remembers his early intellectual encounters with type 2 immunity. "It was crazy. I'm a fairly well-educated person but I knew so little about this. How is it initiated? Why is it initiated? How is it regulated? I was a graduate student working in cancer immunology and had been in multiple labs studying the immune system but had never really been exposed to the incredible parasitic infections that devastate the majority of the world's population. For type 1 immunity, we had identified all these receptors and immune cell populations but in contrast, there was really nothing known about type 2."

By concentrating on this immune module, Siracusa realized that he could "inform therapeutics to treat two devastating disease states: parasitic infections and allergic inflammation. My studies have taken us into the really early events that your body initiates in both." He has developed new ways to understand how epithelial cell-derived cytokines regulate innate immune cells and mediate protective immunity to helminth worms in the gastrointestinal tract. His earlier work focused on understanding acute pulmonary inflammation in response to hookworm infection. And while at Penn, he was on a team studying what is known as the "allergic march," or the gradual overlapping of allergic diseases that can begin in childhood. "We worked very closely with clinicians and allergists who knew that the kids who develop early eczema were going to have substantial allergies down the road." Those research results were published in *Nature* in August 2011.

Perhaps no experience was as motivating as a trip to Peru with his mother right after completing his PhD. "You are burned out. You've written your thesis. Grad school is a long, hard process," he admits. His parents sponsored a group of children at a Peruvian orphanage and his mom wanted to fly down to meet them. When his father couldn't make the trip, "I said I'd go because I thought it would be a nice vacation. I wanted to see Machu Picchu," Siracusa recalls. However, while visiting the villages outside Lima, he finally came into contact with the small children who had "the horrible parasitic infections" he had been studying. "It was incredible to see the manifestations, the stunted growth, for instance, of what I had been reading about. This reinvigorated my reasons for going back to my research." Clinicians down there described "a never-ending cascade" where children were treated, sent home, and immediately re-infected. "You realize the importance of what you are doing."

Students taking his "Advanced Concepts in Infection, Immunity and Inflammation" and listening to his take on innate immunity, mucosal immunology, or parasitology are in for a treat. Siracusa explains that what most students have learned about immunology is dogma. Old stuff. Not in his classes, however. "Fundamental discoveries were made in this area just two or three years ago. To be here at the ground floor in science where discoveries are being made in their time frame grabs them. This is an area of great opportunity in science and one of great need."

Siracusa believes he is in the right place to make these discoveries happen. At NJMS, he joined the interdepartmental Center for Immunity and Inflammation and couldn't be happier. "I was recruited here because we are on the tip of an explosion." The Center is part of the two-year-old Institute of Infection and Inflammation (i3D) that has brought world-class scientists together to build upon cutting-edge facilities located in Newark. "These next few years will be incredible."

Karen Edelblum: Personal Best

For basic scientists like Karen Edelblum, PhD, being able to put a face on the disease they may be studying is crucial. "It is so easy to get caught up in doing the science, writing the papers, and applying for the grants that you don't think about the medical impact of your work on the bench. I've known principal investigators who have inspiration walls in their labs so they can actually see patients' faces," says this new assistant professor of pathology and laboratory medicine at the NJMS Center for Immunity and Inflammation (CII).

"You become more passionate about the science when you have that face and those stories," she adds. CII is a division of i3D (Institute of Infection and Inflammatory Disease). Having arrived just last summer, Edelblum is happy to be here. In her case, finding a face for her research wasn't difficult. It's her own that she sees, along with all the other IBD (inflammatory bowel disease) patients and friends she has known since she was diagnosed with Crohn's disease at age 13. "I'm one of the lucky ones. I've been in remission for 13 years." A graduate of Emory University, Edelblum earned her PhD in cell and developmental biology at Vanderbilt University in 2008 and completed a post-doc at the University of Chicago in 2011, where she stayed on as a research associate. She's been looking at the synergy between immunological, epithelial, and microbial factors during the pathogenesis of colitis and, in particular, gamma delta intraepithelial lymphocytes (IELs). "They are a poorly understood subset of T cells and after 30 years of study, we still don't fully understand what they do."

Since there is no known cause for IBD, there is also no cure. Usually diagnosed in the pre-teens to mid-20s, 1.6 million Americans are battling this gastrointestinal (GI) nightmare. Inside the intestines, a single layer of cells, the epithelium, protects the host from the harsh environment of the gut. Imagine a place with a constant onslaught of pathogens, toxins, waste by-products and cytokines. In IBD, this essential barrier is compromised, contributing to the overactivation of the mucosal immune system.

"I've known since I was a teenager what I wanted to be when I grew up," Edelblum says. "I became single-minded about pursuing this research, looking at epithelial biology, mucosal immunology, and trying to understand the complex components that go into the development of this disease, both on the epithelial as well as the immune side. I was always good at science and I like to think that things happen for a reason. All of my career and academic decisions have been put into motion by my diagnosis and involvement in the IBD community." Edelblum grew up in Houston where her parents liked the fact that she turned what most people would see as a negative into a positive. "As a scientist, I trained in the GI community. Its small circle of investigators has become my role models and mentors."

Edelblum likes science she can see, "as opposed to looking at proteins on a blot," she laughs. She figured that if she could "watch the

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