The Arthritis Foundation funds pioneering scientists with innovative ideas that have the potential to move arthritis research in new directions.

On April 23rd four of these funded researchers presented their findings at the Foundation’s research forum at NYU Langone Medical Center in New York City. They included Postdoctoral Fellowship recipients: Yu Grace Qiao, PhD, Hospital for Special Surgery; Wenzhao Meng, PhD, University of Pennsylvania Medical Center; and Tanisha Jackson, PhD, Feinstein Institute for Medical Research, North Shore-LIJ Health System.

The fourth investigator, Innovative Research Grant recipient, Jose Scher, MD, Assistant Professor of Medicine, NYU School of Medicine, and Director, NYU Psoriatic Arthritis Center, was the keynote speaker.

Stephen I. Katz, MD, PhD, Director of the National Institute of Arthritis and Musculoskeletal and Skin Diseases, NIH, was the evening’s special guest.

Autoimmune diseases are malfunctions of the body’s immune defenses. Instead of attacking foreign infectious agents, the immune system mistakenly attacks the body’s own cells and tissues. More than 5 million Americans have some autoimmune form of arthritis. If left untreated, autoimmune diseases can damage the skin, blood, nervous system and internal organs.

The researchers examined different paths within the human body that lead to autoimmunity and inflammation. Through their research, they have learned more about the mechanisms that cause inflammation, thereby increasing the arsenal of data medical science can use to design new treatments and stop the destructive process in its tracks.

Read more about their investigations on page 3.

Featured speakers met before the forum on April 23rd. They are (left to right): Dr. Jose Scher, Dr. Yu (Grace) Qiao, Dr. Tanisha Jackson; Dr. Stephen Katz and Dr. Wenzhao Meng.
Have there been any changes/trends in the way rheumatology research has been conducted over the past 10 years?

Over the last decade, we’ve seen new kinds of scientific partnerships. Collaborations have formed not only across disciplines and between basic, translational and clinical researchers, but also across sectors. The recently funded NIH Accelerating Medicines Partnership (AMP) in lupus and rheumatoid arthritis is an excellent example. It is a multi-sector effort with government, academic institutions, patient groups, private foundations, and industry working together to achieve the shared goal of identifying and validating promising biological targets for drug development. Research also has become more technology-driven. The AMP is a great example of how cutting-edge technology is advancing biomedical research.

What do you feel will be three important areas of growth in rheumatology research going forward?

I’ll mention computational biology, team science, and patient-centered research.

What would you say to young scientists to encourage them to focus on research?

I would tell them that “you are the future!” Ensuring a robust pipeline of new biomedical investigators is one of our highest responsibilities, and we have taken several steps to support young scientists. For example, the NIAMS leads the intramural NIH Rheumatology Training Program, which was featured in The Rheumatologist in March 2015. Like many NIH components, we have a more generous payline for applications from new investigators. NIAMS funds extramural training and career development programs for researchers in its mission areas. This is a period of tremendous opportunity in science, technology and medicine. I would encourage young researchers to focus on what they see as the most exciting scientific questions.
Dr. Qiao received her PhD in Immunology at the University of Michigan and later joined Dr. Lionel Ivashkiv’s lab at Hospital for Special Surgery. She studied chronic inflammation and the mechanisms and regulation of proteins called interferons in an effort to better understand autoimmune diseases such as rheumatoid arthritis.

Dr. Qiao’s investigation looked at macrophages, which are cells that play important roles in promoting inflammation in diseases including rheumatoid arthritis. Macrophages produce pro-inflammatory cytokines such as TNF and IL-6, that lead to tissue destruction, she explains. “The goal of our research was to better understand how the genes that encode these cytokines are regulated and we did discover new mechanisms that regulate the expression of these genes.”

“We also found that DNA organization plays an important role in the control of inflammatory cytokine expression,” she says. “We discovered that a pro-inflammatory environment changes DNA structures of cytokine genes such as TNF and IL-6, creating a type of ‘snowball’ effect. First, this type of environment sensitizes cells for faster and elevated inflammatory responses to even minimum levels of stimulation. Second, once genes are activated, they are more difficult to turn off as the DNA structure cannot be closed properly. This provides a potential explanation of prolonged cytokine production in chronic inflammation and may help us design safer and more effective new targets for drugs to treat autoimmune disorders like rheumatoid arthritis.”
**Wenzhao Meng, PhD**
*University of Pennsylvania, Perelman School of Medicine • Philadelphia, PA*

**Dr. Meng** received her PhD in Biochemistry at Temple University in Philadelphia and a degree in Molecular Biology in her native China. She is currently a Research Associate of Pathology and Laboratory Medicine, Perelman School of Medicine, and Acting Technical Director, Human Immunology Core, at the University of Pennsylvania.

“B cells are an important part of the immune system as they generate the millions of antibodies that recognize and attack specific infectious agents,” Dr. Meng says. “In normal immune system development, the B cells which produce antibodies that would attack the body’s own cells are eliminated before they mature — but in autoimmune disorders, this selection process fails, allowing faulty B cells to fully develop and begin producing self-attacking antibodies. Therefore, a major challenge of improving the diagnosis and treatment of autoimmune diseases is first figuring out how to pinpoint the defects in the selection process that allow faulty B cells to pass through.”

Dr. Meng explains that “there are millions of different B cells, and trying to find the faulty B cells is like looking for a needle in a haystack.” In an important advance, she and her colleagues have developed B cell repertoire high-throughput sequencing techniques that have allowed them to identify abnormal B cells that could lead to autoimmune disorders. Specifically, Dr. Meng analyzes the genetic coding of millions of B cells and suggests that genetic coding of B cells in lupus patients differs from normal controls. “My hypothesis is that this genetic coding is differentially selected in lupus patients, and that the genetic alterations resulting in possible faulty B cells expansion may serve as candidate biomarkers for early lupus diagnosis or response to B-cell targeted therapy.”

**Tanisha Jackson, PhD**
*The Feinstein Institute for Medical Research • North Shore-Long Island Jewish Health System • Manhasset, NY*

**Dr. Jackson**’s curiosity about how the immune system is regulated drives her interest in the field of rheumatology. She received her PhD in Microbiology from the University of Alabama at Birmingham, and is currently a postdoctoral fellow in the lab of Dr. Betty Diamond at The Feinstein Institute for Medical Research. Tanisha shares with us some of the findings revealed during her Arthritis Foundation-funded study of the effect of CSK gene expression on B cell tolerance and autoimmunity.

“We have found that people with a mutation in a gene called CSK have an increased risk of developing lupus,” Dr. Jackson explains. B cell activation leads to a relay of messages from the B cell receptor on the surface of the cell to molecules that perform specific functions inside the cell. CSK is a molecule that can block the relay of messages during B cell activation.

“The goal of my research was to understand how changes in CSK activity cause lupus. To study this, I used mouse models of the disease in which the mice express higher or lower levels of CSK in their B cells. My research showed that mice with less CSK produce fewer antibodies against DNA and have decreased kidney damage while increased expression of CSK leads to more hyperactive B cells and more severe disease. This suggests that reduced CSK can lessen the effects of lupus. Finding a treatment that can turn down CSK activity may reduce autoantibody production and the ensuing damage caused to organs. We hope that CSK will be a potential target for lupus therapies that will help improve the lives of patients with the disease,” she says.