Judith James honored with the 2020 Stanley J. Korsmeyer Award

The American Society for Clinical Investigation has selected renowned lupus researcher and rheumatologist Judith James for the 2020 Stanley J. Korsmeyer Award, which is given annually in recognition of scientific excellence and outstanding mentorship of future researchers. Dr. James, member and chair of the Oklahoma Medical Research Foundation and Professor of Medicine at the University of Oklahoma Health Sciences Center, has dedicated her career to understanding the pathogenesis of systemic lupus erythematosus (SLE) and related autoimmune conditions and has made key contributions to the concepts of humoral epitope spreading and preclinical autoimmunity (Figure 1). Subsequently, her work expanded to include clinical studies aimed at preventing or delaying SLE development in high-risk populations. Her research group is also seeking to better understand immune imbalances that contribute to flares in patients with SLE. The *JCI* recently spoke with Dr. James about her remarkable research career and dedication to mentoring trainees in Oklahoma.

JCI: What attracted you to a career in medicine and research?

James: I am a fifth-generation Oklahoman from a farming community, and I had horrible asthma as a child. When I was about five years old, I told my pediatrician that I really wanted to be a doctor. He responded that if I became a nurse, he would be happy to hire me. I told him, "That's okay, I am going to be a doctor, and I can come back and take over this practice." He recorded this in my medical chart and left a note to look up this precocious five-year old in 20 years. Later, he actually showed that small redacted part of my medical record to my medical school class, because he came and lectured on pediatric dermatologic conditions.

As an undergraduate, I did everything I could to become a perfect medical school candidate. I was rotating with a family physician, and I would accompany him on house calls. One day, he stopped the car, pulled to the side of the road, and told me that I asked way too many questions and would never be happy just being a physician. He suggested that I find some research opportunities. I went to a small liberal arts school that didn't have any bench research, but I was able to participate in a summer research program at the Oklahoma Medical Research Foundation in the lab of John Harley, who was an MD-PhD. He was my first mentor and very supportive of my career. When I was 19, I saw my first patient with lupus who was also 19. That's when I decided I really wanted to be a physician-scientist.

JCI: Can you tell us more about your early work?

James: I was the first student in the MD-PhD Program at the University of Oklahoma. I worked on epitope mapping of humoral immune targets in lupus autoantigens. That research led to the work that has been my mission in life, which is understanding the early events of disease transition, including genetics, environmental factors, as well as changes in the immune system and regulators of the immune system in the pathway to human lupus. That led to our role in the first lupus prevention trial.

JCI: How did you transition from working on a more basic understanding of disease susceptibility to clinical treatments aimed at prevention?

James: When I started my career, I was more of a basic immunologist. I did mouse experiments and in vitro work, but we still conducted a lot of studies using human samples to dissect what was changing in patients' immune systems over time. My entire career has focused on patients and dissecting mechanisms, and then going back to see which of those mechanisms are important in human disease. As my career has evolved, I have become increasingly involved in the clinical research side. I still take care of patients, and I am very passionate about making sure we do research that helps change the lives of current and future patients.

Figure 1. Judith James is the recipient of the 2020 Stanley J. Korsmeyer award.

We have a wonderful partnership with military rheumatologists who are part of the Department of Defense. Through those collaborations, we were able to access the Department of Defense serum repository, which has longitudinal samples from millions of active duty military personnel. We were able to identify individuals who came into the military completely healthy but later went on to develop SLE, and then we went to the serum repository to access samples obtained before these individuals ever became clinically ill. We saw autoantibodies many years before specific disease manifestations, and then we were able to follow changes in their immune system as they were transitioning to disease.

We have followed up that work with studies looking at family members who have increased disease risk, enrolling them in genetic studies and then recontacting them years later to see who did and didn't

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transition. We've been very interested in identifying the family members who will go on to develop lupus, but equally important are the family members who have significant genetic risk factors and make autoantibodies but never become clinically ill. One of the major focuses of our current research involves trying to understand how these healthy individuals regulate immune responses even after they have lupus-associated autoantibodies.

Through partnerships with clinical trialists like Joan Merrill, we have built the Oklahoma Lupus Cohort, which follows about 650 lupus patients. I have taken care of some of those patients for more than 20 years. I am now enrolling multiple children of my patients or former patients who have passed away into our first-ever lupus prevention trial, and they are so excited to be part of it.

JCI: SLE has been a particularly challenging disease, in part because the clinical symptoms are so heterogeneous. How do you think that modern tools and approaches might help shape our understanding of this moving forward?

James: This is an extremely important area, and dissecting lupus heterogeneity to aid in clinical trials is the primary focus of the recently renewed Autoimmunity Center of Excellence that I lead. In lupus, we have had — which I consider a travesty — many molecules that make complete sense for intervening in lupus pathogenesis, but trials targeting those molecules have not met their primary endpoint in large-scale studies. We think this lack of success is multifactorial, and we have multiple investigators who are working on different pieces of this puzzle. One of those pieces is that lupus is clinically heterogeneous, but in the past, the field has not tried to rigorously dissect the molecular heterogeneity that is happening in patients at the time we are putting them into trials.

Recently, we took a large group of patients with lupus and characterized them from a molecular phenotype perspective. We have looked at immunophenotyping, gene expression profiling, genetics, soluble mediators, and autoantibodies and then used machine learning and clustering algorithms to identify different groups of patients. We have some preliminary data from work with clinical trial samples suggesting that if we can select patients who are in a specific cluster, we may be able to tease out which medicines should be used.

JCI: You have stayed in Oklahoma for all of your training and professional career with great success. Was it important to you to remain in Oklahoma?

James: In the beginning, all of my mentors told me I couldn't do it this way. However, the science was going so well, as we were building patient collections and had substantial support from the institution, so I just never left. I also have a huge passion to help other Oklahoma students to understand that they can have a career in biomedical research. I've had well over 130 people come through the lab who were thinking about medical school, graduate school, or a combined degree, and helping those Oklahoma students (many of whom are either in high school or are undergraduates) and seeing them succeed with physician-scientist training and now with faculty positions at universities like Columbia, Duke, the University of Alabama Birmingham, Harvard, Yale and OUHSC, is something I'm really excited about.

I am also very passionate about training Native American students, because we have a significant Native American population in Oklahoma, but they account for less than 0.2% of all medical students and an even lower percentage of graduate students nationally. I have a tribe-based research clinic, currently with the Cherokee Nation and previously with the Chickasaw Nation. We are working on developing better molecular information to help improve outcomes through early diagnosis and treatment. I've had a number of Native American students who have come through the lab and worked on that project or other projects and who have now finished medical school or graduate school and gone on to productive careers. I've had two Native American trainees who have gone on to obtain independent NIH funding and are both doing really well. That's extremely rewarding.

JCI: What does winning the Korsmeyer award mean to you?

James: I was incredibly excited but also humbled to receive this award. I was not fortunate to know Dr. Korsmeyer, but my institutional president, Steven Prescott, knew him and has shared with me how passionate Dr. Korsmeyer was about mentoring and helping train the next generation. I'm honored to receive the award, and it re-emphasizes to me how important mentoring is. The list of previous recipients is amazing, and I'm very, very honored to be added to that list.

Sarah Jackson