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PEOPLE & IDEAS

Claudia Jakubzick: Work hard, play hard

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Claudia Jakubzick will be an Associate Professor at Dartmouth in the Department of Microbiology and Immunology working on immune homeostasis and how the immune system can recognize and target precancerous cells. She started her own laboratory at National Jewish Health in 2014, becoming a tenure-track Assistant Professor and an Associate Professor in 2017, and will relocate to Dartmouth mid-2019. She is also a member of the American Association of Immunologists' Minority Affairs Committee. We contacted Claudia to find out about her career in science.

Where did you grow up?

My parents were kids who had kids. They were both 20-yr-old, first-generation immigrants from Peru living in South Miami. My neighborhood was filled with Spanish-speaking immigrant kids. Florida doesn't have seasons, so all year long, we ran around the golf course next to our homes, jumped in lakes, and climbed trees. After school and on weekends, we basically played all day outside.

I didn't have books growing up. I don't know why I didn't have any, but my parents' English wasn't good. I didn't know any other kids who read books, either. The only book I read as a kid was *Charlotte's Web*, three times. It was the only book we had in the house apart from the Bible (in Spanish) and some engineering books. The next book I read, apart from textbooks, was after college: *The Little Prince*. Because reading was not a priority at home, I graduated from high school with a third-grade reading level and finished some of my classes in night school. Now my son is in fifth grade and has an eighth-grade reading level. I'm really proud of that.

When did your interest in science begin? What was your first experience of science?

I first got interested in science because of TV, and indirectly because of my dad. He was an electrical engineer. He rigged the TV so that the only channel that would play was PBS. At night, I watched *Nova*, *National Geographic*, and *Jacques Cousteau*—I thought those and a few others were the only shows in existence. The one "fun" show was *Doctor Who*. We had a black and white TV with two knobs and an antenna that needed constant adjustment. However, when Carl Sagan's *Cosmos* series came out, my dad felt compelled to save money and purchase our first color TV. Later, he took me to meet both Jacques Cousteau and Carl Sagan in person, Cousteau at the Miami Marina and Sagan at a lecture at Florida International University. As a kid, I was amazed at the crowd Cousteau attracted, but then discovered that most people were there for the actor who introduced him—Edward James Olmos from *Miami Vice*. Fortunately, this gave a small group of us a chance to speak personally with Cousteau in front of the Calypso. These experiences were inspirational for me.

My parents divorced when I was 15, and things got really hard. My parents were too wrapped up in their own problems and lives to worry much about their kids. At 15, I got my first job, and helped pay the bills until we lost most of our possessions. I had no parental support, and moved out on my own at 17. So, though I was always interested in science, I was worlds away.

I remember the day I decided to change my life and focus solely on my education. I was a senior in high school, and I didn't have enough credits to graduate. My friends and I were sitting together on the grass near the entrance to a dance club talking about life after high school. The girl next to me said she wanted to be a lawyer, and everyone laughed: We all knew that none of us would amount to anything. We went around the circle, about ten of us. When it came to me, I said I wanted to become a doctor. When everyone laughed, for some reason, I was shocked. That's when it hit me: I was on the wrong path. I stood up and told them, "This is the last time you'll ever see me." They said, "Yeah, see you tomorrow at the club." But I never went back.

Claudia Jakubzick

Where and with whom have you studied (undergraduate, graduate, postdoc)?

It takes language skills to do well on standardized tests, and because of my background I didn't have that. My SAT scores were so low that I didn't qualify for admission to my local community college, Miami Dade Community College. I failed the language portion of the alternative entrance examination, too. After that, I remember sitting down and crying on the steps of Miami Dade, feeling like it was all over. A professor, Dr. Roche, sat down next to me and asked me if I was OK. He told me there was another path to get in by taking remedial courses for the first year as an English as a second language (ESL) student. I enrolled, got a 4.0 average, did the ESL courses, and got in.

It wasn't easy. I worked three jobs while going to school, waitressing (mostly night

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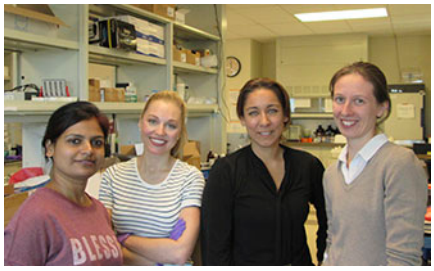

Claudia and her lab, 2018.

shifts during the week until 4 a.m. and double shifts on the weekends at Bennigan's, TGI Friday's, and Green Street Café in Coconut Grove). I also worked as a file clerk, which was the lowest paying among all my jobs, but it was in a hospital. I took it to remind me of the path I wanted to be on. Waitressing taught me the value of teamwork and hard work and that I didn't want to be there forever. So, indirectly, waitressing taught me the value of education too.

Miami Dade was incredible for me. I don't think I would have succeeded in a four-year college at first. After three years with straight As at Miami Dade, I did well on the SAT and got accepted at the University of Florida (UF). I remember the day I got the acceptance letter. UF was the best school I'd ever heard of, and when I opened the mailbox I thought I was the biggest winner in life.

At UF, I was exposed to a whole new academic world. I studied microbiology and loved it. In my second year, I became president of the microbiology club, a group of enthusiasts with ∼100 members representing 1,000 undergrads, and joined the laboratory of Dr. Julie Maupin-Furlow, who studied proteasome subunits. My undergraduate immunology class had a huge impact on me. We used the *Kuby Immunology* book, and something about the way it was written—in chronological order of discovery—captivated me. As I read, I would make predictions: Why didn't they do it that way? Then I'd turn the page and read about what happened next, and sometimes they did what I had predicted. It made me feel like I really understood immunology, that I was good at it. It was a challenging course; many students barely passed, but I was the top student among the 300 or so enrolled. That's when I fell in love with immunology.

It wasn't easy at UF, either, because I was so poor and had to work extra jobs all the time. I tried to mainly work in laboratories stocking and cleaning dishes, staying in the laboratory environment I wanted to end up in, but the pay was minimal. I ate ramen noodles every day my first year at UF, and cooked them every way possible: Baked with a can of beans, fried, boiled with Indian spices, with barbeque sauce, or with Lipton onion soup. I remember once losing my glasses. Today that would be a minor annoyance, but back then it was a really big deal: I had no money to replace them. I called my old boss at Green Street Café, Silvano, who rearranged the schedule to give me double shifts over the weekend from 6 a.m. to 10 p.m. After my last Sunday shift, I drove nine hours back to Gainesville to make my Monday morning classes. This is an example of hard work on my part, but also of support from people like Silvano, who believed in me and gave me a chance to succeed.

Along the way, several programs for minority students helped me develop along my new trajectory, particularly two summer research programs at Penn State University in 1997 and the University of Pennsylvania in 1998. My first paper, on the phylogeny of β- and γ-class carbonic anhydrase, was published in *PNAS* with Dr. James Ferry at Penn State University. This led to the next step: After UF, I spent a year working as a technician for Dr. Steve Thomas, a neuroscientist at the University of Pennsylvania, who encouraged me to apply to graduate school at the University of Michigan.

I was accepted into the first class of the University of Michigan's interdisciplinary Program in Biomedical Sciences, working with Dr. Cory Hogaboam (my primary mentor) and with Drs. Steven Kunkel and Nick Lukacs. Because of the stipend provided to graduate students, this was the first time in my life that I could be a full-time student and only a student, and there was no way I was going to squander this opportunity. This was my pathway to independence.

I worked hard, and loved it. I couldn't tell the difference between Friday, Sunday, Monday, or any other day of the week. I was in heaven, doing what I love: science. I was in the laboratory all the time, sometimes until my supervisor showed up in the morning, when I high-fived him and said I was going to bed. Early on, Cory saw my motivation and drive to succeed and believed in me. I was his first graduate student. Recognizing my language deficiencies, he said, "Oh man, we've got work to do. I'm going to teach you to become a great scientist, even if it kills me." This support, and his ability to lead by example and work side-by-side at the bench, inspires me today. I do the same with my laboratory team.

I also played hard during graduate school, which I think balances out the laboratory work and keeps it fresh and fun. I lived in homes with four other graduate students, trained for and ran several marathons, and never missed a chance to go out with friends. I ran 5–10 miles a day. After four years in the PhD program, I published 15 papers, 7 as first author. But this never felt like a burden; I had a great time, and never felt forced to do something I didn't want to do.

Cory introduced me to Dr. Gwendalyn Randolph, an expert in mononuclear phagocytes. My husband and I moved to New York, and I joined her laboratory as a postdoc at Mount Sinai School of Medicine in 2004. Gwen polished me as a scientist. Although I had published a number of papers, I wasn't really independent yet. With Gwen, I had to learn to read, synthesize literature, and defend my ideas like never before. I also learned to write, a particular challenge given my background. Gwen led by example, teaching me to do the best research I possibly could, and to think through scientific issues in an original way. The norm in the laboratory wasn't just to produce a publishable paper, but to produce a complete story. We worked for years on each project, demonstrating a phenomenon from multiple angles and testing for consistency across multiple methods. Both Cory and Gwen were role models for what I wanted to become: brilliant, passionate scientists.

Even after my postdoc with Gwen, I didn't start out as a tenure-track professor. I moved to National Jewish Health in Colorado, as a Research Assistant Professor in the laboratory of Dr. Peter Henson, a distinguished scientist and pioneer in the field of macrophage biology and efferocytosis. National Jewish Health was a dream job for me because it's a world-class pulmonary hospital integrated with the University of Colorado's Department of Immunology. This was a perfect fit for my focus in pulmonary immunology. In Peter, I found a tremendous advisor and collaborator. He supported me in doing my own independent research, and I was really able to grow as an independent

scientist. During my first two years, I published a senior-author paper in *JEM* (Desch et al., 2011) and was awarded several grants. These included a Zucker award to support women in science, a translational grant to patent and develop a new cancer immunotherapy, a drug development grant, and an NIH R01. This support, along with a brilliant student, Dr. Nicole Desch, and talented super-technician, Ms. Sophie Gibbings, launched my new laboratory (Jakubzick et al., 2013; Desch et al., 2014; Gibbings et al., 2015). Within a few years, I obtained two more NIH R01s to support my research program, and I transitioned to a tenure-track Assistant Professor position in 2014 and Associate Professor in 2017.

I hope that my story serves to illustrate that success in science is a dialog between one's personal drive and love for science, on the one hand, and the societal context in which one is embedded, on the other. I've been fortunate to be surrounded by people who believed that I could succeed, sometimes against all odds, and took action to give me opportunities to do so. They also gave me the support I needed to be increasingly independent, developing and pursuing my own unique scientific vision. This kind of mentorship is truly selfless, and it is so essential. I have been enlightened and enriched in ways I never thought possible growing up, and I hope to return the favor to the next generation of aspiring scientists.

What interested you about your current area of study?

The most exciting projects in my laboratory right now involve understanding how immune cell subtypes work together to maintain homeostasis. The entire immune system, innate and adaptive, works together. When I started working with chemokines, redundancy was the buzzword. Multiple chemokines were thought to play redundant roles, binding to the same receptor types. However, my years of working with T cells and innate immune cells in vivo have made me realize how the maintenance of homeostasis is a delicate balance that involves many cells working together, with each playing specialized, unique roles. Depending on the model, there appears to be virtually no redundancy across cell types. Instead, deficiencies in some cell populations elicit patterns of compensation, a signal that the system is designed to maintain homeostatic function. In some cases, the system cannot compensate for deficiencies, and disease results. I'm fascinated by these interactions across immune cells and the types of compensation and dysregulation that emerge.

What are you currently working on? What is up next for you?

We're applying an integrative approach, studying how different immune cell types signal to and interact with one another to recognize and target precancerous cells. We've found that a series of cells acts in an elegantly orchestrated cascade to prevent cancer in healthy mammals (Atif et al., 2018). This cascade starts with antibody recognition during the elimination phase of the conventional "triple E" hypothesis in cancer: elimination, equilibrium, and escape. Although B cells are known to have a role in the later stages of cancer, I believe the field as a whole, with the exception of a few scientists, has ignored the fundamental role of B cells in the early elimination of precancerous cells. Therefore, I hope to bring to light the importance of natural IgM antibodies in the early recognition and elimination phase and help B cells find a place in the famous diagram of extrinsic tumor suppression. By understanding this, we can understand why tumors can develop even in the presence of dendritic cells, T cells, natural killer cells, and other anti-tumor immune mechanisms. We believe that after intrinsic tumor suppression mechanisms fail, the next line of defense involves immune complex formation. Immunoglobulins form an immune complex with neoantigens located on the surface of precancerous cells, even in the absence of PAMPs or DAMPs. This tags precancerous cells for clearance by macrophages and activates antigen-presenting cells to present mutated self-antigens as immunogens, promoting adaptive immunity (Atif et al., 2018). Our studies, if fruitful, can lead to the development of new immunotherapies for cancer—but understanding how the system works at a fundamental level is the main goal. That deep understanding is what science is really all about.

What kind of approach do you bring to your work?

We do a lot of our work in vivo. Immune cells are specialized for local tissue environments, and in intact organisms, they interact with those environments in complex ways that can't be replicated in vitro. Studying signaling and function in cells' natural, in vivo environment is an important frontier in immunology.

In addition, another frontier is finding the human homologues of immune cells and functions that have been established in mouse models. Humans are different from mice, and we need to understand their parallels in detail to design immunotherapies and prevention strategies that work in humans.

An exciting new technique for identifying cell types and establishing parallel functions across mice and humans is RNA sequencing. Both bulk sequencing of defined cell populations and single-cell RNA sequencing are important. The latter, in particular, can help make sense of the heterogeneity in cell populations within a given microenvironment (e.g., tumor, lung tissue, or lymph node) and identify new categories of cells. We've identified three distinct types of interstitial macrophages in the lung and continue to identify human cell populations with similar properties and functions as the cells we've studied for years in mice (Desch et al., 2016; Gibbings et al., 2017).

What is the best advice you have been given?

When I arrived at Michigan, Cory told me, "You're not here for me; you're here for you. If you fail, it won't hurt me. I'm already made. If you succeed, we synergistically succeed together." This is one of the most important pieces of advice I've received. It may sound hard, but it's true, and it placed the responsibility for and control over my success in my hands. I tell everyone in my laboratory the same thing.

Any tips for a successful research career?

The best advice I have as a PI is to lead by example. Be thoughtful, appreciate everyone's contributions, and organize your life so that you can pursue science. Science is more than a full-time job, and so is raising a family and being part of a community. Get help with the house, logistics, and anything else you can. Try to spend your time doing what matters most to you.

Trust your intuitions and do the right thing. If it doesn't feel right, you're not

doing the right thing. And you must believe in what you are doing. If you don't, you should do something else.

Have integrity, and only publish what you're convinced is really true and will stand the test of time. You can only build a career off of real findings.

Don't compare yourself to others, and don't worry too much about what other people think. There is always the temptation to compare your level of success with others', but that is a trap. You'll find happiness when you set your own internal standard for what you want to do, and do what you find internally rewarding.

Share everything you can, and don't be paranoid. If you're racing to the finish line with other scientists, it's better for you to support each other and get there together than to hold each other back. Excitement in fields is built by people doing things together, replicating and building off each other.

Ignore mean-spirited people, if all attempts to establish harmony fail. Also ignore people who evaluate you not by your research contributions but by their stereotyped impression of you, whether that be because of your gender, background, or something else. You can't control what other people think. Science (like other careers) can sometimes bring out people's less prosocial instincts. When it does, I just focus on my science, and on the mentors, friends, and family members who love and support me. Even if you're not the most popular person, if your science is true, then I believe what my mother-in-law says: The cream rises to the top.

And finally, have fun. My motto all along has been "work hard, play hard," although now for me playing hard means spending evenings with my kids. Scientists have the greatest career in the world. We get to decipher humankind's greatest mysteries, and pursue our own unique, creative visions. There are few things in life more rewarding than that. It's an absolute privilege to be able to spend your work life innovating and pursuing questions no one has ever known the answer to. Remember that.

You are a member of the American Association of Immunologists' Minority Affairs Committee; how do you think we can best increase minority representation in science?

To pursue a career in research, one needs fire in the belly and motivation to find answers or create something new. This has to come from within, but that drive is inspired through a lifetime of exposure to ideas and scientific activities. One way to increase minority representation in science is to support community-based outreach programs that can give kids a chance to try out different types of scientific activities; you never know what will really "click" with someone and inspire them. It can start with Lego building and continue with activities such as robotics club, Science Olympiad, chemistry laboratory, anatomy laboratory, game programming, space exploration, or animal care, to name a few. During these activities, it's important to encourage students to be curious about the way things work and develop their own questions, and then empower them to find answers based on experimentation and evidence. Also, aspiring scientists need positive peer role models, students like them who think asking questions and being smart is cool. All of this requires overall support in the school environment, starting at the top. Furthermore, minorities need to see people like them can grow up to be successful scientists. Lastly, when minority students begin to pursue science, having dedicated mentorship and financial support to learn and develop as a scientist can make a huge difference.

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