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PEOPLE & IDEAS

Erika Pearce: Fitting metabolism and immunity together, to a T

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Pearce investigates how metabolism is tailored to immune cell function.

Growing up on the North Fork of Long Island, NY, there were few encounters with the world of science for a young Erika Pearce. But she remembers as a 4 yr old the set of Collier's encyclopedias her parents owned and was fascinated with the transparent acetate drawings of a frog, an engine, and her favorite one that revealed the basics of human anatomy. A self-revising reference book seems an apt analogy for science and Pearce also remembers "being absolutely fascinated by lifting the layers and seeing what was beneath the next. What I realized later was that science for me now is the same as it was then. We are all just trying to figure out what lies beneath. I still find it extremely exciting when pieces of data fit together to tell us something new."

Pearce's excitement for scientific discovery propelled her through graduate and postdoctoral projects identifying the role of a key transcription factor for CD8 T cell effector functions and the metabolic reprogramming important for memory T cell development. With the aim of understanding the metabolic processes that fuel the generation of T cell effector responses and longer term immunological memory more broadly, Pearce embarked on an independent research career in 2009 at the Trudeau Institute in Saranac Lake, NY. After several subsequent years at the Washington University School of Medicine in St. Louis, MO, Pearce was appointed director at the Max Planck Institute of Immunobiology and Epigenetics in Freiburg, Germany, and head of their new immunometabolism department in late 2015. We contacted Pearce to discover more about her journey.

Where and with whom have you studied?

I studied biology at Cornell University in Ithaca, NY. This was a life-changing experience for me as I was the first in my family to go to college. When I was young my only exposure to science and medicine was either through books or when I went to see a doctor. I never realized what it meant to be a scientist. So naturally, as a child, I wanted to be a physician. However, once I arrived at Cornell and was exposed to a world of research, I wanted to be part of it. My degree was in microbiology, with an emphasis on nonpathogenic microbial organisms, but a series of immunology courses I took during the last year of my program obviously had a great influence. After graduation, I worked as a technician in an immunology laboratory for three years and then in 2001 enrolled in graduate school at the University of Pennsylvania. While there I trained with Steve Reiner and Hao Shen and obtained my PhD in cell and molecular biology in 2005. In 2006 I began my postdoc with Yongwon Choi, also at the University of Pennsylvania.

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What initially drew you to study T cell metabolism?

Throughout my graduate and postgraduate training, I was primarily interested in memory T cells. T cells are critical for controlling cancer and infection, and can mediate autoimmunity, so they are important cells! As T cells engage in an immune response they become activated, differentiate, and undergo extensive proliferation, and all of these stages are tractable to in vivo as well as in vitro analysis. Microarray data from one of my studies pointed to a strong effect of metabolism on memory T cell development (1), and I found this incredibly interesting. I was hooked! We work under the premise that metabolic changes are intimately linked to T cell function and, therefore, metabolic pathways may represent targets for clinical intervention (2).

Erika Pearce. PHOTO COURTESY OF DAVID AUSSERHOFER.

What are you currently working on?

Since starting my own research group, my focus has been on understanding how metabolic pathways regulate T cell function. After I moved to the Max Planck Laboratory, my laboratory became significantly larger, and with more people we have been able to branch out into other areas of immune cell metabolism. Recently we demonstrated that nutrient competition between T cells and tumor cells in the tumor microenvironment can drive cancer progression (3). We also investigated how mitochondria, and in particular the dynamic morphological changes these organelles undergo, can influence function in T cells (4). Because T cell function is intimately linked to the control of infection and cancer, these results may impact how we approach the development of new immune therapies (5, 6).

Currently, we are focused on metabolic and mitochondrial changes in T cells in different tissue sites, substrate utilization by T cells during different phases of the immune response, as well as metabolic processes that regulate macrophage activation. We are

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Pearce laboratory. PHOTO COURTESY OF MARCUS ROCKOFF.

also shifting some of our focus toward more translational aspects of immune cell metabolism, with an emphasis on understanding how suboptimal metabolic programming in immune cells can lead to disease in humans. I hope that this will become a significant part of our research in the coming years as we remain interested in how to better target immune cells for therapy. I also have one person working on metabolism in *Dictyostelium*, but that is a different story!

What kind of approach do you bring to your work?

We integrate as many approaches as possible to support our findings. Using a variety of techniques to arrive at the same conclusion allows us to build confidence in our models and has the added benefit of making our work accessible to a wider group of scientists. While many experiments assessing immune cell metabolism start with in vitro culture systems, like many immunologists we strive to also test our findings using in vivo mouse models. One of the great things about working with immune cells is that we are able to test the biological function of the cells we have manipulated by assessing their ability to protect against cancer or infection.

What did you learn during your training that prepared you for being a group leader?

I was most unprepared for the part of being a manager. Creating a healthy laboratory and work environment is challenging even for people with a lot of experience in this area, and you can't prepare for this during your PhD or postdoc. It is definitely a learn-as-you-go process after you start as a group leader. I quickly realized that research is not just about individuals with great ideas, but rather about a team working together to create a body of scientific work. In my opinion, the team is all-important and plays the largest part in determining whether or not you, or any of your trainees, will succeed. This is the laboratory ethos, and in my opinion it is the key to success.

What has been the biggest challenge in your career so far?

Moving my research group to Germany. Having to learn to negotiate science in a new country with a culture that is much more distinct from that in the US than I expected has been challenging.

"Be bold, and . . . have the nerve to take risks. . . . and perhaps for many women, this does not come naturally."

What is the best advice you have been given?

I have been given a lot of good advice over the years, by a lot of different people. Someone once told me when I started my laboratory that I should be sure to continue working at the bench for a while, because in the beginning I was unlikely to be able to recruit a postdoc with more research experience than I had. I took this to heart and for the first year of my laboratory I worked only with a technician and this allowed me to set things up without having to worry about trainees, as I had enough to worry about by myself! During this time I was able to establish many of the core approaches that continue to be central to our work today. Also, another great piece of advice came from my former division head at Washington University. He encouraged me to be bold, and to have the nerve to take risks. I know this sounds cliché, but for me, and perhaps for many women, this does not come naturally. I was able to follow this advice because of the professional support I received at Washington University. I was very fortunate to have a mentor that made me feel more confident in my abilities and my science.

What hobbies do you enjoy?

I like to draw and paint, but only do this sporadically. My favorite pastime is hanging out with my family. We don't do anything in particular, but we always try to have a laugh when we are together.

Any tips for a successful research career?

Like life in any career, academic research can be challenging and not always filled with palpable successes. It is also difficult to describe what we do to nonscientists, and this can sometimes feel isolating. That being said, I think the best part of our job is that we get to choose the people we take into our research groups. I always tell people to use this to their advantage and be selective. Make sure new people add positively to the group. Work toward creating a laboratory environment where people like to come to work because life is richer when you are part of a team working toward the same goals.

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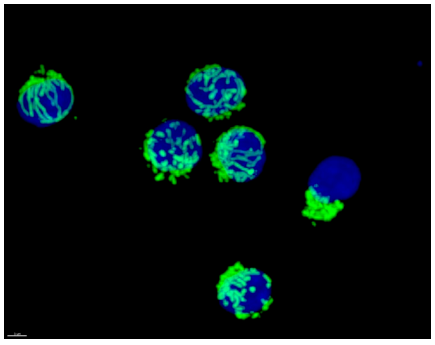

Morphological changes in T cell mitochondria after activation. IMAGE COURTESY OF RAMON KLEIN GELTINK.