

Liise-anne Pirofski is Chief of the Division of Infectious Diseases in the Department of Medicine at the Albert Einstein College of Medicine.

You're an M.D., and your research deals with the role of the immune system in susceptibility to pathogens like *Cryptococcus neoformans* and *Streptococcus pneumoniae*. How did you first become interested in this area?



I did not have any formal scientific training other than pre-med courses, and I did a fellowship in infectious diseases. When I was a fellow, we had a training grant here at the Albert Einstein College of Medicine and I had the opportunity to enter a lab and begin to learn about science and how to be a scientist. I was very interested in immunology, I guess because it's complicated, and I was lucky to be accepted into Matthew Scharff's lab. He told me a story: when you take a mouse and when you give it phosphorylcholine, then every single antibody the mouse makes to that component is identical, and all mice make the same antibody. This idea of restriction captivated me because antibody responses to microbial capsules are highly restricted. The antibody gene family used to make antibodies to capsules was reported to be dysregulated around that time. Since pneumococcus and cryptococcus both have capsules and induce restricted responses derived from this gene family and HIV-

infected persons have a higher incidence of disease with both microbes, I became interested in links between the state of the antibody repertoire and susceptibility to the diseases caused by encapsulated microbes.

The incidence of fungal infections has risen sharply in the past 25 years. Do you think we can reign in this phenomenon? What direction should the science take?

Fungal infections are on the rise and the reason is because there is an unprecedented number of people that don't have normal immune systems. The rise in fungal diseases is very different than the rise in methicillin resist staphylococcus or the other resistant organisms. This is not a problem of resistance (although the rise in *Candida* infections stems in part from antibiotic overuse and misuse leading to a change in the ecology of the normal microbial flora). In fact, there are drugs that are quite active against fungi. The problem is that you cannot eliminate these organisms very effectively from people that don't have normal immunity. The approaches [for reigning in fungal infection rates] are going to have to be those that are focused on immunomodulation and also the identification of even more active antifungal agents.

What is your greatest concern with respect to fungal pathogens in the future?

Their management is really going to require novel approaches, potentially even a paradigm shift in how we approach their management. I worry that before we get there, more patients will suffer. We currently lack some of the critical understanding to manipulate the host response enough to help patients that have very impaired immunity.

What research direction is your lab taking?

Our focus at the moment is predominantly on an effort to understand how the antibody repertoire is shaped and functions in innate immunity. We're really interested in the interactions between so-called "naturally occurring" and "memory" B-cells with microbes, particularly encapsulated organisms. If you have an infection, and I tell you it's going to take two weeks to make a really good antigen-specific T-cell that's going to murder that virus or

whatever it is, you're going to think, "What good does that do me? I'm going to be better by then." And you're right. What we're interested in now is how antibodies play a role in the very early part of the immune response. How did having the right antibody repertoire help you with that? Our idea is that potentially very low-tech interactions help corral the organism, get it into the right sorts of cells that can kill it or manage it, and that this very specific immune response plays a role when you see that organism later or maybe cleaning up after a certain amount of time.

What is your favorite microbe? Why?

My favorite microbe is any microbe that we live with peacefully and happily and that may even help us out, (which, as time goes forth, we're finding out are a whole lot of them).

What advice would you give students about life as a physician scientist?

The advice that I would give is actually the advice that I would give to anyone – that being in science, working in science, is a longitudinal pursuit. It piques your interest and grabs you and then there can be periods when one feels a little bit at sea, not really sure how all of those things come together. Eventually they will come together and the way in which they do provides the piece of the puzzle that makes way for the next set of questions and answers. My advice would be that it's a wonderful life, provided that one is willing to stay the course.

What is something about you that most people don't know?

I was an art history major in college, and I find that it's helpful in my career today.