Williams: This is an interview with Marc K. Jenkins for the American Association of Immunologists Oral History Project. Dr. Jenkins is the Distinguished McKnight University Professor in the Department of Microbiology and Immunology at the University of Minnesota Medical School. He is also the Director of University of Minnesota Center for Immunology. Dr. Jenkins was the President of the American Association of Immunologists from 2013 to 2014. He is a Distinguished Fellow of the AAI and was the recipient of the AAI Excellence in

academic scientist actually did or how one became one, but I wanted to be a scientist, so that started there.

Williams: So what led you to Northwestern? Oh, no. First you—I'm sorry, I'm jumping ahead here. You went to the University of Minnesota.

Jenkins: Yeah, yeah, which is what good Minnesota kids did who weren't—I must say, my parents encouraged me and my brothers to get an education, but they weren't academic people, so there was never a lot of pressure for me to go to Harvard, and, frankly, at that time, I'm not sure I was that ambitious, really. I mean, I knew I needed to get a job and have some kind of way to make a living, so the University of Minnesota was a very solid university, so I thought I could get good training there, and I did.

Williams: And what was your major?

Jenkins: Microbiology. I wanted to be involved in something related to infection.

Williams: Right, right. You have, what, two brothers?

Jenkins: Three.

Williams: Three brothers.

Jenkins: Three brothers, yeah, yeah, all younger than me.

Williams: And any of them in the sciences?

Jenkins: Two of my brothers are in business. One of them works for an insurance company and the other one works for Cardinal Glass, but my other brother is in the humanities. He's at Princeton, and he's a scholar in the Byzantine era. So he has two jobs. He's responsible for a rare book collection there, primary texts from the Byzantine era, which is like the 700s, so these are old, valuable manuscripts, and then he does research on one Byzantine figure, a guy named Michael Psellos, who was credited with being one of the early pioneers in scientific thought, because he was trying to use mathematics to write a mathematical proof to support the trinity, that three things could be the same things, but different. It turns out that can't be done because that's logically inconsistent, but the idea was that you could quantify things in the world, and including things in the Bible. So he's an interesting figure in history, and he had to do that in a subtle way, because that was bordering the line with heresy, which was a capital offense. So he's an interesting guy. I actually went to a Byzantine conference with my brother, registered for the meeting and attended. It was just fascinating. [laughs]

Williams: How long ago was that?

Jenkins: That was two years ago, because it was in Minneapolis, the Byzantine Scholars of America.

[William E.] Paul, famous immunologist. It was a lot of *very* ambitious people. I'm really not sure I had seen that kind of ambition before, overtly—even stated, almost—so that took some getting used to, and it was a very critical place. Everything you did scientifically was criticized, and this was good to produce scientific rigor, try to get it right, but it was really a very intense place. The particular problem that I was working on, like I said, the field of cellular immunology as it applies to T lymphocytes was just in its infancy, so there were a lot of things to discover, and so I was in the right place at the right time to find out something important about T lymphocytes, so that was good.

Williams: So you were there three years?

Jenkins: I was there three years, yeah.

Williams: And did you participate in some major breakthroughs at that point or—

Jenkins: I guess it would be self-serving to go too far with that, but my project, one part of it was to try to understand, basically, the minimum number of kind of signals a T lymphocyte had to respond to something foreign, and a major discovery had been made about the time I started my postdoc, was that there was a receptor on each T lymphocyte called the antigen receptor, and it recognized a peptide bound to MHC on another cell that let that T cell detect whether there was a virus inside that cell.

In the time, the thinking was, based on the model systems that existed, that that signal was necessary and sufficient to make a T cell proliferate, differentiate, kill the infection, and so my research showed that the T cell receptor [(TCR)], although necessary for that process, was not sufficient, and that there was a second kind of signal that was needed for that T cell to become activated. And that signal could be accounted for, in large part, by this molecule called CD28, and CD28 is in a family with other regulatory molecules called PD1 and CTLA4, and that whole idea of signal hat

and Tasuku Honjo, who just won the Nobel Prize. So that was a big deal, yes.

Williams: Right, right. What implications does that particular work have on the clinic?

Jenkins: Well, that kind of signal hat
clinical medicine, so blockade of CD28 is now a clinical therapy for graft rejection(s)-6(i)7(gna)7(l)7( )that
inhibition of signal hat — . And then, of course, the regulators of signal hat ess, they are now the basis of what's called checkpoint immunotherapy, so inhibiting the inhibitor turns out to be an incredible fuel on the immune system, and that's now created this incredible excitement about vaccines for cancer. Treatments for melanoma, now I think the latest evidence suggests maybe 40 percent of people

can be cured, and with much less side effects than we normally get with toxic chemotherapy. So both those things, not that I personally had anything to do with that, but that fundamental understanding that this was how T cells work was a step in that, a first step toward that later application.

I'm worried about funding. And like I said, scientists are kind of in the rejection business, but usually there's always a few successes mixed in there to keep you going, right, a few jackpots to keep you going back to the casino. But when the pay line got so low, there were people who just could not get their grants to run their research programs, and that created a negative atmosphere and started taking a lot of the fun out of it, so that worries me that that's going to discourage people from coming into the profession.

Williams: So how do you define the new normal?

Jenkins: Fifteen percent of grants are going to get paid. You have to write more. You have to write two if you used to have to write one. The system's made it easier to write them. They're shorter, and so developing the skills to be an effective and clear communicator and producing a readable application are all parts of the new skill set.

Williams: They probably don't teach you that in graduate school.

Jenkins: Yeah, they really don't, and I think there's even some confusing messages about the way to clarity is detail, and, in fact, I think it can often be the opposite, of reducing the big idea to some more metaphorical level that can resonate with a reviewer who's an expert but not a super expert in your little niche, you know, make it easy for them to understand your big idea, and that's a different kind of set of skills, although in the end, it's like arguing like an attorney. You're writing an argument to a jury, in essence, and so don't let them guess. But young people now are much better at it than I was when I started, largely because of these mentoring programs where junior faculty are mentored by senior faculty and by other—we have professional writers and professional public speakers working with our faculty now to improve our communication skills, to get our message out.

Williams: Is that common, you think, in the field?

Jenkins: I don't know. I don't think so, especially the public speaking part. They're experts in oral communication. They're not scientists, but they understand the science of oral communication. They're a data-driven group. They know what works, they know what doesn't work. They can help us make better slides, how to use our bodies, how to connect with the audience, how to deal with your nerves, all these things that make you a more effective communicator, someone people want to listen to, not someone people *have* to listen to. So, yeah, I think that's a good value-added program we have.

Williams: Is that targeted to the graduate students?

Jenkins: It's targeted mainly to the graduate students and postdocs to help their job interviewing potential, yeah, but I think I've learned as much as any of them, even

though I’d given hundreds of ta

Jenkins: I do it a little less formally now, although this last year, we started in again. So just because when you've been around a long time, you just have a lot more papers, so trying to figure out how to do that well, I'm probably being lazy. I should do a better job there.

Williams: You know, it strikes me that the field of immunology, you're always so forward-looking that it probably is beneficial to take a moment and look back the other way.

Jenkins: Yes, because there's a trend now to just collect all the information, because we have these amazing methods to collect these large data sets, and that's not a very

Jenkins: Sure. We had developed this new method to measure how these T cells were responding in the body, and it involved this trick of taking these mice made by recombinant DNA technology, where they all had the same antigen receptor, like they were all specific for influenza. We would flood them into a mouse and then we would give the infection, and we could watch those cells respond. It was really cool, but the bottom line was it turns out that flooding the system that is normally designed such that all the different antigen-specific cells are very rare so that you can have a very diverse response, you can respond to almost anything, that that homeostasis was perturbed by all the cells we had flooded in. In our own work, it became clear that that system that I had championed and convinced so many people around the world to use was flawed, at least it wasn't perfect, and so we now rarely use that system. We developed a different way to find the *real* T cells at their ultra-rare state, because that was the bottleneck that other system was trying to solve. It solved that problem, but then it created a different problem.

Williams: And how did you announce that discovery to the world?

Jenkins: We published it. That was hard. But it turns out my career only got better because we went from that path to a better path that was recognized. I wish it was recognized by more people, actually, that still use that earlier method, because it can do certain things that the more modern—it's easier to find one in 100 cells than it is to find one in a million, let's put it that way, and that lets you do things you could never do in the one-in-a-million case, but you still run this risk. So that was hard for me.

Williams: You described, I guess, again, during your President's Message that as far as you'r