The American Association of Immunologists
Oral History Project

Transcript

Paul M. Allen, Ph.D.
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Williams: This is an interview with Dr. Paul Allen for the American Association of Immunologists Oral History Project. Dr. Allen is the Robert L. Kroc Professor of Pathology and Immunology in the Department of Pathology and Immunology at the Washington University School of Medicine in St. Louis. He was President of the American Association of Immunologists from 2005 to 2006 and served as an AAI Council member from 2000 to 2005. We are at the AAI Headquarters in Bethesda, Maryland. Today is Monday, April 28, 2014, and I am Brien Williams.

Dr. Allen, thank you very much for being with us today, and I'd like to start by you recounting something of your own family history.

Allen: Well, I was born in a little town by Hannibal, Missouri, called Louisiana, because my father was a chemical engineer and during World War II worked in Texas making chemicals critical for synthetic rubber. Then after the war, he moved up and U.S. Bureau of Mines was working there, making oil from coal, and so a bunch of chemical engineers went there. Then I was born there, and my sister as well.

Then about 1953, the oil companies pressured the U.S. government to close down this competition making oil from coal, so then at that point we had to relocate, and we ended up going to Midland, Michigan, where my father worked for Dow Chemical.

Williams: What about your early life, elementary school and secondary and so forth?

Allen: In retrospect, it was a pretty idyllic, easy childhood, because Midland is—everybody's father was a chemist or a chemical engineer in a town more or less in the middle of no place in Michigan, and so it was safe and easy. You could ride your bike. Michigan summers are wonderful. Growing up, you would have thought it was bad, or you would think that the town was boring and this and that, but now with the privilege of time, it was really a delightful kind of upbringing, good public schools, and just kind of a place to grow intellectually and then just being busy because you were more or less very accessible to the outdoor home activities of Michigan available too.

Williams: What about teachers, like in your high school and so forth? Did you have some that were particularly influential or not?

Allen: Interesting, when I went into—I took more chemistry and physics, and I didn't take a biology course in senior high school, but I had a couple ones in junior high that really got me interested in biology. And the whole town was all—everybody's dad was a chemist or a chemical engineer, so that was the real push of everything like that.

The schools were outstanding, and so I think that—I'm trying to remember—Mr. Zock [phonetic] was the one in junior high, who realized that I had a quest for

knowledge and creativity and liked science, and I'm sure the English teachers probably, on the other side, realized I did not have a talent for creative writing, etc.

Williams: So you got the science bug pretty early in your life.

Allen: Yes, exactly, because I think it was more by osmosis. You didn't realize that, but that was just kind of—we always used to joke, the toughest job in Midland was being a high school chemistry teacher, because everybody said, "My dad says that the book is wrong," etc., stuff like that. So I think it was just part of that process. Either you embraced science kind of from that environment, or you seemed to reject it. So I was one who embraced it.

Williams: What were the steps that took you then to the University of Michigan?

Allen: Well, I guess I wasn't that adventuresome to go too far away. Ann Arbor in the late sixties and early seventies was a pretty active and dynamic place compared to Midland, Michigan. So I went out there and started out to be in oceanography, but it finally dawned on me that there was no real ocean nearby Michigan. But that was in the School of Engineering, so that was still the same kind of bent, and then I switched to microbiology.

I always thought it was a school that kind of gave you enough freedom. I was confident enough that having a large school—because I think some people feel a very large school, you can get lost, but I really embraced that, because I think it was a fun time in Ann Arbor. You could learn and also now just all the anti-war movement in the sixties and everything like that was happening there as well. So, compared to the quiet, relatively easy life of Midland, Ann Arbor was a pleasant change.

Williams: What led you to microbiology?

Allen: Well, hmm. Good question. I'm trying to think that there was a bunch of people that would go into, like, biology or something, and I just took a course, I think, as a sophomore that had a little bit of it in it, and then it got really interesting, and so I just got interested in it. Then they had a—for a long course that doesn't exist anymore, but it was two semesters. It met twelve hours each week for two full semesters in microbiology undergrad majors. There was this huge full immersion, and once you got into that, you just found it was fascinating. So I just kind of grew into that.

Williams: And that was as an undergraduate?

Allen: Yes.

Williams: So then you did the master's and the Ph.D.

Allen: Yes. So trying to decide what to go into, I remember I had, in addition to one section there was in immunology, I actually took an evening course. There's like three hours a week for once a week, a survey course of immunology. And I took that, and I found it interesting but didn't understand very much. I hate to say that was more the basis of why I went into it. This field seemed interesting, but it was not like I understood it all and this was a really rational decision why I went into immunology. It was a fast-moving field. There was, you know, lots of acronyms and jargon, but it just seemed interesting enough. I'm not sure what sparked it. I just decided that's what I wanted to go to grad school in.

Williams: So you made that decision sometime in your junior or senior year.

Allen: Yes, exactly. So I was a bit of a late bloomer, I think, and I'd never done research in a lab before I went into grad school, so I wasn't exactly a hot commodity. So the truth is, I got into one grad school, Michigan, and so it worked out well for me, but it was pretty funny that that was the one that I guess they knew me from undergrad before and stuff like that. So I stayed in the same department for undergrad and grad school.

Williams: But you made application to other grad schools?

Allen: Oh, yes. When they invite me to give talks, I remind them that they rejected me from grad school. But it was probably with no research experience. Now I look at the kids coming through the research programs now, it's just they all have so much more opportunity and everybody has significant research experience. So I guess I was at the cusp or I'd had it in classwork, but nothing where it was real research.

Williams: What was the status of the university at that time in the field?

Allen: At the University of Michigan, immunology was a tiny field. We had two immunologists. So there was one that had his lab was pretty full. Then my thesis advisor was a full-time surgeon, his name was John Niederhuber, and he had never had a graduate student. So the other immunologist, named Lathe Claflin, convinced John that he should try and have a graduate student. So I was John's first graduate student, and so then his lab grew and he had multiple ones after that.

Then if you fast-forward, he became the head of the NCI here. He stepped down maybe three years ago. So through a variety of his career and my career, that small world, I always tell my students, "You keep in good standing with your thesis advisor no matter what you think where they're headed or not." So that was the one where it worked out. It was just luck, and Lathe kind of championed my position for John to take a graduate student, so that was really lucky.

Williams: So did the two of you sort of sit down and say, "Well, now, what are we going to look at?" or, "Where are we going from here?" Or how did that happen?

Allen: Well, he was a full-time surgeon, so he was busy a lot, and so I think he was more the hands-off kind of approach. So I always liked to do things, so I needed to be reined in, like, "Why are you doing that experiment?" But he gave opportunity. We had a bunch of really creative and energetic people in the lab, so maybe there were about eight or ten of us. He was big into mouse genetics, because another guy had been at Michigan named Donald Shreffler, who was a very good mouse immunogeneticist, and he had been recruited to Washington University to become chairman of the genetics department. John had worked with him, so we had some collaborative projects then with mice that differed just at their major histocompatibility [MHC] gene, and this is the critical locus for determining an immune response. So that's kind of early on, and that's been my theme, more or less, through my entire career. So that was just one of these where, you know, I guess it's a small world in science, and just a few lucky being at the right spot at the right time.

Williams: So how many years did it take for his lab to grow to ten folks?

Allen: So we started out just with a couple technicians.

Williams: You first?

Allen: Yes, and so I was the one where there were maybe two technicians and a couple surgical residents would do that, and then once I got there, then he added—another grad student came on two years later, then another one after that, and he had postdoctoral fellows. So then the lab really kind of took off at that point.

Williams: So at the end or at the point when you received your Ph.D., you were on a strong path. You saw the road ahead clearly, is that correct?

Allen: I guess if you just look at publication records, I didn't have a great graduate career. I mean, I had a couple publications here. I learned a lot, but I wandered a bit, and so I think some of that, in retrospect, I could have been a little more focused. And then John could have helped me out, too, but it worked out because I really developed independence. I didn't rely on an advisor to say, "Well, what are you going to do next?" or, "What are you doing today?" I just charged ahead.

So I think that got me fearless to do experiments, and then I just needed for my postdoc some more, "Why are you doing that?" and etc. So I think it was an overall—I learned a ton. I think I was there seven years, six and a half, seven years, so I was probably on the long side, but I think you have to have enough years under your belt, I think, in science, because some of these programs, just in three years you're not going to learn enough to have experienced the ups and down of science to really be a productive scientist and running a lab.

Williams: Let's just pause here and talk a little a little bit about the creative force in science as you experienced it and as you recommend it should take place universally.

Allen: Obviously it's an impossible thing to teach, but it's fascinating to think about when I great creative ideas, the way I look at it, science isn't done in a vacuum. What you do is I'm sitting there in a big—like an AAI meeting, I could be sitting in a lecture and have this incredibly creative idea because I'm in like a scientific womb. I'm hearing this lecture, but I'm also thinking of other things, and I take pieces *A*, *B*, and *C* and put them together and say, "That's the experiment we should do."

Or sometimes you have some lingering observation that just doesn't make sense, and then you're talking to a colleague, and then they say something and then the spark hits, and then it goes like that. So they don't happen all that often, but it's just a critical part of remembering what you've done in the past, and then trying to think of how it fits into the context of science, and then what could be done to really test that idea with experiments.

If we could teach it or bottle it or do something like that, I guess it would be better, but that's part of the human being, right, of where creativity comes from. It's just a combination of these. You know the Pasteur phrase of chance favors the prepared mind. Because I think some of the laypeople think that we as scientists sit in a room, talk for a couple hours, and say, "That's the experiment we should do," run, and a day later we say, "Eureka!" and we've solved it. More of us, it's a lot of just repetitious grunt or knowing your system, and then, "Oh, there's a little deviation here. Oh, that might be significant. Let's follow that a little." So that's where it kind of comes into this being an observant scientist and then having the training and also kind of the context of the basic immunology and then biology over that of how any observation might fit in.

Williams: Would it be fair to say that some people in the field expect their trainees and whatnot to be more conformist to a particular approach, or is this creativity sort of universal?

Allen: It's a fine balance, because I think if you're trying to conform or just trying to prove what you're predicting isn't very creative, or if you know what the answer is, but it's trying to decide kind of the nose for science what's going to be a novel way to go forward versus some people get off track. So they say, "No, I'm being creative," but you're chasing a wrong lead kind of stuff. So that's the thing where it's really tough to pin down of how this really works. But I think everybody needs some structure, and each one of all the scientists I've trained, they all take different care and feeding. So some of them, you can just push them a little and then they run and they make great leaps in faith. Other ones still need more nudging and getting back on track, and from that they can have creative thoughts.

Williams: So what prompted then the move to Harvard?

Allen: So this is again, I look back, I've gotten very lucky in my career. One of the postdocs when I was in grad school had just come back from a postdoc in Switzerland, and it sounded great. So I'd found somebody who I was going to do a postdoc with, so I had to write for my own money. So this is where fate intervened, because I wrote an NIH grant and it didn't get funded. Then this person, he hit his peak of his popularity right when I was doing it or afterwards, so he dropped out and went back into industry or something. So I would have never been heard from again if I would have gotten that grant.

Then I had three other options, and so I had one with Emil Unanue at Harvard and then Ethan Shevach here at NIH, and then Hugh McDevitt at Stanford. They all kind of worked in similar topics of mouse genetics, MHC, antigen processing.

So I went and interviewed at Harvard with Emil, and it just seemed to work. I paid my own way back then. You flew out, had a one-day interview, and flew home. And, you know, it just seemed like a good fit, so that was the one out of those three. I probably couldn't have gone wrong in any of those, but this one just worked out.

Williams: Where did you fit in in terms of work in his lab with him?

Allen: So Emil was the one who had discovered antigen processing. This is where T lymphocytes recognize antigen not directly, but is handled by antigen-presenting cells such as a macrophage or dendritic cell. What it does it takes a whole protein and chops it up into peptides, which then bind to an MHC molecule on the surface.

So he had been involved in that process, but when I got to his lab in 1981, nobody had figured out how a T cell recognized the antigen, they called it, in the context of MHC. So you knew you needed a major histocompatibility complex and you needed a peptide. But the different models, he thought—we didn't know about the T cell receptor, so it was like all these models you had two receptors and two molecules and somehow this all happened.

So I started out working in Emil's antigen system, which was *Listeria monocytogenes*, a bacteria. Then this is where I realized it was just non-workable at a defined level. It's a whole bacteria. We didn't know what part the T cells were looking at. So I suggested singlehandedly—and I take credit for this one—pushing that we needed to get a model antigen system. There had been a couple antigens around. Most of these are just proteins that are available, some chicken egg.

The one we picked was hen egg white lysozyme, and so that was my—after the first year, then I developed the lysozyme system. And this is where it couldn't

have worked out any better, because this is one where I wanted to reduce a whole bacterium down to a protein and then actually the protein down to the fifteen amino acid peptide that are recognized. So what I did is I started out with immunizing mice and figuring out what portion of lysozyme they recognized, and it turned out when this particular mouse strain, there was one dominant epitope, so I'd identified that and characterized that.

So then this is where we use this system to directly show that peptides bound to MHC molecules, so this was huge in the field. So Emil won the Lasker Prize for this, and rightfully so, and I'm sure he was on the short list for a Nobel Prize too, because this solidified what was going on and how T cells recognized antigen, because people had previously tried to—let's say if you took a cell and you had your peptide antigen and tried to bind it to that MHC, to the cell it wouldn't bind by biochemical means. So then they tried to say, "Well, we don't think it's binding directly to the MHC molecule."

So then what we decided to do was, "Why don't we just try that?" So we purified a whole bunch of MHC molecule, we had peptide, and put them together, and then we actually demonstrated binding. So that was published in 1985, and it's a landmark paper because this really was the first direct demonstration that MHC molecules presented an antigen.

So now with crystal structures of these, I mean, I think the best analogy is like a hotdog on a bun, that you have a binding groove. At the top, there are two helices, and then the peptide binds in between, and the T cell receptor now sits on top of these, kind of binding both bun and the hotdog. So this really solidified this whole field, because now you understood how MHC molecules were involved in the recognition and how T cells develop in the thymus with the MHC molecules, etc.

So I think it was really one of those seminal findings that once you get it right, the textbooks have it, and everybody, with the current students, they're kind of like shocked, "You mean, we didn't know that always? No, back then." So I like to pull out pictures from old textbooks when you're giving a historical talk and show where they have a cell, and a MHC molecule is here, an antigen's here, and they're not touching each other. So it was so wrong. But then once you get it right, it's just the field moved forward.

So that was really my postdoc time, and unlike my graduate work, I published lots of papers, and it was just, you know, you couldn't stay away from the lab, because everything was moving so quickly and it was fun. It was great.

Williams: Is it right that you were the driving force on this discovery?

Allen: So I came up with the whole lysozyme system, and then another postdoc, Bruce Babbitt, and I were the two. So back then, there weren't co-first authors, so we

were definitely equal on all of this. But Emil was the one who finally said, "Why don't we just go and do this?" So we had had the system and we'd kind of been going around the edges, and he just said, "Why don't we just come up with this? Let's just do this experiment." And so it was a team effort of Bruce Babbitt, myself, and Emil that did this.

Williams: And Emil gets the Lasker.

Allen: Yes. Oh, absolutely, because he had done the antigen processing, too, before, that he had shown that the antigen presenting cell had to handle that antigen, it had to go through an acidic compartment and needed proteases and all of that. So it was definitely he had been working in that field and continues in that field.

Williams: So you were only at Harvard for one year, is that correct?

Allen: No, I was there from '81 to '85.

Williams: Yes, now I see that. Yes, I'm sorry. Right. Then you moved to Washington University.

Allen: Yes. So Emil then was being recruited to become chair of pathology at Washington University, and so as a funny aside that there are not very many secrets in immunology, in science, so Emil, we always knew where he went on meetings, and then all of a sudden, one time he disappeared and he wouldn't say where he had gone.

So then I had heard Wash. U. was trying to recruit John Niederhuber, my thesis advisor, into surgery, and they were using Emil as a bait for him too. So I find out from behind the scenes that Emil was being recruited.

So then Emil accepted the job and then took some of us with him. So I thought I wanted to go on a tenure track and be an independent investigator, so that's when I started in 1985 as an assistant professor.

Williams: You were then an instructor at Harvard, is that correct?

Allen: Yes, the last year. So I moved pretty quickly. So after the postdoc, I was an instructor and had a little tiny lab and one technician, and so that was the next step up. I think Emil took faith in me, I guess, a bit, because I was still pretty young and green.

Some of the problems were that most of us go into science because we like to do experiments with our hands, and then the skillset you need as you move forward is—I don't do experiments anymore and haven't for a long time, because now you have to manage people and write grants, etc., and write papers. So it's that

transition that takes a little bit of leap of faith at times, hoping that people have the right stuff.

Williams: While you were doing your master's and your Ph.D., were you ever asked to take a course on how to be an instructor?

Allen: No, there was not—

Williams: How do you walk in the classroom the first day and—

Allen: So one thing is back when I was a grad student, the funding mechanism was a little different, so I had to teach every semester. So I taught like twelve semesters of microbiology courses. They're mostly lab courses. But now our current students teach one semester, and so I got a lot of experience there. But it's still, you learn on the job, but I think being willing just to talk to other colleagues, because that was the best thing I had is when you had people at the same level, because they don't teach you like this crazy stuff, like somebody in your lab falls in love or out of love or somebody has bad hygiene. You know, how do you have conversation with those? But it's just talk to somebody else and then together you can realize, "Oh, yeah, this is what I should do, or just ignore that one."

Williams: And I suppose you acquire the management skills pretty much the same way, by experience and osmosis.

Allen: Yes, yes, and making mistakes. But, yes, it is too bad that we don't give a little more guidance in stuff like that. I try to do some with the postdocs now if we have the resources for them to interview and hire a technician, but in my laboratory. So then there's a structure to it, but then at least they have somebody to answer to and to direct and to learn how to deal with when they're sick one day. Well, you have to pick up the slack, and you can't be mad at them for being sick and stuff.

Williams: Otherwise, what were your five years at Cambridge like? What was it like being there at Harvard?

Allen: Oh, it was wonderful. It was really—you know, you'd heard these stories about the hypercompetitive environment there, but I think it's only in the context that the structure is very different because there you had a full professor and underneath you had associate professors and assistant instructors, etc. So each lab was maybe twenty or thirty people, and so you were self-sufficient, more or less.

So I think the best example was when I was talking about peptide binding to MHC, that we never shared that with any of our colleagues at Harvard. We had competitors there. And so we released it at the 1985 AAI meeting in Anaheim, was the first disclosure of this. So it was pretty exciting, but that was the kind of—but I didn't mind. But it wasn't always people didn't talk to you, it was just

there was certain labs you got along with and then you developed a lot of close contacts and colleagues from that interaction, because there were so many people training there. So it's an amazing institution.

Williams: Niederhuber did not go to Washington University, is that right, or did he?

Allen: No, he ended up becoming chairman of surgery at Stanford, so that was the one.

Williams: But you and Emil continued your own relationship, really.

Allen: Yes, well, my intention was, because I had started this project with the lysozyme, but it was so moving, I didn't have a separate project to spin off. So the question is, so I was going to go there for a like a year or a bit, kind of work, carve out my own part and then move to a different university, was my original intention. So obviously, I was completely wrong on that.

But because Emil I had some frank discussions and were able to carve out how he could have what his lab was known for and what I'd brought, but then also something that I could work with and that we both could play in the same sandbox. And it worked out great because he was very—respected me and the territory and the boundaries, and then it just, after a couple of years, then people could evaluate me on my own, so then it was pretty easy to stay.

Williams: And it's been twenty-nine or thirty years that you've been there.

Allen: Yes, exactly. It's pretty shocking that—because I do have—I used to have the throwaway line when you're interviewing grad students, "I've been here a long time, you know." Now, they weren't born when I started at Wash. U.

Williams: So talk about that span of time in terms of like structural changes in various departments that you've been involved with and so forth. Is there sort of a timeline there that is of interest, or not?

Allen: I think that Wash. U. had some immunology when we got there, but it was headed in maybe the micro/immunology department, and a lot of their key players had been recruited elsewhere, so they brought Emil. Then I think, you know, not speaking too arrogantly, I think we're one of the top handfuls of immunology programs in the country, and Emil has to get all the credit for that. So he just singlehandedly brought in people, spent time, just all the effort a leader has to do to bring this in, set the standards high for what we expect.

So the community has really grown. So we started out. I was one of the few, the first two hires, and then it's just grown, and so now it's huge. So it's fun to see that grow and how to maintain it. When Emil was the chairman, I don't know, till maybe ten years ago, and then he had to step down for an age restriction, and he's still going strong research-wise, but then you're always worried, well, what's

going to happen after Emil? But a new chairman came in, and things have continued. So we built up the community, and it's nice that it's self-sustaining.

So I think it was fun being part of that, where you could really build on it. A lot of us were at Harvard, and so we behave a little differently in St. Louis than we do. If you put us back in Boston, we'll go back to that model and we can exist in it just fine, but in St. Louis, it's a little more collegial, and so that's just kind of the standard that's when you do—a student gives a work-in-progress talk, there's never any discussion about, "Oh, let's not talk about that, because somebody might take our idea," where at Harvard those discussions did enter.

Williams: Other differences between the two institutions?

Allen: They're so different, because I was at Harvard Med School on the Boston side, but it's so enormous, the number of people there. So it's probably not fair comparing the whole enterprise. I was at University of Michigan, which was a public institution, then you went to Harvard, which was just the most wide open, and then you go to Wash. U., which was private, but it's a little more constrained. It has some Midwest judgment to it. So I think the combination of those. So I think Harvard is basically you can do whatever you want, but you have to bring 100 percent of your funds in, kind of stuff, so there are a lot of incredibly bright and motivated people there. Then at Wash. U., there's a little more institutional support. I mean, we still bring in a lot of—you know, but there's still kind of a different business model. Like Harvard would build a building on debt service and say, "We'll just fill it up with bright people." And Wash. U. will save money and build a building when they have the money and then fill it, kind of stuff. So it's just different business models.

Williams: This may be a naïve question on my part, but what is the relationship between pathology and immunology? Where do they kind of cross?

Allen: Good question, because at Wash. U., pathology was considered a basic science, and in a lot of places, it's not. But the department was always known for its basic science. Our previous chairman was a man named Paul Lacy, and so he was a leader in diabetes and islet cell transplants. He had kind of set the standard.

So I think that was why Emil was attracted by the job, because even though he was trained as a pathologist, he's a researcher. So he did the other part to provide departmental resources to run the clinical labs and those decisions. But it was more, I think, reflection when we first got there, was just the Department of Pathology, and then maybe fifteen years ago they changed it Pathology and Immunology. So I think that was reflecting that immunology had grown up in that.

So almost all the processes that you see in immunology, autoimmune diseases, and infection, they're pathological processes. So I see, even though I'm a Ph.D.,

my clinically trained colleagues are wonderful, the insight they have into pathology and the training and stuff. I have so little contact with the clinical side; it's kind of like two worlds. So there's some crossover, but I guess I benefit from the clinical department because there's a bigger department budget. There are more resources because of that. So I think Emil was very good at balancing the two, between the clinicians and the researchers.

Williams: You never have longed to be a clinician?

Allen: No. I think when you start at undergrad, some people—I thought about this, and just once I started working in the lab, that's where I found my calling. I mean, I get more of an appreciation, but I look at it now and it's so hard to do both, so I think I got lucky again. I always joke with the lab, I said, "If I would have gone to medical school, I would have ended up as a pathologist doing research." So I don't know if that was—maybe I would have a little broader training here, but I would probably ended up in the same spot.

Williams: Is there anything to say about the Robert Kroc endowed professorship? Can you just explain?

Allen: Oh, sure. It turned out that was a chair from Paul Lacy. So, an interesting story. So Robert Kroc was a brother of Ray Kroc, who was—I don't know if he was the founder of McDonald's, but the one who really put it on the map. So he was a scientist, worked at Warner-Lambert. His brother set up a Kroc Foundation to study autoimmune diseases, like rheumatoid arthritis and diabetes and multiple sclerosis, because that had affected family members. So he'd given originally three of these endowed chairs, one to Harvard, one to UCSF, and one to Wash. U. So when Paul Lacy stepped down as the chair, his chair became available and then I got it.

So I went out one time—my family lives in California now—and Robert Kroc, who was ninety-eight years old, and so I contacted the family and I wanted to go and meet him up in Santa Barbara. He was a delightful man. You can speak freely when you're older, and like that, and so he would just tell stories about like he was at University of Indiana first.

I said, "How did you do research in the summer without air-conditioning?"

And he said, "Oh, we didn't. We moved to Woods Hole."

Then these kind of stories where you didn't realize research before NIH. He grew up in Oak Park in Illinois, and his family, they knew Frank Lloyd Wright, and he would talk about how Frank Lloyd Wright was an interesting guy but his family life was a bit of a mess. So he would just be honest about that stuff. So I enjoyed meeting him and telling him about the support and stuff like that. So people tease

me about it, because it's named after a hamburger chain, more or less, but it's a nice endowed chair, and I'm really appreciative I've gotten it.

Williams: Let's talk about your science now for a little bit. I think you've probably covered a good deal of it already, but namely about the earlier stages. What have been the accomplishments in more recent years in your career?

Allen: Yes, I think it stems from something we were talking about previously, when Emil and I were—I was trying to carve out my own niche. So we'd known that MHC molecules bind peptides, but at that time we didn't know if they could distinguish between a foreign peptide or a self. Because that's the hallmark of the immune system is it has to distinguish foreign from self. So it's easy to make an immune system that can recognize everything, but then you're going to attack your own body. So how do you develop that fine balance?

So I said, "Why don't I look at self peptides binding to MHCs." So that was where I took off and started this own little line of research. So I first showed that the MHC molecules didn't distinguish. It didn't know if this was a lysozyme from chicken egg or from mouse. It bound them the same. So now I had a fundamental change about how that—and that's where I've taken off of trying to look at how the immune system handles self-antigens and what's their influence in the whole development of the immune system. Because most of us are healthy.

So an antigen-presenting cell in these MHC molecules, they want to have a peptide bound to them. They need to, to be stable. So if you're not infected, their only choice is self-peptides. So you could say, "well, that's just kind of a placeholder till an infection happens." But, no, it really turns out that those self-peptides play an important role in developing your immune system and maintaining it. So that's where I've spent a lot of my career is really working on that fundamental aspect of T cell recognition of a self-peptide MHC.

Williams: And what practical applications derive from that?

Allen: Let's see. I guess if I'm being doom and gloom, I guess we don't have any direct things yet. I mean, it's understanding of how to prevent autoimmune diseases and how to stimulate immune response when you want to do that, so it's two sides of the same coin, so by understanding the basic processes.

So now because if I sit on an airplane and somebody asks, "What do you do?" and I say, "I'm an immunologist," and they say, "Can you do something about my allergies?" You know, we're a little better off, but we still don't understand the basic genetics of that.

Then coming back to this, and now I'll come full circle, is autoimmune disease, we still don't understand some of the components. Because if you take identical twins, same genetic makeup, and let's say they have an MHC molecule that

predisposes them to get diabetes. They live in the same household, they have the same infections, that the chance that both twins will have diabetes is only 40 percent. So there's something else going on here that we don't know. So that's kind of why we haven't been able to make more advances of blocking the autoimmune diseases.

I think most of that is due as your immune system is randomly generated, so Twin A and Twin B will have the same genetic makeup, but their immune system is randomly generated by fragments of genes put together. So from those, maybe one has a few more T cells that might be autoreactive, and then they're not going to cause disease, but then when they both get the same infection, those T cells might then cause a disease. So, fortunately, I think we're getting closer and closer, but it's hard to disrupt the whole process because then you would be sick. If you eliminate CD4 T cells, that's what HIV did. So it's hard to target an intervention at this point.

So I'm trying to think of other things. Yes, the autoimmune diseases have been really hard because you treat the symptoms so you can do that, but you don't yet treat the underlining causes.

Williams: That's just the point at which the science is today.

Allen: Yes, exactly. So we know so much more, and you're getting closer and closer, but a lot of the grants and work is we've learned a lot more. We understand the subtleties here.

Williams: You mentioned AIDS. Have you done some work in that area? I know you're on a review panel for AIDS.

Allen: I did a little bit of work on that when they were opening the floodgates to get as many people in. So I worked on mouse models. I wasn't looking at proteins and epitopes, but I was not a serious—on the review panels I was serious, but the researcher, it was just you realize you have to do it in a species that really infects. You have to do it in human cells and then the SIV model and in monkeys too.

Williams: But then your career has taken you to a few other areas, like the IBD [inflammatory bowel disease] research, right?

Allen: Yes. I had gotten interested in cancer immunotherapy from one colleague, and so I'd made a mouse model of—they had T cells against a tumor. So the idea was that—some of it had been championed around NIH, adoptive immunotherapy—I could make a T cell against a tumor, then you keep putting them in enough and you can eliminate the tumor. So we tried to do those experiments, and we never really got to do a single tumor experiment because we realized that there inhibitory cytokines that we thought—let me back up.

So you could eliminate the tumor if the T cells were there ahead of time or the tumor was small, but once a tumor got to a certain size, no matter how many T cells you put in, the tumor ignored them. So we thought maybe the tumor was making inhibitory cytokines that a T cell would come in and then it would shut them off. So there were two of these: interleuken-10 and TGF-β [transforming growth factor-beta]. So we made mice that didn't have those, respond to those, and that's when we didn't do any more tumor experiments, because these mice got a wonderful model of colitis.

So this is like I was telling you about the collaborative nature of Wash. U. So I didn't know one end of the colon from another, and so I just went up to a young colleague, Thad Stappenbeck, and said, "Thad, we have this interesting model," and he got so excited. Then we did this as a collaboration with my grad student spending much of her time finishing up the project in his lab and so then his grad student who characterized the model. And there were a couple features that were just like human diseases: it was 100 percent penetrant, so all the mice got it, it looked like human disease; and we could cure it with antibiotics. So then it was saying that it was a bacteria and then we could transfer it with T cells, so I was interested. And so then the next grad student figured out what the bacteria is.

So now we've gone back and forth, and it turns out we wrote a grant together, NIH, and it's still wonderful because he's more the inflammatory bowel disease person and I'm the T cell person. So that's one where serendipity comes in, and, we were talking earlier about chance favored the prepared mind, because our mice got sick, you go "Hmm. I wonder what that is." So we could have kept trying to do tumor experiments, but then that took us off in a complete different direction.

Williams: In preparing for this interview, I kept running across the term "self-tolerance," and you have to tell me what that is.

Allen: That's the process where your immune system doesn't respond to self. Because what you do is, I was telling you that when your immune system, you take a bunch of T cells in the thymus and you rearrange all these receptors. So then from that, it's a process called positive selection. So what you have to do is we're talking about how T cells can only see peptide bound to an MHC molecule. So it turns out that they do that in the thymus, seeing what MHC molecules are there, but you don't know what your foreign antigen is going to be because you can get any kind of bug and you'll make an immune response to it. So what it has to do, it's an anticipatory immune system. So what it is is one of these self-peptides that somehow has to, to a developing T cells says, "Oh, okay, you can see antigen on this one." So it's kind of like a surrogate. So that's a process of positive selection. So you pull from all these randomly rearranged receptors. You pull out the good ones that can see something.

And then the problem is some of those could then recognize yourself too strongly, so this is where that self/non-self discrimination and self-tolerance comes in,

because then there's a process in the next stage of the thymus; it's called negative selection. It's like a filter. You rearrange, you get these T cells, then they grow up. Then all of a sudden, if they're going to respond too strongly, they get killed. Then the ones that pass that test then come out into the periphery, and then that's your immune system.

So the self-tolerance process, that if you made it so stringent, the problem would be that you're not going to have enough immune system to recognize every potential pathogen. And so there's always some T cells that are just kind of on the edge of being self-reactive, and then there are other mechanisms that can keep that in place. So this is the whole process of self-tolerance is purging the T cells in the thymus to not recognize self.

Williams: So it's a good thing.

Allen: Yes.

Williams: Good. Let me ask you about disappointments along the way in your scientific career. Have you had some real down moments?

Allen: Yes. Yes, I think there's obviously ups and downs in science, and some of those are where you go off in the wrong direction. You try a project—and the beauty of the NIH system is that you can write a grant, and you don't have to do exactly what you're going to do. You have to be productive, you have to publish papers, but they don't care if you take a turn.

So some of the disappointments are where you start turning and then you get further and further away from your core competencies, and then you're not doing science to the level that I feel comfortable, or the quality. So I got that a bit, and I did a lot on arthritis, because it started out as a T cell model, but it started getting into neutrophils and stuff. So at the end, it was hard to do experiments and things like that.

So other things mostly, I guess real disappointments are grants—that's where you learn—and papers and that kind of rejection. I'm trying to think of—I've been pretty lucky in continuing on that science. I'm not trying to be Pollyanna-ish, but, I mean, I think some frustrations are when you realize that a project is going along, and then the person graduates or moves on, and then you lose a little momentum. So the question is, do you keep going on or do you go another direction, a little turn?

Then there were a couple times when you could have made more hay. Somebody else made more discoveries in an area because you were really close but just didn't push far enough, stuff like that. So those are some of the disappointments. But there are not that many, and you realize it's going to—I view scientists, each one of us, as a catalyst. We make science go a little faster, but it's going to happen

with or without me. I'm not egotistical enough to say that these peptide-binding MHC, it would have been discovered by others very quickly after that too. So I think that's how I view it.

So I haven't had any really major setbacks. You know, sometimes you get disappointed that some of your most talented students didn't go into academics, more for family reasons, not from the science aspect, but other things going on. So you feel a little—those are kind of setbacks because you put your heart and soul into training them, and you want them to do well, and they're doing fine, but within the academic world we kind of view replacing ourselves with like-minded is an important process.

Williams: Talk a little bit about your merit grant. What was that like?

Allen: Well, that was a really pleasant—that they had started this a while ago, because the NIH grants were only ten years, five years, and then what they did was they decided for—at least in the National Institutes of Allergy and Infectious Disease, you get once in your career. So a certain group of people get a merit award. So it's basically that's what my one grant I'm still in now, almost year twenty-nine or something. That's the one I first got when I was a junior faculty. That's the same grant you got a merit.

What it allows you to do, instead of five years, they give you for ten. So halfway through, you have to do kind of check in and make sure things are going okay, but it's just a really nice time when your things are cooking and your lab is going, and they just feel that this is—it's an acknowledgement, but it's not a reward. It's just allowing you, instead of having to stop time and write grants for that one, why not give you a ten-year time, because you already have a track record, and that you're going to continue to be productive. That's what they expect.

Williams: So that was '02 through '11.

Allen: Yes, and it just shows up. It's not like you apply for it. I think they look at the grants, and you can only have one, and they look at it, and then they just all of a sudden they call up and say, "Hi, we've given you a merit." So it's one of those wonderful phone calls.

Williams: Like MacArthur.

Allen: Yes, yes, exactly.

Williams: And that program is still going on today?

Allen: Yes, exactly.

Williams: Shall we move on to talk a little bit about AAI at this point, or are we leaving some things—

Allen: Yes, I think that would be—

Williams: You joined the AAI in '85, I think. I wondered why were you not a member when you were doing your postdoc years?

Allen: Oh, I think—

Williams: I'm not trying to embarrass you.

Allen: No, no, I was always—I think there was less push to get trainees and stuff, so I would subscribe to *The Journal of Immunology*, and then you were a student trainee, but you weren't a full member and stuff like that. So then it was just I think you had to be nominated, and then you had to have a couple papers to become an AAI member. So I remember I had one out of my graduate career. So I finally got those, and then I became a member.

So I'd always attended the AAI meetings or the FASEB meetings, so I've been going to those since—wow. The first one was in Anaheim in 1977 [ed. Anaheim meeting was 1976], something like that. So they used to have some in Atlantic City, so I missed those, but then when I started moving around—so I've been an active participant, but I just didn't, I guess, formalize it till I had enough papers.

Williams: What about today in the organization? Are students more welcome now than then?

Allen: Yes, I think it was even a little bit before when I came on council that there was a big push to increase the membership and to maintain it. So I think you have to realize you have to get the young trainees and the postdocs members. Now with mine, I always—anybody in the lab, I pay for their membership. So instead of them saying, "Oh, I don't want to pay this," or, "I don't want to do this," I said, "Look, we're all signing up because it's our professional organization." So I think that that didn't happen back in the seventies and stuff like that. There was less push from the organization and trying to maintain and increase the membership.

Williams: When I attended the Boston meeting a couple years ago, I was just amazed at the poster exhibits. I mean, so much activity going on, and I suspect a lot of those were trainees and people very early in their careers.

Allen: Yes, I think it's really important. It's our meeting as immunologists and it's a chance where somebody young in their career can get a chance to, if you have a good presentation, you give a talk. Because a lot of these big meetings that you go to are keystone meetings, the program's set. So you can give a poster, but

there's no chance of giving a talk. Well, here, if people read the abstracts and like that, this is how you get your feet wet, and you start at a national meeting. So I think it serves a really important purpose.

Williams: You were an editor of the *Journal* on two occasions. Are there any recollections that you'd like to share about that experience?

Allen: I started out and I was a section editor for the antigen-processing part, and so it was fun because it was my first editorial experience. It was before the *Journal* review process had become electronic, so it was sending things by FedEx and doing all this and calling and faxing, so it was much more cumbersome to do it. And you're more limited on who you could ask for reviewers because you wouldn't send it to Europe because it was really too expensive and stuff like that.

So it really got my feet wet for that, and then it really helped me—I'll come back to being deputy editor. But in between, from '97 to 2000, I was one of the four editors of *Immunity*, and so my *JI* experience really helped me with that, because this is the other thing where you write reviews, but you're never wearing the editor's hat. You don't have much experience. But I did have one where you look at the reviews, and it's amazing how few times there's concordance in the reviews, and you have to decide are these arguments worth, or are they being harsh, or is there an agenda and stuff like that. That really helped me to do this other, the *Immunity* part.

Williams: What does it mean being the deputy editor? It sounds like the Wild West a little bit.

Allen: So what they do is divide up the work, because there's so many manuscripts. So what they do is there's an editor-in-chief, and they mostly do all the really thankless things, where there's fraud or making decisions and keeping the thing going. But all the decisions are made by the—I think there were maybe eight of us, or ten, deputy editors. So basically there's a section editor who solicits reviews, and then what they do is then they take those and they write a summary, and that goes up to the deputy editor, and then they make the decision. So you really are an editor, but not under the official structure.

Williams: Then any recollections about the time, I guess, three years you were on the Awards Committee of the AAI?

Allen: Yes, it's one of those where it's hard, I mean, because you're judging your peers, so it's real easy to say you don't know any and you can pull out these, but now you're trying to decide which peer and with a few awards. So it was really eye-opening, looking at who could write effective letters of recommendation for this and, like, why is this person a good mentor.

I remember things we were debating about how do you define mentor, and, you know, these were all done by phone conversations. We had really lively conversations, because if you define it as success of how many people you put out there who have been good careers in academic medicine or industry, or is it that you're warm and fuzzy and hug and everybody loves you and you're really at a personal level? And both of them of them are right; it's just how you view that.

So that was what my biggest recollection was, that we would have big differences of opinions on the committee, because there would be some of these names that would fit into the former one or the latter. You could say, "Oh, they're obnoxious," or, "They're really harsh on their trainees." But then if you're looking at success, some of these people had trained an amazing number of highly successful scientists.

Williams: How does the awards systems start? Is it through nominations, or does the committee itself look at certain people? How does the process begin?

Allen: It's only through nominations, at least when I was involved. Then I don't know if it still does, the council still has the veto power kind of thing, that it's still making recommendations. So they have different awards, and they keep added those where there's distinguished career, and mid-career, and young investigator. People nominate them. Then there are more than qualified ones, so those can roll over, because I think they realize that somebody just missed—they ask letters again from somebody, "Why can't you just recycle the package the next year?" Then they have a whole package, and then you have a long phone conversation, I think is what it is.

Williams: Then you were the AAI representative to the international union [International Union of Immunological Societies]. What was that experience like?

Allen: That must be on paper only. I was officially on that one, but really, you know, because there's the AAI, there's this international organization, they have every three years an international congress [International Congress of Immunology]. So we're one of the U.S. representative of that. So this is where it's much more worldwide political, about where the locations are and stuff. So AAI, we participate some, but we're a little bit more on the edge because we get outvoted. That's the reality of things, because of where they're going to be going and stuff like that. So we spent some effort on that, but not a lot.

Williams: I was going to ask you about international versus domestic issues and perspectives and whatnot. Do you have any thoughts on that? It's a big topic, I know.

Allen: Well, you know, each country and region does science a little differently. There's always a question of how inclusive should it be. Is it American Association of Immunologists? And we thought here the criteria, anybody can be a member, and you get a reduction on your pages for charges for *Journal of Immunology*. So I

think AAI made the decision that we could be an international organization. So I still think it's the strongest and the biggest of those, so I think it has a prominent place. Also where the U.S. is in biomedical research, we're worldwide, but that's changing, you know, and if the funding situation kind of stays in the same vein, we could lose some of our prominence and stuff like that. But I think there were some of these where it was the international politics that AAI tried to stay away from, if you're having somebody who's a scientist who's being persecuted by the government or something like this, I think we decided as a society that's not a venue we wanted to get into.

Williams: So in '05–'06 you were president of the organization.

Allen: Yes.

Williams: Looking back on that period, what do you consider the highlights?

Allen: So I think there was the NIH doubling, so there was movement trying to get more money into Congress, and then one thing is with Lauren Gross and other AAI staff, I got aware of that, you know, you go to these staffers on the Hill, and you just want to argue, like I want a success rate of grants to go from twelve to thirteen. It's very difficult, but you say, "Let's double the NIH budget in five years." They had a good message, they got support on both sides of the aisle, and they agreed to that. So from '98 to 2003, the NIH budget doubled, and so that was a wonderful thing. So you started putting more money in, and it was pretty much proportional over the years.

So then where I came on council was then the question is, when in 2003 we hit the doubling, now what happens? So my presidency was, vice president, right in there, was like how do you hit, is it a soft or a hard landing? So that's where the real intrigue went about what was going on, and so that is what I most remember about that.

We'll come back to another issue about publications, because we would have to go and lobby Congress, and this is where another one of my eyes were opened about, that both sides of the aisles have votes. So I have to put my own personal political views aside and go and try to convince them to increase money or keep the money going. So even before I was president, you would go and try to lobby to make sure they maintained the doubling. But then the question is trying to get them to not have—you know, if we just stopped it or keep going a little, then it was going to be a hard landing, and that's more or less what happened because then the country got involved in other things and other priorities. And so I think this was a hard part, a hard time when the success rate was going up, the grants, because previous to that, when NIH has to deal with budgetary constraints, they work really hard at it and they do the best they can, because how do you do it?

So some of this, what they do is they trim down. You might be awarded a grant for 250,000, but I'll give you 225,000, and then if I have nine of those, I can then fund another grant. So they were able to do that. And then with the budget doubling, everybody's budget went back up to what it originally was awarded. So it really was really a wonderful time because the pay lines were about 20 percent, which is about probably the good comfort zone, because much above that, you're funding not the best science. So it was exciting time to be in that.

Then when my presidency hit, then you're spending all the time trying to go and trying to convince Congress. We had lost some of the real champions of NIH. There used to be [Senators Tom] Harkin, [Edward] Kennedy, used to be—let's see. Who else were some of the other ones? George Miller in the House. There's a couple of other ones here that they really liked NIH, and Arlen Specter was another one. Then those all seemed to be moving on, and nobody else has come back. So then this has been the hard part, that everybody likes the idea of NIH and biomedical research, but then there are just other agendas going on.

Williams: So when was the last year of the doubling?

Allen: 2003. I understand it's Washington and it won't happen, but if you just told scientists they could get a defined cost-of-living increase with NIH, no more, no less, they could live with that because then you have kind of a defined budget that goes up. But now it's so hard because you'll get more money one year, but these are five-year grants, so then it's a long process to not overcommit and stuff like that.

Williams: Right. These issues became really salient while you were on the council.

Allen: Right.

Williams: And I didn't ask you about your experiences on the council. What was that like?

Allen: Well, that was good. I really liked—when you first hear it's like a seven-year process, you kind of go, "Wow, that's a long time," but you realize it really is, because you kind of go through the experiences, so you're four years as a councilor and you just hear the budget. When I first got on, it was just coming out of previously that the society wasn't in good financial straits, and I'm sure you've heard from other ones that it had no reserves.

So then Michele [Hogan] came along, and then others, and they started. So I was in the part where they kept building up, and the goal was to get one year operating funds. You can see each time you're on council, you're getting there, and you understand. You went through the budgets, and you're involved. Then by the time you got to president, you've done this for five years, so now you understood how it worked and what decisions had to be made and where you put your effort.

Williams: So some of the other issues in your year of presidency, what else were you dealing with besides convincing Congress they should give you more money?

Allen: Well, one of the issues is open access in electronic publishing, because it was just starting to come out, and so the business models were complicated. So AAI fought pretty hard, because there's currently now in its existence that what you have to do is when you have a published paper that's supported by NIH dollars, that you have to send a copy to the National Library of Medicine, and then that's publicly available after each journal has maybe after six months or something.

So, my understanding, all this originated from is some congressman from the Midwest, maybe Oklahoma, had some niece who was trying to do a report, and she looked up something on the internet and found this, and then it said, "You have to buy that article for $25. You don't have access to it." So I guess she tells her uncle, who then starts this whole thing.

So this was a big issue, too, that we took a stand that this was really not necessary, because who owned this? It just was a matter of timing. It's not that this is not publicly available, but to have a journal viable, you can't give your content free. So it was this whole electronic publishing and all these issues about in journalism. So we spent a lot of time on trying to do that, and NIH was trying to work through what should the requirements be. So they still have that requirement. Everybody sends these papers here. I don't know how effective it is.

Williams: And it's still the six month—

Allen: Well, I think some journals are instant, and I think each author can do a little bit. But it seems like it's shaken out that the journals now have adjusted to the electronic world, I think, because it was just the beginning of all these discussions about like *The Journal of Immunology*, because to make your first printed copy costs a whole lot, and then each one is very little after that. So what's the archive if we say we're only being electronic? Back then, you kept going from floppy disks and the storage media and stuff, so it was a very scary thing to say we're not going to print a paper copy. We got some advertising revenue and stuff. So there were lots of really interesting discussion about this, about the fast-moving field and how this affected it, because that's a big source of revenue for the society is the *Journal*. So you didn't want to lose that. And it's also important for society to run a journal, not a for-profit company.

Williams: I think you dealt with the reauthorization of NIH during your year.

Allen: Oh, yes, that's right, because that was the one where they were always worried, because every so—I forget how the periodicity, because then that was the one could they change all the rules, because they can change anything, because the big one they were always worried about is NCI. Because of Nixon's War on Cancer, the National Cancer Institute has its own separate budget, and that's coming from

the reauthorization. So the money's all in one big pot from Congress, but they're viewed as differently. Where the other ones come from the Institute director down to the institutes, NCI is different. So there were all sorts of worry about that's going to go away or what's going to happen, and they talked about merging. Because there was so many different little institutes, why not just put them together? But then there's a bureaucracy. So there was some discussion, but it went through and we sent letters and things. But it was mostly beyond us, I think.

Williams: And Congress didn't do—

Allen: No, I think they reauthorized just the same old, same old. They didn't really change much.

Williams: Then there was a move to centralize power in the NIH in the director versus the institutes' directors.

Allen: Yes, that was the one, because previously the NIH director had no budget or a little tiny budget. So then that was always an issue, because money is power in this. So they got the director's fund, and he would tax each of the institutes, and slowly it's getting more a powerful position. The institute directors are still very powerful. So in immunology, Tony Fauci has been an amazing AAI member forever and stuff, and so he's been great. So I think that was critical for the power structure, and I think that's why probably reauthorization didn't change much, because I think the power structure works, but the director was able to carve out a little bit of funding source that then they could have some initiatives or have some control.

Williams: And AAI's position on that was what? They were in favor of it?

Allen: No, I think we probably weren't. Boy, I mean, if I had to guess, I think that would be probably not.

Williams: Another thing you wrote about in your presidential messages was developing and keeping young scientists.

Allen: Yes.

Williams: You've expressed that quite clearly, that you were concerned about retention, I guess.

Allen: Yes, I think it's still a real big concern. I think we do a great job of training, but then it's that next level, like I see it in my students and postdocs that they look at what I do and how hard it is to get funding and stuff, and they're just trying to say, "Gosh, is that the way I want to go?" So I think we're really losing not a whole generation, but I think the best and the brightest aren't always going into academics or research.

Williams: But they are finding places to go.

Allen: Well, I think the Ph.Ds., right, will, but then I think we're also losing even at the graduate-school level, that they're going to go into computer science or they're going to go into something else instead of going into biomedical research. And I think some of that has to start way back in junior high, like we were talking about. I'm the Sputnik generation, so I don't remember my parents saying, "You have to go into math and science because of the Sputnik launch," but I think there was an emphasis on that.

It seems like we don't want to have a Cold War crisis to do that, but somehow we have to spark to get the young kids really interested in this research, because, you know, most of the people who are successful, it's a passion. You love science, that you go into it because you want to know what the answer is. So there are a bunch of people who have that, but we just have to make sure we nurture that and get them and get them interested in that, because I think it's a good career.

I got really lucky. I get to do interesting science. It changes every day. It's not like the same thing I learned in college is what I'm doing today. I always view as like an accountant. Could you imagine? It would just be like what you learned is more or less what you're doing now. I mean, science is so different than from when I graduated, and so that's what's exciting. But then there's some things that don't change at all, so it's kind of a combination.

Williams: What do you see as challenges ahead for AAI?

Allen: I think the real thing is trying to make there an effective lobbying, I don't know, thing or just an advocate for biomedical science in unison. Because the problem with the FASEB that works, because if we just go to Congress and say, "Support immunology." They're not going to do that. They've worked really hard not getting earmarks. But how do you support all of NIH and how do you get that where there's this budget? It's a really tough one.

So I think that's the real challenge, because without the external funding support, it's just that that's where all the members are, and all the research, the endeavor, and stuff like that. So that has to be the engine that drives it. It just seems that there's so much economic benefit coming from NIH dollars, discoveries that have moved forward, small companies that start out. All of these things fund from that, and it's still a pretty lean machine. We never get enough money to do it, and nobody's getting rich on this. So I think it's really, at least from my biased point of view, I think it's really important to have AAI be an advocate for immunology in the context of biomedical research.

Williams: Do you see spending and leadership going to other countries now? I mean, NIH has been sort of right at the pinnacle of scientific research. Is that slipping, do you think?

Allen: Well, that's interesting. I think there's some—I can use Singapore as an example. I mean, some countries, they say, "We want to open up the money and attract scientists," but I think the question is, is it long-term money? Because sometimes they switch a little. So Singapore brought in a lot of really from around the world people and gave them huge amounts of money. Then all of a sudden five years into it, they decided to change their funding model for doing things. Then some of the people, oh, that's not what you want. So some of these countries, they think they can do it.

But the one thing the world has never really been able to mimic, and who knows how we had it, is our research universities. It's hard to define how do you make one. So if you said, "I gave you a billion dollars, go and make one." It's a really hard—you know, we have this wonderful education system here, and then in that these are formed and you have all this research going on. So it's hard to exactly mimic. You can have research institutes that people can do it, but I still think it's where you have the trainees want to come and the people go, because it's only as good as the people you have available.

So I think there's some movement to that one, and I think we have to be careful, because we could lose some of the edge. But I look at now that we're still training, a lot of our best and brightest students aren't coming from the U.S. So we're attracting them here, and then the hope is we can retain them here. But you can see that if they don't have jobs here and somebody at their home country says, "Hey, you're well trained. Come back." Yes, that could really change.

Williams: How do you describe the current and near future of immunology just in general? Is it spinning its wheels, is it on the cusp of, or stagnant, or not? Where are we?

Allen: Oh, I think it's still in its ascendancy. We've had a few conversations about things we still don't understand, because I think we finally understand a lot of the molecules, but then how the whole process works and how it's regulated and what can go wrong, we still are just at the beginning stages of that. So I think it's still a really exciting time, because I remember Charlie Janeway wrote in this Cold Spring Harbor book in 1989 about are we reaching the asymptote for our discoveries in immunology? So he was arguing he didn't think so. I completely agree. I mean, you look at that from then till now, there's just innate immunity. We've known about it, but now all of a sudden you have molecules, and it's just blossoming. And then that's still in the context of the adaptive immune system.

So I think it's just a really exciting time. That the mouse is a pretty good model for the immune system, where some other systems might not be perfect for doing drug discovery or stuff like that, but with the mouse, it works really well. So I

think then we can manipulate, we can change things, so we can really test these. I think the whole field of cancer immunotherapy now, with all these checkpoint blockades, I mean, this is an exciting time.

If you look at immunological things, there was like TNF [tumor necrosis factor] blockers for autoimmune diseases, and now you have antibodies against like CTLA-4 [cytotoxic T lymphocyte-associated protein-4] or PD-1 [programmed cell death-1] or PD-1 ligand. Those are huge. So instead of like pinpointing when we were talking about individual T cells or peptide MHC ligands, this is more global. And I think most immunologists thought if you had initially blocked tumor necrosis factor, everybody would get sick. Well, they really don't. Occasionally somebody does, but it's an amazing how once you start proving there. So I think it's an exciting time for immunology.

Williams: And you encourage young people to go into the field?

Allen: Yes. I think it's still just—I look at this. You can eliminate an immune system if you keep your research animal like the mice clean. So it's wonderful. You can do so many things, and it hits all sorts of aspects of it. It's not just one little molecular detail. You can look at cellular reactions. The microbiota is now clearly involved when we're talking about inflammatory bowel disease, and so it impacts in so many different other physiological systems and stuff like that.

If it was really simple, we would have figured it all out of how this all works. So I think you can say the complexity is there, but that's what the immune system is there. More or less, it works pretty well. I mean, we get sick. We can't cure the common cold yet. We still haven't been able to make good vaccines. We can make some good vaccines, but other ones we aren't. But now people have been making all sorts of—you know, influenza, because there's some areas that are completely conserved of the influenza molecules, and then if you attack that with an antibody, that can provide protection, and now they've figured out a way to have the immune system just focus on that little part.

So it's a really exciting time with structural biology and molecular modeling and stuff that you can start coming up with vaccines Because I think that's where—you know, you really look at what benefits has immunology done so far, and vaccines has probably been the biggest contribution to human health.

Williams: I've been asking everyone this question. What does a scientist do for fun? What outside interests do you have?

Allen: Oh, I have lots of—I love sports. I like golfing. I just love to travel. So one of the benefits you get being in this business, you get to travel around. So with groups we've done and gone on photo safaris in Africa and gone to the scientific hajj going to Galapagos. So I think doing that, gardening, woodworking. I realize that science is so demanding, I need a break. And so the excuse I say is

making sawdust in the basement is much cheaper than a psychiatrist because I need something tangible to see, like I made something or I grew a plant and stuff like that. So I find that really helpful to me in getting away.

Williams: You mentioned that your family is in California? Is that—I heard you say—

Allen: Yes, I have a sister. Yes, they all lived out there and stuff.

Williams: Anything else you want to add to this today?

Allen: I think I'd like to still talk about a little bit the AAI staff. I think it's just an amazing group of people, that they really are dedicated in their—and I think it's obviously a good place to work, because the continuity. I look here, I haven't been in the building in like eight years, and most of the names look familiar. So I think Michele runs a great organization. Because putting on the national meeting is just so much work, and they put that on, but they keep the thing going, and they run an efficient organization. They do it. They're advocates for us. *The Journal* is incredibly done well. So I think that's what I'd really like, to give kudos to them, too, because I think they're the power behind the scenes that sometimes they don't get as much recognition as they should. But I think that's the one where Michele makes your job easy as being on the AAI Council and president. She tells you here are the issues you have to deal with, or here's a phone call you have to do and stuff like that. So in any organization it's the staff that really make it work.

So for the future, I just am very optimistic still. I think no matter what level of funding, there's still going to be NIH. You know, good science is still being done. You have to tighten your belt a little, but it's wonderful to have the public to support us to go and chase whatever the discoveries lead and trying to make progress and make human health better.

Williams: Is that it?

Allen: Yes, I think that's—

Williams: Good. Okay. Thanks so much.

[End of interview]