The American Association of Immunologists
Oral History Project

Transcript

Matthew D. Scharff, M.D.
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Interview conducted by
Brien R. Williams, Ph.D.

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Transcript copy editors: John S. Emrich, Ph.D., and Charles L. Richter, M.A.
Final edit by: John S. Emrich, Ph.D.

Williams: This is an interview with Dr. Matthew D. Scharff for the American Association of Immunologists Oral History Project. Dr. Scharff is Distinguished Professor at the Albert Einstein College of Medicine. He was awarded the inaugural AAI Award for Excellence in Mentoring in 1998, and the AAI-BioLegend Herzenberg Award right now [2015]. We are at the IMMUNOLOGY 2015™ annual meeting in New Orleans, Louisiana. Today is Saturday, May 9th, and I'm Brien Williams.

So, Dr. Scharff, thank you very much for doing this today, and I'd like to ask you, go back as far as you can in your family background.

Scharff: Well, I can actually go back, my mother claimed, nine generations.

Williams: Oh, dear. [laughs]

Scharff: But I don't intend this—there's a whole huge book of—but the only relevant thing about that is, I think, somewhat amusing, is that there's an ancestor that we claim who was a famous mathematician, and my mother was convinced that—I was the seventh generation, and the seventh generation is supposed to inherit some of the characteristics of the predecessor, and so she was sure I was going to be a mathematician. And I'm completely nonmathematical. I'm just terrible at math and barely could get by school. That was solved when we discovered I was really the eighth generation, if all of this was true, and she was supposed to be the mathematician. So that explains that.

My mother's side of the family were second- and third-generation Americans. My father's side, he was first generation. They came from Germany and from Russia, and I guess we were close enough that education was very important, so that was a key issue with my parents.

Williams: You say "close enough." Close enough to what?

Scharff: Close enough to having immigrated. My father came from a very poor family. His father died when he was quite young.–So my father went to work, quit high school and went to work when he was sixteen, to sort of make enough money for he and his mother and one brother, to contribute to that. So he was very obsessed with not having gotten even a high school degree and that I should certainly get a college degree, and he was also pretty obsessed with the fact that I should become a physician, because where he was growing up, the only people who ate steadily and had a house and a car were the physicians. So I don't know whether it was a mistake, but my first initials are M.D., and I don't know whether that was something he laid on me because of that or not. [laughs] But, anyway, so they were very concerned with education. My mother was a schoolteacher. My father was a salesman.

Williams: In New York City?

Scharff: He traveled. It was with women's clothes, but he traveled to the West Coast. So when he was eighteen or nineteen, he went for his first trip to the West Coast, selling things that were manufactured in New York to West Coast stores, womenswear.

Williams: And did you have brothers or sisters?

Scharff: No, I'm an only child.

Williams: So what about your early education in New York City?

Scharff: Yeah, it was painful. [laughs] So I went to public school, grade school, and I couldn't read. I got to the beginning of the third grade, and I still couldn't read. And luckily for me, my mother, being a schoolteacher and, as I said, their being very concerned with education, she couldn't believe that I was retarded, although the school wanted to send me to a special school because I just couldn't read. It was difficult, to say the least, and so she started taking me around New York City to various whatever there was for people who couldn't read, and, luckily, she got to Columbia Education School. People didn't know about dyslexia, but they'd just sort of discovered dyslexia, and I had right-left dominance dyslexia, and I couldn't read because I couldn't follow the lines. It turned out there was someone there who was studying this, and the solution was that you read down the page instead of reading across the page. So this is now called speed reading. But at the beginning of the third grade, this person taught me how to read down the page. So you don't read all the words. You miss a lot, but you can read. And I suddenly could read everything. I mean, I was reading what were then Book of the Month Club books and so on. So if she hadn't been so persistent, I probably—I don't know what would have happened to me. [laughs]

Aside from that, I wasn't a terribly good student, and they were anxious for me, so I went to public school, I went to a private school in Brooklyn, and eventually went to a private—it was a prep school, a day school in Brooklyn, a very good school, very difficult teachers who really were on you about working, and I was still just really a mediocre student through high school.

Williams: What school was that?

Scharff: It was called Poly Prep, Polytechnic Preparatory Country Day School, and it emphasized Latin and foreign languages and math, which I did poorly at, and athletics. I mean, everyone had to be on a team and so on. It was a very good school, and there were teachers that were Ph.D.s in high school. I had a French teacher who hit you with a ruler if you didn't say things right. I was a mediocre student, but I had an English teacher who was very, very good and inspiring, and, all in all, you got a very good education there, even I. He just told me, although I thought I was working hard enough, that I just didn't work hard enough.

I applied to college, and in those days, Brown was sort of the bottom of the Ivy League. This was a prep school where they took pride that you got into good schools, and, luckily, I got into Brown. He told me that if I didn't really work hard, I was going to flunk out, and it wasn't the first time I had heard that. So when I went off to college, I really disciplined myself and worked very hard and did various things to force myself to study hard, and I did very well in college.

Williams: And did you see a path ahead for a career and life's work?

Scharff: So in those days, parents like mine took you to see some consultant who talked to you and told you what you should be for the rest of your life. So considering my mathematical abilities and they gave me some tests and so on, said, "Well, the one thing you shouldn't do is anything quantitative, like science or math. English is fine. Maybe you should be a lawyer or something like that." So I went off and was an English major at Brown for two and a half years.

I liked biology in high school. It wasn't, in retrospect, very sophisticated, but I liked it, and I took biology courses in college and they really stimulated me a lot. I really loved it. I had to do, I guess, my first big paper that I had to write in college for my biology course was on neurosecretion, which had been discovered shortly before that, and we'll come back to that. But anyway, it really captured my imagination, I loved it, so I switched to being a biology major and a premed, actually.

It wasn't so easy to get to work in a lab, even as a volunteer, in those days, so I didn't. I mean, I tried, and I didn't. But I did well, excepting I didn't have to take math, actually, because I had sort of placed out and took a logic course, and I didn't have to take French because I placed out of that. I didn't have to take that. Those were the things I was terrible in. So I graduated with a very good academic record.

Williams: Dyslexia stays with you for a lifetime.

Scharff: It absolutely stays with you for a lifetime.

Williams: So you were still facing all the challenges associated with that.

Scharff: But, you know, I guess there's all sorts of dyslexia, so because of the kind of dyslexia I had, I had trouble writing on a line, too, but typewriters were there in those days, so it solved that. I couldn't spell, because if you read down, you don't look at individual words, and if you don't look at words, you don't know how to spell them. So my spelling was awful, my grammar was not so great either. I don't feel that I suffered from it greatly, but it's not easy to read scientific papers if you just read down. I mean, now all the words are important, you know, and so I could read fast and I can certainly get the essence of things quickly, but I've really got to struggle to read a paper very carefully.

Aside from that—this is going to sound strange, I guess—I'm colorblind, I'm tone deaf, and those actually have been bigger problems for me in some ways. Colorblindness has been a bigger problem, I think, than the dyslexia.

Williams: In what way?

Scharff: Well, almost anything you do in science, there are colors. So, I mean, one, I suppose, illustration of this was I became a biology major and I took a histology course. So in histology, you look at tissues, and they're stained and you recognize them by the stains and the shapes and so on. At the end of the course, there was a final exam, and after the final exam, I got called in by the teacher, who said, "You cheated on this exam, and we're going to throw you out of college."

I said, "What do you mean?" [laughs] I'd done okay, I thought.

Said, "Well, you got 100, and the next highest grade was 40, and so you must have known what the questions were or something."

So I said, "I didn't know anything. What are you talking about?" You know, I was very shocked and upset.

He said, "Well, didn't it bother you that we changed the color of the stains?" So you can stain tissues with different color stain, but I never saw the colors to begin with. I'm terribly colorblind. I don't see any color. In the tests they give you, I don't see anything. There's an Ishihara test, where you can see numbers and figures. I can't see anything in the whole book. Didn't bother me at all. I didn't know they had changed the stains because I'd never seen them to begin with. I'd learned to look at the shapes rather than at the colors, and it just didn't bother me. It was a breeze.

So, luckily, I had been a subject for colorblind studies in that same department where there was someone had a grant from the navy and he was studying colorblindness, and I was severely colorblind, so I was part of those studies. So it was immediately verified that I was terribly colorblind, and that was the explanation, and they didn't throw me out of college.

But when I went to medical school and when I took care of patients, it's hard for me to see red ears, it's hard for me to see red throats. Early in medical school, my daughter, who was born when I was in my second year of medical school, was complaining about an earache. And, of course, I was going to take care of it, so I looked in her ear and I said, "Oh, there's nothing wrong." And then in the morning, her drum had broken and there was pus on the thing, and my wife has never let me do anything with her. In fact, I couldn't see the red ear. I mean, that's the bottom line.

And these days, all sorts of things are plotted in various sorts of colored graphs. I see something that I know what I see, but often unless the colors are—I'm told that people like me see colors based on the intensity. I've learned that pure red has a certain intensity, and if the stoplights or if the things in the journal articles are pure colors, the intensity is good, then I can see red from blue and so on, but if it's at all off, I can completely mistake it or not see it. So that's really a bigger problem than the dyslexia has been.

Williams: So what prompted your choosing to go to NYU [New York University]?

Scharff: Well, mostly it was the only place I got into. [laughs] So I had an outstanding college record. Those were hard times to get into medical school. We were told there were quotas for Jewish people. I actually don't know how documented that is, but I didn't get interviews at most places.

Williams: You did not get interviews.

Scharff: I did not get interviews. I did get interviewed at Harvard, didn't do very well in the interview. I applied to a number of medical schools. In the end, NYU was the only one I got into.

Williams: And do you suspect there was a quota system?

Scharff: Well, I'm quite certain there was a quota system. I don't know whether my not being interviewed by some of these places was related to that or not. I mean, there are many manifestations of that that were real that I know of. My medical school, Albert Einstein Medical School, was sort of founded because of those quotas. I mean, people were going to be accepted irrespective. Yeshiva University [(YU)], which is the parent university, sort of founded this medical school so that anyone could apply and be treated equally, and it hired a fantastic faculty of very famous physicians, the people who wrote the textbooks in the areas that they were expert in, largely because they could never be promoted to be the chairmen of the department at the places they were at because they were Jewish.

So how do you prove that? I'm not sure. But there was just no chance. And even years later, I mean, I had friends who were my contemporaries who had budding careers in science and surgery, for example, and were approached by the chairman of a department of an unnamed medical school who said, "You know, we've never had a Jewish faculty member in this department. I think it's time we hired one, and we want to hire you." So it was pretty well known. I don't know of any cases where people were sued and it was proven and things like that.

Williams: What year was Albert Einstein formed?

Scharff: So, approximately 1950, ’52, something like that. [Ed. Albert Einstein College of Medicine was established in 1953. The first class started in 1955.]

Williams: While he was still alive.

Scharff: He was alive, and it was the only institution to which he formally gave his name. He came to the opening ceremony. His name is on other institutions but he participated. He came and he had no socks but he had shoes. They asked him why he didn’t have any socks. He says, “I’ve never understood why you need two coverings for your feet.” [laughs] There are these pictures of him at the dedication of the original building. And he said he was doing this, in part, because of the idea that there would be a school that would treat everyone equally.

Williams: You did not apply to that because you already—well, you went to NYU in—

Scharff: I graduated in ’59. So I graduated from college in ’54, and it was just opening. I don’t know whether they had graduated a class yet.

Williams: At?

Scharff: At Albert Einstein at that point. Is that possible?

Williams: Okay. So you were studying at Albert Einstein or you were at New York University?

Scharff: No, New York University. I thought you were asking me did I apply to Albert Einstein. I don’t think I did. I was going to get in everywhere because I graduated with very, very high academic honors, but I didn’t. [laughs]

Williams: So describe NYU College of Medicine as an environment.

Scharff: It was fantastic, actually. NYU also interviewed everyone, and I don’t think discriminated in any way. I should just go back. I mean, there were all levels of this. For instance, Columbia Medical School had taken women for years, and some percentage of their class was women, small, but for decades, whereas other places did not take women. There’s all levels of this sort of thing. NYU at that particular time, especially in immunology, had a faculty that had determined that it was time that physicians were encouraged to do research, and so they sort of did everything they could to encourage us.

I was very interested in doing some research. So the leaders of the school did everything they could. So I got interested in immunology because I had a—in those days when you took a course, there was a lab in every course, so we had a lab in microbiology. My lab instructor, who was a faculty member, I asked him a question, why is it that antibody response is so diverse, which is what I’ve worked

on all my life, and he handed me a book, which was the book by Burnet and Fenner on the clonal selection theory of antibody production or something like that, and it was fantastic. I said, "You know, this is really interesting," and we talked about it.

And he said, "Well, would you like to work on that?" He was not an immunologist, but he said, "I'll help you find between your first and second year a summer research opportunity." And he did. I went to work for a guy, same guy that Jonathan Uhr worked for, A.M. [Alwin Max] Pappenheimer, Jr. In fact, I worked for Jon Uhr. He was a postdoc. I was a medical student.

Williams: And this was all at NYU?

Scharff: All at NYU. I don't know whether you know who Lewis Thomas is. Lewis Thomas wrote *The Lives of a Cell* and other things, and he was chairman of Pathology and then the chairman of [the Department of] Medicine there, and there were others like him. So as soon as you showed any interest and any talent at it, they did what they could to help you find ways to do research, even to the extent of not always going to all your classes and things like that.

So they encouraged me and other people there to apply for something called the post-sophomore fellowship, which the NIH [National Institutes of Health] was beginning what became the M.D.-Ph.D. program, and they offered you, after your second or third year of medical school, $4,500 if you would take a year off medical school and work full-time in the laboratory. You had to have a sponsor. You had to have done something sort of in the laboratory. So I applied and got one, so I took a year off between my third and fourth year of medical school, worked full-time in the lab for Jon Uhr, basically. He was a postdoc and I was his medical student.

Williams: At the time, was NYU offering both M.D.s and Ph.D.s, or not?

Scharff: Yes, there was a Ph.D. program there and there were Ph.D. students, not the way one sees it now, but I'm quite sure there were Ph.D. students. But for various reasons that I'm not sure I understand, they had acquired a number of immunology faculty. Lewis Thomas was one of the most distinguished, but there were others. Herman Eisen, whom you've interviewed for this, was actually a practicing dermatologist in New York who they had given a lab to, and he would come in in the evening and sometimes on the weekend and work in the lab. I was on the same floor, and he was fantastic. He was one of those people you could go and talk to, and he was always interested in what all of us were doing. But others, there were a lot of immunologists. So they encouraged us. The overall environment of the place was very open in that sense, and encouraged people who were interested in clinical research, encouraged students at all levels to do this.

Williams: So your next move then was?

Scharff: So then I had decided I really liked research, it turned out, but I wanted to get an internship and residency, and I did like taking care of patients. I liked it intellectually and I liked it personally, and I liked talking to people. I liked all parts of it. So then I was going to take an internship and a residency, but that was the time of the doctors' draft also. So it was post-Korean War, but there was still a draft, and if you graduated from medical school, you had to go into the armed forces in some form. So I was encouraged by the people at NYU to apply to the Public Health Service for my time, because it had to be done while you were in medical school, at the end of your medical school time.

So I applied for that, and I applied to be an intern and resident at various places, and, again, these same people sort of shepherded me in certain directions. So Lew Thomas called me into his office, I knew him but just in passing, and he asked me where I wanted to be an intern and suggested certain places. I went to interviews, and I got into the Boston City Hospital, which was then a Harvard service, a very distinguished Harvard service at the Boston City Hospital. About 30 percent of the deans of medical schools in the U.S. had gone through there, many of the chairmen of medicine. It was also very clinically oriented, but very research oriented as well. So I was thrilled to get in there, and I went to be an intern and resident.

At the same time I got into the Public Health Service then, because that was the way you got to the NIH. So the NIH was essentially a part of the Public Health Service and part of the Coast Guard. So you could go and have interviews with various people if someone would take you. Instead of going off and being a physician in the Aleutian Islands or some place in some clinic, you could go to the NIH and essentially be a postdoctoral fellow.

So I did that, and, again, this same group of people at NYU, Al [Chandler A.] Stetson, Lew Thomas, Pappenheimer, got me an interview with Harry Eagle, who was at the NIH, because I had sort of in my time at NYU, I had been exposed to what was going on in bacterial genetics at that time. If you read about Len [Leonard A.] Herzenberg, who this award is named after, he went through the same process. A little different, he didn't go to medical school, but he had gone to the Pasteur Institute where [François] Jacob and [Jacques] Monod were setting the tone for modern molecular genetics, basically.

Pappenheimer, who I worked with, who Jon Uhr was working with then, had just come back from five years of having been at the Pasteur Institute with Jacob and Monod in bacterial genetics, and how one could study other things using those tools was very exciting. So I decided I wanted to grow antibody-forming cells in tissue culture and treat them like they were bacteria and do bacterial genetics on them. It wasn't a very original thought. I mean, Len Herzenberg had exactly the same thought. Many other people did.

So the way to do that was to learn to grow cells in tissue culture, and Harry Eagle, who was at the NIH, had developed the media that you could use to grow cells. He was the world's expert in growing cells. So that's who I wanted to go and work with because that's what I wanted to do. So I got accepted there as well. So I did a year of internship, a year of residency, and then went off to the NIH.

Williams: So what amount of time were you in Boston?

Scharff: I was there two years.

Williams: Right. And then to NIH. And then how long were you at NIH?

Scharff: So I was at the NIH for two years. These were two-year appointments. They were your service time. If they wanted you to stay there as a more permanent or temporary permanent member of the NIH, you could do that. What happened to me was that I arrived and I wanted to learn to grown antibody-forming cells in culture, but the day I arrived, Harry Eagle left, and he left to go to Einstein, actually, to form a new Department of Cell Biology. But I was there, and so I was moved to one of the people in his department who was a virologist.

Eagle had had the idea that the way to learn to do molecular biology of animal cells was to use viruses. He was not a virologist. But viruses have lots of protein and lots of nucleic acids, and when you infect a cell, there was, even then, molecules that you could isolate and look at and analyze relatively easily. So I did virology for those two years that I was there. I tried to try and grow antibody-forming cells in culture, too, and I knew some immunology, so I helped other people with immunological techniques, but I basically did virology.

Williams: So did someone else come through then with the other area?

Scharff: No. So I spent the two years doing virology, and then at the end of those two years, I had to make a decision. I was offered by NYU a faculty position at that point, and Eagle, who had left, offered me a faculty position, along with the chairman of [the Department of] Medicine, at Einstein. So I went. So then I had to choose. I mean, my family was all from New York. My wife wanted to go back to New York. But Eagle had founded a really fantastic new department devoted to the molecular biology of animal cells, and he himself was an immunologist. So I elected to go to Einstein.

Williams: And never looked back?

Scharff: I certainly have not looked back. [laughs] I've been there fifty-two years, going on fifty-three years.

It was a very unusual place also at that time. It was new. The school was ten years old or something like that. They had recruited outstanding faculty, and they

had decided to expand the school in the area of molecular genetics, and Eagle was the first one to come and then he recruited other people. A whole new building was built. One of the people [Jacob V. Maizel, Jr.] who had also been at the NIH with Eagle and had come then to Einstein developed a technology called sodium dodecyl sulfate gels, SDS gels, which allowed you to separate molecules by size and not by charge, which meant you could look at almost anything you wanted, which you couldn't do before very easily. You didn't have to be very smart. Before, it was done in ultra centrifuges and it took a lot of skill. This took virtually no skill at all and you didn't have to understand very much. You didn't have to solve formulas, mathematical formulas. Every molecule ran according to its size in these gels, and you could just look at them and know what was going on. So that was a real opportunity there. It was animal cells, and there were analytical techniques, and it was a great place to be.

Williams: And you were also chair of—

Scharff: I became—at Einstein, you're talking about?

Williams: Yes.

Scharff: So I became chair of Cell Biology when Eagle stepped down from that and became first head of the Cancer Center, then associate dean.

Williams: I thought you said that from the NIH you went to Einstein as chair of something.

Scharff: No, no, no, no. Sorry. [laughs]

Williams: I thought it would be pretty young in your career to be chair.

Scharff: I went as a very beginning assistant professor. [laughs]

Williams: Right, right. So over the years, how has Einstein grown and developed and so forth? Give us a portrait.

Scharff: Well, I think these are bad times for Albert Einstein at the moment, very bad times, and for American science, and we're suffering from it. So it was always what we call soft-money institution. It depended upon NIH grants. When I was medical student, grants were just first becoming available, but by the time I was a faculty member, the NIH had Congress and the then administrations had decided to fund research completely. They would fund the buildings, they would build the buildings, they would fund all the expenses, pay our salaries, and so on. So Einstein was sort of built on that business plan. You got a grant that paid for everything, so it had attracted very good people. There was a very open environment, and it enabled us to communicate easily and to do what we wanted to do. Is that what you asked me originally?

Williams: I'm not sure, but it was a very good answer. [laughs]

Scharff: And, you know, because it was so new, we were sort of all young. There were senior people, but a lot of new people had come in. And Eagle was an autocrat, having lived almost all his scientific career in the Public Health Service, actually. He was accustomed to running things the way he wanted to run them, but the way he wanted to run them was that he wanted to attract people he thought would do original things, and he wanted to do everything he could to make it possible for them to do that. He insisted that we share equipment, that we share ideas. If you were one of these people who didn't want to share, then he didn't want you. And because he and some others like him played a very important role as the school grew, people who wanted to build an empire and run a big operation and control a lot of resources, it wasn't a very good place to do that, but if you really just wanted to do your science and you wanted other people who were excited to do their science to also be interested in your work and you to be interested in their work, he set a tone for that.

Williams: That's interesting because you describe him as an autocrat, but—

Scharff: Benign dictators can be very good. [laughs]

Williams: So he didn't get in the way. He actually encouraged.

Scharff: More than that. He encouraged. He watched us. He thought I had data that I wasn't writing up, and so I would get called in and he would say, "You know, you have to write one chapter at a time. You've got data, this is interesting, and now you should write that up." So I was slow at that, so he would push me in that direction. He had nothing to gain from that, but he would push me in that direction. So he looked after us. We called him "Papa"—not to his face. [laughs]

Williams: And this slow rate of publishing, was that also a reflection of the dyslexia?

Scharff: I don't think so.

Williams: What you're describing is NIH and this infusion of money. That was an aspect of the Great Society, I suppose. Is that right?

Scharff: It was, although, you know, it was a special set of decisions. I mean, I was too young to really understand, but someone had this idea that the way to promote biomedical research and basic research, the business plan was to basically pay for everything, and that encouraged institutions to do this. So I think it was, you're right, but it was a special—I think the Great Society didn't have to go in that direction. It had to go in certain directions about generating new information and better medical care and so on, but they decided to do it that way. Very few other countries really fully run it that way; everything would be paid for.

Williams: Along those lines, Nixon and the War on Cancer, did that produce a real uptick in funding?

Scharff: It did, and at Einstein, we were one of the first places to have a cancer center. We were. There were only three cancer centers originally, and one of the three was us, and we were one of the three first M.D.-Ph.D. programs, and when the War on Cancer came, we had a cancer center that was built on this model that Eagle had propagated, in a sense, that not only would you have a bunch of independent individual investigators, but there would be shared facilities; that is, if someone developed or had a special technology.

So I was very interested in immunology and antibodies, and when the hybridoma technology was reported by [César] Milstein, we didn't do that, but we were doing very similar things, and immediately we knew how to make monoclonal antibodies. So we set up a shared facility where anyone in the school could come in and we would assist them in making their monoclonal antibodies, and then they were theirs and not ours. They would go back and they would have these reagents.

So those were set up, and that really was the model for cancer centers, that there would be an intellectual group interested in cancer, but they would be supported by these shared facilities that allowed relatively small labs that didn't have enormous resources to have very sophisticated equipment and skill and technology. I've run a hybridoma facility at Einstein for thirty-five years or something like that. We're still doing it. We help people do this, and then they go back and have their reagents.

Williams: You say number three cancer center. What were the other two at the time, do you recall?

Scharff: I'm trying to remember what. So I'm not sure that I—

Williams: That's an unfair question.

Scharff: No, it's not an unfair question. I don't remember exactly. We were one of three.

Williams: Looking over the, I think, fifty-three years that you've been there—

Scharff: Almost, right. My wife would correct me and say fifty-two and a half or something. [laughs]

Williams: Oh, okay. See, I'm a little mathematically challenged too. [laughs] There was a period which was sort of the golden years of those fifty-two?

Scharff: Scientifically, I would say. Yes, people from all over the world applied. Young people who wanted to do molecular immunology or molecular biology of animal cells would apply to Einstein to come, and they wouldn't apply to me, necessarily; they would apply to the Department of Cell Biology, and Eagle would hand me the CV and say, "You should consider this person." And that was in part, I think, because they were good at getting people and selecting people; secondly, because they did everything they could to help people get going; and, in part, this technology of SDS gels, which allowed everyone to do things that had been very hard to do before. One guy discovered that, Jacob Maizel, and taught us all how to do it and made a machine that would do it for you, and it took maybe two or three or four or five years before the rest of the scientific community completely stumbled to what a superb technique this was. So that enabled us to really do, I think, what appeared to be innovative work, but to certainly make new discoveries because of that technology. So I think that had a big, big role and attracted all sorts of people to come there, both faculty and students and fellows.

Williams: So you're sort of describing all fifty-two and a half years as golden years.

Scharff: Well, no, no. If I did that, I would be wrong. So I think we did very well for sort of the next ten or fifteen years. I think, at the same time, the rest of the world was also growing scientifically because of the funding, because great progress was being made. It was a time of great advances, and I think, you know, we became just another place.

Williams: About when did that happen?

Scharff: You know, it's a little hard. I think that, well, we never were able to really compete with Harvard and with Yale and with Berkeley and with Stanford. Almost, but in certain areas, but not—they had a prestige, and within New York City, Columbia had a prestige. NYU was a very good going operation. Cornell was less, in those days, research oriented. But in certain areas like in immunology and like in virology and some other areas, we were competitive.

I think, you know, science expanded, very good people all over, and we became a good place, still a very nice place to work. It may be that this decision—I'm almost afraid to say this, but this decision to favor the person who wanted to focus their attention on their research and on other people's research and not build an empire, not have lots of people working in their lab, not have control of a lot of resources, many very good people who were there left because they wanted to do that. It's just another way of working, but it wasn't a good place to do that. We didn't have a lot of endowment. We didn't have a lot of donors. We've never done very well in raising money. You couldn't garner all of these resources. You were completely dependent on what you could get out of NIH grants. So a big lab was five, ten people was a very large lab, and we were set up in a way where to be an active participant, you had to also be interested in what other people were

doing, and you had to be willing and interested in hearing what other people were doing and helping them in various ways and being helped by them. So people who had a different sort of ambition, which is very productive in some ways—there's a so-called star system, if you want—we weren't very good for that. So I think probably, although I like personally working in our environment, other people wanted something else, and that became a very successful way of—you know, in all of the good senses, a successful way of doing science.

Williams: Would it be fair to say that that shift was towards a sort of empire-building?

Scharff: Yeah. But I don't want to say that because it sounds bad, and it was, but I think that those people decided to do their—I mean, they're doing the same science, but to do it in a slightly different style. It's been very successful in a good sense, but I think that we lost out to some degree by not having that.

Williams: But for the benefit of science, is your model more productive than the empire model or not?

Scharff: You know, I wish I could say it was, because I like it, but now almost anything you do takes a variety of people with a variety of skills, so even I need an informatics collaborator, you need all these other things, and you need expensive technology and you need resources that aren't easily obtained even when money wasn't so hard, an NIH grant.

So I have to say that at the moment I think they're contributing different things. I think the way that I'm pushing, number one, it makes you as a scientist remain completely tuned into what's going on in your lab, the smaller lab, because you don't have another faculty member working for you. We've never had that at Einstein. So, I mean, I've never had, nor has anyone else there ever had an assistant professor in their group. Each faculty member is expected to be an independent investigator with their own branch and their own projects and so on. And if everything falls on you, you've got to keep up with what's going on, and you've got to watch over every student and every fellow, and you've got to personally be there to work on every paper and so on. I like that, but it's not necessarily favorable for big science the way it's being done now.

So I think there's a need. So I think that students and fellows and faculty remain very tuned into what they're interested in, and the system is tolerant of all sorts of people. By that I mean different personalities, different sorts of intellects, and so on. And I think that's great, and I think ultimately that's essential for new innovation, but at the moment a lot of science is being done is data collection, big science, and we're learning a lot. So I think they're both absolutely necessary, and I think the mistake now is that sort of the big science is squeezing out the little science. I think that's sad.

Williams: Your successes in little science, did that mean that you received a lot of offers to move elsewhere?

Scharff: I did receive a number of offers over the years. I don't know whether it was a lot, but I received a number of offers over the years, yes.

Williams: And resisted the temptation to move?

Scharff: Well, probably I only looked seriously at two or three jobs in the course of all these years. I did internally at Einstein some—I mean, I was chairman of the department, I was head of the [Albert Einstein] Cancer Center for ten years, I've done those sorts of things, and that's the kind of job I was being offered in other places. And I liked where I was. As you can gather, I liked the style of where I was. And some of it was personal. I mean, my family was there. My wife likes it. Maybe some of it was a lack of courage, I'm not so sure, but when I went to look at these other places—I guess I should say it this way. Where there are lots of resources, people compete for those resources. Where there are less resources and you're sort of dependent on grants as we were, there's nothing really to compete with your colleagues for. So in many of these other places where there were lots of resources, when I would go to interview for a chairman's job or something like that, most of the discussions was, "You should get rid of this guy next door, and he has resources he's not using right," and so on. We largely didn't have those resources, and we have very little politics and we have very little of that sort of competition. I wasn't interested in participating in that sort of thing, so I was happy where I was.

Williams: So the grant model, which is what you're describing, is under attack now because of the financial situation.

Scharff: Yes. I think a lot of places may not survive, or they certainly won't look like they have in the past. Einstein is in a particularly difficult situation because its parent university has sort of squandered its endowment in various ways, and we're actually being taken over by Montefiore Hospital, which is our major teaching hospital, because, basically, YU can't afford to have us any longer. Even under the optimum situation, it always costs some money to run a research endeavor, so now where a lot of our very good faculty can no longer get grants and after a while the labs are closed down and so on. It's very hard times. I don't know what's going to happen to biomedical science in the United States. I mean, certain places that have lots of resources and deserve them—I mean, I'm not saying they don't deserve them—they're going to survive all of this, and I don't know what's going to happen to other places like Einstein. I just don't know.

Williams: That's a sad note on which to end that part of our interview. Talk about what you will always be known for in terms of innovation in immunology.

Scharff: I've never completely understood that, to be honest. I think it's sort of interesting. If one was listening to what Linda [Sherman] said last night, and others, there was a period when many of us who were interested in B cells or T cells were trying to grow them in culture and understand them and doing animal experiments as well, and everyone wanted to find a way to make monoclonal antibodies. We may not have called them that, but that's what everybody wanted to do. So Linda described her trying to do that. I was trying to do it. [Georges J. F.] Köhler and Milstein were trying to do it. You could run into maybe a hundred people back then, even, or more, who were trying to do that. A student of mine, David Margulies, and I were busy trying to do that, and we were developing certain tissue culture and ability to fuse cells and so on at the same time that all these other people were doing it, and I guess we were very close. We didn't do one critical experiment. We published a paper that was on all of the same subjects as Köhler and Milstein, but they did a critical experiment that we didn't do. We just never thought of doing it. And in the act of that, they discovered the hybridoma technology. But I think that they were not overly communicative. It was hard to get their cell lines to do it on and so on.

As soon as David Margulies and I saw what they had done, when we read the paper, we knew we could do exactly what they did. We had all the reagents and so on. So we did it and we wrote about it, and we were asked by many people in the States to help them do it, to give them the reagents to do it and so on. So I think one thing that happened was that I became known as someone who you could get what you needed to make monoclonal antibodies, and I think that people appreciated that.

Also, with the use of SDS gels, we had done, I think, what was useful experiments, important experiments, on how you make immunoglobulin molecules, how it's controlled, some of the genetic controls of it and the biochemical controls of it. That was largely because of SDS gels.

So, very early in my career I was able to do a number of things that no one else had been able to do, both in virology and in immunology. So, early on, I think I became pretty well known, and then I think Harry Eagle did a lot to push me as well, getting me to the right meetings, making me write papers and getting me elected to societies and things like that. So I'm sort of known for having failed to discover the technique, as are a lot of others. I felt that they had just been smarter than we were. It's sad that we didn't think to do that, but it hasn't bothered me that much. They were just smarter, that's all, and there are always smarter people around. And we did develop modifications to the technology that made it much easier and feasible to do to make lots of monoclonal antibodies, so I think I'm probably known for that and probably because I like being helpful to people and so on.

Williams: Let's take a moment here to talk to the layperson who doesn't understand the science. What is a monoclonal antibody and what is its importance?

Scharff: So every day we're exposed to many different things in our environment, viruses, toxins, allergens, and we've evolved the ability to make both T cell responses and antibody responses in order to protect us largely from infections but from everything, all these foreign substances. And to do that we make an enormous number of antibodies and of T cells that allow us to respond to every possible antigen. So every day we're making hundreds and thousands of different molecules.

So how can we do this? We even are making things against foreign threats that we've not yet quite seen. So to do this, there's this huge variety, and in order to understand what's going on, it's been very difficult, until very recently with deep sequencing techniques and so on, for anyone to really dissect this out because of the enormous heterogeneity. But if you could take a single antibody-forming cell and grow that cell in culture to very large numbers, then you could take an individual antibody that you made, which was one of the hundreds of thousands, and you could characterize it. And you could do that on a number of different ones, like your response to influenza virus or your response to Ebola virus. If you had one of the antibody-forming cells that was protecting you from Ebola, you could understand exactly how that antibody was protecting you and how you could make more of them if you could isolate just one of those thousands. So a monoclonal antibody is essentially the product of a single antibody-forming cell and its clonal progeny. It's a homogenous antibody, and it differs in many ways from another antibody made by another cell.

Of course, in addition, if you can isolate one of them and you can fully characterize and understand it, then you would be in a position to use it to administer to patients, for example. Polyclonal antibodies are the product that we normally make, is sometimes used. Hyperimmune globulin is used to treat some diseases, but it's very hard to know exactly what's in each new batch, whereas with a single antibody-forming cell, we really know what it is, and then when you give it to a patient, you really know what you're giving them. So a monoclonal antibody is just pulling one little fraction out of the total response that you make.

Williams: And what triumphs have there been—I'm thinking now about translational science—because of your ability to produce these monoclonals?

Scharff: Well, one thing is that they've turned out—so as soon as you have that, you can begin to use them to treat various diseases. So, for example, monoclonal antibodies now are being made that can protect you against—if you just give those antibodies to someone, it appears you can protect someone against a virus like HIV or against influenza, but they're also being used to inactivate various things we make in the body. So Crohn's disease is an inflammatory disease, and the inflammation is being caused by a certain molecule, and if you make a monoclonal antibody against that molecule and you administer it to people, then you can decrease the inflammation that occurs in Crohn's disease.

So there are, I think, seventy or eighty monoclonal antibodies been approved by the FDA [Food and Drug Administration] or in the act of being approved, that are being used to treat inflammatory diseases, autoimmune diseases, infectious diseases, so they're biologicals. They're, unfortunately, expensive to make, but they tend to be much less toxic than like a chemotherapeutic agent that kills all the cells. So Crohn's disease is being treated, as one example. And also that antibody allows you to develop a vaccine that you could use so that you could make lots of that very good antibody, and that's the major effort now in AIDS and in influenza and things like that.

Williams: What are the patent implications of all of this?

Scharff: Well, the hybridoma technology, when Köhler and Milstein described it and they took their discovery to the experts at their institution, the experts said, "This isn't going to be so useful and we don't want to patent it." So they never patented the production of monoclonal antibodies. There was subsequently some patents, but they never did it. So I'm not fully expert on this, but I think there was a patent to Hilary Koprowski, having learned the technology from them, filed a patent in the United States, which has run out a long time ago but which enabled some biotechnology companies to get started. I'm really not expert on this, but I think that you can patent a sort of use, but I don't think you can patent a monoclonal antibody.

Williams: Well, see, it's like the genome issue.

Scharff: Yeah, yeah. But the other part of that was the next step originally was you could make monoclonal antibodies in mice. What are you going to do about humans? And the idea there that, not me, but that others had, was to isolate the genes that would encode the antibody, express them in cells, and produce human monoclonal antibodies. There are at least three or four patents around that. One came out of work that Sherie Morrison and Len Herzenberg and Paul Berg and Vern[on] Oi did, where they made the first chimeric, so that was partly mouse, partly human, and you wouldn't have an allergic response against it. And there are three or four patents on making those kinds of a process and making those kinds of antibodies.

Williams: Right, right. You received the AAI Award for Mentoring in '98. Just briefly, how important is mentoring in the whole field?

Scharff: Well, you're asking to me individually or just in general? Either way?

Williams: Well, maybe both.

Scharff: My view of it is that as scientists, we are interested in certain things. We do certain things in the lab. I think it's very unlikely that if any one of us had never

gone into science, someone else wouldn't have done the same things we're doing. So one of the really rewarding and more permanent things about science is that people come to your lab or come to make monoclonal antibodies or something, and you help them in doing that, and you help them—it's called mentoring, but I think you're helping them to do that and to do the things they want to do, and you're helping them to learn what they're strong at and what they're weak at and to use their strengths and sort of compensate for their weaknesses.

That's what mentoring is, in my view. To me, it's a more permanent outcome of what we do as scientists, as the people who I've interacted with through various sorts of things, but mostly having come through my lab and have gone on, most of them have gone on to be successful scientists, and we've remained good friends and it's really rewarding. I mean, it's like having children with, I suppose, not some of the minuses but only the pluses, over and over again. That is, if they turn out to be failures or they turn out to have difficulties, it doesn't fall upon you, but just like with your children, although you can't really take credit for what they do, and shouldn't, you feel good about what it was. So I think as scientists or almost anyone who's an educator, you can feel very good about that, so I feel very good about that. I feel very good about the people who have come through the lab, and I feel like they're—you know. Some of them I probably spend more time with than I spend with my children. [laughs]

Williams: You've mentioned Len Herzenberg several times today. I suspect there's a kind of special amount of—the fact that you're receiving this first award in his name is kind of special for you, is that correct?

Scharff: It is. Well, it is because although our backgrounds are virtually identical in many ways and we certainly were acquaintances and so on, we were never really very good friends. I mean, he was on the West Coast. I was on the East Coast. But he developed or was mainly responsible for having developing fluorescent-activated cell sorting, without which I don't know where immunology would be at all in a lot of the clinical applications of it. And, like me, he came from Brooklyn, and actually we have very similar beginning scientific experiences. He worked for Harry Eagle at the NIH two years before I worked for Harry Eagle.

So I think he's done really important science. Technologies are always the most important thing you can contribute. I mean, they really make a difference for everyone. And he was also a person who believed in trying to help underprivileged people, and things I admire him for. So I feel sort of embarrassed because I think he clearly would have deserved this award much more than I would. I mean, if he were still alive, he should have been the one getting this award. So, yes, I feel very good about that. I think he's an admirable person in lots of ways.

Williams: And I'm going to force you to be self-serving here. Why are you getting the award this year?

Scharff: I'm not completely sure. I think in part because some of my former students and fellows decided to nominate me and took the trouble because—and I think because I'm looked upon as a good guy, which I'm proud of. And I think I probably don't deserve it. So in that sense, I can identify other people I might have given it to, okay? So I'm not quite—I was surprised.

Williams: In the words of the AAI, part of it is because you are considered an elder statesman in the field.

Scharff: Well, I guess I've lived a long—yes. [laughs]

Williams: But do you cousin to that description? I would think you would.

Scharff: Well, I am older and I managed to survive in quite good health and to still be functioning in the lab, and I think some of it has to do with—I don't know what that really means because I've never been politically active in the AAI or in organizations. I mean, I've spent the time that some people spend doing that, which I think is very worthwhile, I've spent more involved in having to do with organizations that pick postdoctoral fellows and serving on their boards and serving on NIH advisory committees and so on. But I hope part of it is because I really am enthusiastic about science, I'm enthusiastic about immunology, I'm enthusiastic about training people to do it. So if that's what an elder statesman is—to me an elder statesman is someone who has some authority and uses it well, and I don't have any authority, so I don't see that.

Williams: Well, admiration from the field does convert to authority, I imagine. What do you see as the future of immunology?

Scharff: Well, I mean, one could argue with everything that's been done—immunology has had an interesting role, I think, in biomedical science. In my few minutes I'll try and say that this evening that I have. But if you look at major advances that were made in the molecular biology of animal cells and of higher organisms and so on, many of the major discoveries were actually made by immunologists and then generalized. I think the first gene that was cloned was [Susumu] Tonegawa cloning the antibody light chain gene. The first transcriptional enhancer was separate discoveries by [David] Baltimore and by Sherie Morrison and by Len Herzenberg on enhancers. So, many of the things that have played an important role in our understanding about molecular and genetic control of animal cells have been done by immunologists studying antibodies or T cells, and I'm not sure why that is, excepting that there are a lot of immunologists and there are real translational opportunities in immunology that keep driving it in a sense. So I don't see any reason why that won't continue and why people won't be attracted to it, because it has the opportunity to improve human health, to prevent diseases, but also because it's really a fascinating subject.

Someone pointed out that early on in immunology there was a debate about how you got this enormous diversity. If every antibody molecule had a different nucleic acid sequence, there was not space in the genome for all of that. So there had to be special mechanisms for that, and that attracted many famous scientists, like Sydney Brenner and others, to have theories about the generation of antibody diversity. And I think immunology will continue to have those characteristics, so I think people will continue to want to study and be immunologists. So I think it has a very good future, which is being encouraged even more by the translational opportunities that comes out of immunology. I mean, we've evolved this mechanism to protect ourselves from all sorts of things, sometimes it hurts us, but it tells us a lot about human physiology and so on. So I think there's a very good future in immunology, maybe better than in many other areas.

Williams: I'm asking everyone this weekend about how you mix family and career.

Scharff: First of all, if you have a family and you have a wife, they have to be very tolerant, because I think science in general, any kind of science, there's an infinite number of things to know and learn. I mean, it's what's exciting about it. Although I'm an immunologist, we have daily seminars at Albert Einstein with outside speakers from all sorts of areas, and I go to them because I really like to hear all these different things and I want to learn about them and I want to keep learning new things and doing new things, and it just is terribly time-consuming. It's infinite. You can keep reading papers and going to seminars and going to meetings, I suppose. So it's a real hard challenge to do that and to have a family, if a family includes children or includes any other people.

So, in my case, I certainly think I've probably not done as well as I should have. My children are fine and I think they like me okay, but I haven't spent as much time with them as I should, or with my wife. I spend a lot of time working. I work, still, pretty much seven days a week, and I come home every night and I try and read and learn new things. So I think that in that case, it's somewhat to the detriment of the family, and you need to have very tolerant people that you're living with to do it. I've been very lucky to have that.

Williams: How many children have—

Scharff: I have three children and four grandchildren.

Williams: And your children, what career paths have they taken?

Scharff: Not science or medicine. One of them's a computer person. He actually works for the Cancer Center at Albert Einstein. My youngest son was for many years an aspiring musician, a punk rock musician, and it's only in recent years that he's really had a job. He works for the Annenberg Foundation and he's got a title of something like creative director, but he does a lot of their communicating with the outside world, web pages and displays and so on. He's a very creative person, but

I'm afraid never made it as a musician, although they're reissuing his original punk rock records these days.

My oldest child is a political activist. She's a founder of a political party in New York State, co-founder of the Working Families Party and a founder of an organization—or she's the chief executive director of an organization that seeks to help underprivileged people, minorities, to exert their rights to vote and to get them elected into all New York state legislature, working. So that's the Citizen Action of New York. So that's what she does. She's a political activist. She started out being interested in science, but as a freshman in college, a group of what we would call progressive professors spotted her as someone who was going to be a political activist and attracted her into that, and organic chemistry was sort of dull. [laughs]

Williams: What recreational activities have you undertaken?

Scharff: So I play tennis and I play golf occasionally, and that's basically what I do.

Williams: Okay. You came with some notes today. Are we not saying that we covered those?

Scharff: No, I had your list of questions, and I just didn't want to forget—make sure I mentioned the names of some of these people. That's all.

Williams: Oh, yeah, good. Well, this has been a charming experience, and thank you very much for being here today.

Scharff: Thank you. I hope I didn't make a fool out of myself. [laughs]

Williams: That certainly is not the case.

[End of interview]