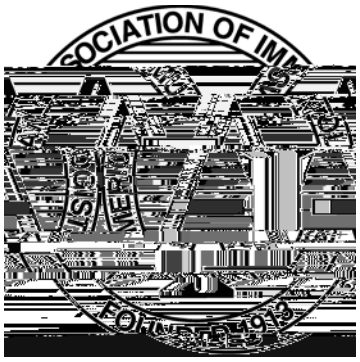

The American Association of Immunologists Oral History Project

Transcript

Betty Diamond, M.D.
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Manhasset, NY

Interview conducted by
Brien Williams, Ph.D.

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Williams: This is an interview with Dr. Betty Diamond for the American Association of Immunologists Centennial Oral History Project. Dr. Diamond is head of the Center for Autoimmune Diseases and Musculoskeletal Disorders and director of the Laboratory of Autoimmune Diseases and Musculoskeletal Disorders at The Feinstein Institute for Medical Research, North Shore–Long Island Jewish Health System. Dr. Diamond was president of the American Association of Immunologists from 2009 to 2010 and served as an AAI Council member from 2004 to 2009. We are in Dr. Diamond's office at The Feinstein Institute for Medical Research. Today is Tuesday, February 5, 2013, and I'm Brien Williams.

Dr. Diamond, let's start out with a little bit of your family background, where you come from, and maybe your ancestors a little bit.

Diamond: My ancestors. Wow. I grew up in New York City. I really have lived most of my life in New York City, with the exception of college and medical school, and I love New York City. My father, my uncle, my brother were all interested in history, and it's hard to compete against that many people in a family, so I went into science.

Williams: What areas did your brothers and uncles—

Diamond: So my father was interested in American history. My father actually began his life very politically involved and worked with the UAW and was a union organizer and the UAW historian, and then he went to graduate school. So in my

used to from my high school experiences. So I took some science courses but decided I wasn't going down that route.

I got to my senior year, and I thought, "What am I going to do with a classics or art history degree? I don't want to teach. I want to do research." But actually I thought that I wasn't qualified to apply for a Ph.D. because I hadn't been a science major and I hadn't taken enough science courses. But medical schools are always looking for well-rounded individuals, so I thought, "Okay, I'll apply to medical school, and I'll get into research through the back door," and so I did.

I fell in love with clinical medicine, and so I went on and did residency, which I wasn't planning to do. But at the end of that I decided that I really wanted to get back into doing some research. I had done one year of research in medical school, and so that's when I went off to [Albert] Einstein [College4(a)4(lutm10(I)23( )]TJ-1

Williams: And it was a tribute to your mastery of things general that Harvard accepted you. Was that—

Diamond: Well, you know, it was during the time of the Vietnam War, and there were some young faculty members who were politically involved, and they wanted more women in the medical school class and more minority students in the medical school class. I had the advantage of being interviewed by two of them. I actually was one of four women in the class, so it wasn't that they were so powerful, but I had the sense that every woman or minority candidate that they interviewed got accepted.

Williams: Your modesty is showing through here.

Diamond: But, you know, over the course of the next two or three years, that number went from four to about thirty and then was half the class very quickly. It really was the beginning of a big transition.

Williams: Did you feel any particular pressure or anything stand out for you, being a woman at the time when you came in and there were only four of you?

Diamond: I think that there are always particular incidents you can look at and think that that only happened because I was a woman, that wouldn't have happened if I hadn't been a woman, and there's some that are perhaps not so nice and some that are nice. I think that I'm a great advocate for women in science and women in medicine, and there still are barriers that need to come down for women, but for myself I think I've had a pretty gratifying career.

I should just say one thing, because I had a wonderful postdoctoral mentor, and I came into his lab after finishing my residency really deficient in my basic science background, and he would routinely tell me that he thought that women made the best scientists. I don't for a moment believe that he really thought that or thinks that, but there was nothing so reinforcing as having somebody have a great confidence in your abilities that way. It's a lesson that people need positive reinforcement.

Williams: And that mentor's name?

Diamond: "Matty" Scharff.

Williams: Do you want to say anything else about him?

Diamond: Oh, he's a wonderful scientist. I hope that he's being interviewed in this project. I think he is, actually. He has been involved in immunology research for half a century.

disease mechanisms to designing a therapeutic that might actually work, and that would be fun.

Williams: In layman's terms, talk about what lupus is and how you're attacking it.

Diamond: So lupus is a disease where you make antibodies against some of your own cellular constituents in your own tissues, and it's a disease where you make very many different autoantibodies, but antibodies to DNA are the most common. As far as we know, wherever there is organ system involvement in lupus, it is initiated by these autoantibodies. So the autoantibodies are very important in at least triggering the disease.

The disease is nine times more common in women than in men. It's clearly, in part, hormonally regulated, because before puberty it's a three-to-one incidence, after puberty it's a nine-to-one incidence, and after menopause it goes back to the much closer ratio of men to women getting lupus, but by that time very few people get lupus. So the age of onset is primarily twenties and thirties. Any organ system can be involved. It can affect your kidneys; it can affect your heart; it can affect your lungs; it can affect your skin. It can affect, really, any organ system. About a third of lupus patients die of kidney disease, about a third die of infection because of the immunosuppressive therapies used to treat the disease, and about a third die of accelerated atherosclerosis, which is probably contributed to in large part by the chronic inflammation that's part of the disease.

Williams: So maybe you don't want to talk in much detail about how you are currently attacking it, but do you want to go into that a little bit more?

Diamond: So the lab started off studying the origins of these DNA antibodies, which we knew at the time contributed to kidney disease and were the major autoantibody present in lupus patients. We actually went against the orthodoxy of the time, and we showed that these antibodies arose by B cells that had matured through a germinal center reaction and had mutated to acquire reactivity with DNA. At the time, the prevailing wisdom was that antibodies arise with some autoreactivity present in their structure and that they mutate to lose autoreactivity, and here we were showing that in a disease they could actually mutate to acquire pathogenic autoreactivity.

We've gone on to show that a subset of these DNA antibodies can actually target the brain, which is affected in about 80 percent of lupus patients, and there really was no understanding of what causes the brain disease in lupus. We showed that these antibodies can cross-react with a particular receptor on neurons called the NMDA receptor, and this receptor is critically important in learning and memory. We've gone on to show how these antibodies affect the NMDA receptor. We've modeled this in mice, and we've shown that this is consistent with what we see in humans with the memory disorder that is especially prevalent in people who have these antibodies.

Whether through running an M.D./Ph.D. program or through running a clinical division or one-on-one or through establishing an organization of women

how much money should go into each pot. It would be nice to see something like that.

Williams: What was the Common Fund mechanism? Just define it.

Diamond: It was different kinds of grants, different kinds of grants that were sort of where each institute gave up some money to go to the direct me-10(gTj -38 fu-38 n-38 d-38 d-3

Diamond: This is going to sound very grandiose on the part of the immune system but I think that the immune system, we're learning, has incredible connections to the brain and we're going to learn more and more about the relationship between the immune system and the brain, the brain govo tst blA6M0(ut)-2(t)-2(he,4(s)-11(y)20(s)-1