The American Association of Immunologists Oral History Project

Transcription

Stephen M. Hedrick, Ph.D.
May 10, 2019
La Jolla, CA

Interview conducted by:
Brien Williams, Ph.D.

Transcription: TechniType Transcripts
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. Stephen M. Hedrick for the American Association of Immunologists Oral History Project. Dr. Hedrick is Distinguished Professor in the Molecular Biology Section in the Division of Biological Sciences at the University of California San Diego [(UCSD)]. He is also the Chancellor's Associates Endowed Chair in Biological Sciences at UCSD, and he is a Distinguished Fellow of the AAI and was a recipient of the AAI Distinguished Service Award in 1997. We are at the Scripps Research [Library] in La Jolla, California. Today is Friday, May 10th, 2019, and I'm Brien Williams.

Thank you very much for joining us today, and I'd like to start by asking you to tell me a little bit about your family background.

Hedrick: My family background. My parents—I was born in Los Angeles, in Hollywood, California, only because that's where the hospital happened to be. Cedars of Lebanon [Hospital] was in Hollywood at the time, and they lived in West L.A. My father had come down from Oregon. He was born in Oregon. My mother was born in the Philippines, and she was in a prison camp during World War II and then was liberated by [General Douglas] MacArthur and then came to Los Angeles, where she went to UCLA. They met on Avalon Beach in Catalina, and they got married in 1950, and nine months later, I was born, May 1st, '51.

Williams: So tell me a little bit about—well, what did your father do then out here?

Hedrick: My father started in the automobile business, and he eventually worked for Chevrolet Division of General Motors and did that for almost an entire career, and then he left and had his own dealership in the San Fernando Valley. My mother was a teacher for about twenty-five years, and then she had a career as a travel agent and then another career as a realtor. She just retired about two years ago, and she turned ninety this last year.

Williams: Wow, wow, yeah.

Hedrick: So we lived in Los Angeles almost my whole life, yeah.

Williams: Are you an only child?

Hedrick: No, I had a brother, and he passed away in 2009 from esophageal cancer.

Williams: Was he also a scientist?

Hedrick: No, he was a teacher. He taught at Santa Monica High [School]. So it's a family of teachers. My mom was a teacher and her two sisters were teachers, so that was kind of in the family.

Williams: Right, right. So tell me a little bit about your educational background.

Hedrick: So, I started at UCLA and followed a girl to UC Irvine, so I transferred. That lasted about two weeks after I got to UC Irvine. I was an environmental engineering major and then I took on a second major in biology, and about halfway through my senior year, after I'd done all the hard engineering classes, I gave up the engineering major and finished up in biology.

And the way I got into immunology was tied up with that. There was somebody living above me who was a premed student, and one summer, I was working in an engineering lab and he said, "Why don't you come to something called a Journal Club, which is a weekly meeting where people discuss the current literature." And he happened to be going to this one at somebody's house down in Laguna Beach, and he said, "Come on down and we'll discuss—." They just discussed current literature in immunology. And I didn't know any immunology, but I thought, "This might be interesting."

So I went down there, and the topic of the day was something I ended up studying for the next forty years. So then that sort of motivated me to not finish in engineering and finish in biology and then go to graduate school in biology, and I stayed at UC Irvine as a graduate student and finished there.

Williams: What was that like, immunology, at Irvine?

Hedrick: Well, there weren't very many people that were practicing immunology at Irvine, but there was enough, and the topic caught my interest. I'll come back to this a little bit later, but the topic was this, easily explained: everybody knew about one part of the immune system, which was antibodies, and they were well characterized as how they were produced and their structure. But there was a whole different arm to the immune system that was mediated by cells, not by antibodies, and these were called T lymphocytes, and there was nothing known about the way T lymphocytes could recognize the universe of infectious agents. So this was the topic, and it was a complete mystery to the field. And from that day on, I thought that was an interesting thing to study.

Williams: So that's been your forty years of work? So you were really at the front end of that whole line of discovery.

Hedrick: Yeah, I definitely participated in some of the early fundamental aspects of the way that T lymphocytes recognize infectious agents or cancer or whatever they happen to recognize.

Williams: Mm-hmm, mm-hmm. What turned you off engineering?

Hedrick: Oh. It's—well, I never practiced it, so I don't know what it would be like to be an engineer, but it's very mathematical, especially the way it's taught at the University of California. And, you know, I have some strength in math, but I

wasn't the best mathematician in the engineering school, so I think I struggled in thermodynamics and differential equations and linear algebra and things like that. So I was much more taken and interested and I had much more facility with biological sciences. It seemed to be my forte.

Williams: Besides this meeting that you attended, give me the sort of through line that really committed you to immunology.

Hedrick: Well, once I'd made the decision not to finish engineering school, I was pretty committed to going to graduate school in biology, and this topic of immunology was something that really caught my interest, as I said. So I started out with one advisor at UC Irvine and, unfortunately, he didn't get tenure, and so I needed to find another lab.

It turned out that a fellow down at the Salk Institute was taking a job at UC Irvine, and so I went down to the Salk Institute for a summer and worked with him and then came back up and carried out my degree with him at UC Irvine. So there was a whole community of immunologists in Southern California. It was more centered down in San Diego at UC San Diego and at Salk Institute and here at the Scripps Clinic especially, so I had a connection and I would go back and forth often for seminars and for meetings and so on, but the thread was really just interest in science. I just thought that the field was fascinating. Because there was this major lack of understanding of the way cellular immunology worked, that really motivated me to continue in graduate school and on as a postdoctoral fellow and so on.

Williams: And you felt at that time that you were involved in something that was pretty kind of niche?

Hedrick: I did. We didn't really have the tools to discover how T cells recognized infectious agents early on, especially in the early seventies. It wasn't until, really, recombinant DNA technology was made available that we had the tools really to clone the genes and to understand what they look like and sequence them and so forth.

Williams: Right, right. So after you got your degree, you then went back to the NIH [National Institutes of Health], is that correct?

Hedrick: Yes. So there was a group at the NIH who had recently published that they could grow T cells in a dish, and the ability to do that allows you to grow a very homogenous group of T cells so they would all have the ability to recognize the exact same infectious agent, and the homogeneity was, I thought, important in order to isolate what that receptor was all about. So I decided to go there as a postdoctoral fellow. I thought about going to Europe and I applied to several places in Europe, but I also had a wife and two little children aged nine months and two years, and the dollar had recently fallen against the European currencies,

and so it just became financially too difficult to go to Europe, so this was the best alternative. They paid a little bit better, and it was a place where I thought the technology might be available.

Williams: So you applied or—

Hedrick: I applied. I flew across the country and interviewed with two or three labs. I noticed one of the first histories was with William Paul, who recently passed away, and it was his overall laboratory where I interviewed, as well as another in the Cancer Institute, and then it was just a matter of choosing which of the labs to join.

Williams: And which one was the lucky one?

Hedrick: [laughs] Well, so it was a fellow by the name of Ron [Ronald H.] Schwartz that was in the greater lab of Bill [William E.] Paul's, and I worked with him for about eighteen months, and we published a couple of papers on the ability to grow and characterize these what we call clones of T cells. And I was fortunate that another postdoctoral fellow had come from Caltech and brought with him all the technology for recombinant DNA manipulation. He was also interested in the way T cells could be distinguished, for instance, from antibody-producing B cells, and so after eighteen months with Ron Schwartz, I connected with him and we set out to find the clones of the encoded—the receptor on T cells that recognize infectious agents. So we thought cloning the gene would be the way to characterize what it looked like and how it worked.

Williams: John Emrich [Ed. AAI historian] told me that you had an epiphany experience on the way to the zoo? [laughter]

Hedrick: Yeah. So we were deep working on it and screening all of these clones that Mark Davis and I had worked on. He was the fellow that brought the technology and with whom I collaborated. And I was going through dozens and dozens of clones, characterizing them to see which one would be most likely encoding a receptor, and the way we had to do that involved electrophoresis and then radioactive blot, so you put it onto film and you could see how the different clones migrated on a gel. There was a characteristic that we predicted that should be there that was called gene rearrangements, so we were looking for a gene that rearranged in T cells, and it's a very, very unusual characteristic. I know this is a little bit past what we're talking about here.

So, on a Sunday morning, it was common for my wife and I to take our little kids and go someplace, and in that particular case, we were on the way to the zoo. So I usually stopped by the lab to check on results and so forth, and I took this film that was exposing the radioactive gel and I had developed it. We had development tanks and so forth then. We didn't have automated film development. And I pulled it out and I could see that the genes that we had cloned were rearranging in

T cells and not other cells, and that would be a characteristic you would never see in any other gene, so I was pretty sure in that moment that we had isolated the right genes.

So we went off to the zoo, saw the animals, came back, and I called Mark Davis, my collaborator, and I said, "You ought to come down here. I think we have something that might work out." So that's the way it worked out.

Williams: And that was the birth of?

Hedrick: The T cell antigen receptor. That was the first gene cloned for one of the two subunits of the T cell antigen receptor. So immediately then we could use DNA sequencing technology and sequence the genes and look to see how they related to other genes like immunoglobulins and so forth, but they were in their own unique family of genes.

Williams: Mm-hmm, mm-hmm. So you were at NIH from '80 to '83, I think, and then you came back out here to UC San Diego. What prompted that move?

Hedrick: Well, I needed a job. [laughs]

Williams: So why did you separate from NIH?

Hedrick: Oh, I was just a postdoctoral fellow. It was never intended to be a permanent position. And, you know, as a Californian, I kind of wanted to come back to California. In fact, that was one of the motivations for going to the East Coast or going to Europe, was that I felt that that would give me a better chance, actually, to come back and have a job in California.

So I interviewed around the country and I had a couple of opportunities other places, but this was by far the best opportunity I was offered, so I came back as an assistant professor and we moved.

Williams: Mm-hmm. And you've been here ever since.

Hedrick: I have. There were a couple times when I considered moving other places, but didn't work out, and I'm really glad I stayed.

Williams: Describe the department and the immunology activity when you got here.

Hedrick: When I got here, really immunology in San Diego was really focused over here in Scripps. There were more immunologists here. It was better supported and there was just much more immunology activity over here at Scripps. There was a small group at Salk and maybe an even smaller group at UC San Diego, but there was a community overall, it just wasn't supported quite so much at UC San Diego. And over the years, between myself and other people who came to UC San Diego and

who were already here, we managed to build a pretty nice group in immunology. In fact, right now we're starting a program in immunology which is a joint program with another institute that's located on campus called the La Jolla Institute for Immunology, and so we've pulled together the faculty from UC San Diego and the La Jolla Institute, and we have about seventy people who consider themselves close enough to immunology to be members of this program.

Williams: Were there certain breakthroughs through the years where you really experienced a major jump or some grants that were really significant?

Hedrick: Well, so when I came to UC San Diego, we had just cloned this gene, I mean literally months. Mark moved a few weeks later to Stanford [University], Mark Davis, and I moved about a month and a half later to UC San Diego, so we were communicating by phone and by modem, by slow modem, with the computer in NIH where all the data was still located, to finish the writing of the work.

But anyway, there was a rush of experiments that came out over the next two or three years where people were able to use this information to finally characterize what the receptor looked like, so that occupied us for quite a while. And I would say the next breakthrough came when people invented, I guess is the word, transgenic technology, where you could put a new gene into an organism, in this case a mouse, and change the way that the immune system of the mouse worked. I set up a transgenic facility based with some funding from a National Science Foundation grant. It was a Presidential Young Investigator Award that allowed me the freedom to set up a transgenic facility in my own lab, and so we had dedicated personnel that would produce these mice, and we must have produced, I don't know, a dozen or two different kinds of transgenic mice that allowed us to probe the immune system in different ways.

Williams: So your alliance with the La Jolla Institute, that's been quite recent, is that correct?

Hedrick: Yes. So the president and I have been working on setting this up, and we've got joint seminar programs, we've got a little grants program. We're trying to set up a freestanding graduate program in immunology, and we'll see how that goes, but we're in the process of doing that at the moment.

Williams: How does UCSD respond to that proposition?

Hedrick: Well, they've been supportive so far, and it's just a matter of convincing them to continue their support through the sort of trial phase where we're still building the program and we still need support. Eventually, we hope to be able to get support from the NIH, but it's difficult until you have the program up and running to convince them to fund a new fellowship program.

Williams: In what particular direction are you steering yourselves in?

Hedrick: Well, there's interest and strength in several areas. Cancer immunotherapy is one, for sure. We have a strong connection with the [Rebecca and John] Moores Cancer Center. There's a lot of us that are interested still in infectious agents, especially chronic viruses, chronically infectious viruses. Those have been understudied in previous decades, and it turns out that that's a very interesting interaction with the immune system when you have an infectious agent that's never cleared by the immune system, and yet it has some sort of a stasis in that it doesn't overwhelm the body and the immune system doesn't overwhelm the body, so there's this sort of equilibrium. So, for instance, all of us—or most of us have cytomegalo virus as an infectious agent or Epstein-Barr virus that causes infectious mononucleosis, but once it's established in the body, it doesn't cause any disease. But the immune system is constantly interacting with these chronic viruses, and so we're interested in the way that works, in addition to these other aspects like cancer immunotherapy.

Williams: So taking off from that, what do you look at the status of immunology today? Where are we in the field?

Hedrick: Well, when I started, there were lots of mysteries about how genes could mutate and rearrange, why we had so much diversity in certain genes of the immune system called the major histocompatibility complex [(MHC)], that there's tremendous diversity within the human population, and that's unique for all genes. Usually, genes are very similar between all of us. These are very, very different.

And there are many other mysteries that were difficult to understand because the biology was different than other biological systems. The physiology of the immune system is such that it's just very different than other systems, and it's probably because it's under constant evolutionary selection by infectious agents to be different and to change and to come up with novel mechanisms in order to overcome infection. We've solved a lot of those basic mysteries, and so now immunology is coming to the point where we're trying to understand it in really much more detail so it can be repurposed, if you will, in terms of, for instance, immunotherapy. So the metabolism, the microbiome interaction with the immune system, as I said, chronic viruses and acute viruses, bacteria and fungi, all of these sort of details are now really the focus of the immune studies.

Williams: Mm-hmm, mm-hmm. And looking at the road ahead, do you see constant sufficient support and interest on the part of politicians and so forth, or is there a battle there?

Hedrick: Well, there's two answers to that. One is that especially with cancer immunotherapy being at the forefront of even the public's understanding of science and Nobel Prizes given this year and so forth, I think everybody's really excited about that, and so immunology's been able to—and the people that did

those experiments were able to come up with ways that a few cancers can be treated and a percentage of the patients actually cured, and so the excitement is that this could be applied across the board to other kinds of cancer. That will take a whole lot of work, but there's enough interest in the community and in the federal government that there's at least support for it. Whether there'll be financial support for it sufficient to bring it about in a short period of time is another issue.

Necessarily, getting grant funds is very competitive, so, for instance, in National Cancer Institute, someone just told me that the percentile funding is around ninth or tenth percentile, so every grant you put in, the chances of it being funded is about one in ten. For the National Institute of Allergy and Infectious Diseases that funds most of immunology research, it's a little higher, it's more like twelfth percentile. [laughs] And for new investigators, it's a little better still, it's about fifteenth percentile, but still, that's very competitive, and this is all by peer review. It's a necessity of the system. I mean, it has to be competitive. There's no other way around it. There are other ways of giving out competitive funds, but for now, this is what we have. It requires a lot of effort by all the investigators to maintain good levels of constant funding to keep the research going, but I think there's the will to keep the funding going. It's just very competitive. That's the part of being in science and being any kind of a biological scientist or any other scientist that is the most challenging, is to maintain funding, and some people do it easier than others, and that's just the way the world works.

Williams: And it's probably something that keeps you awake at night from time to time.

Hedrick: From time to time. [laughs]

Williams: You mentioned the immune system and all of these various diseases. Is there any coordination within the field that, "Well, we'll look at this cancer," and, "Well, we'll look at this cancer," or is it all you're just sort of doing it on your own in a sort of silo fashion or not?

Hedrick: Well, I wouldn't say it's silo fashion, but people are pretty independent and different laboratories are pretty independent. There's certainly a lot of collaboration that goes on, but I would say that it's sort of like a free market in that if there's a need, someone will fill that need quickly, because if there's low-hanging fruit or if there's something that is obvious that isn't being pursued, somebody will be there. So, you know, it works sort of the same way as in an economic system, I suppose, and you collaborate when it's in your interest, and when it's not, then there's even rivalries in terms of trying to get someplace first or trying to find results.

Williams: How do you know what the other guys are doing?

Hedrick: Well, the Internet has made that pretty available. Research is published pretty quickly and it's available online, and you can access the entire history of immunology through the National Center for Biological—what is it called? [Ed. [National Center for Biotechnology Information, which houses PubMed] It's the NIH's online system for publishing articles, which is a huge change from before the Internet days, where you'd go to the library and photocopy these big volumes of journals. Now it's at your fingertips, so there's lots of communication. There are even ways of publishing work before it's even peer reviewed in Bio Archives [bioRxiv]. You can put up a paper and people can see what you're doing even before it's been peer reviewed, and that's becoming a little more prevalent, but mostly the communication is via meetings, like the AAI meeting that's taking place down in San Diego right now, or through publications.

Williams: Mm-hmm, mm-hmm. So, I think you've already answered this question, but let's just review it if you haven't. [laughs] If you have. What do you want the public to know about the significance of your work?

Hedrick: Of *my* work? Well, you know, we all stand on the shoulders of giants, and this is an interaction that occurs with the entire group of researchers in the field, so in my opinion, no one person makes that much of a difference. We all contribute a bit, and, you know, to be perfectly honest, if I weren't here, somebody else would be doing the work. I don't think there's anything particularly unique. I think I sometimes bring a unique perspective to immunology. I'm very interested in the coevolution of infectious disease and the immune system, and I think one of the aspects of immunology that's lacking, to an extent, is the way that infectious agents actually determine the outcome of an immune interaction.

Whereas people studying immunology tend to think about the immune system as determining whether or not you cure a disease or not, it's actually much more important—well, it's at least as important to understand how an infectious agent, like, for instance, tuberculosis, why do they form these granulomas and why are they sometimes latent in some people and they're active in others. That's probably largely coming from the mycobacterium and not so much determined by the immune system. The immune system responds, but the mycobacterium is so much more facile evolutionarily, because it has a short generation time, that a lot of this is coming from the infectious agent. So my goal has been, over the last five or ten years, to push this as a notion and a philosophy in immunology to take more into account the infectious agent as opposed to the immune system.

Williams: So that's really an expansion of the narrow definition of immunology.

Hedrick: Yes, and certainly I'm not the only one who feels this way, but I've published two or three articles, just perspective articles, trying to put this point of view out in the literature.

Williams: And has it had legs?

Hedrick: The first one was novel enough so that I think it got a lot of notice. I don't know if it's convinced the field yet, but it's evolving that way. There's certainly many more people now who consider themselves immunologists and virologists or immunologists and microbiologists and interested in this coevolution, so I think it's slowly making its way into the field, for sure. And, believe me, I'm not the one that has done this, by any means. I'm a supporter of this idea, but I wouldn't give myself credit for bringing it to the field.

Williams: But you're an advocate.

Hedrick: I'm an advocate, yeah. Thank you. That's the word.

Williams: So virology and immunology have always been sort of close together over the years, haven't they?

Hedrick: To some extent, but not so much. I mean, more recently, they have, for sure. So we started in immunology looking at very synthetic infectious agents, just a foreign protein like the albumen from eggs. This is a common way of looking at the immune system, is to inject a mouse with the albumen from an egg, a chicken egg, and ask how does the immune system respond to this foreign entity.

A number of years ago, other people who were more virologists, like Dr. [Michael B.A.] Oldstone, who I think you're going to interview next, brought to the field this idea that you can understand the immune system much better if you look at a real infectious agent, and he brought the idea of using this particular virus, lymphocytic choriomeningitis virus, in mice, and that has, I think, really revolutionized the understanding of the immune system, to use real infectious agents.

Williams: Hmm. Interesting. One question I wanted to ask you was when you encounter a scientific endeavor, sometimes things don't work out very well. How do you handle disappointment in your field?

Hedrick: Well, it's like the song. Pick yourself up, dust yourself off, and start all over. [Williams laughs.] You know, most experiments don't work and many hypotheses that you start out with are incorrect, and if you're doing good science, you prove yourself incorrect. I think it's part of the fascination of science, is to succeed and fail.

Williams: And the failures have significance.

Hedrick: Yeah. I mean, some of them don't where you just drop the tube on the floor. You're not going to learn too much from that, but many of them do. You have to have a real love of science, and I think it's easy to generate in people, because once you see the—I don't want to be corny, but the beauty of understanding

nature from observation and experimentation, I think it can keep your interest for a—it's kept my interest for a very long time. But you have to understand that most labwork is just going to be not so fruitful. You don't have so many eureka days where you pick out the gel out of the tank and you see that you've achieved what you set out to achieve.

Williams: Maybe you ought to go to the zoo more often. [laughs]

Hedrick: I don't think that's the correlate. [laughter]

Williams: One thing that, in a lot of these interviews, we really haven't talked about is the importance of technology in your work. Can you speak to that for a moment?

Hedrick: Yeah, that's a real driver of moving the field forward. If you don't have the tools to work on something, it can be pretty futile, and, you know, with the way technology is increasing so fast in visualization and, for instance, microscopy, and especially recombinant DNA work with massive sequencing capability or the ability to sequence a human genome in a day, really, whereas the calculation was, when I was doing DNA sequencing, it was almost impossible to sequence that many bases. So now as technology is improving, it opens up whole fields that just weren't accessible before, and some people are facile enough to incorporate all this technology in real time, but some of this happens with younger people coming into the field, and they bring expertise in this new technology and sort of enliven the field, so that's interesting to watch.

But, yeah, technology's huge. It's instrumentation. I can give you just an example. We were talking yesterday—we have this machine called a flow cytometer and it's able to detect single cells and tell you which proteins are found on these cells, and you can see a certain number of proteins on each cell at each single cell, so you can look at millions of cells and look at the whole population cell by cell and know what's expressed on each cell. Well, we were limited previously to about fifteen different proteins at a time, and now there's a new technology—well, there's one technology that came out that allowed it to go to thirty or forty, but that was very, very expensive and a little more cumbersome, and now there's a new technology that allows you to do twenty-five different colors or different proteins at the same time, and that will enable experiments that couldn't be done previously. But that's just one example. There's super-resolution microscopy and there's all sorts of things that really allow you to understand new aspects of not only immunology but just all kinds of biology.

Williams: Mm-hmm. Is there some type of technology that you are particularly interested in their discovering?

Hedrick: Oh, that's an interesting question. In other words, what's our technical limitations at this point. Well, so for my own work, the limiting factor is the time it takes to do genetics in mice. So you can't speed up the way mice breed and develop,

except there's the possibility of speeding that up in a certain sense. With CRISPR-Cas technology that's come along recently, one of my colleagues at UCSD has come up with a way of—they call it active genetics. Now, this is a little bit technical, but we're all diploid; that is, we have two copies of each of our genes. And so to do genetics, you have to breed male and female, and they each contribute one copy of the gene, so now the offspring have the paternal and the maternal copy of the gene. And in order to get, say, two maternal copies plus the mother gene, you have to breed them, and it takes several generations.

Well, they've come up with a way in which a gene can be transferred from one chromosome to another almost in an infectious way in each generation, so each time you breed, you would get both genes from, let's say, one of the parents into the chromosome, which it defies Mendelian genetics and, in principle, will allow you to speed up breeding manyfold. If you made these active genetic principles all over the genome, you could pull them all together in one or two crosses, which would tremendously speed up the way you do genetics.

Now, it's not feasible quite yet, but people are working on it. So that's a great technology. I mean, the CRISPR-Cas technology in general is just going to revolutionize human beings, I mean not that we're going to necessarily alter human beings themselves, but the way you can alter, let's say, mosquitoes or tomatoes or something is unbelievably powerful. I think that's one of the most revolutionary breakthroughs of our time.

Williams: Do any other breakthroughs occur to you at this point?

Hedrick: Oh, my gosh. [laughs]

Williams: Well, you speak so well of that one. Are there others?

Hedrick: Well, that's the one that really has excited me, and we're working with other groups on campus, and this isn't my work at all, but they are engineering mosquitoes so that they would be resistant to malaria plasmodium. They're engineering plants so that they would be more productive in terms of producing canola oil, for instance.

Then there's another group that's made this active genetic principle work in mice. So there's a whole program at UC San Diego on this active genetics that is funded by the Tata Foundation, and there's just almost endless possibilities. For instance, you can engineer a plant so that it would have a gene that would be more productive in terms of pulling carbon dioxide out of the atmosphere and carrying out photosynthesis, and if this plant had an active genetic principle, every time it mated with another plant, it would spread through the world—this is sort of a science fiction idea that might be a little bit dangerous—it could spread through the world and pull carbon dioxide out of the atmosphere and solve global warming. Of course, it might freeze the planet also. [laughter] So I wouldn't

advocate releasing that at the moment, but these are the kinds of technologies that you can do with genetics and CRISPR-Cas and active genetics that are *really* going to revolutionize the way we interact with the environment.

Williams: Great, great. In 1981, you joined AAI. What caused you to do that?

Hedrick: Well, let's see. I was just a postdoctoral fellow, and it was kind of the thing you did. I was an immunologist, and so I wanted to join. I really just did it. I mean, I had gone to the meetings. I had gone to the meetings as early as maybe 1970—there was one in New York City, and I went with my first Ph.D. advisor to New York City to attend—no, maybe it wasn't New York City. Anyway, we attended a meeting, and, actually, that meeting was the meeting in which a scientist presented this ability to transplant skin from one mouse to another, from a black mouse to a white mouse, and so you'd have this white mouse with a black patch of skin, and this was a big deal because transplants are usually rejected by the immune system, although it turned out that this mouse had a black patch because they had used a Sharpie, a marker, to color it in, so it was a big scandal. That was my first meeting that I attended, was this big presentation of this wonderful new technology to allow transplants to occur, and it turned out to be fraud. What can you do. Anyway, that's not what you asked me. [laughter]

Williams: Well, it's fascinating, though.

Hedrick: It's just a little anecdote, yeah. What caused me to join AAI? Really, it's just what you did as an immunologist; you joined the AAI. Then I guess the first thing we did that was really significant for the AAI is about 1995 or '96, the Internet became a thing, as people say now, and there was the World Wide Web and there were a few thousand sites. [Williams chuckles] And I had a graduate student who was quite interested in this and had learned a little bit of coding to make a website. So we made the first AAI website for them, and I designed it, poorly, I must say, but it was the first time there was a website for the AAI. And it had an interesting little feature. We had an "Ask an Immunologist," so the public could just go on this website, type in a question, and then I sort of would triage the question to some immunologist who had expertise in this, and they would answer it, and then we'd put it back up on the web and people could learn about the things that they wanted to know about the immune system. It was really interesting. I enjoyed doing that. Then, of course, they wanted a professional website very soon after that, and so they moved it and made much better designs and so forth, but we did lose that one functionality, which was this "Ask an Immunologist." It was sort of like the earliest podcast or discussion group. I don't know what you'd call it.

Williams: So you regret the passing of that feature?

Hedrick: Yeah. Yeah, we could institute it anytime, I suppose, if they were interested in it.

Williams: It sounds like it was labor-intensive for you.

Hedrick: Well, it was, yeah. You had to constantly be reading these things and finding people to answer the question, but relative to other things that we do, like reviewing papers takes hours, so I could do this in an hour a day, probably, or half an hour a day, usually.

Williams: Mm-hmm, mm-hmm. What about your participation in the Advanced Immunology course?

Hedrick: Yeah. So I first participated back quite a while ago and then I actually ran it for a couple of years, and I think we brought it down here to UCSD, so the class was here at UCSD, and then it rotates, so somebody else has been running it for quite a long time, but I've been lecturing in it for the last, I'd say, four, five years. The lecture I give is on the coevolution of microbes and the immune system, so I try to bring my perspective on this coevolution to each new generation of students, which I find to be really fun.

Williams: The typical student in the advanced course would be what?

Hedrick: Well, there's two courses the AAI gives. One is the introductory course, which is still pretty intense. People come and give their talks over a period of five or six days. Then there's an advanced course. I teach in the introductory course that's held up at UCLA, and the students that come typically are students that have had a little bit of immunology, but want to get exposed to more in-depth focus from the different faculty members that come and give them more detailed lectures on different topics in immunology. And I've never been to the advanced one, so that must be even more intense.

Williams: Have you encouraged some of your postdocs and whatnot to attend?

Hedrick: Oh, yeah, mm-hmm. In fact, for this program in immunology, when we have a graduate program, we're going to require a background in immunology to start the program. It would be difficult for us to garner the resources to bring someone in that has absolutely no immunology background and start them in the graduate program. We just don't have the faculty to teach those early classes, so what we want is for people to come with at least an undergraduate course in immunology, but if they don't, they could attend the AAI course and probably come up to speed and be able to then attend graduate courses in immunology. So we intend to use the AAI resource in that way.

Williams: Mm-hmm. You received the Distinguished Service Award in 1996.

Hedrick: That was for this website that we put up. [laughs]

Williams: Well, you're recognized for it and appreciated.

Hedrick: Yeah, yeah. No, they're great. AAI is wonderful. They really take care of the people who serve, and they acknowledge them, and it's a great organization to be affiliated with.

Williams: And now you're receiving the Distinguished Fellow Award. Maybe you just did yesterday.

Hedrick: Yes, they handed out these little plaques, and it was really quite nice. It was a wonderful surprise. I just logged on one morning to my email and there it was. I had no idea it was even something they gave out, so it was a very nice surprise. I was glad to be included.

Williams: So you've dusted off a little area on your shelves and—

Hedrick: I'm going to. I have it in my car right now. [Williams laughs.] There were four Nobel laureates included and a lot of other people who have been in the field a very long time, so I was honored to be included.

Williams: Do you recommend a career in immunology under present conditions?

Hedrick: Yeah, absolutely. I mean, being a scientist is the very best job you could have, with one exception. So it's the very best job in that you come to work and you really pretty much work on what interests you, and you work with very smart people, and if you're lucky, you bring young people along and they surpass you, and you just see the march of information and knowledge accumulate. This sounds corny, I'm sure, but it really is a fulfilling way to spend your life, I have to say.

The only downside is the competition, especially for funding, and everybody complains about it, and there's just nothing to be done, probably. It's a system that, to some extent, competition is absolutely required. How it's actually administered, you could argue there's different ways to do it, but the competition is always going to be there. And everyone complains about getting their papers in the best journals. You know, that's less of an issue, because if you have a good story, you can publish it someplace. You may not get it in *Science*, but it'll be publishable someplace.

And it's just fun. I like writing. I like writing scientific papers. I like plotting data. I like seeing how it works out, and it's just fascinating constantly. And there's still many, many areas of research that will move forward forever. I mean, there's just no end to discovering new aspects of nature. It's changing in that—I think I discussed this—at least in immunology, we're not trying to solve big mysteries that we have no idea about. We're more focused on understanding the nuances. I don't want to just say details, because they're really important aspects that we haven't really encountered before, like, for instance, the interaction with the

microbiome. That's *huge* in the immune system, and that's a brand-new field that's exploding. So there's always going to be new fields. It just wasn't the same mysterious questions that we had when I started, which was how does the immune system recognize an infectious agent and what are all these novel aspects of biology that you find in the immune system. But, still, there's always going to be interesting things to study, and it's really a wonderful career.

Williams: What's the exception?

Hedrick: Well, the exception is the competition for grant funding. That's the hardest part of science, but as I say, I think the competition is necessary. There's no way of getting around it.

Williams: How does family life figure into the life of a successful scientist?

Hedrick: Yeah, that's an interesting question. The culture of science is whoever works the hardest gets the most respect, and so there's these phrases like who's a serious scientist and who's not a serious scientist. I suppose a serious scientist is someone who just goes all in and devotes his or her entire life to scientific pursuit, without so much regard to their personal life. Personally, I don't subscribe to that, and so when my kids were little, I coached soccer for six years, and I spent many weekends at home with my kids and family. And also I'm lazy. But, yeah, it figures in, and some people are much, much more dedicated and put it in six and a half days a week in their labs. So, you know, you just have to find your own balance.

Now I've forgotten exactly what your question was.

Williams: Well, how family life collaborates with scientific endeavor.

Hedrick: Yeah, you know, because science does take so much time and it is competitive, you can continually work at it without stop, so that can certainly—you have to balance it, that's for sure, and each individual has to decide how much he or she wants to devote to one or the other. Then there's issues of gender in terms of many women devote more time to family or feel a need to devote more time to family, and some don't. I mean, it's all over the place, but it's well known it's a little bit more difficult for a female scientist if they take time off, for instance, to have a family. It can be a little bit more difficult, and I think we're moving toward accommodating those family issues a little bit better, but there's probably still lots of room for improvement.

Williams: You have two kids?

Hedrick: Yes.

Williams: And where are they headed professionally?

Hedrick: Well, they're both artists of a sort. One is a glass artist and lives up in Los Angeles, and the other is a graphic designer and runs a website and an event space, and she has a little company with two other women that they run this. So neither of them went to science, and I don't know why. I asked them, "Why didn't you go into science?"

And they said, "Well, we don't know. We just found our way in someplace else."

Williams: Is your wife a scientist?

Hedrick: She is. She's a lab manager at the Salk Institute for a scientist there, and they work on metabolism. We met in the lab, actually. She was a lab technician in the lab in which I did my Ph.D., and we met there and got married during graduate school. So she's continued as a lab technician and lab manager ever since, and she's thinking about retiring, but she's still working in the lab. In fact, right now she's doing an assay, and we are having a party for all my lab alumni tonight, and so I'm hoping she gets home not too late so that we can finish getting ready for this party. We have about fifty people coming.

Williams: Wow, wow. You mentioned coaching soccer. I've been asking people, as a scientist, what do you do for fun?

Hedrick: I'm an enthusiast for exercise, so I run and ride a bicycle, and we have a house up in the mountains and we go skiing a lot and we hike. So we try to take a trip someplace in the world every two or three years. We have a group of people we go with and we hike. So the most recent one was to Patagonia in November, and so we spent two weeks hiking in Patagonia. And I enjoy reading both science and trash. [laughter]

Williams: Well, on that note— [laughter]

Hedrick: Oh, no, you can't end on that note. [laughter]

Williams: Is there something else you'd like to say for the historical record here?

Hedrick: No, I don't think so. It's been a pleasure to be a scientist. That is kind of the theme you were bringing out, and I recommend it highly.

Williams: Thank you. Thank you very much.

Hedrick: You're welcome.

[End of interview]