The American Association of Immunologists Oral History Project

Transcript

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Lanier: Okay. After I got out of high school, I left engineering and started in microbiology at Virginia Tech. There what really turned me on—was I think when I was a senior of college or a junior in college, I was in a virology class, and there was a guy named—I think Dr.

So my first project was to work on the skin graft transplantation. But as it turned out, the first year I was in Geoff's lab, these mice that we had made genetically to study the skin graft rejection were spontaneously developing lymphomas. At that time, there weren't any good models for human B cell lymphomas, and these mice started spontaneously acquiring these tumors. So my project ended up understanding and studying these mouse B cell lymphomas and making therapeutics to help cure them.

Williams: At what point did you first publish results of your work?

Lanier: I think that was about 1978, so I was a second- or third-year Ph.D. student. So it was on this novel mouse model that we had generated. There's a tumor called CH-1, or Chapel Hill-1, we named it. It's a B cell lymphoma and serves as a good model for human B cell lymphomas.

Williams: So why did you choose the Ph.D. versus the M.D.? You just never thought of going the clinical route, is that correct?

Lanier: When I was living with my grandfather as a little boy, he had a really bad heart and was in the hospital several times for months on end, and I just got a bad feeling about being in hospitals, so I didn't like being around sick people. I really liked the science of medicine, but I think that experience I had with my grandfather kind of gave me a phobia of hospitals.

Williams: Widely shared. So talk about your postdoc work then at UNC, I guess.

Lanier: Yes. So I stayed on and finished my Ph.D. with Geoff in about three years and wanted to finish up some projects. We had made antibodies against the surface immunoglobulin on these B cell tumors to serve therapeutically. So we treated these mice, which we'd given this lymphoma, with these antibodies against the surface Ig. They're called anti-idiotype antibodies that cured the mice. I wanted to finish up a few of those experiments and also then look around and decide where I wanted to go for a postdoc.

There were three places that I really seriously wanted to go to, was, one, in Sweden, to a guy named Hans Wigzell who was doing some exciting work at the time. The second one was Len Herzenberg at Stanford [University]. And the third was a fellow named Noel Warner, who was in New Mexico at the University of New Mexico but also working at the Los Alamos labs.

Well, Len sent me a rejection letter that my wife subsequently found in his filing cabinet when my wife was working for him many years later. [laughs] And I didn't hear back from Hans in Sweden, so I thought, well, he just ignored my letter.

But then Noel Warner flew me out to New Mexico. I went up to Los Alamos labs They'd just invented flow cytometry in Los Alamos a few years before that, so I saw this fantastic new technology, appreciated what it could do for me as a cellular immunologist. Noel offered me a position, which I accepted. The day I accepted, I got a call from Sweden from Hans, telling me that he'd like me to come to Sweden. [laughs] But I'd already given my word to Noel by then that I would join him in New Mexico. So off I went to New Mexico for the next couple of years.

Williams: Looking back, if you'd gone to Sweden, might you have had a cells, but we didn't have any really definitive markers. The T cell receptor had not been identified. We knew about surface immunoglobulin on B cells. That was about it. By the time I left BD, there were a couple of hundred known surface antigens. We'd developed antibodies against many cell subtypes and differentiation stages, and that was where I first also started working on natural

Lanier: Yes. We started on the edge of Palo Alto in Mountain View new lab on Garcia Avenue. The last year I was at BD, we moved to San Jose, but I was there about six months and then started phase two of my career.

Williams: So BD not only was making products, they were making products based upon the science?

Lanier: Right. So what they wanted to do was make products to initially allow researchers to understand how the immune system works. I think the main breakthrough that happened for them commercducts Bottomo2tsd12(ar) to do wdum-2(h

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Williams: Have you developed ways to increase the population of NK cells in an organism?

Lanier: Yes. You can increase NK cells, again, with cytokines. Again, when people have been treated with IL-2 therapeutically, the number of NK cells increases. Jerry Ritz and his colleagues at Dana Farber [Cancer Institute] have shown this quite convincingly. Also, many of the antibody drugs now that are used, like Herceptin for breast cancer and Retoxan for B cell involvement, it's actually the CD16 receptor on NK cells which is involved in killing the antibody-coated tumors. CD16 is the receptor for the FC portion of those antibodies.

Williams: So you're several ye

Williams: And you did none of that work yourself?

Lanier: [laughs] Not the mouse work. Not the mouse work.

Williams: So this was sort of a continuation, then, of your DNAX interests.

Lanier: Absolutely. Like I said, one of the reasons I had left DNAX was I really wanted to understand what the biological function was of a lot of these molecules we had discovered at DNAX, without worrying about putting them to therapeutic use in a five-year timeframe, because I knew that that was probably not going to happen.

Williams: Was there any expectation that some of this work would flow back into DNAX, or were you completely severed? That relationship had been severed?

Lanier: No, I stayed on as a consultant for them, an advisor for a few years, and, in fact, I'm going back and advising the Merck group. Last month I was meeting with some of my old colleagues from DNAX who were still there, discussing the science. So it was a pleasant separation.

Williams: But it was understood that the work you were doing there may have been built on the work you had done there, they would have no proprietary—

Lanier: Well, you know, when I was working at BD and at DNAX, the understanding was if we discovered something potentially useful, you would file the patent before you submitted the paper. So many of the molecules that we discovered in my lab at BD or then at DNAX, the patents were filed. So, in essence, by continuing to work on some of those molecules at UCSF, I was doing their work for free now, because if we found something interesting, we'd file the patent through them and they could potentially benefit from that.

Williams: And that did happen?

Lanier: They still are pursuing some of the things that I had started there a decade ago.

Williams: So talk about the high points of your career to date here. What have you been doing?

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So that really set the stage for much of what I've done since being at UCSF. We had a receptor that's on all NK cells, it's on all gamma-delta cells, and on human CD8 T cells. So when those cells, those immune cells are circulating through the body, typically there's no ligand for that receptor in healthy tissue, but either cancer or viral infection or autoimmunity can cause the expression of those ligands on the surface. It's good if you have cancer or have a viral infection. It's bad if you have autoimmunity. So we've set up several models, autoimmune models, viral infection models, and cancer models to show the importance of that receptor system.

Williams: In layman terms, describe the ligand.

Lanier: The ligand, they're a protein that's not expressed in healthy cells. When cells become unhappy and they're disturbed by infection or by cancer, they then will put this protein on the surface of the cell like a flag, saying, "Something's wrong with me. I need to be gotten rid of." The receptor on the killer cells can now see that flag, know that that's the cell to take out. So there's a variety of ways that those—stress can do it. Many types of stress of the cell causes that process to turn those genes on.

Williams: Now, it would sound like—a simple-minded person would say, well, you've cured cancer.

Lanier: [laughs] We've cured cancer in a lot of mice. That's the interesting part. Both viruses as well as cancer cells find a way to escape this mechanism.

Another good surprise was when we started working with a postdoc here, Courtney Crane

women has become infected with papil

NK cells are long-lived. We studied them and showed that they would then respond better the second time they saw a virus, saying, like B and T cells, they remembered, and they were also long-lived. Now it suggests that maybe you can vaccinate NK cells like you vaccinate other components of the immune system.

Lanier: Well, I always thought the AAI was a good organization. I joined, I think, when I was a postdoc in about 1980, and initially it was one of the first few places that as a young scientist I was invited to talk about my own work. That's something unique about the meeting. At a lot of meetings, like some meetings, they invite the famous people. When you're just starting out, you're never going to get on the podium. AAI allows the people who actually do the work to talk about their own work. So as I was starting my own lab, I was invited several times to come to the AAI meeting, present my own work.

The Journal of Immunology is a fantastic journal. People say, "Oh, it's just a *JI* paper." Well, the first paper on the T cell receptor is published in that journal. The first description of Th1, Th2 is in that journal. My first NK paper is in that journal. So before things are fashionable, the journal and the society have really contributed to everyone's career early on in that fashion.

Williams: You were an editor, associate editor for a while?

Lanier: Yes. So as I started my relationship with AAI, they started inviting me to chair sessions at the meeting. The first papers I probably reviewed for a journal were for *JI*. Then they asked me to help with the editorial process. Then at one point they asked me to join the Program Committee and then become head of the Program Committee, which organizes the annual meeting. So that was kind of my steppingstones up to the Council and the presidency.

Williams: You received a distinguished award from the AAI, and I'm trying to find it in my notes here. Was that for your service on the Program Committee or not?

Lanier: Yes, that was largely for my work as program chair for a number of years, yes.

Williams: What was outstanding about your programs?

Lanier: [laughs] I'll let other people judge that. They were well attended, and I think everybody congratulated us on putting together good meetings that were well run and were exciting.

Williams: Did you introduce any innovations in the format or anything of that sort?

Lanier: It's been quite a while, so I don't remember. I think the key, though, is persuading the best people to be involved and present their best science, because AAI, unlike some other organizations, is all pro bono. You don't pay anyone to speak there, so you have to convince them that it's such an honor, and to get the top people in the field to come to the meeting and present their latest work without getting paid for it or getting the travel expenses paid. So I think my distinguished service was convincing a lot of really good people to come for free. [laughs]

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