

**The American Association of Immunologists
Oral History Project**

Transcript

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transferrin. We also went on to show that females who are heterozygous for these two alleles at the transferrin locus are more fertile and that the fertility at least in part can be ascribed to the fact that the heterozygous that is having both kinds of transferrin present are better or more bacteria static than having only one kind.

Then I finally went on. This is one of the great things where I learned that sometimes it's really good to collaborate. We tried to make a mathematical model for how to do this, for how that kind of fertility, which is not the sort of standard over-dominance for fitness that you think about for resistant to malaria by sickle cell anemia, because it's kind of a twist on a fertility model.

I tried really hard for about three weeks to figure out how to make an algebraic model to do this, and Ray said, "You know, I know this guy [James F.] Jim Crow in Madison [Wisconsin]. You should just go over and see Jim, and he'll help you figure this out." So we bought a plane ticket. I flew to Madison. I stayed at Jim's house. Jim just died recently. In about three days, really one hour of his time, three days of my time, we figured this out. We published a paper full of equations in *The American Naturalist*.

It showed me that the right person can really fix a problem, and you don't have to know how to do everything that you need to do; you just have to know how to get help to do it. I don't know if you know about Jim Crow. He's a really famous population geneticist, but just the nicest man. I think he played the viola. Maybe it was the violin.

Williams: Now, this sounds like you were a postdoc, but you worked.

Frelinger: I was a graduate student.

Williams: You were a graduate student, so at the same time you were taking courses.

Frelinger: Sort of. So Caltech requires you to take a small number of courses outside of what your major is. So what I like to say is I took management accounting, I took a seminar in population problems, and I took another course. I can't remember what it was. It was another economics course. So I took no biology courses. I did T.A. [Teaching Assistant] in immunology every fall for the whole time I was in graduate school.

Williams: So your interaction with immunology was limited pretty much to what you were doing in the lab, is that right?

Frelinger: Yes.

Williams: And talking to people.

Frelinger: And talking to people. Ray was an interesting guy. He didn't require very much of you, but he required you to show up for coffee twice a day. So you had to be there at ten to have coffee in the morning, and you had to be there at three, and you had to arrange your day around that, and there we talked about everything. Ray was a real Angel's fan, so we sometimes talked about the Angels, so a really

The problem I was interested in was in short-range recombination in the major histocompatibility complex. I was interested in it for two reasons. One is it was clear it caused tissue graft rejection, but it was also clear it was a place that you could look at very closely linked genes recombining because there were good markers.

So I said, "That sounds good," and I met Don at a meeting, and he seemed like a good-enough guy, and so we went. So we wrote up a proposal which was

Williams: What were the students like at USC?

Frelinger: Awful. No. The very best students were okay, and the worst students were bad and there weren't very many. I had two students at USC, and they were okay, fine. They survived. They survived me. It was okay. The postdocs were better. I had great postdocs. My first postdoc was a guy, Peter Wettstein, who is now a professor at the Mayo Clinic. So they were good. I really was lucky in getting really good postdocs to come work for a new assistant professor, which was kind of fundamentally insane to do, but they did anyway.

Williams: So what reason did you have for moving on?

Frelinger: It was really clear by then that USC couldn't keep its act together. In retrospect, its problem is/was certainly that it had a huge clinical operation to provide indigent care to a huge number of people, so that means a very large number of service-oriented clinical faculty whose job it was to take care of sick people, and that makes it very hard to create an academic environment. Walt Kelly wrote, as Pogo, said, it's really hard to think about draining the swamp when you're up to your ass in alligators, right? Really, that's a big problem. So the academic atmosphere certainly never was able to be generated, while I was there anyway.

Williams: So what's the weather like on Monday (9) 40.4 (42) 3.8 T w 10 T 0 T w 33.6 (34) 10.5 (1) T n E M C 0.0 2 T

build a state zoo, and he said, “We don’t need to build a state zoo. We can just put a fence around Chapel Hill.” And that was okay, because you lived in Chapel Hill, there were like-minded people. Occasionally the town had a foreign policy. [laughs] Never understood exactly why we needed a foreign policy, but we had one.

So it was fun and it was a nice place to live. We ultimately built a house on ten acres five miles from the lab. On a bad day it took eighteen minutes, and on a good day it took twelve minutes to get to work. I mostly biked, and it took twenty-five minutes on the bike. It was an easy place to live. For her, there’s a big vibrant writers’ community, and that was a big part of her life. So it was a really nice place to be.

Williams: For you in terms of medicine, what was the allure?

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that he failed to get—he probably hired twenty-five or thirty people between the time he was in ID and the time he was in Micro. I can only think of three people that he didn't actually manage to sign.

Williams: So with all this influx of new people, did you coalesce into various groups and study groups and so forth, or were you pretty independent?

Frelinger: Yes and no. I mean, so I had really serious interactions with a large variety of people over time. I had a very close collaboration for a long time with an x-ray crystallographer called Ed Collins, and as a result, if you screen the x-ray crystallography database, I have about eight structures that somehow I'm associated with, although I could never solve an x-ray structure if my life depended on it. So we had those.

I had a long collaboration with a guy called Roland Tisch on Type I Diabetes, and so both Ed and I and Roland and I had grants

people now call BLT mice, bone marrow, liver, thymus reconstituted, gamma C-null, SCID, NOD mice, reconstituted with human fetal liver and human thymus and human bone marrow. Those mice

course that's not a didactic course for all the graduate students in immunobiology. That's our only required course, and we spent a lot of time this year, because this is the first time we did it, but we put together a series of modules, which we did as two-week modules but we'll probably do as three-week modules next time, with a sort of six-week introduction, "Everything You Needed to Know About Immunology, Bacteriology, and Virology in Six Weeks," which is really fast and really shallow and really a 30,000-foot view.

Then everything else is focused on a question or disease or something. So we just

In Arizona, the legislature is almost exclusively made up of high-school-graduate small businessmen, and so it's not the same, and they're much more actively antagonist towards the university than they were in North Carolina. North Carolina, they didn't like the university because they were full of them northern liberals, but, boy, they loved the basketball team, right? You could, and I did, I've been to pig pickings out in the country and you didn't talk about where you went to church, but you could be for any basketball team as long as it was UNC or State. [laughs] That was fine and you could talk about that, and that was sort of a unifying principle.

Williams: So where are you getting most of your funding for the department in Arizona?

Frelinger: So the university has been very generous to the department, and a lot of it's coming from the School of Medicine. We've been successful in getting NIH [National Institutes of Health] funds. Three of us, led by Janko, got a \$12 million contract last year from the NIAID [National Institute of Allergy and Infectious Diseases], and I came with grants, so that's what we're doing. I mean, the old people, that is, Maggie and me and Janko, are well funded. One of the young people, Felicia Goodrum, has two grants. She's done very well. She's kind of an old young person. So we're trying hard to do that and to bootstrap(nd J)-11(a)-1(t)-2(la)-2(n)-10(

we're just not trained right. But we've had a good collaboration with people in electrical engineering at U of A who design gaming chips for games processors, and so they've designed and built a hardwired gaming GPU to analyze these kinds of sequences and to make models of them. So we're trying to write an NSF [National Science Foundation] grant with those guys to sort of forge ahead with that, kind of different from what we did before, but exciting and fun.

Williams: Let's turn to your experiences with AAI for a bit. You became a member in '76, I believe.

Frelinger: If that's what it says, that's probably true. [laughs]

Williams: What are some of your outstanding memories of the organization?

Frelinger: So I got involved really with AAI in the advanced immunology course. They got us to teach the course for a couple of years, and then I got asked—I guess they probably did it for five years, but I did it only for a few. They had a person come for half the course, and they called him the guru. What you did was you provided some continuity because the advanced-course people come in, they give their two-hour lecture, and they're around for a couple of hours and they bolt. So they wanted some senior people to be there to talk to the students, and when the students didn't understand something, they could ask questions of you and you weren't quite so forbidding because you didn't just pontificate for two hours about it, and they could ask.

So I did that. That was really fun. Bob Rich, one of the years I did that, was one of the other gurus. I'm trying to figure out exactly what Bob was doing then. I think he was probably an associate dean at Emory [University] then and was interested and realized that I was interested in kind of broader issues of policy. He was chair of the Public Affairs Committee. The sort of professional person on the Public Affairs Committee was a guy called Pat White, the Lauren Gross equivalent of the time.

So I was on the Public Affairs Committee for probably three or four years and made some [Capitol] Hill visits, and it was at a time when—so it must have been George [H. W. Bush] the first's time when the Republican legislature was very big on getting rid of all these onerous regulations. We were going to deregulate everything. So we tried to figure out ways to make life easier for people by pushing back against—there's always been this increasing regulatory burden that we have that's driven by someone's afraid for safety, someone's afraid that you're going to throw some deadly germ down the drain or that a terrorist is going to walk in and be able to find something in your lab. No one can find anything in the labs. But to try and figure out how to push back against increasing regulatory burden, and so he got me interested and I got interested in the larger policy questions.

So when Bob stepped down, I was asked to chair that committee, which I did, and I think I did it for three or four years, which now we don't do that anymore, but which was really good. I really got interested in trying to push AAI and push the government into thinking harder about support for biomedical research, how we do that, the things which are important to our members in terms of regulation and in terms of how we live our daily lives.

My personal feeling of the most useful thing I did on that committee is I had lunch with Pat White and the chief of staff from [Thomas R.] Harkin's office in the Senate cafeteria. It was at a time when one of the things I was and I'm still interested in, postdoctoral salaries, which I still think are too low, but at that time were really too low, so we were chatting about this, and this fellow says, "Well, how much do they get paid?"

I said, "Well, I had a fellow in my lab who was an M.D./Ph.D. board-certified pediatric rheumatologist, and he was making \$32,000 a year."

He said, "That's not possible."

I said, "Trust me. That's possible. That's what he gets paid on a T-32 with that much experience."

He said, "Well, we'll have to fix that."

So that year postdoctoral stipends went up about 25 percent. Now, I don't claim that I did that, and there are certainly lots and lots of people worried about postdoctoral stipends and not just me and people inside NIH, but it was clear that this was a really important guy who was the chief aide to a congressman who was really important on the right committee, and maybe it creates the receptive field for ferti

Frelinger: That was less work and more interesting than I thought it was. It's way less work than being public affairs chair. I mean, the real work of being a councilor is showing up twice a year and paying attention while you're there. So you've got to read the book on the plane on the way, right? But really its function is as part of the board and trying to be responsible and thinking about what's best for the organization, how can the organization help its members, and why we do particular things the way we do, and should we change them. That's really what we do. And keep Michele Hogan happy. That would be the other thing that the councilor is supposed to do.

Williams:

Williams: What was that like?

Frelinger: So this is difficult for me, because my father, who was then ninety, wanted to come to the conference, and so we brought him to the conference and he heard my presidential address. The next night we were getting ready to have this sort of fancy party like they did last night, and he fell and broke his femur. So he spent the next four weeks in San Francisco General [Hospital]. One of my former fellows, Bruce Cairns, the surgeon I told you about, actually had come to this meeting because I was president, and Bruce spent the night in the ED with my father. My brother was there, who spent a lot of time there, and I showed up here handing out pictures and signing things and presenting plaques. But it wasn't that much fun, and afterwards my brother and my wife and I sort of tag-teamed the time he was in San Francisco, going home, coming back, and staying with him. So it was less than wonderful personally. I heard the meeting was good.

Williams: A few last questions. I've been asking people what they think of the state of science today in the United States.

Frelinger: So that's a really complicated question. It seems simple, doesn't it? So science is great, right? And we have tools and ways to do stuff that we couldn't even imagine when I started doing science. In my lab, Adam Buntzman, this guy who's been doing the informatics stuff on T cell receptors, out of essentially our back pocket we have just completed the sequence of the hummingbird and the ostrich. The reason for the hummingbird is it's got a heart that beats 400 beats a minute, and they live twelve years. So how do they do it? I mean, there are enormous physiological adaptations you should be able to figure out, at least get clues from the sequences. So we can start to do those kind of things which are just insane, and it costs almost nothing now compared to what it used to. So the tools are awesome.

Our ability to understand things and drive things from ideas to the clinic, I mean, it's better now than it's ever been. The downside is the healthcare system is in total disarray. We're driving it in three directions at once, all of which are wrong, and so that makes things really hard to do. The societal appreciation of science, I feel like is at a new low. I think soon we'll pass a law saying that the world is flat and that you're going to fall off the edge if you go too far.

Our inability to communicate effectively with the public is amazingly bad. I mean, it's horrifying to me. And when people like our former president [George W. Bush] says, "Well, global warming is only a theory," well, gravitation is only a theory. Evolution is only a theory. Right? So I make some alternative explanation ad hoc and that is equal? So, I mean, we've done a really bad job of trying to teach people what science tells us and how it tells us those things, and I don't know how to fix that. I mean, I think all of us need to work harder at it, but if I had a way to work harder and smarter, I would be doing it right now.

We had a session here about scientific outreach, and we don't do that very well. So we've done that. We've degraded science as a perception, and people have this simultaneous awe and distrust of it. You can find people that believe we really have the cure for cancer and we're just holding out on them, and at the same time they don't believe in evolution. And those are so discordant. I can't resolve those in my own mind.