The American Association of Immunologists
Oral History Project

Transcript

Michael J. Bevan, Ph.D.
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Interview conducted by
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Williams: This is an interview with Dr. Michael J. Bevan for the American Association of Immunologists Oral History Project. Dr. Bevan is a Howard Hughes Medical Institute investigator and professor in the Department of Immunology at the University of Washington. He was awarded the AAI Excellence in Mentoring Award in 2000 and the AAI Meritorious Career Award in 2009. We are at IMMUNOLOGY 2015™ in New Orleans, Louisiana. Today is Sunday, May 10th [2015], and I am Brien Williams.

Thank you very much for doing this with us today.

Bevan: Thanks for asking.

Williams: I like to start the interviews with as much family background as you want to share. So please tell me a little bit about your background.

Bevan: I was born in 1945 in South Wales, part of the United Kingdom, in a village which sounds all very nice, but actually it's in the coal mining valleys, in the Taf Valley, close to the Rhondda Valley. My father was a coal miner, as were his father before him, and my mother's father was also a coal miner.

In about 1900, they built these—I don't know why we call them villages. They were just terrace houses on the sides of the valleys, you know, close to the colliery pit, the mine, the coal mine, whatever. I still have vague remembrances of my father coming home, taking a bath, but pretty soon his health made him give up that, and after that he sort of just did menial jobs in factories and so on.

My mother was a housewife; she had lots of sisters, and was born just about 200 yards from where we used to live. She, apart from looking after two kids, me and my brother, and my father, of course, also was a dressmaker. She used to make dresses, usually just for family members. I still remember she would make a dress, cutting the patterns out in tissue paper, and then sell them—not sell them. They were requested for ten shillings, which is like half a pound, maybe half a euro now, one would say.

So it was a pretty good life. I, obviously, walked to school, to my primary school in—my village was called Cilfynydd, which means "farm under the mountain." The closest market town was Pontypridd, which translates into "bridge of mud." But I could walk to my primary school in Cilfynydd.

In those days, we did the eleven-plus, this horrific exam that people in England used to do, which split you into two. Either you passed the eleven-plus and you went to grammar school, which I obviously did, or you failed it and went to what we called secondary school or maybe something else.

So I then went to grammar school, a boys' grammar school, unfortunately, a boys-only grammar school in Pontypridd, until I was eighteen, did the O-levels, did the

A-levels. And all that education was free, of course, and then I applied for a few universities and eventually had to choose, or wanted to choose between [University of] Leeds and University College London. I went to University College London on Gower Street, and my bachelor's degree was in zoology. So in retrospect, I don't think that zoology was terribly useful as my career, but it was terribly interesting. What I wanted to do, I wanted to do some biological research, but it was split into one year we would do the invertebrate year, and the next we would do the vertebrate year, and the third year we were supposed to just study for finals, which was just a one week-long session we had.

But the best thing about going away to London, leaving Cilfynydd and Pontypridd in South Wales, were the people in my course, people from Yorkshire, people from North Wales, people from Birmingham, you know, the most intelligent. The other students I'm talking about, not the faculty so much. But we used to have terrific arguments about scientific things, things we were learning about, speciation and evolution and things like that, and I think that really formed me. Now, I always knew that I wanted to do biological research. I don't know how I knew that.

Williams: When did that bug get to you?

Bevan: I was always liking animals and being fascinated by them. I'm wandering around on the hillsides, finding skulls of sheep, lots of sheep in Wales, you know, and that always used to fascinate me. Then at a later stage, looking at articles as you'd find them in *Scientific American* in those days, and pretty early on I was pretty fascinated by the antibody problem. Nobody knew how the diversity of antibodies were made. It ended up I would never contribute to that, but that kind of turned me towards immunology in a way.

During my 3 year bachelor's degree doing zoology, we learned no immunology. We learned normal molecular biology, but the bug was still there. So after doing my bachelor's degree in zoology, I then did a one-year master's degree in biochemistry at the same institution, at the University College, and that was just packed with molecular biology. That really turned me on to the cracking of the genetic code and so on. That was wonderfully exciting.

Then I applied, just made one application. Somebody recommended I should go to Mill Hill, the National Institute for Medical Research in North London. I wrote one letter, and I don't think I was interviewed, but they said, "Well, you can come." I came, and that was it, to do my Ph.D.

Williams: Describe, first of all, what was University College London like?

Bevan: Well, it was a fantastic experience for me, meeting these—there were only twelve students per year in the zoology course. We were fused with a year ahead and then later put the year behind, so there were twenty-four of us. It was just, well,

the first intellectual experience I'd ever had. We would be taught things, complex things about speciation and things like that, and then we would be in pubs arguing about these things, fighting about these things. It was a great experience.

Williams: You make it sound like the greater value was among your colleagues than—

Bevan: I think it was. I think it was. [laughs]

Williams: That's not high praise to the faculty.

Bevan: [laughs] Well, most of the faculty are gone now. My professor was Michael Abercrombie, who was a wonderful, wonderful man, a cell culturist, so we did learn a bit of what I call more modern biology, but most of it was dragging us through the animal kingdom, which was fun. I mean, I still love mollusks. I mean, a fantastic phylum, my favorite phylum. [laughs]

Williams: So what was Mill Hill like then?

Bevan: Mill Hill was very different. Most of the guys that were in my year stayed on and did Ph.D.s at universities or places like that. I was going to the National Institute for Medical Research, where there were probably just two or three Ph.D.s. I was one of the last ones to be—not necessarily involved in getting a grant, but to go on the staff of the Medical Research Council, which gave me a little bit more money. Didn't really make terribly much difference. It was very, very different. It was very formal, very dry. It was tea time at ten-thirty—I mean it was coffee time at ten-thirty, and it was tea time at—and there was a faculty lounge. I mean, it was pretty staid and not so enjoyable as being at the university again. I mean, I was still only fifteen miles away from my buddies who lived in North London?.

I wasn't doing really what I called basic immunology. I wasn't attacking the big problems of how variable regions came about and so on. I was studying myeloma immunoglobulin synthesis in myeloma cell lines, and that was okay. My Ph.D. supervisor was Brigitte Askonas, who died just last year at age ninety. I had enormous help from Michael Parkhouse and Alan Williamson in the same division [Division of Immunology].

But, again, I got lucky, and luck is a big thing in all of these things. My research, it was just basic biochemistry, actually, studying heavy and light chain association and so on and polymerization of IgA and IgM. But two floors before us in Av [Avrion] Mitchison's group, which was experimental biology then, that was a fantastic hotbed of discovery, which absolutely fascinated me. Av had brought lots of these people. Martin Raff was there. Harvey Cantor was there. Roger Taylor was there. And they were figuring out exactly what the carrier effect meant when you immunize mice, all these mice for Av, with a protein where you can isolate one determinate called the hapten on the protein called the carrier. They knew that there was such a thing as a carrier effect. If you came along and asked

the animal to respond to the same hapten but on a different carrier, the response was much less than if giving it the same thing.

There were numerous explanations for why the carrier effect should exist, but Av, by doing lots and lots of adoptive transfers, and Martin Raff, in particular, defining markers that distinguished T cells from B cells, was able to show that this was cell cooperation. The T cells were helping the B cells make the best antibody against the hapten. So B cell specific for the hapten, T cells with specificity for the carrier. The B cell had to take up the hapten carrier physical complex and then make the antigen the T cell saw to make [unclear]. And that was absolutely so exciting.

Then the Salk Institute was formed only in the sixties sometimes, but Michael Parkhouse, who was senior to me but was in the same laboratory as me, had been at the Salk Institute early on. He really encouraged me to go there. It was a fantastic place. San Diego, La Jolla was a fantastic place, and so was the Salk Institute. And Melvin Cohn came through the institute one day, through Mill Hill at one stage, and I met him, and pretty soon it was decided that I would be going to the Salk Institute to work with Mel Cohn. And that was so different from Mill Hill. I sort of implied that Mill Hill was rather formal, you know, with faculty lounges and tea times and things like this. Well, Mel's lab was not chaos, but there you worked, but Mel always had the opinion that it's much more important to think about an experiment than actually start it. He would encourage people to go to the beach and to think about things. He was a great theoretician, Mel.

Then I'm not quite sure, but I was still absolutely fascinated by cell cooperation in the immune response, and Mel was encouraging me to work on suppression, using an in vitro system, mixing T cells and B cells together and looking for regulatory T cells, or suppressor cells, as we called them in those days. But the only culture of lymphocytes that really worked extremely well for me was mixed lymphocyte cultures where you take lymphocytes from one strain of mouse, mix them with the other strain of mouse, and a fraction of the cells go crazy. They respond to the MHC antigens of the other cell in a process called alloreactivity. And that was fine. When we, me and another person [ed. Ruth Epstein], discovered that adding mercaptoethanol to these mixed lymphocyte cultures made them so much healthier, these became the most reproducible things in the world, and I did some, I hope, relevant experiments on alloreactivity in vitro.

I went to the Salk Institute in 1973, I was there for four years, and then in 1974 the bombshell hit, and that bombshell was Rolf Zinkernagel and Peter Doherty's and discovery of, as they called it, "altered self" or MHC [major histocompatibility complex] restriction. They were working with viruses, and their simple discovery was that when you made a killer cell response in one strain of mouse against this particular virus and asked it to kill virus-infected cells, they would kill them. They'd be nice. But if you used the same virus on an allogeneic cell, one which had different MHC antigens, it just didn't see them.

And there had been other indications that MHC restriction existed from macrophage and T cell interactions. Ethan Shevach and Alan Rosenthal had shown that. But this was a four hour assay. It was just doing the killing assay, the kind of assays that I was doing with these alloantigens. And that was an absolute revelation. I mean, it led to the Nobel Prize for Zinkernagel and Doherty.

I was just poised at that moment and so, as always, setting up my mixed lymphocyte cultures with MHC different stimulators and responders. I asked myself, well, what about all the other minor histocompatibility antigens that we have? Even in those days, 1974, 1975, one knew there were fifty different loci that scored as skin rejection antigens or kidney rejection antigens. And to do that, I had to prime mice, because they're much, much weaker, and then having those primed mice and being able to mix and match different congenic strains of mice, I was able to show that all the responses of cytotoxic lymphocytes to unmodified cells to minor histocompatibility antigens fifty different loci, probably hundreds of different loci were all MHC restricted. And this was a pretty cute finding, I mean more than cute, because what Peter [Doherty] and Rolf [Zinkernagel] had done was shown that when you insult a cell by giving it a virus infection, and what Gene Shearer had shown when you chemically modify the surface, that these responses are MHC restricted. What I was showing is that all of our cells, in all circumstances, the MHC is modifying all of our antigens. Of course, we now know that they're presenting as tiny little peptides.

One unusual thing about my postdoctoral work is that I published all of this work without my supervisor, without Mel Cohn as an author, because we totally disagreed on the interpretation. [laughs] I was the most loyal commitment to altered self. It was a single receptor recognizing these unknown complexes. Mel absolutely believed in two separate—dual recognition, two separate receptors. It was impossible for me to publish my papers with him, but generously, he let me go ahead and do it, so I got a little bit of success for that and fame, whatever fame is.

Williams: So you were working pretty much independently, would that be true to say?

Bevan: I was working independently, but Mel Cohn and another postdoctoral, Rod [Rodney E.] Langman, an Australian guy, they were together, they were dual receptorists, so I spent hours and hours of discussion and arguments about this and that, obviously, for me. I was working independently, yes, but I was right about the conclusions, I believe, but it was so much fun to be able to argue with these people, and it clarifies your mind. I still think discussions are one of the most meaningful things, "Ah! Let's go in this direction."

Another important person was actually Polly Matzinger, who you may have heard of. At the time, she was a graduate student at UCSD [University of California, San Diego]. You know, the Salk Institute is just half a mile from UCSD. She was

a graduate student in a drosophila lab, had no interest in immunology, but since, I guess, to get a graduate degree, you have to write a paper on something else, and she picked immunology, and we met, and she, like me, just fell in love with it. It explained everything you wanted to know about the MHC, which had been a mystery for so long, the HLA [human leukocyte antigen] antigens and so on.

So interacting with her, we agreed—we used to talk about it for ages, and that's the way the experiments came about. In fact, one—well, I published a couple of papers with Polly, but the most relevant one is a hypothesis paper we published in the journal of *Cellular Immunology* with the title "Why Do So Many Lymphocytes Respond to [Major] Histocompatibility Antigens?" That's the alloreactivity thing that I had been studying before. It was just that MHC wasn't one antigen; it was a thousand interaction antigens interacting with all the other surface proteins. Well, we called them surface. Now internal proteins. We know any protein that makes a particular peptide that fits in that group. So when you say I'm responding to your HLA antigen, your HLA antigen probably exists on every cell in your body and probably 10,000 different species because of the 10,000 different peptides that are presented. That was a pretty nice hypothesis, not knowing anything about peptide presentation or what the MHC was actually doing that came out of that.

So then in 1976, I think, the Salk Institute used to have these meetings, usually cancer meetings, some of them supported by Armand Hammer, the oil magnate. And I was a postdoc, so I wasn't a speaker at this meeting, but certainly I was attending, and also Herman Eisen attended, and so did David Baltimore. These were both at the time at the newly formed Center for Cancer Research [now the Koch Institute for Integrative Cancer Research] at MIT [Massachusetts Institute of Technology]. Herman had moved there in 1973 from [Washington University in] St. Louis, and in 1976 was still recruiting, and although I wasn't a speaker, I guess I made a bit of a nuisance of myself in asking questions and so on, and Herman approached me and asked if I would be willing to come to MIT and interview for an assistant professor position. The Salk Institute, those are the best years of my life, the four years there, being single and having fun and doing these experiments. My first question to Herman was would I have to teach, because I didn't have any particular interest in it.

He said, "Yes, of course." [laughs] So for a while, I declined to go there, but I guess he persisted, or maybe I think other people, other Americans at the Salk Institute said, "You can't say no to MIT. You have to go and interview." They didn't really mean that, but I did go and I was just overwhelmed by the smartness of the faculty I met there.

So in 1977, I did make the move across country from San Diego, from the two corners of the states, to Boston to join the Center for Cancer Research in 1977, which was another great move, actually.

Williams: Well, you might as well carry on with this narrative.

Bevan: Well, we've only got to 1977 yet. [laughs]

Williams: Well, at some point we may have to accelerate. But anyway, so what was your work like at MIT?

Bevan: Well, again, I was becoming an assistant professor, going from having a bench of 200 square feet to having 2,000 empty square feet, and getting a grant, which was kind of easy in those days, it seemed. But the best thing that happened at MIT was the graduate students there. I arrived February 1st, I think, was my start date, '77. The next flock of graduate students had probably arrived in September of '76, and two of those students decided to join my lab. We all had to give presentations to the students, and that was David Raulet and Pamela Fink, two absolutely amazing students. Plus, I got a wonderful postdoc, Thomas Hünig, who's now in Würzburg, came to me from Würzburg and is now a director in Würzburg.

So that lab, the four of us, Raulet, Fink, Hünig, and Bevan, was just the most efficient lab I can possibly imagine. We were all being productive. Nothing was being wasted. It was just wonderful. They've also helped me enormously because some of the work I'd been doing at the Salk Institute right at the time I was leaving, I think I can say I discovered this phenomenon of positive selection, whereby when cells are maturing in the thymus, T cells are maturing in the thymus, they are selected by these MHC antigens presenting this range of peptides again and decide which ones are going to mature. That is positive selection. So I'd done that along, but then I needed—well, I didn't need, but then Pamela Fink, one of my students, was adept and able to do thymus grafts and show this was all happening in the thymus.

But everyone was successful. Herman was a wonderful, supportive colleague. There was a little Cancer Center call grant that we all shared in. All in all, it was this theoretical, always discussing this aspect of what is altered self. We still didn't know how did this explain cell cooperation and so on.

Williams: Were you on the bench, the four of you, at this point, or do you have techs?

Bevan: Yes. No, I was still wearing a white lab coat. We used to wear white lab coats then. We were all—well, some of us, three of us, Tom Hünig, David Raulet were always smoking in the lab, and that's my memory of lab benches, where they have cigarette burns often, but that doesn't happen anymore. Within a few years, I probably wasn't doing very much at the bench. I still did in my next move. But my team was wonderful. It was a wonderful way to start your faculty position, being so lucky with three wonderful colleagues, students, and postdocs.

But it wasn't the West Coast, and there was a possibility I could have moved back to the Salk Institute, which didn't work out, but the neighboring institute, the

Scripps Clinic and Research Foundation, as it was called then, offered me a job. Bill [William O.] Weigle was the chairman of the immunology department then. But I have to say that it was Norman Klinman and Linda Sherman who really made it very attractive to me. They always hosted me when I came there for talks, and made dinner, and in terms of funding, made it possible to move. So in 1982, I moved back from Boston to San Diego and set up my lab there as an associate member, associate professor.

Williams: Did any of your team from MIT come with you?

Bevan: Well, I had a small lab. One postdoc, John Klein, came in. That is all. So I had to rebuild again, but things seemed to be going pretty well. It was exciting times, and I was doing relevant work, and, again, I got another wonderful set of postdocs. When you're at Scripps or Salk, you have an adjunct faculty position at UCSD, and I got a couple of students from there, most of whom are absolutely wonderful.

Williams: Were there ways in which Salk and Scripps were very different places?

Bevan: Yes, they were. Yeah, absolutely.

Williams: How so?

Bevan: Well, they're neighboring. Well, Scripps is associated with a hospital, so much more sort of clinically inclined. Scripps was founded by Frank Dixon when he moved from [the University of] Pittsburgh, actually, with the "gang of seven," as they used to call them, and most of those guys are still there. Weigle was one of them and so on.

The Salk was founded on March of Dimes money after the Salk vaccine. So Scripps was more clinical. You'd see many more people, the professors wearing lab coats. They were all M.D.s. The "gang of seven" were all M.D.s who'd founded this place, and they were all wonderful people, no doubt. But the Salk was much more basic than that, and it recruited their senior faculty from all over the world, from molecular biology. Mel Cohn, my boss, had actually been in [François] Jacob and [Jacques L.] Monod's lab. He's responsible for IPTG [isopropyl-β-D-thiogalactoside], for inducing E. coli and so on. So there was a different feeling about them, yes, absolutely.

Williams: Were you more at home emotionally in one place than the other, or did you just adjust accordingly?

Bevan: If I'm honest, I would have preferred the Salk, if it made it possible, but as you know, they have to offer you a job, there has to be support, and things have to work out. Like I say, Norman Klinman, in particular, did a great job in—he wasn't actively recruiting me. He just made it seem fun, that's all. Financially,

there were opportunities to become involved in program grants then, which meant I had funding, but made it more possible.

Williams: And do you still have teaching responsibilities or not at all at Scripps?

Bevan: No, but if you are an adjunct professor at UCSD, which I was, which I think I gave one or two lectures a year in courses that Dick Dutton, Richard Dutton, who you've also interviewed, would be organizing. No, no, not much in terms of teaching responsibilities. Being on thesis committees, serving as mentor for a thesis student and one or two lectures per year, so not burdensome.

Williams: So you were there for, I guess, what—

Bevan: Eight years.

Williams: Eight years.

Bevan: '82 to '90.

Williams: And then you were lured elsewhere.

Bevan: Yes. Well, as I've told you, I am British, and at some stage, my wife by that time, Pamela Fink, who's now the editor-in-chief *The Journal of Immunology* (*The JI*), we got married in 1985. Actually, two days ago was our thirtieth wedding anniversary. Anyway, that's not relevant. We had vacationed up here—well, not up here, in the Olympic Peninsula on a camping trip, which just seemed like it was just one of the most perfect vacations where you're backpacking in the Olympic Mountains. I don't know if you know them, but they really are spectacular. Plus the climate, you know what I mean, the physical climate in Seattle is very similar to what I grew up with, long springs and kind of moist.

Williams: Lots of rain. [laughs]

Bevan: No, it's not so much. It doesn't bother me at all. Much less rain in Seattle than there is in the valleys of South Wales, let me assure you. I think most of my memories of childhood were standing on our front porch saying, "Mammy, Mammy, can I go out?" She'd say, "No. It's raining."

And, yes, Roger Perlmutter, the Department of Immunology at the University of Washington, Seattle, where I've been for the last twenty-five years since 1990, was recruiting to the new department that had split off from Microbiology, Microbiology and Immunology in 1989, and he offered both me and Pamela Fink jobs, the first outside recruits, me, the first professor along with Roger, and Pam as an assistant professor.

So we came up here, and that's been wonderful, the University of Washington, twenty-five years I've spent there. This time a couple of postdocs did come along with me. When I left Scripps in 1990 to come here, I was very fortunate. John Harty was at the Scripps, not in my lab, but came with me. Eric Pamer had been in San Diego, not in my lab, but came with me, and Steve [Stephen C.] Jameson, also not in my lab at Scripps, had come with me. I was at the time getting Howard Hughes [Medical Institute] money, so I guess they figured I could afford it. [laughs] And maybe some of them had fellowships too. That was another fantastic way to go.

Williams: So were you head of this group of people that came up?

Bevan: Yes. Well, they were postdocs. Yes, I was the head. Roger was the chairman of the department, but I had my lab.

Williams: Right, right. And that started a now eighteen-year—

Bevan: Twenty-five years I've been—

Williams: Twenty-five. My math is off.

Bevan: At the University of Washington.

Williams: I read that *U.S. News* [*& World Report*] ranked—was it your department—as number five in the world? Or is it in the country? In the world? In immunology.

Bevan: Oh, that's nice to know.

Williams: I mean, you must have built something really special.

Bevan: Oh, yeah.

Williams: Tell me about that.

Bevan: Oh, it was a fantastic department in those early days, for the first fifteen years, Department of Cellular Immunology, T cell immunology. Things have changed dramatically now and people have moved on. Roger left in about 1997 to go to Merck, and my other closest neighbor, Alexander Rudensky, left about ten years ago to go to Sloan Kettering. So things have changed dramatically. It's still a wonderful department, but it's very different now.

Williams: Different in different directions or different in—

Bevan: Different directions, absolutely. Like I say, we were a basic T cell immunology department, adaptive immunity. Now it's, as it should be, as the fashions go, I mean, it's largely innate immunity now looking at cytosolic sensors, NK cells

[natural killer cells], and things like that, which is fine. I'm still stuck thinking about T cells and what they recognize.

Williams: Talk about just briefly about being a husband-wife immunology team.

Bevan: Well, there are quite a number of husband-wife, and sometimes I think the easiest way to do it is when you're the same age. You meet as postdocs, you get married. [laughs] Or you meet as students, you get married. And you're both thirty years old or forty years old or fifty years old. Pam is much younger than me—well, not much. She's eight years younger than me, and we basically don't publish together. We've never run labs together, which I think is good, and that's because I was a senior guy and she had to establish herself.

So we've collaborated on a few papers, usually always with her being last author because I was just helping in some ways, but we've published very, very few papers together. It's tough, of course, because sometimes you're up and the other one's down. But we've always had group meetings together, as we do with others. But all in all, it's been terribly enjoyable. We work on rather similar things. She was my graduate student at MIT. I hope I made that clear. She's gone her own way now and I've gone mine, but we still have basically the same instincts about what to do. We proofread each other's papers—not proofread; hopefully giving some more input than that. It's been good. It's a different way from—I think it would be easier if we were both at the same stage in our—not in our—now we are in the same stage of our career, but to run the lab together sometimes would be pretty nice, actually.

For example, for me, [unclear] are the most famous pair, Pippa [Philippa] Marrack and John Kappler run a lab together, and I'm very pleased to say that Steve Jameson, who was my postdoc, and Kris [Kristin A.] Hogquist, who was my postdoc, they've run a lab together in Minnesota. It doesn't exactly lessen the burden, but I think you then have a bigger group, you have a bigger lab, there's much more interaction and so on. But that's not the way Pam and I have done it, mostly because of the seniority difference. I couldn't be the professor and she the assistant professor. She had to establish her own path, which she did successfully.

Williams: Right, right. And is now the editor-in-chief at *The JI*.

Bevan: She is. She is two years into her five-year sentence. [laughs]

Williams: Well, that's quite a distinction.

Bevan: Oh, absolutely, yeah. She does a great job. It's enormously time-consuming but very worthwhile.

Williams: Are you able as a couple to talk about other things at the breakfast table?

Bevan: Oh, yeah. Sure, we do. Absolutely. She's a rower, so she goes on Lake Washington and Lake Union two or three mornings a week. So she's gone by—

Williams: What about the dinner table? [laughs]

Bevan: She's gone at seven a.m. No, but I'm talking about the breakfast table.

Williams: Yes, I know.

Bevan: But when we're there, we sit there, she first starts with the *Seattle Times*, I start with the *New York Times*, and, yes, we discuss things about that. Our kids are gone. They're twenty-seven and twenty-nine, but obviously for all parents, that's a main topic of conversation. Any other topic is what the heck are we going to do this weekend. Are we going to go hiking or kayaking or what the heck are we going to do?

Williams: What career paths are your children following?

Bevan: Well, my younger one, Graham, is in his second year now at medical school in the University of Rochester in New York. He was toying for a while—he did work in a couple of labs doing benchwork during high school or during the holidays, and toyed with the idea of going the Ph.D. route, but he's much more a people person and has chosen to go the M.D. route, and I'm sure he'll be wonderful. He's doing it at Rochester, and the University of Rochester is a wonderful medical school. He's doing extremely well there and he's adapted to that. People know more than I know; I don't know much about the American education system. But the first two years, they just cram you full of stuff. It's a hard thing to survive, but he has survived. And I think he would like to be involved in doing some kind of clinical research if there's the opportunity to do that, but first of all, he'll be a wonderful M.D., I'm sure. He can talk about any subject, he listens, and he's going to be good, I think.

The other one is two years older. He's twenty-nine now. He had a special skill. He's gotten much quieter. So Graham's the people person, an outgoing kind of guy, talk to anyone. Thomas is more like his father and his grandfather, my father. He's much quieter and can sit alone by himself and doesn't seek out conversations and so on. But one thing he did do, which surprised the heck out of us when he was still in medical school, was make this movie, basically like a claymation movie where you move things in takes. It's a fantastic movie, which he won prizes for. That was okay, but then he decided he was—then he went to Cal Poly [California Polytechnic State University] in San Luis Obispo to do a mechanical engineering degree, which took him six years. He had a stroke in his third year, which set him back a while, but then decided he wasn't really terribly interested in mechanical engineering.

I'm glad to say then we sent—well, he wanted to go up to Vancouver, Vancouver in British Columbia, just 150 miles from Seattle, to do a course in CGI, computer-generated imaging, and has been in Vancouver ever since. We think he's doing pretty well. He works for a company, which when people are making movies, every movie, even one you wouldn't suspect, even a situation like this, you and I talking, would have special effects, computer-generated effects in it, make me look better or make you look better, and that's what he's doing, and we suspect he's pretty good at it. Of course, this is a parent speaking. Pretty soon, he might move from the company he's at now to Sony Pictures Entertainment, which is also in Vancouver. So it looks like he's going to be in Vancouver, in Canada for quite some time. But we're happy with them, actually. We have no grandchildren. [laughs]

Williams: Well, there's still time. [laughs]

Bevan: There's still time.

Williams: You were described to me as a "Titan T cell biologist," and I'd like for you to continue talking about some of the triumphs that you've had, and in particular, the applications that laypeople would be interested in knowing about.

Bevan: Well, I think it all starts from being lucky and being in the right place at the time, being close to Av Mitchison when I was a grad student, or not close, but aware of what was going on, and then that bombshell, the Doherty and Zinkernagel bombshell. So for the first ten years, I think I understood everything about T cell recognition, and maybe that's why people call me a Titan, because maybe I was rude about certain things.

Williams: And it starts with *T*. [laughs]

Bevan: Yeah. But I think my greatest—well, two things I'm known for is maybe being the third person to see MHC restriction, but then for minor histocompatibility antigens. But the thing I'm most proud of is positive selection, this notion that the T cell repertoire gets selected in the thymus.

And also I'm credited with discovering that dendritic cells can take up exogenous antigens, take them into their cytoplasm, which is pretty amazing, and then present them to cytotoxic T cells, a process that I called cross-priming, which is now better called cross-presentation. That, of course, has tremendous implications. I remember when it became clear that for MHC II, one would say takes in the outside world in phagosomes and presents that, so they take in extracellular bacteria, things like that, extracellular toxins or dead viruses or whatever, whereas the Class I world, the MHC Class I world just involves itself with whatever is synthesized in that cell can be presented, and that is true. For some people, that was it. There was the outside world for Class II and the inside world for Class I.

But I knew from work I'd done on this cross-presentation that that wasn't true. I mean, again, having the fortune to work with minor histocompatibility antigens, where I knew absolutely that some cell within the body, some antigen-presenting cell, could take up things from the outside, could phagocyte those, and present them for this Class I pathway. So partly why I'm saying, so while the rest of the world—and lots of people simply didn't believe that. How could something get into the cytoplasm, into the Class I processing machine? Lots of people simply did not believe that, and I knew it was true.

But at the time, companies were being formed, and I would occasionally consult with companies, and they would say to themselves and to me that in order to vaccinate for a tumor antigen, to make cytotoxic T cells, one had to get the antigen into the cytoplasm of the presenting cell. One had to devise a virus that would do it or a kind of mechanism that would push it across the membrane. All of which is simply not true. I mean, dendritic cells are perfectly capable of taking up any dead cell, any dead virus, and doing it all by themselves. So cross-priming is important, of course, and, I think lots of these companies didn't—now they realize it. Nobody speaks in those terms that only the synthesized proteins within the cell get presented. I mean, again, a subset of cells, probably the professional antigen presenters have a way of taking up the outside world too.

Now, positive selection is much more difficult to imagine how one could—I mean, it's relevant, of course. Let me explain, if I can, what positive selection is. But in a Carl Sagan way, when genes rearrange in the thymus, the T cell receptor genes, they make billions and billions of receptors, and eventually the useful repertoire is going to come out into the periphery and is going to recognize these MHC restricted antigens. They're going to recognize they're self MHC presenting certain peptides, hopefully, foreign peptides, pathogenic peptides.

But as we discussed, the MHC is the most polymorphic genes we know. So the peptides that you're presenting are probably very different from the ones I'm presenting. So from these billions of T cells that are generated in the thymus, expressed on the surface, those which interact with low affinity, with self MHC, are the ones that are allowed to mature. Some people think, oh, well, so what? But it's a huge effect. I mean, I estimate, I don't know what the real answer is, but only between 1 and 5 percent of the, let's say, the many millions of receptors that are formed in the thymus and expressed on the surface, only 1 to 5 percent of those actually are allowed to mature because they have this correct low affinity recognition of self MHC, and that's relevant in terms of bone marrow transplantation. I mean, for many reasons the cells that get positive selected on in the thymus should match the rest of you and should match antigen presenting cells. But it's a highly theoretical thing, and, again, people have problems understanding, you know, grasping that, and we still don't understand it, I must say. I haven't contributed to the field for a long time, but it's the most fascinating thing for me.

One more thing I would say, I was discovering positive selection in 1977, 1978 with Pamela Fink, and we had no idea what was going on, but by 1995, when these two people I mentioned before, Steve Jameson followed me from the Scripps to the University of Washington, and Kris Hogquist joined my lab as a postdoc from Wash U[niveristy] in St. Louis, and together they were such a great team, and by that time we knew that peptides were involved. We knew certain peptides. We had certain T cell receptors as transgenic mice which could recognize them, and by making variance in these peptides, we could set this affinity scale and then figure out that really it was probably low affinity recognition in the thymus. Kris Hogquist did most of this work in fetal thymus organ cultures. They designed the experiments. They did it. Steve Jameson did all of the work in characterizing the affinity of peptides in various assays. The three of us produced very strong evidence that it was affinity for self MHC, low affinity that allowed you to positive select it.

And I would like to say and that's where the story ends, but, of course, it doesn't end there. [laughs] In work that I have not been at all associated with, it now turns out that the cell within the thymus, which is presenting MHC to [unclear] MHC molecule, which determine which T cell receptors are going to be selected for maturation, those cells and only those cells express the specific protease expressed in the proteasome, which no other cell in the body makes. So there's something special about those thymic peptides, which nobody understands yet. I haven't been at all involved in that work, I wish I was, but the mystery is still there. And once that mystery is solved, I still don't know how one could possibly think about applications for that.

Williams: What about applications for the work that you've done? Are there real breakthroughs on the clinical side or not?

Bevan: No. Everything I've done is purely basic. I've never focused on a disease. I mean, certainly I might use vaccinia to immunize or influenza to immunize. Recently I did have one paper on malaria, but I've never been focused on how to vaccinate or any autoimmune disease, although we've touched on those things, but personally I haven't been involved in applying.

Williams: During the course of your basic research, have you run up against some real dead-ends and big disappointments in your work where you've had to abandon? [Bevan laughs.] Talk about that for a little bit.

Bevan: No, none that I recall terribly now, but maybe that's because I have this way of not admitting to myself that something has happened. [laughs]

Williams: I guess Titans aren't disappointed.

Bevan: I'm sure there are. Well, let me say this, in the 1980s while I was at Scripps, guess what everyone wanted? Everyone wanted the T cell receptor [laughs] via molecular biology or by making monoclonal immunizing. A couple of guys in my lab were making one T cell clone. We'd had one T cell receptor, so let's immunize some other mouse or maybe a rabbit with that and make an antibody that would be specific for that thing. Well, we failed in that. It wasn't a terrible disappointment, actually, because people were way ahead of us and had discovered things which were useful to us. But, yes, I'm sure we've had lots of disappointments, actually.

I also wanted to figure out how cross-priming works, and I wanted at some stage, much more recently. There is a specialized cell type which can take up, phagocyte, let's say cellular debris from a tumor cell or what have you, and they can translocate those proteins which then become peptides into their own cytoplasm, present them on MHC Class I. That's what dendritic cells do in tumors as they take them to the lymph node. So we did look at some gene signatures and come up with things. What's special about these APCs [antigen-presenting cells], and let's knock down a few of those. Well, we did knock down a few, with no significant changes in their ability to cross-present, cross-prime. So, yes, there have been disappointments, but the disappointments don't match up against the successes, and I think I've had three or four pretty good successes in my life, and those I certainly remember. The disappointments, who knows. [laughs]

Williams: A good philosophy. Let's talk about the AAI for a moment. You became a member in '78, I believe.

Bevan: If that's what my CV says, then I did. That's a long time ago, '78.

Williams: Right. You were only a few years in this country.

Bevan: I was at MIT. Yeah, that's when I moved MIT, in 1977.

Williams: And then you have done a fair amount of work on *The JI*.

Bevan: Oh, yeah. I was editor, the sole editor for the "Cutting Edge" section of *The JI* some years ago, and that was pretty easy. You got so much help from the staff. Every paper that comes in is submitted to *The JI*, which is one of the good things. Every paper gets reviewed, so you don't have to make this decision, say, "Oh, let's not waste our time with this." But then what you got from *JI*, or at least what I was getting, and I was the only person doing it, I think now they do the "Cutting Edge" with a couple of editors. I was doing it all alone, and everything used to come by fax in those days, f-a-x, fax, which I despise and hate more than anything, a list of potential reviewers, because reviewers have keywords. That all worked very well, and I think I only did it for two years, but it was fun. It wasn't exactly fun, but it didn't take up too much of my time.

Williams: Did you inherit that section or did you create it, the "Cutting Edge"?

Bevan: Oh, no, I didn't create it. I was possibly the second or third person to do it for a while.

Williams: And then you received the Excellence in Mentoring Award.

Bevan: Yeah, that was pretty amazing to get that. I was the third recipient of that award. People said I was too young to get it. [laughs] But it was just shows how lucky I was, starting at MIT, continuing at Scripps, and then into the University of Washington.

Williams: Can you talk about the special skills you present in terms of being a mentor?

Bevan: Well, I always like to say that I have a good nose, that if there are a few things happening in the lab or a few things happening in the literature, I can kind of sniff out which one is going to be productive. But let me say, I don't have a real philosophy, except discussion, discussion, argument, and more discussion. Many people—and maybe I used to be like this when I was really starting out. Somebody would come to my lab, like these two MIT students who came to my lab, they didn't know any immunology, well, very little immunology. Maybe I would think, "Well, let's get started on this approach," or something. I just don't do that. I can't claim that I do that. When I get a good postdoc, the postdoc is picking me, and I'm picking them for a certain reason, and we don't have a design project in mind. But the most important thing that can happen is that she and I, he and I, this new postdoc, discuss, discuss, and discuss the things that we're jointly interested in. And that is why sometimes before postdocs come, and mentors, particularly in this funding climate, they're always encouraging the incoming postdoc to write a fellowship application before you come or let's plan one before you come, and that sometimes locks you in. "I've written this fellowship application on this topic. I'm going to work on this topic." No. I don't particularly want that.

So I don't direct people at all. Well, sometimes I do direct people, a person, if a person needs direction, but if a person is somebody I can talk to and discuss it, everything comes out of constant discussion and comes out of group meetings and things like that. It comes out at journal clubs,, have been another incredibly important way for me to get projects moving.

So I can't really—I can take credit. I was a postdoc. I was successful. I had people to discuss, Mel Cohn and Rod Langman and Polly Matzinger, to discuss things with them, and I can take credit for some of those things, and then maybe until the time when I was a junior faculty person. But, no, I can't say that I suggested that experiment. I cannot say that. [laughs] Everything comes out of mutual discussion, arguments, finding papers, going to a certain talk at an AAI meeting, or to go a conference.

My philosophy is never to force people into something, and sometimes I'm too lenient like that. I've had Howard Hughes money for a while now, and sometimes having too much money, you let people, well, sometimes, you know, do something which you don't think is the most productive way to go, but you're going to let them do it anyway because they'll find themselves and they'll discover this for themselves. Maybe that's wrong. Maybe I should enforce certain rules on what we're doing, and of course I do. We all work on cell immunology. But I don't have a philosophy that I will start you off with these two projects and one might—I think postdocs should start with two or three projects, and hopefully one out of three will work out, but I don't pick those projects, but I help them. I think I can tell, you know, that I have good sense of what's going to go somewhere. Some people have said that I have a pretty good data-assessment thing. When I look at data, when I look at the figure while I'm sitting in a seminar or reading a paper or if it's a journal club, I can see the flaws pretty well, and that probably becomes less and less true now as I get older, but it used to be true. [laughs]

Williams: It sounds like a very organic process that you're describing.

Bevan: Yeah, it is. Absolutely, yeah. And I won the Excellence in Mentoring Award, which is a wonderful thing, and I've had fantastic people, thirty very successful students or postdocs. People ask me is there a—well, first, the most important thing is to get good people to come to you, have to apply, right? But then I guess I would feel that why they're successful, is, though, I do good have good taste. I'm not claiming to have the ideas that put them on that track, but I kept them on track and helped them decide which track was the better track to do. Plus, again, this notion of continually gnawing at your project, you know, meeting somebody in the corridor and boring them with what you're thinking about and so on. It's very important, I think. You can't work in isolation. Well, at least that's the way it used to be when there were challenges and questions.

Williams: Right. Was there any particular thing that prompted the AAI then to give you the Meritorious Career Award?

Bevan: What year was that? You probably remember better.

Williams: 2009.

Bevan: 2009. No, I don't.

Williams: The body of work, I would imagine.

Bevan: Yeah. I think it was for positive selection, cross-priming, maybe, being early with altered self.

Williams: How does the Howard Hughes fold into an academic program? How does that work?

Bevan: Well, Howard Hughes is a wonderful organization, and I've been supported by Howard Hughes for twenty-five years. They pay 100 percent of your salary. You can't get salary from outside. I guess there probably are some ways of doing it. As a result of being a Howard Hughes investigator at the University of Washington, I am still a professor without tenure at the University of Washington, which is fine. It doesn't bug me at all. I mean, if I had to depend on them, I'm sure they'd step up. But that's the joy for a department to have a Howard Hughes person. It removes all of their response for that person's salary, and whatever the university or the state has given them, they can now use to recruit a second person to fill your slot, which means your slot is gone. It's not sitting there idly waiting for you, of course, which makes absolute sense.

But I think all Hughes people, certainly me, we do everything as any other professor would do for the department. We teach just as much, absolutely. I mean, maybe there are some people who don't want to do that, but we're totally integral people within the department. Sometimes we can buy equipment that somebody else couldn't buy, and that's always shared, as far as I'm concerned, and every other Hughes investigator I know is willing to do that. So it's maybe—I mean, I don't know if you're searching for some jealousy, maybe there's some jealousy with other faculty members, but if you're a good citizen and if you can buy a certain piece of equipment which then you share, that makes things better. It's special to have that pot of money.

Williams: Is there a kind of periodic review of your work?

Bevan: Every five years.

Williams: What would you say about the importance of the AAI to the field of immunology?

Bevan: Well, I think the AAI, one of the most important things is *The Journal of Immunology*. I'm not saying that because my wife will kill me if I don't say it. But what I love about *The JI* is that all papers get reviewed. I mean, it's not some small bunch of editors deciding. Everything goes out to, hopefully, experts who will spend the amount of time it requires to give good or bad thumb's up. And although we, including myself, all like to publish in some other journals, which maybe published only six or maybe ten papers per month, the rest being filled up with previews and reviews but only basic science, *JI*, of course, comes out twice a month and publishes many more than that. But if you look within *JI*, for every month you can find papers which are possibly equally as important to some of—not all of them, of course. There's chaff and then there are wonderful things that appear in *The JI* too. So I think that's a very important function that *JI* [ed. AAI] serves in running that that journal. It's a really big organization, as I'm finding out from conversations with Pamela Fink.

The other thing is these meetings—for me, I have never done any lobbying for the AAI. I haven't been to Congress. I haven't been on the council, as you know. But these meetings I think are special because they're good and they're bad. I mean, they're bad because they're so big and they're good because they're so big, because people meet everybody. When you get kind of old, it's impossible to walk down the corridor without bumping into something and you can't get to the next talk you want to go to. But for young people it's very important. I mean, the breadth of stuff that's going on is enormous.

And, again, I mean, I don't deal very easily anymore with poster sessions. There's just too much information too suddenly for me now to take in. But to see young people explaining their poster sessions and hopefully arguing about them and discussing them is wonderful. Running the jobs, having job applications and just meeting people, forming, maybe, collaborations. I think these meetings are very important.

My favorite meetings used to be—I'm talking about the seventies—with the Gordon Research Conferences, which are, in some ways, the exact opposite of the AAI meetings. They would only allow in 100 or 120 people, and very frequently they'd be held in boarding schools in New Hampshire, where you'd sleep in a dorm, there'd be no screen and you'd be eaten alive by mosquitoes. Food was terrible, white-bread sandwiches. But those meetings, they were very cliqued. I mean, there was a core group of twenty people who used to go, but they were pretty amazing. There were very competitive discussions going on forever.

One thing we have to do at them—not we, but since I'm not involved, one thing we have to do is keep everyone on time to the minute. They do that. They do a spectacular job. I don't know how they do it with all these egos around, but they do it, and it has to be that way because there are so many concurrent sessions. I would prefer that there was just one major session that suited my taste, but that obviously can't be true. And these meetings give postdocs and students their first opportunity to present, and it's good for them. They sit there listening to professors and the famous people. Well, let's see if you can do it too.

Williams: Have you been in the habit of attending annual meetings fairly regularly?

Bevan: Oh, absolutely. I've been to the last three. Of course, two years ago I was in Honolulu, 100 years old—that was wonderful—last year in Pittsburgh and a couple of times in Seattle. Seattle, actually, my hometown now, so I do go.

Another thing I'd like to say about AAI is everyone agrees that Michele Hogan has done a fantastic job, managerial job in making it financially stable. But I want to give a particular call-out to Marc Jenkins. Marc Jenkins is the past president before Linda [Sherman]. What I understand and during that time, they come up with a number of new awards to give—you know, money is tight now, but I'm

not sure if it was Marc individually, but during Marc's tenure, they came up with a notion of making these Travel for Techniques Awards, such that a postdoc or a student could apply to the AAI and get money to find out how to use that 15-kilohertz cell sorter or how do you use that mass spec [mass spectrometer]. I think that's a good idea. AAI has always given a few travel awards, you know, a thousand bucks or whatever it takes, but I think now they're also supporting giving salary support. And, again, in times like this, if the AAI can afford it and if they can remain solvent, then I think enormous kudos goes to Marc for changing that. Let's not hold the money. Let's spend it wisely, hopefully. Travel for Techniques is good.

Williams: Right. So that leads naturally to my next question, which is what do you see as the future of immunology?

Bevan: Well, for me, it's always been basic, but the things that fascinated me as a student, as an undergrad and even when I was in high school, the antibody problem's amazing. MHC restriction was amazing. All these things are amazing. The Tregs are amazing nowadays. But so many people now are focusing on—their research starts with a disease. That has never been the case for me. They're working on malaria or they're working on this particular autoimmune disease, they're working on diabetes, and that's wonderful, because, I mean, there's so much information out there now, and it's so easy to do genetic linkages amongst families and focus on this, and it tells you new and unexpected things, which is wonderful. But I think like most of the sciences, it's information technology now. So from systems biology and from informatics, that's where all of science is going, as far as I can tell.

What are we going to do? Well, human immunology, the techniques are becoming available. We can't do the kind of experiments we can do in mice with human immunology, but we can certainly get lots and lots of information from blood samples and so on and also from new ways of doing confocal imaging. So it used to be from humans' blood that's what you get, but now you can get other tissues and get much more information out of them with all these wonderful new technologies. So is there something new and wonderful to be discovered, something really major? I don't think so. I think it's all been done, the antibody, the rearrangement of antibody genes. So there are some spectacular things that I won't discover, but I'd like to discover.

Williams: What about the cloud of funding?

Bevan: It's getting slightly better now. Percentage points of NIH funding have gone up. That's why I think it's important that AAI did what it did. Any other source of funding is important. Now, I think it's tragic. We have three junior faculty in our department and they've all been successful in getting R01s, but guess what? One R01 is simply not enough. You have to pay a fraction of your salary. As soon as you start paying a technician or a student or a postdoc, there's not much left over.

One thing that's always—maybe I haven't heard many people say it. Some people say it, and one of the institutes does it. I think there should be cap on funding per individual, certainly caps on what comes from the NIH. I mean, that's the American way. You can apply for one grant or you can apply for ten grants, and maybe if you get them all, I don't think that's a terribly good idea.

The other thing which I hear lots of people saying, and I certainly agree, too much emphasis now is given on these group grants, these program-project grants, or core grants, where somebody at the NIH decides that they're going to have this funding announcement, and people are always on the lookout for these things, not in terms of "What can I do?" They want money to do what they want to do. But like most basic scientists, I really believe that investigator-initiated research, obviously has to be—you know, the public has to be satisfied with what we're doing, translational immunology and new discoveries that are fantastically important. But I think the NIH should move away from allocating to specific areas. If it's Ebola—I mean, one can't argue with spending money on HIV, right? That has led to fantastic basic discoveries. But I would, as would most people in my position, prefer that more the investigator initiated the R01 type that's unfunded, but it's not focused on anything that the NIH is suggesting.

And there are lots of other sources of money. Howard Hughes supports a couple of hundred people very richly. The Gates [Foundation] gives money. There are lots and lots of fellowship applications. But I'm afraid I see junior faculty, they get one grant, they're successful, they're immediately searching for the second, and I think you need at least two or three grants to run a reasonably successful and stable lab. You don't want—your grant is running out in five years. "What the heck am I going to do?"

Williams: What do you advise young people about a career in immunology?

Bevan: Well, if they want to do it, if they really want to do it, passionate about it, willing to devote twenty hours a day, do it. If you're just drift—well, I think lots of people used to drift into becoming a faculty person. Don't do that. [laughs] I mean, the times are just too tough for that. So if I know somebody or have somebody in my lab or know somebody who's just so devoted to research, you know, they're there on weekends, they're coming back at nights, they're always talking about it—that's another thing I always stress, is talking about it—I say go for it and you can be successful. I mean, it's not going to be easy. It's going to be tough.

And then there's the thing about when you go out, maybe you write six different applications to different institutes or universities, and maybe you get offers, which one to pick. Should you pick the ones where the best faculty are, where the best colleagues are, or the one with the biggest startup package? That's much too difficult for me to—but I'm not negative. I mean, we have overtrained people,

maybe. It's a pyramid. There's a professor and there are students and postdocs. But I'm not negative about the best young people, the passionate people going into science, going to universities or research institutes. It's been a wonderful life for me. It can still be, but not as easy, perhaps. It seemed easy when I—my first grant, moving to MIT, was $70,000 a year on a three-year grant. Different now.

Williams: You talk about twenty-hour days. Is that really—

Bevan: No, not really. But it's passion—

Williams: You're exaggerating a little bit, I guess.

Bevan: Well, when I was a postdoc, it was all about getting results from a gamma counter, counting chromium-51 cytotoxicity assays, and gamma counters only take 300 of these big vials, and I used to go back at midnight or two a.m. to change it, just so I'd get the results the next morning. But, no, I don't really mean—but you know what I mean; working hard.

Williams: You've mentioned hiking and so forth. Are there other outside pursuits that allow you to relax and get away from the field?

Bevan: Sure. Yeah, absolutely. Well, Seattle's a wonderful place to be, as you know. I built my own kayak recently, and I do that sometimes. Hiking is a big thing everywhere. Ask anyone in the Pacific Northwest and they say that. More recently I've started working with wood, and I have a lathe, which is pretty addictive, actually, to take a block of—I don't buy wood. It's important that the wood be free and it be green, to make it easier, and then forming that with a chainsaw and with a bandsaw and then finally on the lathe into something which looks like a bowl or resembles a bowl is kind of exciting. So that's what I'm going to be doing when I retire, I guess, and reading, of course. Looking forward to the next Jonathan Franzen novel.

Williams: Is retirement on your calendar or not?

Bevan: Absolutely. Yes, I'll be retired in September. I'll be seventy in September. I want to say again I think people should retire. [laughs] Sixty-five to seventy, I think, is—I know some people who say, "Oh, he's still wonderfully productive." But who knows. I mean, maybe that thirty-year-old guy is going to be more productive. I think people should move on.

Williams: Do you look to September with any foreboding?

Bevan: A little bit, yes. I'll be bored sometimes. I'll still go in occasionally, you know. I can't imagine staying home or kayaking or hiking seven days a week. But not too much, actually. I think I'm ready for it. I'm just not as fast as I used to be. I'm not as fast mentally as I used to be. We talk about the complexity of this meeting

now. There are so many new things that I'm not expert on now. Maybe I was a Titan in the old days and I could ask the right questions, but that's not so true anymore, and be much more competitive than I am now.

Williams: Well, is it always true that the field has expanded so much?

Bevan: It's changed a lot, and certainly, yes, it's so diverse now. It would only seem twenty years ago to be only a couple of things that were terribly important. That ain't true anymore. [laughs]

Williams: Right. What about your brother's career path?

Bevan: My brother? Well, he did pass the 11-plus, but he left grammar school when he was about fifteen or sixteen to go to what one might call—we used to call mining school Technical College, which was fine, and he became a draftsman and has worked all his life. He's two years older than me. He's produced four kids, three of whom all still live locally and within twelve miles of where we were both born. And I really admire him. He's stayed on the same street as we used to live, and three of his kids have been through college, which I think I was the first person in my family to go to college from this Welsh coal mining background. So I just admire him a lot, and he's perfectly happy.

We enjoy going back, and my wife and my kids particularly enjoy it. It's quite an eye-opener for those to see what pub life really is, and the countryside there, you know, different from the Pacific Northwest, but some of the mountains and the coastline is just spectacular. So we enjoy it.

Williams: Any last thoughts you want to add to this?

Bevan: No. I think we've covered most things. I mean, the notion that I have a recipe for being an excellent mentor is not true. It just really is based on passion and discussion. That's all.

Williams: Good. Thank you very much.

Bevan: Thanks, Brien. It's my pleasure.

[End of interview]