The American Association of Immunologists
Oral History Project

Transcript

Philippa Marrack, Ph.D.
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Interview conducted by
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Williams: This is an interview with Dr. Philippa Marrack for The American Association of Immunologists Centennial Oral History Project. Dr. Marrack is a Howard Hughes Medical Institute investigator, senior faculty member in the Integrated Department of Immunology at National Jewish Health, and distinguished professor of immunology, biochemistry, and molecular biology and medicine at the University of Colorado-Denver.

Dr. Marrack was the president of the American Association of Immunologists from 2000 to 2001 and served as an AAI Council member from 1995 to 2000. We are in Dr. Marrack's office at National Jewish Health. Today is Wednesday, August 29, 2012, and I am Brien Williams.

Delighted you're with us today.

Marrack: Thanks for coming.

Williams: I'd like to start with you talking a little bit about your own background and maybe your family's background.

Marrack: Well, I was originally English. I'm still British, actually, citizen and an American citizen, which is a good thing if you're going through the relevant airports. That's its really chief advantage, because the disadvantage is, you know, if the plane is taken over by terrorists, the joint U.S.-U.K. citizens are the first to be shot, actually. Yes, anyway.

I was raised, as my father was in the Royal Navy, I was a military brat, essentially, and we moved from one place to another frequently so I went to a lot of different schools and lived in a lot of different houses. The place I lived the longest in England was the university I went to, which was Cambridge, where I took my undergraduate and Ph.D. degree.

Then I came to the States, as many British people did at that time, to train more to do a postdoc, and there I met my current husband. Yes, that's a long story. A short story, actually, I suppose. At that point, I suppose people have adventures in their lives. Adventures? Points in their lives at which they do something that changes everything that they were going to do. So after my postdoc in La Jolla [California] with Richard Dutton, I was supposed to go back to Cambridge. I had a position there to go back to, and, of course, my family was in England and my then-husband was British, etc., etc.

But in about five seconds I decided not to go back to my country, not to go back to my job in Cambridge, not to continue to be with that husband, and go to someplace I'd never heard of, Rochester, New York, which was a big difference from UCSD [University of California, San Diego] in terms of climate and everything else, and live with and eventually marry an American. So that was part of an adventure, I suppose.

There are different kinds of adventures in life. There are adventures that are automatically happy. You go on vacation or something, and it's wonderful. Then there are adventures that are not happy at all, but they're still adventures because they're life-transforming, and this was sort of in between the two. It was sad to give up all those things that I had, my British heritage and my family and so on, but on the other hand, it was a completely new life with John [W.] Kappler and one I've never regretted. I think everybody should have an opportunity to have an adventure not maybe quite like that, but something in which they know that they've done something that changes their life completely and they can pinpoint almost the exact second that they did it at.

Williams: Was John Kappler at UCSD too?

Marrack: Yes. He was a postdoc in the same lab as I was, and we were friends for a long time and then suddenly decided we were going to do this, go to Rochester and work together, live together.

Williams: So you went back to England and closed books on things or—

Marrack: I did, actually. I went back with my previous husband to see his parents—that was a little unnerving—and cleared up the books and dealt with possessions that I had left at Cambridge, dealt with my parents who were in England at the time, came back to the States to Rochester where it snowed continuously for six months, but didn't regret it.

Williams: So your first husband was also with you at San Diego?

Marrack: Yes.

Williams: Was he a scientist?

Marrack: Yes, he is. He's still at the Salk Institute.

Williams: I see. Well, that's very interesting, a good place to start.

Marrack: Did you ever have an adventure like that?

Williams: This is about you and not about me.

Marrack: But it's about our interaction.

Williams: Yes, yes, I think probably not quite as major as that, but I've had some in my life.

Talk about your great-uncle for a moment.

Marrack: Yes. So, my father was a naval officer and obviously not a scientist, although at one stage in his life he designed guided missiles, which is, you know, not exactly politically correct in our current environment, but that's what he did.

His father, my grandfather, was a mathematician, a very good mathematician in England, and my grandfather's brother, John Marrack, was a well-known immunologist in the thirties, who was the first person to suggest that the reason that antibodies precipitate antigens is because each of them is multivalent. This was antiserum, and they make this sort of lattice that builds up and then eventually brings the whole thing out of solution. So he was well known for the so-called lattice theory of immunoprecipitation.

He was an irascible son of a bitch, I think more or less a communist, so he was blackballed. He never was elected to the Royal Society, in spite of being an extremely distinguished scientist, because the Royal Society at that time was not particularly pro-Stalinist, which I suppose was what that great-uncle was. He's also the only person I ever knew who had—he was an M.A., M.B., M.C., M.D. That meant he had all these medical and academic titles and a military cross for service during the First World War. So he was a character, I guess.

Williams: Did you spend much time with him?

Marrack: Very little, actually. My grandmother, my grandfather's wife, did not approve of this man on political and other grounds, so we actually hardly ever met him. In fact, I don't think I ever met him with her or with my grandfather. But later on when I was at Cambridge, he was also living in Cambridge still, and so I met him then a couple of times. But I didn't know him very well, no, just that he was reputed to be short-tempered and outspoken and not politically correct at all.

Williams: So his being involved in immunology had no bearing on your—?

Marrack: Yes, it did. No, on the contrary, actually. The reason I had studied what I did was because of him indirectly. The reason, as I've told the story lots of times before and you've probably read it, after I finished my undergraduate degree in Cambridge, I was going to go and work on something I've forgotten with some other scientist at Cambridge. But then I went to a cocktail party and probably drank too much and met Alan Munro, who became my thesis advisor, who cornered me and said, "Why don't you come and work with me instead of—and I'm going to start studying T cells." Alan previously had been studying protein synthesis. He was interested in immunology and needed a graduate student to help him out, I guess. He was a good-looking guy and he had blue eyes, and I had drunk too much, and whatever, so I said, "Fine." So I went to work with him. The reason he asked me was because he thought it would be really cool to have a relative of John Marrack's work with him on a subject that was John Marrack's subject. So that's how it happened.

Williams: So this was another of these pinpoint moments, in a way.

Marrack: Yes, it was. You're right. It was a pinpoint, right. If only I could remember it. [laughter] It was a pinpoint five seconds. I guess you would say that's true. And certainly I think like all pinpoint moments, you don't ever regret them, because, of course, you don't have the controlled experiment, right? You have no idea what would have happened if I'd have gone off and done the other thing. So we live our lives in this constant belief that we did the right thing. So we never regret all those moments when we changed the course of our lives.

Williams: Munro was at what institute?

Marrack: He was in the Department of Biochemistry at Cambridge at that time, and then together we went, after my first year, down to the Laboratory for Molecular Biology, which was south of Cambridge at the time. It's still south of Cambridge, four miles south. That was another reason to go and work with Alan, because he knew he was going to go there. It was that place, that relatively small building, was absolutely a hive, a really wonderful place for biological research at that time in Cambridge, much more interesting than the rather staid biochemistry department at that time.

When I went there, it had four Nobel Prize winners in it, living in it, and a huge number of American postdocs, many of whom I still know and contact today, and they were all very interesting, vigorous, intellectually smart, curious, different kinds of people. It was an amazing place intellectually to work at the time.

One of the reasons it was so successful, it had been set up, I think, by John Kendrew or Max Perutz. I'm not sure exactly who started, who set it up the way it was. At the time, it was four miles south of Cambridge and there wasn't really anywhere else to eat around there. The nearest pub was a mile down the road or somewhere, and there was nothing else. They had built a cafeteria on the top floor of this building, a large room, and they had furnished it with long tables, tables that took six or eight people, not small tables.

And because it was British, we had coffee in the mornings and then lunch and then tea, so there were three occasions at which everybody in the institute arrived in this cafeteria to consume something or another. Because the tables were large, one always could sit down with anybody. You could be sitting next to the janitor, or you could be sitting next to Francis Crick, and so the interactions were really fostered. The intellectual discussions of science, and, I suppose, my knowledge of how to sweep a floor in a lab, were really fostered by this arrangement, how they set up the meals. Since there wasn't anywhere else to eat, you were forced, really, to eat with this huge variety of people who were so interesting. So that made it really a wonderful place to do a Ph.D.

Williams: The way you describe this runs counter to the sort of proverbial thought that the British tend to be quite reticent.

Marrack: I don't know if you know anything about Francis Crick.

Williams: I'm here to find out.

Marrack: He was not a reticent man, and, of course, the American postdocs were what American postdocs are. Whatever they want to say, they'll say. I don't think British scientists are particular reticent, actually. There were one or two people there. Fred Sanger, for example, was there at the time. He'd already got his Nobel for sequencing insulin, and he had decided at the time that I was there that he could sequence nucleic acids. He was a very quiet, reserved man, is a very quiet, reserved man, and he was working away at different kinds of methods to sequence nucleic acids. About ten or fifteen years later after I'd left, I guess, he eventually did develop the methods which were used to sequence DNA and which he got his second Nobel for.

So, yes, of course, some British scientists, or any scientists in any country, we have the same personality spectrum as anybody else, and I don't think the British are particularly reticent.

Williams: You're here to dispel.

Marrack: I don't know. Have you been to London recently? They're all over the place.

Williams: Oh, now. We were talking about the seventies.

Marrack: Well, we were talking about the late sixties and early seventies, yes. We messed about just like anybody else.

Williams: Talk about Sir Francis Crick for a moment.

Marrack: Well, I don't know him very well. He had an office right next door to our lab, so an office that he shared with Sydney Brenner. So in spite of his considerable intellect and reputation, he still shared an office with somebody else. He was very outspoken and abrupt, I suppose, but so smart and perceptive, even about things that he wouldn't necessarily have—. But I'm told by his technicians that the idea that he would step in the lab and actually touch a test tube was not encouraged, but he, yes, of course. He's a wonderful intellect.

Williams: Now, you may have touched on this before, but what motivated you then to leave this halcyon place and come to San Diego?

Marrack: Because everybody has to do a post—if you're a scientist and a serious one. We all trained to do a Ph.D., and then we're considered to be still baby scientists, and

we have to do postdocs. Often people are encouraged to do postdocs in subjects that are slightly different to what they did in their Ph.D. to increase exposure, I suppose, to different kinds of approaches and so on, and so need to go to a different lab to learn about different ways of doing science and so on.

So in that time it was considered desirable to come to the States from England, and my then-husband and I, I remember sitting by the cam at some pub or other, deciding where we should think about to go in the States. We had to find a place where we both could find somebody we wanted to work with. So one possibility was to go to Boston, and then the other place that was a good fit for both of us was San Diego, La Jolla. We decided it rained too much in Boston, it was going to be too much like Cambridge, so we'd go to La Jolla instead, where it was presumably going to rain less and be more different. California would be more different from Cambridge than Massachusetts. I don't know if that was true or not, but, anyway, that's what we chose to do.

Then I'd already met Dick Dutton at that time, and he was working on more or less the same subject as I was, actually, so you would say it was not an ideal choice but actually he turned out to be just fine. My then-husband went to work with somebody at the Salk Institute and continued there.

Williams: So how important was Dutton to your career?

Marrack: Tremendously. What did I learn from him? I learned how to write, I learned how to lecture, and we, John Kappler and myself, we hope we learned how to run a lab in an egalitarian way to try and get the best out of everybody. What Dick was very good at was even the technicians, everybody, went to meetings, national meetings, for example, because he felt—and I think he was right—that the techs have actually more to put into the lab in terms of ideas than some of the postdocs and graduate students do. They, as the permanent members of the lab, like us, have a lot to contribute and a lot at stake. So we learned from Dick how to try and treat everyone in the lab, regardless of rank or position, the same. That was a really useful lesson.

Then, as I say, what he really taught us, especially me, to do was how to think clearly enough about what—in trying to explain a difficult scientific concept, it's useful to put myself in the position of the person who's listening. How can I explain this to them so that they will understand it and they will enjoy understanding it? They're not just going to say, "Ah, she's going on about something or another, and this is really boring." To try to make it interesting, to tell a story about it that will fix it in their minds, make them curious about it, make them excited about the idea, etc. And Dick taught us how to do that. He was really terrific. He was a great advisor.

Williams: What was it that Rochester offered you other than bad winters?

Marrack: [laughs] Snow. When John and I went to Rochester, I didn't have a position at all, but I went at the last minute, just as John was leaving to go to Rochester and take his assistant professorship there. I didn't have a job, and the chairman of the department at that time, the Department of Microbiology, which is where we were going, Frank Young his name was, it was very kind of him, actually. He arranged some way of paying me through John's startup money that didn't involve nepotism issues, but I was basically working as John's technician.

So then after about a year, it turned out they didn't have anybody to teach the undergraduate immunology course at Rochester, so I said I would teach it. So I taught this entire course, all forty lectures or whatever it was. Off the bat, I think I did an okay job. Also I went out and got myself independent funding from the American Heart Association—thank you to them—as an established investigator, and I got a grant, an American Cancer Society grant.

At this point, the university began to think, "Well, maybe she's not really a technician after all," although they were pretty reluctant about the whole thing, as a matter of fact. For example, Frank Young, when I got the established investigatorship, the American Heart Association thing, the chairman was supposed to suggest what my salary should be. So he suggested to the American Heart Association it should be so much—I've forgotten what it was—and the Association wrote back and told him, "Well, that's lower than our minimum."

Whether that's an example of outright sexism or an example of, "Well, she just showed up and we didn't ask her to show up, and who the hell is she and what is this woman?" I don't know. They just didn't pay any attention. They didn't believe I had any—I don't know what it was an example. I don't think I was even taken aback by it, frankly. I've had other examples in my life, and I'm sure lots of other women have, too, where somebody behaves as though you should be behind the kitchen sink and not doing whatever it is I'm doing. Most of the time, I deal with that by just ignoring it. I have enough confidence in myself and my own abilities not to worry about the fact that the guy suggests I should only get this much money a year. Why do I really—I care a bit about the money, but I don't really care about his opinion of me, because I think it's rubbish.

Williams: The Heart Association struck out in my mind too. What were you investigating? That seems a little bit far afield from your—

Marrack: Yes, it was. So it was nothing to do with the heart, of course, at all. We were just studying T cells. There are some ideas now, of course, that heart disease has something to do with inflammation, misactivity, untoward activity of the innate part of the immune system. But at that time there wasn't any, but they had a category in their list of things, which was any old biological science I don't think was written like that, but whatever it was. So I applied for that, and it was on those grounds I supposed they funded me. It had nothing to do with the heart at all, but I really am grateful to them and the American Cancer Society, both of

whom funded me when I was young and really untested, and without their support I would not be whatever it is I am.

Williams: But it was T cells that you were working on then?

Marrack: Yes. We didn't make any pretense about studying the heart or anything. I said, "This is what I'm doing. These are the experiments. This is the question I want to address." I don't know if it was good for them or not, but it was certainly good for me.

Williams: So then at some time you must have been let into the inner fold at Rochester, or not?

Marrack: You mean, they said, "Oh, we'll give you an academic position"? Is that what you mean? Yes, particularly when we said we were leaving. [laughs] Then, "Oh, my goodness, let's make you an associate professor," and so on. But the University of Rochester never put one penny into my salary, because I was paid indirectly off of John's grant to start with, and then I got the established investigatorship, etc., etc. And I didn't ask them to. Why should they? After all, I showed up unasked. I don't really resent that, actually. I wasn't invited to show up. I did. They did their best to be hospitable. There was a little issue about salaries and sexism and whatnot, but it was fine. They did a good job.

Williams: But you did have an academic position at Rochester.

Marrack: I did in the end, yes. They gave me an assistant professorship and then, as we were leaving, as associate professorship, yes.

Williams: I guess you'd been working with your husband all along in this activity.

Marrack: Yes.

Williams: So what motivated then the coming here, this part of the country?

Marrack: Well, first of all, the sun shines in the wintertime, and we were sick of sticking the kids out of the door in the winter and then them coming back in fifteen seconds later. But, actually, most importantly, we came here to work.

I forgot to say this about Rochester. We were basically just the two of us working together without any input, intellectual input, from other people, because nobody else was really interested in what we were doing. That was great, actually, in some ways because we were free to do whatever we wanted. There was nobody doing a similar experiment down the hall to sort of dampen our interest in anything, so we could do what we wanted.

Then we realized that if we came here, there were a lot of really excellent immunologists here that we could talk to and learn some techniques from and interact with and have a more vibrant scientific life, and all of that was true. So that was really the reason we came here. The fact that the sun shines 310 days a year instead of 80 or whatever it is in Rochester was a lucky break.

Williams: So you packed up the car and drove west.

Marrack: Well, John packed up the car and he drove west. I took the plane with the kids.

Williams: You'd already looked for a house here and so forth?

Marrack: Yes. We came for a weekend, and there were three houses for sale in the area we wanted to live, and we bought one of them.

Then my parents. I forgot to mention my parents. So my parents, a couple of years before we left Rochester they had decided that I was a completely inadequate mother and that they should come to the States from Britain and take care of our children, our two children, so they did. They lived around the corner from us in Rochester.

Then about a year and a half after they arrived, we said, "Oh, we're going to Denver."

So they said, "All right." So one weekend we came and bought a house, and the next weekend they arrived and bought a house around the corner.

Williams: So there was only one of those three houses left?

Marrack: That's correct. It was a very tight market at that point. [laughs] Yes, exactly.

I'm very grateful to my parents. They were terrific, took care of our kids all that time, and everybody else's kids in the neighborhood too. They were the only grandparents around, so everybody dumped their kids on them. They were great.

Williams: Are you an only child?

Marrack: No, I have a brother. He's an M.D. He lives in Canada.

Williams: So when did he emigrate?

Marrack: About a year after I did. He went to western Ontario, where he still is.

Williams: So you are definitely part of the brain drain.

Marrack: If you want to put it that way, yes.

Williams: You don't want me to put it that way?

Marrack: People go back. Now there are Americans flocking back to the U.K.

Williams: But that's amazing, your parents gave up Britain as well.

Marrack: They did. There were reasons to do that. My mother was schizophrenic, and my dad, who was retired from the navy at that time, she wanted to come and take care of the kids, and my dad also knew that from time to time he would need help with my mum because every so often things would really go insane. I mean, she was insane, but she was on the major tranquilizers, chlorpromazine or whatever, and that kept her pretty well under control most of the time. But I think he knew that he would need help with her, and that turned out to be true as time went on. So, actually, they took care of our kids, and then when they got older, we took care of them. So it was a completely reciprocal arrangement, how a family should function, I think, if they can, if they got the opportunity.

Williams: And they adjusted relatively easily to American life?

Marrack: Very well, and they were really welcomed and continued to be welcomed by the people who lived around them. Yes, it was wonderful. The people in Denver really took care of them. They took care of their kids. It was mutually great, yes.

Williams: Do you look back on your mother's disability as having an effect on you?

Marrack: Yes. I never wanted to be like my mother. She wasn't diagnosed until quite late in her life, so I thought when I was growing up that all mothers hated everybody, including their children some of the time. She didn't hate her children all the time but from time to time. So I thought, "Oh, well, that's the way mothers are."

And she couldn't hold a job, even before she went on. I don't know if you know people who've been on the major tranquilizers. They do allow the person to live in society without locking them up. You know, the mental hospitals emptied when these drugs were discovered in the fifties. But they flatten out the personality. So my mother was a pianist and interested in the arts and reading novels and whatnot. All of that disappeared when she had to go on the tranquilizer, on Stelazine or whatever it was. The only thing she had left that she could still do, apart from more or less run the household, was paint, so she painted a lot, but she could no longer play the piano or concentrate long enough on a book so as to remember in the next chapter what she'd read.

Almost every family has people in it who are disadvantaged for some reason or another. They have diabetes. They have health problems. Lots of people have mental problems of one sort of another. They're chronically depressed. They're

manic depressive. One percent of the time they're schizophrenic. So this is not an unusual phenomenon to have a close relative who has some problem.

For me and for our children, because they lived through all of this, they were raised by this woman and my father, I think what we learned was—and I hope, I'm sure, this is true for other people too—that it's society's job and the family's job to accept and cope with these things. People who have problems like this are entitled to and should have as fulfilling a life as you can manage for them. It gave us some understanding of how to cope, how to help this person live productively, I suppose.

Williams: Did it call upon your father to—

Marrack: Tremendously. So my dad coped with all kinds of issues with my mother, and when we would say to him, "Why don't you lock the old bitch up and get rid of her?" he truly loved her in spite of the fact that sometimes she was awful, violent, and unpleasant. And sometimes she was fine. So, first of all, he really loved her, and second of all, he was a Royal naval officer. It was his duty to take care of her, and he got satisfaction, almost pleasure, out of doing his duty, because that was what he was trained to do. I think the rest of had various combinations of those feelings, and in a way it was a privilege to help deal with somebody who has problems like that.

Williams: At what stage in your life did he have to step forward?

Marrack: To have to take care of my mum?

Williams: Yes. Just maybe in the earliest stages of—

Marrack: Well, she was always paranoid, and I remember when I was growing up, not always, but I mean from time to time, so he was always coping with that, I guess. I don't know, but I imagine he married her knowing that she had these issues. But there wasn't a name for it in those days. It didn't have a disease. She was just occasionally off her rocker.

But he loved, because it had a lot of spirit associated with it and all these—yes, it's not a completely nothing, not a complete negative. He loved all that, and he even loved it when the drugs took it away. It had its Dickensian aspects. I don't know if you can imagine what that's like, but in Dickens there's often these sort of grumpy women sitting at one end of the table and everybody's trying to make polite conversation at the other end of it. Had moments like that.

Williams: Was your parents' assessment of your skills as a parent accurate?

Marrack: [laughs] Yes. I don't know. You'd have to ask my kids. They would never say that, I don't think.

Williams: How did you find a balance between work and family life?

Marrack: Only thanks to them and my husband, who was tremendously supportive, you know. We did an equal job. I think women who have a job, we rely on the parents or people in society who don't have to go to work every day and who deal with, but who do more of the parenting for the whole community in a sense. They go to the daycares. They go to the schools and help out, volunteer in the classrooms and so on. So I'm very grateful to those people who did that so that I didn't have to. They're friends now. We all raised our kids together, and we're still friends, so they were.

As a parent, I think it's a problem being obsessed with something else as a scientist. We have our obsessions with some little widget thing, in my case how do T cells see the foreign material that gets in the body, and that's on our minds all the time. Then how to switch from that to reading a bedtime story to a kid, they're running in parallel in your brain all the time. Whether that matters as a parent, I don't know. Or maybe it even helped being a parent, because however ghastly the kids were being, I could still think about the widget.

Williams: So on the balance, you enjoyed being a parent?

Marrack: Oh, yes. Now I'm a grandparent, so now we're all besotted.

Williams: So talk about the ambience that you and your husband created here and what it was like over time.

Marrack: In the lab, you mean? Well, I think we did a good job, but that sounds very self-serving, but I really think we did. Not only us, actually, but the whole community in this. So I work in a small hospital with a relatively small department, and not just because of us, but because of all the other people in the department, it's a very collegial, interactive community, which I think has been for us, and I hope for all the other younger people and older people in the department, made it a place that you want to go to every day that you're not afraid to go to talk to your colleagues about anything, and that same feeling in the lab, too, that the lab members, I hope, feel they can interact with us and everybody else in an enjoyable profitable-for-the-science manner. I don't think we deliberately aimed for it. I think that's just the way it evolved because of the people and partly, I suppose, because of us. That's what we were luckily enough to achieve it.

Williams: You say you got your grounding in that kind of an approach with Dick Dutton.

Marrack: We did, right, exactly. So his example told us how to do it, but amongst the entire department, community here, it wasn't just—Dick didn't teach all those other people as well. Somehow they were either like that or they learned from us or they were good people anyway or whatever. It worked very well.

Williams: So where did the Howard Hughes come into the picture?

Marrack: In the early times of the Howard Hughes Institute, they were a relatively small foundation. I don't know if that's what they call themselves—Institute, I suppose—and they were funding a few sites around the country. Then in the mid-eighties, I suppose—I don't remember exactly the dates—some judge in Utah decided that the entire Hughes estate should come to this medical institute that Howard Hughes had created. So they went from being financially a relatively small operation to having a huge amount of money all of a sudden. They decided to start funding individual people around the country—this is my understanding what happened—not just these few sites, UCSF [University of California, San Francisco], Yale [University], etc., that they were funding at the time.

We were, I think, the first round of people that they decided to fund in this way. So one day we got a call in the lab from them on the telephone that said, "How would you like us to give you a million bucks a year?"

I said, "Oh, sure, why not?" [laughs]

Williams: Really? That's the way it happened?

Marrack: Yes, exactly, it was a phone call, I think, if I remember.

Williams: Wow.

Marrack: So we've been very fortunate over the years to be supported by Hughes. Now they're going to phase us out because we're not studying things that they're interested in anymore. But that's okay. We were lucky to get the money we did.

Williams: Because they've moved on or because you've moved on?

Marrack: I haven't read the full sheet on why they've decided to do that, but I think John and I are not working in a fashionable area of immunology at the moment. We're working on what we think is interesting, but other people, of course, have their own opinions. I suppose Hughes thinks that's not where they want to go. But we've been very lucky to have had their support all these years.

Williams: That money came to you at National Jewish?

Marrack: Yes. Me and John, so we were jointly funded. I think Hughes funds a few people jointly. Mostly it's individual grants, but because John and I worked so closely together, there's no way to divide up our budget, so the budget comes as a single lump sum to the two of us.

Williams: Then you also took a position with the University of Colorado?

Marrack: That was required in order to get a position here at National Jewish, so we came to National Jewish and took a position here and got joint positions at the university at the same time. That allows us to take graduate students and so on, because otherwise we don't have an academic position that allows that.

Williams: So do you have to, quote, unquote, "split your time" between the two institutions or not?

Marrack: No. In what way would you do that? I don't understand the question.

Williams: What are your responsibilities to the University of Colorado?

Marrack: To train graduate students to teach, participate in committees for other graduate students. For example, we use mice in our research, and there are Animal Care Committees that govern the treatment of the animals in the different institutions. We have a Care Committee here at National Jewish, and there's another one at the university. We'd never be asked to serve on a committee like that at the university, whereas we might be asked to serve on a committee like that here at National Jewish. So most of our mundane administrative commitments are to this institution, not to the university. But we do things with the university, of course.

Williams: So I have problems asking this question, because what often happens is people get mired in lots of scientific detail. But describe to me the high points of your academic achievements.

Marrack: So all my academic achievements are co-earned by my husband, John Kappler, and, in fact, in some cases they are his achievements, although I'm perfectly happy to take credit for them.

Williams: When I say "academic," I mean scientific.

Marrack: Yes, I understand that. When I started my Ph.D., these cells, T cells, had just been discovered, and there were a lot of arguments in the seventies about how T cells know that something foreign has arrived in the body, what's the nature of their receptor for foreign material, and for a long time a number of people thought it was actually an immunoglobulin molecule just like B cells use, an antibody molecule. It turns out that, actually, for my thesis I had done some experiments that suggested it wasn't an antibody molecule. Alan Munro and I did these experiments.

Williams: So you were introduced to T cells very early on?

Marrack: Yes. That's what I worked on my whole career. Fortunately, in my entire career, they turned out to be interesting and unexpected.

Anyway, so I think people would probably say, and we would, too, that our first achievement was definitely John's, actually, which was it had been discovered by other people, for which Peter [C.] Doherty got a Nobel Prize, that T cells see foreign material and these things called major histocompatibility complex proteins at the same time. These MHC proteins are part of us, self. They are not foreign; at least the ones in our body are not foreign. There was a long debate about whether T cells had two receptors, one of which binds the MHC protein, and then another of which binds the foreign material, whatever it is, the bit of the bacteria, virus, and so on.

So I think almost within a week of our arriving here at National Jewish, John had devised an experiment to test which idea was correct. It involved making hybridomas, actually, these things where you fuse two different cells together. In this experiment, we took a cell that was able to recognize one foreign thing, ovalbumin from egg whites, plus a particular MHC molecule, and another cell that recognized a different foreign thing, keyhole limpet hemocyanin, I think, the oxygen-carrying material from a keyhole limpet, plus a different MHC molecule.

The idea was if you fused these two cells together, if the MHC recognition was independent of the antigen recognition, you should get the cross; that is, this thing that was recognizing egg white plus one MHC and this other thing that was recognizing keyhole limpet plus another MHC, then this MHC should be able to match with that egg-white thing, and this MHC should be able to because they should be operating independently. Did I make that clear? Did you understand it?

Williams: I think so.

Marrack: Anyway, we fused the two things together, and they didn't act independently. This thing continued to recognize egg white and MHC-A, and this, and the same. Now it's a single cell that has all four things on it, or two, continued to recognize keyhole limpet plus MHC-B, and you couldn't get the egg white and MHC-B to be recognized or the crisscross didn't work.

Williams: So they were independent?

Marrack: They were dependent. Only this MHC plus that protein worked together, and that MHC plus that protein worked together, and you couldn't get the mix to work. So it was a single receptor that recognized the two things together. So that was really a cool experiment. But John figured out how to do the experiment, and together we did the experiment with a technician, Janice White, who's still in our lab, actually, today. So I think that was really the first time we did something that was really different and unexpected, and totally convinced the field that I think that somehow T cells saw the two things together at the same time.

Then we went on to find this receptor with some other people, a lady called Katie [Kathryn] Haskins, who's still here. We identified the protein at the same time as two other labs, actually, also found the protein for the T cell receptor and showed that it was not an antibody molecule. It was like an antibody molecule, but not an antibody molecule. So we identified the protein, and then later on other labs discovered the genes that coded for these proteins and how they got put together and so on.

So I think that was our work in the early eighties that sort of cemented our position in the field, and sometime after that we accidentally found out—so I'm going to try and explain this to you, because anybody who—who watches this, really? [laughs]

Williams: We can talk about that later.

Marrack: Anyway, they're immunologists. They know all this stuff already, right? Or if they don't, I might as well not have lived.

So we knew, everybody knew, at this point that T cells could potentially recognize anything, foreign things, bacteria and viruses and whatnot, and then go about their business, which is to try and get rid of it so that you're not infected with it anymore. If they can recognize anything, why don't they recognize us? Right? They can generate these receptors that could just randomly recognize whatever you like, influenza, but they also might be able to recognize your own pancreatic beta cells and knock them off so you now become type-1 diabetic. So the question is how do they tell the difference between us and everything else.

So there'd been a lot of theories about that, and, actually, it turns out that most of those theories are correct, but as it turns out, it's done in a lot of different ways. But the question is how do you test what's going on. So one of the hypotheses that had been put forward in the fifties, actually, in a sort of indirect way by a guy called Joshua Lederberg, was that when the cells first develop and they first start to express these receptors for foreign things or for self things, they're fragile. So if their receptor binds to the thing it's destined to bind to, foreign or self, they die. So all that means is, if you're a human being and you're developing these cells all the time, as the cell pops out in this immature fragile state, it's bound to see you, because you're always around, right, and it's going to go off and die.

Well, the ones that see foreign things like polio virus and influenza, they get through that fragile stage because they're not infected with influenza at that very moment, and now they turn into the more stalwart robust guys, and when the influenza comes in, they can do something about it. So you filter out self, all the ones that can react with self all the time, because you're always around, and influenza is only sometimes around. Did I make that clear?

So the question was how to test it. So we accidentally discovered a tool to test it, that idea, and it turned out to be right, yes, indeed, during development, the cells that can recognize something that's around at that time. Self, or even if you're infected with influenza, at that actual moment, the influenza-recognizing cells will die, and you're rescued because some of them got through and got out the other end and got turned into stalwart guys before you caught influenza. Did I make that clear?

Whereas you are always there, always there. It's like I always say, when you go to the lavatory, you're the only one in the room. That's how you know you're you, because you're always around. Anyway, that's not a very good analogy, but that's one of the ways to think about it.

Anyway, so we showed that the cells that are specific for things that are always there constantly killed off in this fragile state before they can turn into the guys that are going to knock off your pancreas or whatever. But, of course, that's not always true because people become autoimmune. They do. So the question is why is that, and that's a problem that all of us, us and other people as well, are trying to deal with today.

So those are the early things I think that probably we'd be best known for. Later on we went on to discover special kind of proteins that are made by bacteria called superantigens that gives you toxic shock and diarrhea and whatnot. We studied a lot more about how cells die, why cells die, and recently we focused a lot on what is it that constitutes these autoimmune cells, what are they actually reacting with, why do they suddenly turn on the pancreas and knock it off or give you rheumatoid arthritis or whatever.

Williams: I read somewhere where you were also looking into gender based—

Marrack: Yes, that's true. So about five or six years ago, I was on a thesis committee of a woman who worked with a guy called Brian Kotzin, who's since gone to work at Amgen, and she was trying to understand this business that some autoimmune diseases occur much more frequently in women than in men. I hadn't really thought about it much before, but because I was on this committee and Brian left so I could do what I liked, he wasn't studying it anymore, we began to think, well, it may be that just being a woman, just being female, regardless of anything else is a predisposing factor, because, after all, the biggest genetic polymorphism in the human population is gender. Some of us have two X chromosomes, and some of us don't, like fifty-fifty. There are a lot of other genetic polymorphisms, but that's the biggest, the most frequent one for sure.

So is there something about being female that makes you different? So we started to look in mice, normal healthy mice. Is there something different about the way the immune system is in a healthy female versus a healthy male? Unexpectedly, we found a kind of a B cell that's only expands in female mice and not male mice,

and it appears in autoimmune mice and not in non-autoimmune mice, and it's also in human beings, in human females with autoimmune disease and not in males with autoimmune disease. Now we're trying to figure out are these cells causative; that is, do they cause the disease, are they essential for the disease to occur, or are they just sort of manifestations of these byproducts of the disease afterwards, so are they important or not really? Is it worth trying to tackle them and get rid of them?

So we're doing those experiments now, and I don't think we know the answer. They may just be byproducts, and therefore not clinically useful to treat in terms of trying to treat via these cells or they may turn out to be actually contributory to the disease, in which case it might be interesting to figure out ways how to get rid of them. So I would say those experiments are under way. We don't know the answer. The cells certainly exist.

Williams: I want to go back to the first major accomplishment with the—

Marrack: With the mixed cell?

Williams: That's right. How many times did you repeat that experiment before you were ready to—

Marrack: You sound like the reviewers. [laughs] I'm trying to remember the paper. I think we did it two, three, or four times, with three or four different combinations of cells.

Williams: So it was a fairly limited sample?

Marrack: Yes. Hmm. That's not nice.

Williams: I'm not trying to embarrass you.

Marrack: It was the right answer, actually, as it turns out.

Williams: I'm trying to get more of your sense of the scientific approach, the methodology.

Marrack: Yes. Hmm.

Williams: Let's move on to something else.

Marrack: It was a tough experiment to do, actually, as it turned out.

Williams: I can imagine. You describe this as a sort of self-contained unit of scientific activity here at National Jewish. How much is the interaction going on with other labs and other people around the world?

Marrack: For us personally?

Williams: Yes.

Marrack: Of course we interact with other people in several different ways, especially in the past. We had reagents. We made reagents that other people found useful. At first we thought, "Oh, well, there are different ways that you can interact with people on that front." One way is to say, "Okay, we're doing this experiment, so we wouldn't like you to do that experiment, but we'll send you this reagent so you can do this experiment." Or you can say, "We'll send you this reagent to do an experiment we're interested in sort of peripherally, but you have to put our names on the paper."

Or—this is a particular kind of interaction—we can send them the reagent and say, "I don't want to know what the hell you're going to do with this thing, because it might stop me from doing it too. So please don't tell me anything about it. You can do whatever you'd like with it. Don't put my name on anything." Actually, over the years, we have tried to drift toward that third possibility. Usually, trying to control people who you don't meet day to day what they do with things, it's impossible and it just engenders resentment and whatever. It's a pain.

Now, putting your name on other people's papers, especially these days, is a dangerous pursuit, because you don't know what they really did, and with all this interest in, well, is this Western blot really what it's supposed to be, are you sure this is, one could end up publishing something that I know nothing about at all but actually turned out to be wrong. So, you know, why not just give the thing away and let them get on with it. So, nowadays, I think if we possibly can, we try to do that, but not always because it depends on exactly how much labor we've put into it and whether our postdocs' careers depend on—it's not fair to give away some reagent that some postdoc has sweated on, because they need the credit. So the other way to do it is to say, "Postdoc, you can put your name on that paper," or whatever, but not us.

So I think that that's the ideal way to deal with the reagent issue, just give it away and have done with it, and not ask what's going to happen to it. Of course, we don't always do that, because we're not ideal human beings.

Williams: That's talking about a product.

Marrack: Yes.

Williams: What about intellectual—

Marrack: Intellectual interactions?

Williams: Right.

Marrack: We haven't done a lot of cross-institution work, especially recently, so that could be because nobody else cares what we do, so they don't. It doesn't come up. Of course, we talk to other people about what we're doing, I think, so we never try to hide anything. We interact a fair amount with the people here in this institution. You've talked to Art Weiss recently, I think. He asked us if we could help him with a particular experiment a few months ago that I hope we're going to do with him, and that probably if we put enough work into that that probably we would put our names on the paper if there ever were one, if Art decides he wants to continue with the project and so on. Yes, I don't think we've done a lot of, and I don't know why not, just hasn't come up. It wasn't a deliberate choice.

Williams: Where have you gone wrong in the eyes of the Howard Hughes?

Marrack: [laughs] Oh, you'll have to ask them that. I think, first of all, we're getting old. We've had support from them for many years. Maybe they think we've had our turn. I can't read their minds. I think, correctly, they think that John and Pippa have gone off on some pathway that's not leading the field anymore, that we are following our own interests, that the field itself has gone off in some other direction and we're not leaders in that other direction, and I agree with them about that. That's true, because we, John and I, are interested in a different problem that the rest of the field is not so interested in anymore. We still think it's not only interesting but important, but the rest of the field doesn't. Well, that's true. I don't know how to counteract that.

Williams: So what area of interest is leading the rest of the field?

Marrack: Well, I think the rest of the field is very interested in, of course, what's going on in the gut and the flora, the bacterial flora, the viral flora that we have in our bodies and how that impacts our immune response. Of course it's a tremendously important and interesting subject. We don't have the tools to study it here, and I don't see a way into it that would be innovative for us. The field is interested in all the different cytokines, these different hormones that the immune system uses to talk to itself and other cells, and although we worked on that early in our careers, we certainly haven't been innovators in that field.

I think all the time we've tried to do something that was not just following the herd, and, of course, you could imagine that actually that would lead you away from the herd. That sounds sort of derogatory to the herd, doesn't it, and I don't mean it to do that. But we always tried to do something that was not just the standard stuff, and as it turns out in our case, that's led us down a different path. Maybe we just don't do good work anymore. I don't know. We think it's good but other people might not. So we try to be honest about it.

Williams: You've covered the areas of interests now that others might not see as being herd-worthy.

Marrack: We study subjects now which most of the rest of the field doesn't think is interesting or is not going to drive the field in a new direction, so some of the questions we study are old questions that have been around for a long time. To some extent, people have forgotten our questions, perhaps. I can't speak for other people. Maybe that's why.

For example, these receptors that T cells have on their surface, they're different. It's a different collection in your body than in mine for various reasons, and the question is, how are they different. Structurally, what's the difference between the receptors on your cells and the receptors on mine? We know they're different. We've known that for more than thirty years, but we have no idea why. It's a basic question in immunology. Why are mine different than yours? So we're trying to tackle that question now. I can't speak for everybody else. They may think, first of all, it's of no clinical relevance at all. We don't care why mine are different than yours. But it's a fundamental question about how the whole thing works. So it's not clinically relevant, and most people have forgotten it's a question, so I don't want to justify myself too much because I understand that people would think we're going off on and away from the herd, if you like.

Williams: So in 1972 you became a member of the American Association of Immunologists.

Marrack: Oh, yes, I did.

Williams: Maybe John did, too, at about the same time?

Marrack: I suppose, yes.

Williams: What motivated you to do that?

Marrack: Dick said so. [laughs]

Williams: What, in general, has been your feeling of association with that, feelings about the association?

Marrack: Hmm. I think they do a very good egalitarian job, meaning that the Association has to represent all immunologists of all different ranks, and I was going to say notorieties, but I don't really mean that word. I mean public persona. Some people are very well known and some people are not. But the AAI has, I think—I don't know deliberately, but has really tried to level the playing field so that everybody has a voice, selected people, but not just the big honchos, whatever, have a voice in organizing the annual meeting, who's going to speak, who's going to get honors, what have you. So I think that that's been a really valuable aspect of the Association. As I say, I don't know if it's deliberate or not or just by

chance, tried to represent lots of different kinds of people and not just the people that one might think were the, quote, "most important."

It runs its journal which has the same sort of philosophy, actually, *The Journal of Immunology*, and also trying to level the playing field so that everybody has a place to show, and that's true for the society meetings. Then also it's been a force in this sort of international organization that represents all the immunologists around the world, which I don't know if we're going to talk about that later on. The IUIS, are we going to talk about that?

Williams: Yes, yes.

Marrack: So there's an international organization that represents immunologists from everywhere, and they have this triennial meeting once every three years in different countries, and that's valuable, really a terrific event, I think, for many reasons. First of all, you get to visit all these different countries, if you have the money, you can afford the travel expenses. It's the only time I've ever been to India, just a wonderful experience, Rio a couple of times ago. Next time it's going to be in Milan, etc., etc., so it exposes Americans, who could do with a bit of exposure, some of them, to the rest of the world, frankly, to all these different cultures and different approaches, Budapest, whatever. So because the AAI is part of that, I think, it has helped foster that organization.

Yes, I think the AAI has done a really good job. I don't have so much knowledge of how much impact it's had politically in terms of Congress and so on. Other people that you've talked to I'm sure know more about that.

Williams: That was an issue that you brought up, I guess. Yes, I have a note here on the newsletter. You were bemoaning the funding crisis, and that would lead one to think that probably some work had to be done with Congress in order to try to steer them differently.

Marrack: But I would be surprised if AAI had much effect on Congress's opinion about the funding situation at NIH [National Institutes of Health]. It may do and I don't know. You need to talk to Jeff Frelinger or someone like that.

Williams: What about FASEB [Federation of American Societies of Experimental Biology] and their public affairs?

Marrack: I don't know very much about it.

Williams: You, I guess, were asked, but chose to go into that process to become the president of AAI.

Marrack: Yes.

Williams: Yet you're a very, very busy person doing all these other things. What led you to commit to that?

Marrack: It was an honor. I think probably that. I wouldn't say I had a tremendous drive to do something innovative, useful, just maybe a little bit.

Williams: Did you come in with an agenda?

Marrack: No, I think I just came in with keeping it steady on the rocks, steadily going forward. No, I wouldn't say I had much to do, and I don't think I achieved much of an agenda, actually, frankly at the time.

I think my major contribution to AAI, incidentally, was probably at about the time I got elected to the Council. As far as these international meetings was concerned, the once-every-three-years meeting, the meeting was scheduled to be in San Francisco, and I was supposed to be in charge of the program. How did it go exactly? There were two other people who were associated with us: Bill Paul, who decided at that time to become the AIDS czar at NIH and so stopped doing this, and so I took over his role as president of this thing, of running this meeting.

Then the program was then to be organized by a guy called Charlie Janeway, who's since died, and he became ill with lymphoma during the time we were organizing this meeting. He was really a terrific person. I'm sure other people have talked to you about Charlie. Anyway, so I had a certain amount of picking up, helping out with him, and also running this meeting. It turned out the meeting made a lot of money. I don't know why, but it did.

Williams: Selling t-shirts?

Marrack: Selling t-shirts, being in San Francisco, whatever. It was a big success. So the AAI, I guess, were happy that I made all this money for them, so I think that was one of my major—at the time this happened, they were almost bankrupt, so they needed bailing out financially, and we bailed them out. I only had a miniscule contribution to the fact that we made money. There were people like Pat Jones and Charlie and Bill Paul and others who organized the meeting, but I had the luck to be in charge of a real moneymaking event.

Williams: That was the AAI meeting or was it the international meeting?

Marrack: No, it was the international meeting, so people came from all over the world to this meeting in San Francisco.

Williams: So it didn't replenish the coffers of the AAI.

Marrack: Yes, it did, because the host organization picks up the profits if there are any. Or the losses, if there are those too. But as it turned out, we actually cleared the bankruptcy issues and filled the coffers at the same time.

Williams: You have such an impressive list of elected memberships. What does that mean to you?

Marrack: Do I? I'm a fellow of the Royal Society.

Williams: I mean, I read about Darwin being a fellow. [laughs]

Marrack: They always show you, actually, the book when you go to sign in the book. They show, the 1600s part of the book, so you get to see all these—

Williams: Right. So that must have brought a flush of pride, excitement.

Marrack: Yes, I'm happy to be a fellow of the Royal Society, although it's British, right, so you could write the initials after your name, FRS, but I never do, because I'm American now. I don't write things after my name. But I am proud to be a member of the Royal Society, yes, and I think my family was gratified.

Williams: And the National Academy of Science.

Marrack: Yes. I worked quite hard for them, on their editorial board for their journal. Yes, I am proud of that.

Williams: And the American Academy?

Marrack: I don't do anything for them, so there's no connection. I mean, it's nice.

Williams: Then the list of awards.

Marrack: You know, perhaps you feel this in your life too. It counts what you did today. They're just things. It's nice. I'm grateful to the people who worked, because people write letters, and it's a lot of time to write letters for people to get this stuff, and I'm grateful to those people who did that kind of work, but when I die, they won't be the things I'm thinking about.

Williams: Have you decided what your last thoughts are going to be about?

Marrack: They'll be about my family, of course.

Williams: And not T cells.

Marrack: Oh, they might sneak in too. [laughs]

Williams: Particularly if they're involved, right?

Marrack: That's right. That's right. They failed me. I'm dying of pneumonia. [laughs] If I'm lucky. Yes. You know that. Everybody knows that.

Williams: Of course. A few quotes that I've picked up from researching you and your career. You've said that it's easier being a foreign woman.

Marrack: Yes.

Williams: Explain what that means.

Marrack: So I talk about this quite often. It's easier being a foreign woman because foreign women are not tied down by the expectations of the country that I live in. What do I mean by that? And I don't even know if this is true. This is my hypothesis. Let's say I'm an American woman raised in the United States, so there was all this cheerleading, what have you, stuff that happened in high school, universities, indoctrinated, unaware you pick this up, that this is a particular approach that one should have to life, men, women, whatever.

If I come from another country, I can pretend I don't know any of those rules at all, and which I don't, actually. I know the rules back there in England, but I'm not living there anymore so I don't have to deal with them. So I'm much freer. I think Tom Wolfe wrote a book called *The Mid-Atlantic Man*—I don't know if you've ever read it—which is about exactly this phenomenon, that you don't belong in either culture, so you don't have to obey the rules of either culture, and that leaves you free to be whatever you want to. Actually, it's not whatever you want to be, but whatever you're inner thingies drive you to be, because we don't usually, I don't think, or we would wish to be saints or what have you, wonderful, gorgeous kind people. Of course, we're not really. So our inner demons drive us, and we're free to exploit those inner demons because we're not hidebound by what society expects. Well, we probably are but we're unaware of it.

You know, I picked up my dad's death certificate the other day. It's a page like that. I think, shit, you've got the whole life on one page.

Williams: That was Dick Dutton telling you how to write.

Just one small question here. Do you think that American women are required to follow more rules, that growing up in England there are fewer strictures?

Marrack: No, they're just different. And, anyway, I think there are lots of American women who don't follow any of the rules, of course.

Williams: You have called yourself a very competitive person.

Marrack: Yes, that's true.

Williams: So how has that served your science?

Marrack: Gets you in here on Christmas Day.

Williams: That's why you needed grandparents here.

Marrack: Absolutely. Somebody's got to be with them when they're unwrapping the presents.

Williams: How crucial is competitiveness to the pursuit of a scientific career?

Marrack: Hmm. It's so ingrained in me that it's difficult for me to answer that question for other people. I think once we are competing with different people, right, to a certain extent with other people, but also with ourselves, that we each of us have expectations of ourselves and a drive, which in a sense is kind of competitive within ourselves to get there first, to fulfill this thing. That inner drive, unless you're extremely lucky, and you fall on something really interesting, completely by chance, that inner drive is probably crucial for all kinds of endeavors, whether we're going to be Neil Armstrong and jump on the moon or just be a little ordinary scientist like me and do this thing.

Williams: "I'm not arrogant. I'm not going to cure any disease."

Marrack: Well, I shouldn't have said the arrogant thing. That's not right. I am arrogant.

Williams: Because you're curing disease?

Marrack: No, just because I'm an arrogant bitch.

Williams: Where has that gotten you?

Marrack: It's part of the competitiveness. I know I'm a fairly smart person, etc., etc., so that makes me arrogant. I doubt whether I'll ever cure a disease, maybe. We just have an influenza vaccine that's in trials in ferrets. Maybe that will be helpful. I don't know.

Williams: From your perspective, what do you see as the road ahead for immunology?

Marrack: [laughs]

Williams: Good question.

Marrack: Yes. Well, I think the immunologists and vaccinologists between them will develop better vaccines for certain diseases. I think some diseases we may never

have a vaccine for. HIV, for example, I would give it 40 percent chance that there will ever be a useful vaccine, maybe less, for HIV.

This business about manipulating the gut flora, it's going to be more complicated than we think it is, but maybe there will be something there that will be useful for some conditions, human conditions. There's a lot to be done about inflammation, how damaging it is to the body, but, on the other hand, useful, heart disease and so on, and understanding how it's controlled is what I mean. An immunologist's job is to understand how we control inflammation in the body, and can that knowledge be used to help control, treat certain types of diseases.

Other people have fallen on this sword before, but I'm going to say it. My guess is that we probably have a lot of the building blocks, the things that we need to know already, and the question is how to adjust those building blocks to make the immune response more useful and less damaging to certain people. But we don't know how to do that to make the construction for that to happen now, so it's going to be a lot of how do we understand the whole now we know the individual parts. Did that make sense?

Williams: You have said that T cells equal the human genome project of the cell world.

Marrack: Did I say that?

Williams: I think you did.

Marrack: Really?

Williams: Yes.

Marrack: I don't remember that.

Williams: I guess that puts it in a pretty central position.

Marrack: Yes. I suppose what I mean by that, if I said it at all, was it's to do with this assembling the parts into a coherent whole, that when you have a system that has four different variables and you ask how many permutations can you put those variables together in, especially since they are each of them on a sliding scale, so you can have values one, two, three, or four for each of them, there are so many combinations that you can put them together in, in a human immune system. How do you reach? How do you understand how they interact with each other? And that makes it a very complicated project, problem to understand, in fact, more complicated, you might say, that the human genome project where all you're doing is sequencing a whole bunch of DNA in a whole long line. I know that's not really true.

Williams: But it strikes me the number four comes up again.

Marrack: Yes, it does, but a different kind of four.

Williams: Do you recommend scientific co-marriages?

Marrack: It was outstandingly satisfying and successful for John and myself, I think. You're not talking to John. Maybe you should ask him. The reason it worked for us and, I think, for people who are married to each other that it works for is although we're both very competitive people, we never compete with each other. We always feel that, I hope, the other person's achievement is ours, too, so it's a joint endeavor. If we competed with each other, it would be a disaster. We'd have to work separately.

So the positive aspects of the thing are that there's always somebody to back me or him up and that we have different skills so we can provide some element that the other person doesn't have to an experiment or an idea, and there's always some intellectual thing can be provided by the other person. And we always have something to talk about that's not, "Oh, you didn't pick your socks up the other day."

Williams: I was talking to Jo—

Marrack: Alamri?

Williams: —Alamri beforehand, and she enumerated about five couples that are working here.

Marrack: Yes, there are a lot of us.

Williams: Is that unusual?

Marrack: Yes.

Williams: Is it deliberate?

Marrack: No, certainly not deliberate. Is it something to do with the fact that there were couples here already and they felt comfortable coming here? Maybe. When we were recruiting young faculty and they're a pair, married or not, I suppose you could say that because the department has had experience with other partners, organized systems, whatever, we understand how to deal with them and that it's not unacceptable that they should both be associate professors or whatever it is that they are. So there's an element of acceptance and accommodation about it, I suppose. Personally, I think it's terrific.

Williams: I've been asking this question of everyone. What do you do outside of science that gives you pleasure?

Marrack: [laughs] Well, let's see. I play the piano, not very well. I take lessons from a Chilean lady right now, who I enjoy very much. I run with our dogs, and there are these rivers that run into the Platte, which is the major river. So the dogs, they're Labradors, they run with me and they jump in and out of the river and they chase the rabbits and they have such a good time. So I couldn't fail to have a good time running with them.

On my runs, which are along these paths alongside these rivers, on the way back, I pick up the trash. That's very satisfying. "Oh, I'm so noble. I picked up all the garbage." Of course, it's on the way back, right, because you don't want to carry it out and then carry the whole damn thing back. There's always a plastic bag involved in the trash, right, as people throw things off their cars or whatever. So there are plastic bags around to put their trash in, carry it back. So I find that—I know, stupid isn't it?

Williams: Well, it's small, but—

Marrack: It's satisfying. I recommend it if you need to feel that you've done something worthy, even though it was small.

Williams: Pick up the trash.

Marrack: Pick up the trash on the way back.

I take care of my granddaughter a day a week, the one that lives in town. I think that's about all.

Williams: You and John had two children.

Marrack: Yes.

Williams: What are they doing?

Marrack: One of them lives in town. She's married and she has one daughter and she works for an organization, a company that writes software for universities to interact with the students at the universities and for the students to interact with each other. It's called eCollege.

Our son took a Ph.D. at the Rockefeller and then decided not to go on with science, and now he works for a small company that coordinates interactions between drug companies and continuing medical education things for M.D.'s. So he lives in Brooklyn, he has two kids, and his wife is a literary agent, so they have a lot to do with writing in various ways.

Williams: Understanding that this becomes an oral history document, so to speak, in the archives of the AAI and that some portions of it may be used in Honolulu next year for the hundredth anniversary of the Association, I have two questions. What would you say about the organization on the occasion of its hundredth birthday?

Marrack: Offer them congratulations. Keep up the good work as far as egalitarianism is concerned. Good for you.

Williams: My other question is are we leaving something important unsaid here, something you'd like to communicate?

Marrack: I think if you possibly can, if you have some lust to do something that's not illegal or hurtful to other people—that's facetious—just get on, do it. It's not a subject, I realize; it's just an approach. And that's partly why we've gone different way from other people, because we want to understand this thing, this little widget over here, really understand it in depth. And it's not worth it to me to do it. I'm old, right? So now I don't have that many years left. I'm just going to do what I really desire to do. But I think I always did that, actually.

Williams: The way that you describe that, the word that comes to my mind is propulsion.

Marrack: Oh, yes.

Williams: It propels.

Marrack: We were propelled, yes.

Williams: At what point did you first feel that propulsion?

Marrack: I think it happens to some graduate students. You can see it happening. They get hooked, and I think that happened to me about sometime during my graduate career. I realized I could sit down and design an experiment myself out of my head and do the experiment and get an answer to a question I wanted to know the answer to. Then that's very addictive.

Then because I was studying T cells and they turned out to be important and interesting, and everything they did was exactly the opposite of what you thought they did, it's like a detective story that somebody didn't make up. It's in there. What could be more wonderful than that? So, yes, we get completely obsessed with our own little widgets. You probably are completely obsessed with talking to various people about things.

Williams: I am. Thank you very much for this interview.

Marrack: Thank you.

[End of interview]