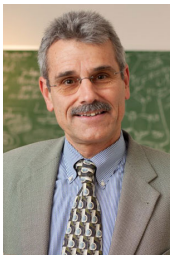

Balz Frei Oral History Interview, January 10, 2014

Title
“Leading the Linus Pauling Institute”

Date
January 10, 2014

Location
Linus Pauling Science Center, Oregon State University.

Summary
In the interview, Frei discusses his upbringing in Winterthur, Switzerland, including his family background and early interests. From there, Frei recollects his undergraduate and graduate experience at the Swiss Federal Institute of Technology, including the beginnings of his work in biochemistry, his first research program, his mentor Christoph Richter and meeting his wife, Simone. Frei's first trip to the United States, for a fellowship at the University of North Texas, is recounted as is Frei's tenure in the influential Bruce Ames Laboratory at the University of California at Berkeley. Frei notes the development of his research while in Berkeley as well as his impressions of and contacts with Linus Pauling and the struggling Linus Pauling Institute of Science and Medicine.

After a discussion of his years in New England at Harvard University and Boston University, Frei moves on to his tenure at OSU. He begins by recalling his initial recruitment and hire as Director of the Linus Pauling Institute at OSU, including his first impressions of campus, early allies of LPI and the sharpening of the Institute's mission statement. He describes the ways in which his worked changed as he assumed a heavier administrative burden and, in particular, recounts the story behind the fundraising, design and construction of the Linus Pauling Science Center. The interview concludes with Frei's thoughts on the future of the Institute and with words of advice on how we all might live longer and healthier lives.

Interviewee
Balz Frei

Interviewer
Chris Petersen

Website
http://scarc.library.oregonstate.edu/oh150/frei/

Transcript

Chris Petersen: Okay, Balz, if you could please introduce yourself by giving your name, today's date, and our location?

Balz Frei: Okay. My name is Balz Frei. Today is January 10th, 2014, and we are in the Linus Pauling Science Center.

CP: Great. So we'll begin in the beginning. You were born in 1958 in Winterthur, Switzerland, is that correct?

BF: Yes, yeah. Winterthur. [Laughs]

CP: Could you tell me a little bit about the town that you grew up in?

BF: Sure. So, it's a town of about 90,000, in the German speaking part of Switzerland, about fifteen miles north of Zurich. Just an average Swiss town; nothing really special. Of course, a European town, old town, and mainly, kind of white collar, but some—some blue collar areas. There's some major industry there, in terms of—there's one big company called Sulzer, actually related to my family. My mother came out of the Sulzer family. And they started this company that builds big engines for ships and trains, and now has branched out to do some other areas like medical equipment. That's the biggest company in town; employees probably tens of thousands still. And that was one of the big companies in the town.

The other one was Winterthur Insurance Company, that actually [laughs] is fairly well known around the world. So that's more the white collar-type company, and that was a big employer in town as well. But, it's a very nice town—lots of museums, actually. I grew up close to a beautiful museum called the Oskar Reinhart Collection. And Oskar Reinhart was one of the big kind of philanthropists in the town, and he had this beautiful collection of classical art—a lot of impressionists. And that museum was very close to where I grew up, and that attracted quite a lot of tourists as well. So.

Yeah, I love to go back there, and it's always great to see how the town has changed since I left. It's been now 30 years, so. Yeah, good memories of all of that growing up.

CP: You mentioned your mom briefly. Could you tell me a little bit more about your parents' backgrounds and occupations?

BF: Sure. So, my dad was a family doctor. And his background was actually he came from family that didn't have anybody who had studied. So he was the first one in his family to go to the university, and became a doctor, and a well-to-do professional in Winterthur. He was very well known because he had so many patients there. And he kind of made me interested in science in general, but also in medicine in particular. I was fascinated by what he did, and I would often go with him to his practice on weekends, and he would do some work there, and I would just hang out there in his practice and look at [laughs] the equipment, and instruments, and whatever was around there, and kind of became curious about his work in general. I have fond memories of spending time with my dad in his practice on those weekends and learning more about his work.

My mother was basically a housekeeper. We had a traditional family, with the father being the breadwinner, and the mother staying home and taking care of the house and the kids. But yeah, she came from this wealthy family, this Sulzer family, with a background in this big company that they founded. I think it was her great-grandfather who actually started that company. So, yeah, we were very traditional family. And my dad being a physician influenced me quite a bit in terms of where I wanted to go in my life. [0:05:03] My brother became a physician and took over my dad's practice.

So I felt when I came to that point in my life where I had to decide what I want to do, I didn't want to do the same that my brother already did, and he kind of followed in the footsteps of my dad. But I wanted to do something that was kind of related, and more focused on figuring out what holds life together, and what are the underlying biological mechanisms and issues that are leading to disease? And kind of more get to the cause of it, rather than just treat the disease, or treat the symptoms of the disease. So I decided to go into biochemistry, to understand the chemistry of life, basically, and dig a little deeper than just treating symptoms with pharmaceutical drugs, so to speak.

CP: How early on did this interest emerge? At what point did you make this decision that you wanted to follow this line?

BF: It actually was fairly late in my career. I mean, not in my career, in my upbringing. I went through high school, and I had lots of different interests in high school. Geology was a big one. I really enjoyed geology classes. I loved physics; I loved chemistry, but there were some other classes that are not related to science that I also enjoyed a lot. So I wasn't quite sure when I entered university what exactly I wanted to do. And initially I [laughs] signed up for engineering, mechanical engineering, because I just didn't know exactly what I wanted to do. But then I quickly realized that that was not what really was my calling.

And I found out about the biochemistry classes that were offered at the ETH—the Swiss Federal Institute of Technology, where I studied, and I felt this is something that I'm much more interested in, again, because I was at that stage in my life, kind of interested in what holds life together and who are we, what makes us function? And biochemistry seemed to me at the root of life. And that's kind of what I became interested in. I wanted to stay away from medicine, again, because my brother already did that. I think going into engineering was [laughs] way too far away from medicine. But with biochemistry, that was kind of the sweet spot where I felt, yeah, this is really something now that resonates, and this is something that I really would like to do. But it took until I started to study at the university before I really realized that's what I want to do.

CP: Were you a good student as a boy?

BF: I was a very good student, yeah. I was a nerd. [Laughs] I was almost always the best in my class. And when I studied, I had very good grades. I mean, I really enjoyed studying. I enjoyed learning new things. I wanted to do a good job at it. Yeah. [Laughs] I was kind of a nerd, and some people think I still am a nerd [laughs], but I definitely was one when I was studying in high school and also at the university. I loved it, because it was so interesting.

CP: What were some of your hobbies or recreational interests growing up?

BF: One of my interests were rocks and collecting rocks and minerals. That's why I was so fond of geology classes. Then I would do some sports. I liked to play squash a lot. That was maybe when I was in high school. Before that I was in soccer and all those things [laughs] that kids do. But yeah, squash was one of my passions. And let's see; what else? Collecting stamps, which was something that I did together with my dad. He was [laughs] collecting stamps! We grew up on a dead end, [0:09:59] and we had lots of kids in the neighborhood, so when I had some free time after doing my schoolwork, I would just go out and play with the neighbors. It was very different from now, when you have kids sit behind their computers or watch TV. We spent all of our free time—of course, especially in the summer—outside and playing with the neighborhood kids, and hanging out for hours and hours, catching lizards or [laughs] or playing tag, or whatever you do as a kid. Or what you used to do as a kid in those days.

CP: Your interest in rocks was shared by Linus Pauling as a young boy, too.

BF: Yeah, I know. Yeah. So that's kind of similar, and interest in chemistry in general. Yeah, yeah, that's true.

CP: Did your family travel much?

BF: We traveled quite a bit, yes.

CP: Memorable trips?

BF: Yeah, we had many memorable trips. Usually in the summer, we would take a major trip, go south, from Switzerland. So we spent time in Italy, a lot of trips to Italy. Sometimes we would go to France, Spain, Greece—we would kind of go to the warmer climates. My dad was very much into history, and we often took trips to Rome or some other ancient cities, and would look at all the interesting buildings, which I always enjoyed a lot. And he would always tell us about the different buildings and the history. He was very educated in that. So he wanted to show us all these places. And I really enjoyed that. We also went hiking in the Swiss Alps, and then skiing in the winter. Yeah, we took a lot of trips. We had this big Chevy Malibu [laughs] I remember, which was, you know, a great thing to have, this American big car. [Laughs] It was a white, big Chevy Malibu that we used for many of those trips. We were four children, and parents—six people in this Chevy Malibu, and loaded it up and off we went to France or Italy. That's always a great experience. Summer vacations in particular.

CP: So you have two other siblings?

BF: I have three. I have two sisters and one brother. I'm the youngest of four.

CP: Did the sisters pursue science and medicine at all?

BF: No. The brother did, yeah, but the sisters, no. They are into more gymnastic—my sister, the younger sister, she's teaching kind of gymnastics classes. She's not doing it anymore; she's retired. And the older sister, she kind of didn't know for a long time what she wanted to do, and I think about—was it six or seven years ago? When she was fifty years old, she started studying psychology, and she now has a degree in psychology and does some professional counseling. And before that she did—she was making jewelry, and more into arts. But she didn't have a formal education.

CP: Did they all remain in Switzerland?

BF: They all are in Switzerland, yeah. They still live very close to where they grew up. Kind of the European model, you know, where you don't move too far away, and you stay close to where you grew up. I was the only one who left.

CP: Gymnasium Winterthur—was that the equivalent of high school?

BF: That's the equivalent of high school, yeah. Right.

CP: Okay. Were there any mentors that you had during this time, or people who made an impact on you? I know it sounds like you didn't find your direction until college.

BF: Yeah. You know, I wouldn't say mentors, but of course they were teachers that I—liked. I liked the geography/ geology teacher, the French teacher. But, nobody that I would consider a mentor during that time really.

CP: Well, tell me about your transition to the Swiss Federal Institute of Technology.

BF: Yeah.

CP: And kind of your time there.

BF: Right. So that's where I started initially with engineering, and switched fairly quickly to biochemistry. It was a rather rigorous schedule. I mean it's not like you had a lot of electives. [0:15:00] Actually, for the first two years, you pretty much had to take the classes that were required for your degree. And that was kind of nice, because it gave us a clear direction and schedule, and we didn't have to worry about missing [laughs] credits that we were supposed to get. It was just: you have to take these classes, and that's your entire schedule for the year, and then, you know, you go with that. I didn't mind to have that kind of a structure.

We had very good teachers. I mean, the Swiss Federal Institute of Technology is kind of the MIT of Switzerland. Of course, not as prestigious as the MIT, but it's a very good school, a very good university. You also don't have to pay for university education in Europe. So, it was kind of—it's a free education, but you had to meet certain entry criteria, like here, you have to have a certain GPA, and take tests to get into the university. Like, in Switzerland, if you didn't go to the highest level of the high school, which is called the gymnasium in Switzerland, you were not allowed to go on to a university. So if you were in the secondary school, Sekundarschule it's called, which is high school that's at a somewhat lower level, or any other high schools that were not gymnasiums, you were not allowed to go on to study at the university. So that was kind of a minimum requirement.

I had a great time during my studies at the ETH. I had lots of great friends. We [laughs] had a lot of fun, too. Sometimes, almost too much fun. But, it was a very, very good time of my life. I really enjoyed my time at the ETH. I took one year off in 1980, which was my third year into my studies there, and traveled in South America with a friend of mine for about six or seven months, which was a great experience, too. And then came back and finished at the ETH. Well, first I got kind of a master's degree after four years, and then I stayed on for another three-and-a-half years to get my PhD degree. So I was at the ETH, overall, for about eight years, almost.

CP: Who emerged as being influential for you, during your time there? Did you have an advisor or a professor who made an impact on you?

BF: Yeah, it's interesting. You really don't have an advisor like you have here in the United States; it's a different system. But certainly, my supervisor, or my advisor for the PhD thesis, was a great influence on me, obviously. I worked very closely with him for three-and-a-half years.

CP: What was his name?

BF: His name was Christoph Richter. He was actually from Germany, and commuted every day. The German border is only about 50 kilometers, 30 miles from Zurich, so he just came from across the border every day to Zurich. Yeah, he was a very intelligent and interesting person. He was always looking over my shoulders, because he was eager to, you know, find out what I was doing, and what results I was getting. So he kept a very close eye on me. [Laughs] I was one of his few graduate students. He had only a small group of about three or four people. And I was a very productive graduate student; I had about ten or twelve papers coming out during those three-and-a-half years. So, he was of course very supportive of what I was doing, and very eager to get more publications out together with me.

He was a very passionate runner, too. So a lot of the time he would just disappear about eleven o'clock and come back two o'clock from his long run. Back then I couldn't quite relate to that because I was not a runner. Now I'm a runner myself, so I can kind of understand that he was a bit addicted to running. [0:19:57] But he was a very good scientist, and I really learned a lot from him, obviously. He really helped me get all these publications out, and become kind of more established, or at least get on a good track for my career, make the good start, and lots of publications.

He was a little frustrated with the Swiss academic system, or in general the European system, where you kind of have to wait to move up in the ranks until basically the chairman of the department steps down, and then everybody moves one notch up. And he actually had to include the chairman of the department on all of the papers that he was publishing, including my papers. And you know, I knew that the chairman didn't really know what I was doing. It was really between Christoph and me. We were designing the experiments, and writing all the papers and getting them out, and then the chairman would put his name on it, which I felt was kind of not right.

And in fact, it came back to bite Christoph, because when he wanted to get promoted from Assistant to Associate Professor, one of the main reasons why they turned him down was that he didn't publish independently, that he had his chairman on all of his publications, who sometimes was even the corresponding author. And I felt that was not right. And he was quite frustrated about that himself, of course. It was a major blow when he didn't get promoted, because that was one of the main criticisms. Or it made it more difficult for him to get promoted in the end. But I think that was one of the reasons why, not too long after I left his lab, he basically got out of academia. And he's now breeding horses, and running, and doing other things, living in England.

So he ended up as a non-academician, which did have an influence on me, in terms of whether or not I would want to go back to Switzerland after I came here for a post-doctoral fellowship. I think the academic system in Switzerland, or in Europe in general, is very hierarchical and very rigid, and it certainly doesn't give you as many opportunities as it does here in the United States, especially as a young investigator, or a young scientist. You have many more opportunities here in the United States. Whereas in Europe, you have to know the right people; you have to know the right connections. Maybe it's not as bad as it used to be when I was going through the system there, but it clearly was more based on hierarchy, and who was ahead of whom, and not so much based on your actual merit and the work that you're doing, but more on your connections and where you are in the hierarchy.

CP: So what was the line of research that you were pursuing at this time?

BF: At the ETH as a graduate student, I did a lot of work on mitochondrial calcium transport. [Laughs] So, mitochondria are the power plants in your cells, and they basically convert fat into energy that can be used by the cell in the form of adenosine triphosphate, or ATP. But they are also important in many other ways to the normal function of the cells, and one of them is to regulate calcium homeostasis.

So calcium is a very important molecule or ion in regulating different processes in both the mitochondria, as well as outside the mitochondria, in the cytoplasm, the rest of the cell, basically. So they have mechanisms of taking up the calcium from the cytoplasm, and then releasing it back into the cytoplasm. And the calcium levels both inside the mitochondria and outside are very, very tightly regulated, because they play such an important role in many biochemical processes. You don't want to have too much or too little at any given time.

So, I was interested in how the calcium is being taken up into the mitochondria, but more importantly, how it is being released, [0:24:59] to understand the mechanisms that cause these calcium gates to open up and let the calcium get out of the mitochondria and into the cytoplasm. And this was very much related to oxidative stress or redox regulation. So if the mitochondria became oxidized, or a certain compound called NADPH or NADH became oxidized, then that would trigger kind of a chain reaction that ultimately let to the release of calcium from the mitochondria. So I was investigating that whole mechanism, and trying to understand how oxidative stress triggers calcium release, and how antioxidants may prevent this from happening. So we tested various compounds that would induce oxidative stress and release calcium from mitochondria, and others that would protect against that.

CP: It sounds like you thrived in the laboratory environment, judging by your publication track record at the time.

BF: Yeah, yeah. Yeah. Yeah, I loved to work at the bench, and I had a colleague there, a good friend of mine. [Laughs] As I say, we had a lot of fun, too, in the lab. It was just—just goofing around quite a bit. It was a great time. I really loved the bench work, and the science, and getting into the nitty gritty details of understanding, again, kind of what I mentioned earlier: what are these mechanisms that make up life? What are the processes? Because eventually it boils down to chemical processes. I mean, that's what kind of life is. I mean, there's a lot more to life than that, but if you are really looking at what is at the foundation of life, or what is it that holds life together, it's all these nitty gritty mechanisms and the chemistry that occurs in your cells and your tissues that makes you live, and makes you tick, so. I was fascinated by that, understanding these mechanisms and going all the way to the cell level or the molecular level, and really get to the bottom of all of it. Yeah.

CP: Did you ever meet Jack Dunitz, a colleague of Paulings? He worked at the ETH.

BF: No, no, I never did. No. Yeah.

CP: Was it at the ETH that you met Simone?

BF: So, I met Simone in high school. Yeah, yeah. That was going back to high school. And yeah, now she's my wife. [Laughs]

CP: Were you together this whole time, or—?

BF: We were together for about three or four years initially, and then we split up for quite some time. That's when I was in South America for a year, or not quite a year. I traveled for about half a year, and took one year off from my studies at ETH, but we were not together for a couple of years. And then got back together, and got married shortly before we moved to the United States.

CP: Was she a student as well? At ETH?

BF: Yes, yes. No, not at the ETH. She was a student in the high school, but she studied at the University of Zurich, but didn't get too far before we moved to the United States. So she actually got a degree in Social Sciences from the University of San Francisco, and a master's degree from another institute in Berkeley.

CP: In 1984 you took on a fellowship at the University of Texas?

BF: Yes.

CP: Was that the first time in the U.S.?

BF: Yes, that was my first time in the U.S.! And it was a great experience. So I got a fellowship from the European Molecular Biology Organization, EMBO, which was quite prestigious, and I was really happy to get it. With the help of Christoph; he was instrumental in helping me get that fellowship. But, what I was supposed to do was go to the United States to this lab in Denton, at North Texas State University, to learn a method that was very much related to the work I described earlier, which is the mechanism of calcium release from these mitochondria. So there's a process called ADP ribosylation, so this compound NADP, nicotinadmide adenine dinucleotide phosphate, is being split up into two molecules, and one of them is ADP Ribose. And this ADP Ribose modified a protein in the mitochondrial membrane, and then opened up this gate for calcium. [0:30:04]

So I went to learn a method to measure ADP ribosylation of proteins. And this lab in Denton had developed such a method and published it, so we contacted them and asked whether I could come and learn that method, on this EMBO fellowship. So I traveled to the United States, and it was my first time. I remember I landed at the Dallas-Fort Worth Airport, and this professor of this laboratory actually was there to pick me up. And I was kind of, wow, this professor comes to pick me up! I'm just a graduate student. And he was there. He was fairly short. And he had this big sign with my name on it. And I'm whoa, kind of embarrassed, everybody would see my name. And he was there with his cowboy hat, and we went to his truck, and he had a gun in the back of his pickup truck, and [laughs] I was like wow, welcome to the United States, or to Texas in particular!

But I was very impressed, you know, that he would come and pick me up from the airport, and drive me to Denton. And he was such a nice man. I mean, it was an incredible experience there! Everybody was so welcoming, and they helped me with this method. And they took me out, and showed me around. And it was a fantastic experience. And that's when I kind of fell in love with the United States. You know, it was Texas, but the people are so nice! And my experience in that lab was really fabulous.

One of the things I remember was during that time, it was February, there was the Super Bowl. And I had actually no idea what football was all about. I mean, football in Switzerland is soccer, right, and I didn't know the rules or anything of football. But, I went to this party, and they had this pool where you could bet on the spread by which—which team is going to win. And I can't remember who played—maybe the Redskins against—I can't remember. But I just you know, picked one team, and picked the spread, like fourteen. And I turned out to win the whole thing, because it's exactly what I had predicted. And I had no idea what this game was all about; I was watching it, but I didn't quite understand. Then in the end, I win that whole jackpot! [Laughs] So it was kind of funny.

The other thing I remember when I was there, there were some ice and rain, and everything was covered in ice. And the whole town was basically shut down, and all the cars were kind of on this side of the street, and couldn't move anymore. It was an amazing experience, because the next day, it was like 60 or 65 degrees. I mean, it was these huge swings in temperature. So, yeah, I had a great time there, and you know, it was a critical experience for me, too, because later on when I applied for a post-doc position in Bruce Ames' lab at Berkeley, this professor in Denton—Myron Jacobson is his name—he wrote me a very nice letter of recommendation to Bruce. And so to have somebody in the United States who was writing a letter of recommendation for you is obviously, you know, very important, if you want to get a position here. And so it was a really great experience, and it helped me a lot in my career.

CP: Well, you returned to Switzerland after that for a couple more years, to finish up your PhD?

BF: That's right, yeah.

CP: Was that just a continuation of your work that you had already started with the calcium?

BF: Yeah. Exactly, yeah. And then I tried to use that method that I had learned, and put it—or establish it, set it up in Switzerland, but I never was quite successful in doing that. So. But there were lots of other things that I still had to finish up. So it was just a fellowship to learn that method, and then I'd come back and finish up my PhD thesis, yeah.

CP: Well, you mentioned in 1987 the post-doc at Berkeley, with Bruce Ames. Could you tell me a little bit more about how that evolved? Ames was an important figure for you.

BF: Yes. Ames—the Ames test is something you learn when you take classes in molecular biology or genetics, or carcinogenesis. I had heard about the Ames test, and we were taught the Ames test in molecular biology classes, [0:35:00] I believe it was, at the ETH. And I remember when I first heard about the Ames test, and how it works—it's actually a very simple test, but it's a sort of ingenious way of how you test substances for potential mutagenicity. So you measure whether a compound can cause mutations in the DNA, in a very simple manner, but very effective. I was very impressed by this Ames test. And this is the Bruce Ames in Berkeley, who then became my mentor.

So in 1986 after I finished my PhD degree at the ETH and got married [laughs] the same summer, I came to the United States in December to start my post-doctoral fellowship with Bruce Ames. And the first day I walked into his office, he got up and said, "Hello, I'm Bruce. Welcome to Berkeley." And I was kind of flabbergasted, because no professor in Switzerland would introduce themselves with their first name. You always say professor, doctor, such and such. You know, you have to use all the titles before you [laughs] come to the name. And he was just saying, "I'm Bruce, and this world-famous scientist who had gotten the National Medal of Science, and was always very close to actually getting the Nobel Prize! He should have gotten it. And he just says, "I'm Bruce, and let's talk about what you want to do in my lab." So, yeah, that time was absolutely instrumental in my scientific career. Bruce was a fantastic mentor, and he still is, to some degree. I mean, now he's more a colleague, but still calls me up a lot, and we talk on the phone.

I was in his lab for three-and-a-half years. And did a lot of work on, again, oxidative stress. That's how it kind of started. And that was an interest of Bruce's because he had written, just shortly before I joined his lab, a very important paper on oxidative stress and cancer, and how oxidative stress causes DNA damage, which in turn causes mutations, hence the Ames Test to kind of measure those kinds of mutations, and how these mutations can lead to cancer. He was very well known, and had done a lot of work on oxidative stress and DNA damage, and cancer. So I became interested in oxidative stress, and damage to fats, lipids, and how that relates to atherosclerosis and heart disease.

So it was the oxidative stress as kind of the common theme. But instead of looking at cancer, I looked more at heart disease, and instead of looking at DNA damage, I looked at damage to lipoproteins, so, you know, molecules in your blood that transport fat and cholesterol. At the time there was this hypothesis that oxidation of LDL, which is the low-density lipoprotein, or the bad cholesterol—that oxidation of the LDL is a very important contributing factor to atherosclerosis, which is the hardening and thickening of your arteries that leads to heart attacks or strokes, and heart disease in general.

So I became interested in that. I was investigating how the fat in your blood can get oxidized. And then more importantly, I was interested in how the antioxidants in blood would protect against that type of oxidation. And that's where I really stumbled across Vitamin C. That was my first discovery that related to Vitamin C. And what I found in those experiments quite astounding. When I took blood, or plasma, which is the liquid part of blood, and exposed it to oxidative stress to get LDL oxidized, so it would be more pro-atherogenic, there were certain antioxidants in plasma that would protect against that. And there were kind of different lines of defense that were used up sequentially before the LDL would get oxidized.

And the first line of defense under all different types of conditions and oxidative stress that I tried was always Vitamin C. [0:40:02] So you have about fifty-micromolar of Vitamin C in your plasma, which is a decent concentration. You have other antioxidants, like Vitamin E at about thirty-micromolar, or you have metabolic antioxidants like uric acid at three-hundred-micromolar. So all these compounds have antioxidant activity, and can protect lipoproteins from getting oxidized, but Vitamin C was by far the most effective. And in fact, it was so effective that as long as Vitamin C was still present in plasma, you could not see any oxidation of the lipoprotein. So, it was basically a hundred percent protective.

But once the Vitamin C was all used up, because it got oxidized, then you started to see oxidation of LDL and other lipoproteins, while the other antioxidants got consumed. So Vitamin E, for example, was not able to completely protect the LDL from oxidation; it just lowered the rate of oxidation. But Vitamin C, again, was the first line. So I was really intrigued by that. And this was the work that then led me to become more interested in Vitamin C and micronutrients in general, which is what I'm pursuing now. But, this time in Bruce Ames' lab—he gave me a lot of freedom to do what I wanted to do. He just said, kind of, "Here's what we're doing in my lab. I'm obviously very interested in oxidative stress." Kind of gave me the parameters, but then said, "Now you come up with a project that you think is fitting into this whole overall framework."

And that was exciting, that you would have so much freedom to design your own project. And then he would come into the lab every day and always ask, "What's new?" He was always very curious what you're doing, and whether you had some new results, because he loved to talk science and new results. And he would always have so many great ideas! I mean, he would make suggestions, "Oh, why don't you do this? Or that?" He is a fountain of great ideas, and the key was to pick the good ones, and just a few good ones. And that's kind of what Linus Pauling always said. [Laughs] To have good ideas, you have to have a lot of ideas, right?

And that's kind of how Bruce is, and he always has these kind of just visionary ideas, and out of the box! You know, he can think of different ways of approaching your experiment, and it was really—the key was to pick the best ones that he was throwing out there, and then go with those. It would take time to pursue these suggestions in detail, and really follow through on it, so you couldn't consider his next great idea until you had focused on that first one, and done that work that was related to that first one. So. And he became a really important mentor for me, also, because when I was in his lab, he introduced me to a lot of well-known scientists here in the United States, because they would come and visit him, and everybody wanted to talk to him. And so he would always bring them to the lab, and I was able to get to know these scientists, which was very important, of course, to start networking as a young scientist in this country, not knowing anybody, and nobody knew me.

It was very important to kind of start to become part of this science network here in the United States. I mean, it was fascinating for me to come from Switzerland, you know, which is a very conservative, traditional country, very old, lots of history, to the Bay Area in particular. I mean, not just the United States, the Bay Area, and even more UC Berkeley. So it was a fantastic experience. Initially, kind of a little bit like a culture shock. But it was like starting from scratch. I mean, nobody knew me. I didn't know anybody. It was like being reborn. I had another chance to kind of reinvent myself.

And I walked into this experience with wide open eyes, and all the different ethnic groups, and this whole spirit of freedom, and entrepreneurship, innovation. It was very new to me. And Bruce himself was kind of—[0:45:00] kind of experience that opened my eyes to a lot of new experiences, and seeing things in different ways. So it was a very important time of my life, and very productive. And it really made my career. I mean, being in his lab and having him as a mentor has been absolutely crucial for my scientific career here in the United States.

CP: Well, at the time that you were discovering Vitamin C, Pauling had been talking about it for quite a while.

BF: Yes.

CP: Certainly your sense of his—his rhetoric or research at that point related to Vitamin C, because it was pretty extreme and fairly controversial.

BF: Yeah. [Laughs] Yeah, it was. And Linus Pauling was very interested in the work I was doing. He found out from Bruce—Bruce and Linus would talk to each other every now and then. But yeah, my view was, back then, that Pauling did very interesting work on Vitamin C. And I remember shortly after I came to the United States in '86, I went to a conference in Washington. And the book *How to Live Longer and Feel Better* had just been published, and I found it there in a book store and I bought it right away, and I read it. And I was fascinated. I thought it was absolutely intriguing, what he was saying in that book. Obviously it focuses a lot on Vitamin C, and then it focuses a lot on dietary supplements, and probably puts too much emphasis on supplements and not enough on diet itself.

But I was very, very intrigued by that book. But I also felt that he was going a little too far. And he made quite extreme statements, or maybe you could call it hypotheses, that Vitamin C can cure the common cold, and it can treat cancer, and may also be useful in heart disease. You know, there were certain things that panned out, but many of his predictions didn't quite pan out. And because he was so passionate and almost extreme about Vitamin C and its role in the common cold, in particular, I think in the end, among the scientific community, he may have actually caused more harm than good for Vitamin C, because they felt he was just getting too far out. He was too extreme. And many of his predictions, or his hypotheses didn't actually quite work out the way he had sort of envisioned.

So, yeah, it was certainly very important work that he did. And this book was a big influence in my life—the *How to Live Longer and Feel Better*. But overall in terms of the Vitamin C science, he may have caused a little bit more damage than

good. And still nowadays, among scientists, they are kind of critical when it comes to Vitamin C. They think, well, yeah, it's Pauling, and he just overdid it. We don't think there's anything special about that Vitamin.

CP: Yeah, a stigma kind of developed around it.

BF: Yeah. Yeah. Yeah. Unfortunately, because Vitamin C is an absolutely fascinating vitamin. And it is, as I mentioned, a really, really good antioxidant, and I think it's the best antioxidant we get from our diet. And being an antioxidant has many important functions in the body, because oxidative stress and oxidative damage is a contributing factor to many chronic diseases. It's not the only factor. Of course, all diseases are multi-factorial with a few exceptions, but if you can lower oxidative stress and oxidative damage, you do have a lower risk of certain chronic diseases.

I mean, there's no doubt that oxidative DNA damage is mutations, which in turn can cause cancer. And if you can prevent oxidative DNA damage with Vitamin C, or other antioxidants, then you should see the consequences, in terms of a lower risk of certain types of cancer. And the same with heart disease, you know, if oxidation of LDL really plays a role atherosclerosis, which is still somewhat controversial. [0:49:57] But my work showed that the best antioxidant to prevent LDL oxidation is Vitamin C, because it is so highly reactive, and it is present in human fluids and cells and tissues at fairly high concentrations, or even very high concentrations. So, there must be a role of Vitamin C as an antioxidant in the human body, otherwise we wouldn't accumulate it in these large concentrations.

And so there certainly is something to all these ideas that Linus Pauling had, but he just went a little too far, I think, and he got ahead of the science and the evidence. And you know, he was the first member of the National Academy of Sciences who had a paper rejected by the *Proceedings of the National Academy of Science*, which back then was unheard, because the members could just send in their papers and they would get published without even being peer reviewed. That's no longer the case, but he was the youngest member ever to be in the National Academy of Sciences, in his early thirties, but he also was [laughs] the first one to have a paper rejected by *PNAS*. So.

CP: Somehow fitting.

BF: And that was on Vitamin C. He published up to a very old age, related to his work in chemistry, in *PNAS*. And those papers are mind-boggling. I don't understand what he's talking about there. So he did top notch science up to a very old age, but in terms of Vitamin C, he went out on a limb and it backfired a little.

CP: You met him, correct?

BF: Yes, I met him twice. The first time was at the Institute in Palo Alto, the Linus Pauling Institute of Science and Medicine. And he had invited me, together with Bruce, to come to the Institute and give a seminar. And for me, it kind of was a job interview. They wanted to hire me. I was at the end of my post-doctoral fellowship looking for jobs. And so they were interested in me, and asked me to come and give this seminar. And I did that back to back with Bruce.

And this was the day the big earthquake in the Bay Area, in 1986 in October—I think it was October; I can't remember—16th or whatever. But I'm always joking that it was an earth-shattering experience to meet Linus Pauling for the first time. And it truly was. I was in the office of Steve Lawson, who is still here at the Linus Pauling Institute. He's the only survivor, we call him, of the original Linus Pauling Institute of Science and Medicine. And I was sitting in his office, and we were talking about science, and what's going on at the Linus Pauling Institute of Science and Medicine. And all of a sudden these eucalyptus trees outside the window started to kind of dance back and forth. It was like—first I thought it was some strong wind, but then I realized these big trees wouldn't move in the strongest wind.

And so it was the earthquake. We heard all the glassware shattering, and things coming down from the shelves in the laboratories, and then we realized, oh, this is an earthquake. Got up and ran out, which you shouldn't do. You should crawl under a table, or under the door frame, but no, we just ran out as quickly as possible, ran down the stairs, and out into the big parking lot behind the building. And I remember there were these waves going through the parking lot. It was like, surreal. You know, these like—and then it lasted for about 45 seconds or so, and then everything was totally quiet after that. Nobody was saying anything. Everybody was kind of in shock. There were no cars moving. It was very eerie. And actually, Bruce had already left. So he gave his seminar, and then left shortly thereafter.

I gave my seminar, and then talked to a lot of the people in the Institute, because, as I mentioned, kind of a job interview. So he had already left, and he was on his way back. And we were very concerned that he might have gotten into one of those critical spots, like the cypress structure that collapsed, near Oakland. But fortunately he wasn't near there. He was already back in Berkeley at home, so. And then when I had to go home there, I had to go all the way south to San Jose, and it took me about three hours to get back to Berkeley.

But, yeah, so that's the first time I met Linus Pauling. I didn't talk to him at length. I went into his office and we had a ten minute conversation, and he came to my seminar and asked some questions. Then the second time I met him, it was at a conference at the National Cancer Institute, which was a conference that Linus Pauling had tried to set up at the NCI for a long time. [0:55:00] He wanted to really discuss this issue of Vitamin C and cancer. And I was invited as a speaker there to talk about my work in the Bruce Ames lab. So this was on Vitamin C, and oxidative stress, and antioxidant protection as kind of an underlying mechanism for how Vitamin C can also work in cancer by preventing oxidative DNA damage. I saw him there a second time, and that was also a great experience, and I learned a lot from that conference that the NCI.

CP: What was your sense at the Institute at that time? It was going through some tough, tough periods.

BF: Yeah. In '86, I think it was still doing okay. There was—this fellow Matthias Rath was there, and we might not want to get into that. [Laughs] But that was one of my concerns, too, that he was kind of doing very questionable things, and his science was not very convincing. But he had a big influence on Linus Pauling, and misled him in a number of ways, so that was a concern. But I was actually quite impressed with some of the other scientists there at the Institute, not doing work on Vitamin C, but lots of other things going on at the Linus Pauling Institute of Science and Medicine.

I think financially they were kind of struggling a little bit. But, you know, that is not unusual for [laughs] research institutes. It didn't have a lot of NIH funding, and part of it was because Linus Pauling had become so controversial and he was himself not successful in getting any NIH grants anymore. So they were struggling financially a bit, but they had also some big donors that kind of kept them going. The building was pretty old. I remember kind of not being very impressed by that. I ended up, obviously, taking a different job, and I felt that taking a job at the Linus Pauling Institute of Science and Medicine as an assistant professor—they didn't have an official affiliation with a university—would not be a good move for me at that time in my career. So I wanted to really go to an established university, you know, kind of get the best job I could. And I had a number of offers, and so I didn't go to the Linus Pauling Institute. I took another offer.

CP: You wound up at Harvard?

BF: Right. Yeah, yeah. I got a position at Harvard School of Public Health in the Nutrition Department, and was very happy to get that. I mean, when I was at the end of my post-doctoral fellowship in Bruce Ames lab, I had to kind of decide: do I want to stay in the United States, or do I want to go back to Switzerland? Because I had a grant from the National Science Foundation in Switzerland—so it was a fellowship, and it was for two years, which of course, made it more easy to get this post-doctoral position in Bruce Ames lab, because I brought my own funding basically. But that was only part of it. And I remember, I made $16,000 the first year, and $17,000 the second year! [Laughs] Not that much to survive in the Bay Area!

But, there was a stipulation to that, that you had to come back to Switzerland. So they wanted you to go abroad and get some top-notch science training, in a great lab in the United States, which I did. But then they were expecting you to come back, and not contribute to the brain drain, so to speak. So I had to get a waiver. Also for my visa, there was this two-year clause that I had to go back. And so I liked it so much in the United States I decided I'm not going to go back to Switzerland.

And one of the things I really was very impressed with was that, as a young scientist, again, as I mentioned earlier, I felt you had a much better chance of becoming independent early on in your career. So, you had a chance to start your own lab, and have your own research program, if you were successful. I mean, it was more merit based, I thought, than having the right connections, like in Europe. [1:00:00] So, if you did a great job, if you published a lot of papers, if you were successful in getting a grant, then you could have your own show, and you could have your own lab, and run your own research program—which is almost impossible in Switzerland, at least back then. So I decided this is where I want to be as a scientist. It was much more exciting. There was much more going on, too. There's lot of scientists, obviously,

here, and a lot of top-notch science being done. So that was a fundamental decision I made at the end of my post-doctoral fellowship.

So I was looking for positions, as I mentioned, and then I got this offer from Harvard. So, Harvard was a tough place. I was successful there, and got my first NIH grant, and ran my own lab. But, you know, they didn't give you a whole lot of support and a whole lot of encouragement. You get there, and they give you a lab, and a modest salary and a modest start-up package, because you know, they're Harvard. They don't have to pamper you, and give you extra stuff that they would maybe give you at other universities. And initially I missed to have a mentor who could help me, you know. Getting into grant writing and trying to establish yourself is difficult in academia, as a young researcher or an assistant professor.

So the initial grant proposals that I wrote were not reviewed by anybody, and I just tried to figure it out myself. That was not the right way to go, because you need support, you need help, you need feedback from your colleagues, and you need some kind of a mentor to really help you get your first NIH grant. So my initial proposal I did not do well at all. Then I decided I need to find somebody to help me with this because I can't do it myself. Nobody really can at that stage in their career. So I did find a few people who would read my proposal and give me good advice, and eventually I did get a nice grant. But there was not a whole lot of collegiality at Harvard. I mean, we were three assistant professors who had started fairly new in the department, and even we three assistant professors—we had labs next to each other, but we didn't talk a whole lot to each other. You kind of were a little isolated, because it's such a competitive place.

I mean, there's lot of big sharks at Harvard. You know, there's a lot of elbowing going on, and it's not a very supportive atmosphere, for a young scientist in particular, I thought, an assistant professor. And they tell you, basically, you're having three years to get your first grant. And if you do that, you can stay another three years, and then maybe you get promoted to associate professor, maybe you don't. Then there's this kind of eleven year up and out rule—if you make it to associate professor, once you get to eleven years, you are up for promotion to full professor—on average, eleven years. But at that point, your position is basically advertised, and everybody can apply for it. So you have to compete with people who also are interested in your job. [Laughs]

And if you don't happen to be the best candidate among everybody who is applying for it, then you're out. And so a lot of people at Harvard don't stay beyond associate professor because they don't make that step to full professor. So in general, I think it was a very important time of my life. It was tough; it was really tough. I struggled, initially, and I was stressed a lot during that time. I did make it and got my grant, and could have stayed longer, but I decided, after three-and-a-half years, I got a very good offer from Boston University, and they kind of recruited me away from Harvard. I had started some collaborations with people from Boston University, and I really enjoyed those collaborations, and they recruited me. They made me a really nice offer. [1:05:00] I got promoted to associate professor just by moving across town. Got a brand new lab there, and had colleagues there, already. So that was a good move.

CP: How did your work develop over the course of time in New England?

BF: Well, I continued to do the work on LDL oxidation and the atherosclerosis. I started to look at other dietary compounds that may also be important in preventing oxidation of LDL. But the first grant that I got was actually on Vitamin C and LDL oxidation, so I certainly continued that work and became more deeply involved in Vitamin C research. But with the influence of some of the colleagues I had at BU, I also started to become more interested in endothelial function, which is related to atherosclerosis, but it looks at more the function of the arteries, not just atherosclerosis itself.

So the endothelium is the cell that lines the arterial wall, and this kind of interface between the blood stream and the arterial wall itself. And this endothelial cell layer—it's a mono-layer, a single layer—produces a number of substances that regulate for example, blood pressure. So, the vessel can dilate, or it can contract, and this is regulated by substances that are released from these endothelial cells. So I became interested, again, through the influence of my colleagues at BU, in how this regulation occurs, and what the role is of oxidative stress and antioxidants in vascular function, or endothelial function.

And when I was at BU, I started to work more with—well, not me personally, but I got involved in work that involves patients, and MDs, who were willing to collaborate with me on ideas that I had, in terms of oxidative stress and antioxidants in endothelial function. And we did one study, together with Joe Vita at Boston University School of

Medicine, to look at the role of Vitamin C in vasodilation, again through the regulation of these molecules that are produced by the endothelial cells and cause the blood vessels to dilate. And we found that Vitamin C was very effective in doing that. And it was really the first paper that showed that Vitamin C has a role in vasorelaxation, and by extension, possibly in blood pressure, because vasodilation and vasoconstriction is important in blood pressure regulation.

We had this hypothesis that Vitamin C acts as an antioxidant, and scavenges these free radicals called super oxide radicals, so this is what causes oxidative stress, these super oxide radicals. And we thought, okay, that Vitamin C can scavenge these radicals, prevent them from causing damage to the endothelial cells, and that's why they can better dilate and contract. It turned out that was wrong, and we did some additional work to really figure out what the mechanism is. So we were right that Vitamin C can improve vasodilation, but we were right for the wrong reasons, and later on figured out what was going on, with the help of my good colleague and friend John Keaney, who was my very close collaborator during that time at BU.

He did that work on the mechanism of Vitamin C, and figured out that it's something different than scavenging of super oxide radicals. So, the time at BU was very important, because I was at a medical school. I was the only PhD, or one of a handful of PhDs, in that institute where I was—that was the cardiovascular research institute, the Whitaker Cardiovascular Institute. But I kind of got some insights into the medical community in the world, and the hospital, and with patients and all that. And doing human studies was very important because—first of all, just the experience of what that is, and what it means, and how different it is from doing bench work, [1:09:59] and second, because I wanted to see how the research I was doing in the lab would translate into the real world, so to speak, and make a difference in people's lives. I mean, that was first time I really felt, okay, what I'm doing is meaningful, and has real consequence in human physiology—or human disease, maybe, and it might help prevent heart disease, or high blood pressure.

So that was a very important formative stage in my career, because I started to have that connection to human studies. And I'm still very good friends with Joe Vita and also John Keaney. John Keaney is younger than me—not much younger than me—but he kind of had a big influence on me, because, first of all, he is, and still is, incredibly smart, one of the most intelligent and smart people I've ever met. And he just has this background as a MD, and he taught me a lot about how he as a medical doctor approaches research. So he's both an MD, and has been doing a lot of research in the lab himself. He kind of bridges the bench to bedside better than anybody else I know, and he was a strong influence on me. And I learned from him also how to navigate the medical world, which is very different from the PhD world. [Laughs]

CP: Well, in 1997 you moved back across the country, and became the director of the Linus Pauling Institute at OSU.

BF: Right.

CP: Tell me about your recruitment and hiring at LPI.

BF: Right, so when I saw this position advertised, I first thought, well, it's kind of interesting. Well, it's certainly right up my alley, with Vitamin C, and micronutrients and dietary supplements, and something that I was interested in ever since I discovered this role of Vitamin C in the Bruce Ames lab. But I was very happy at BU. I was successful; I had great collaborators, and so I wasn't looking for a job outside of BU. But I thought, ah, well, I could give it a shot, and just see what happens. You know, maybe it's going to be an interesting experience just to find out what the position is all about, and go out to OSU. I hadn't heard about OSU. I didn't know anybody at OSU before that, except for one person, Don Reed, actually. I did know Don Reed. He was a big scientist. He was known in the glutathione oxidative stress field. But that's the only person I knew from OSU.

I didn't know much about Oregon [laughs] in general. Well, that's not quite true. I was in Oregon before when I was a post doc in Bruce Ames lab and I came up to Oregon to hike on the Pacific Crest Trail for two weeks, in the summer of 1985, I believe it was. But in any case, so I applied for the position, and I thought I may have a decent shot, but I wasn't trying desperately to get the job. So I came out here, and the interview went fine. I thought it was an interesting position. [Laughs]

I remember one particular episode. When I was giving my seminar—you know, back then we had the slides, the slide projectors, not the LCD projectors we have today. So I had all my slides there in the carousel. And the chairman of the Department of Biochemistry and Biophysics, Chris Mathews, who was the chair back then, and the chair also of the

search committee—he was in the back of the room and operating the slide projector. And a slide got stuck very early in my talk—I think it was maybe the third or fourth slide—because it was too thick. You know, that used to happen every now and then. So the slide got stuck, and he took the whole carousel out, and was trying to get the slide out of the carousel, and he couldn't do that. So he turned the whole carousel upside down, and all the slides came out. They were all on the floor! [Laughs] [1:14:58] And of course he had no idea how to put them back in what sequence; I hadn't numbered them or anything. [Laughs] And so I basically had to give the talk without slides. And at some point he got them back on, and they were kind of scrambled, and not in the right sequence, and upside down, and what have you. [Laughs]

So it was kind of comical, but I think I impressed the audience, because I was pretty much able to give my talk without the slides. I talked through it, and you know, it was hard to explain it without the slides. And at some point I did get the slides back up, but it's kind of, very interesting, and funny episode that I remember from that first interview. And then I came out for a second interview. They asked me back because they were interested in me. I think I was one out of two finalists, so to speak. And that was—I think it was a very dark day and was raining, and was really kind of depressing! [Laughs] And my wife came with me, Simone, and she kind of was wondering, what the heck is going on here? This is not very inviting. You know, we got treated very well, but it was horrible. And I remember we got picked up at the Eugene airport, and this guy didn't know where he was going, and we got lost. And it took us about two hours to find the place where we were staying, and so it was interesting. Simone wasn't too—wasn't too excited about this whole thing, but yeah, so then one thing led to another and I got the offer.

And it was clear to me that there was one big issue that I think other candidates had brought up, too, which was that the offer didn't include any faculty lines. So you had basically an institute, that would be the director, and then some staff, including some that they had brought up from Palo Alto, one of them being Steve Lawson. But they also brought some bench scientists who continued to work here at OSU, just to keep the Institute going while they were searching for a director. But in the start-up package, so to speak, there was no faculty line. So I said, well, if I can get three faculty—if you allow me to recruit three faculty and you provide the start-up for the recruitment package for these three faculty, I think that would become an attractive offer, but without that I'm not going to be interested in this position.

And then Dick Scanlan, who was the Dean of Research at that time, he actually managed to get three faculty lines, which was very unusual, that faculty lines would flow through the research office. They are all going through the deans and the colleges to departments, but these were three faculty lines that went through the research office to the Linus Pauling Institute. So it's a completely different set-up. And the Institute in and of itself is not an academic unit that can provide tenure for their faculty, so the faculty had to have an academic home department, where they would do some teaching and some service. So it was a different way of setting up a faculty line, and it's still not officially considered a faculty line, but it was money that was committed to the Linus Pauling Institute for these three faculty.

So I accepted the position, against my original plans. But I was excited about the position, and also about moving back to the West Coast. I mean, I like Boston a lot; intellectually, academically, it's an unbelievable place. But I didn't so much care for the lifestyle there, and I wanted to come back to the West Coast. That was not the driving force behind my decision, but it was a nice bonus [laughs] to get back to the West Coast, and to a very nice position where I saw a lot of opportunity for me to really build this institute up from scratch. I mean, it was very small. It was just a handful of scientists from Palo Alto, plus Barbara McVicar, who is still my assistant today, seventeen years later, basically. And then Steve Lawson.

So that was basically five people in the Institute, plus then, some people that I brought with me from Boston University. And so the start was modest, but I had these three faculty lines. I recruited three outstanding faculty. And I was really, really pleased when we advertised these positions, [1:20:01] we had so many people who applied for it. And the applicant pool was outstanding. You know, I was concerned that Linus Pauling could be a liability. The name could be a liability, especially among scientists. You know, "Linus Pauling, he really went out on a limb there with Vitamin C. I'm not sure how serious this kind of institute is." But that was not an issue at all.

And so initially we advertised two positions, out of the three that were part of the start-up, but then we got so many good applicants, we said, "Well, we'll fill all three positions with this, because we have so many great candidates to choose from." And so we did that, and we brought in three outstanding scientists who—well, two of them are still here. One of them just left a couple of months ago, so he was here with the Institute for fifteen years. And the other two are still

here. So, Maret Traber, Tory Hagen and Rod Dashwood were the three founding faculty, I would call them, together with myself, for the Institute here at OSU.

CP: Why do you think the pool was so good? Was it the work they were attracted to, the idea of what you were going to be pursuing? In terms of the research?

BF: I think that was an important part of it. You know, what was very critical early on was to have a very well-defined mission of what we want to do with the Institute. I know some people think, yeah, mission statement is kind of useless, but it turned out to be really a key thing, because it allowed us to build the Institute in a very focused manner. We would only hire people who were interested in contributing to the mission of the Institute, which was to understand the role of micronutrients, vitamins and minerals, and also phytochemicals, which are chemicals in plants—fruits and vegetables in particular. So dietary components, and how they can be used in disease prevention and health promotion. And not only understanding the effects, but the underlying mechanisms, so we really do high-quality nutrition research, mechanistic research, that would explain how these micronutrients and how these dietary components can inhibit disease initiation or progression at molecular and cellular level. So really good quality research, and research that could have great impact, because disease prevention is really the way to go, I think in general for medicine in this century, and the twentieth century, too, to really get a handle on healthcare costs, and prevent disease in the first place, rather than treat it.

So, it's a fundamental approach, based on diet and dietary supplements, to prevent disease, which I think resonated a lot, and created a lot of interest in the Institute early on. And that's why I think we got such a great pool of applicants. So, yeah, that gave us a great start with these three faculty I was able to recruit. And then over the years, we added one faculty at a time. A few of them we basically recruited from within OSU, and most of them actually we brought in through searches. You know, we have been really successful, I think, in adding very high quality scientists to the Institute over the years. My approach was always if you want to have a great Institute, you had to hire great faculty. The Institute can only be successful if the individual faculty are successful, and I think we have been very successful at bringing in successful faculty, and that was one of the key elements of building up the Institute.

So I was excited when I got the position offered because I saw a great potential for it. And the potential really has—I mean, we have reached all the goals that we originally set out for this institute, including building a state-of-the-art facility. And so I'm very, very pleased with how things have been going, and OSU has been extremely supportive through all these years. [1:25:03] And for me, obviously, this is my—I'm very proud of what the Institute has achieved, and where we are today with the Institute.

CP: Who were some of the early allies here at OSU that helped you sharpen that mission statement, and kind of get going?

BF: George Bailey was a very important ally. He was on the search committee. And he had done great work before I came here on chlorophyll and some other phytochemicals in cancer chemo-prevention. And this was something that obviously the Institute was very interested in, because it's dietary compounds and how you can prevent different types of cancer. And it's still a major focus of the Institute today, cancer chemo-prevention through diet and dietary factors.

So he took on a very important role in the Institute, kind of as a mentor for me, or certainly a very close advisor and supporter of me and the work we were doing at the Institute. And he was kind of the wise elder for the Institute, and still is. He's now retired, but I really thought he was very influential for me, and a top-notch scientist. And in fact, one of the first three faculty that I hired was a former post-doc of George Bailey, and he had encouraged Rod Dashwood to apply for this position, because he was so convinced that LPI would be successful and a great place to be. So yeah, he was very important, George Bailey, in the early stages and throughout the seventeen years that I've been here at the LPI.

Dick Scanlan, as I mentioned he was the Dean of Research, but he was very supportive of the Institute as well, and helped me navigate more the administrative aspects of being the director of the Institute. But being such a strong advocate of the Institute, and having an advocate of that level of the university was certainly critical for our success as well. And then Chris Mathews, who was the Chair of the Biochemistry and Biophysics Department. He has been very successful himself, but also very supportive of the Institute over the years. And then Don Reed was important. As I mentioned, he was the only person I knew here at OSU before I came out for the interview in 1997. So these people also were on the scientific

advisory board, and some of them are still on the scientific advisory board for the Institute. Yeah, so those were the key scientists here who helped me establish the Institute at OSU.

CP: One of the people who kept the Institute afloat at some of its darkest times, and also helped the Institute locate to OSU was Linus Pauling, Jr.

BF: Yes.

CP: I wonder about your—the times that you spent together with him, and memories you had.

BF: Yeah. Yeah, Linus Pauling, Jr. I think he was very, very happy that the Institute moved to OSU, and he was even happier when we got this fabulous building that's basically a working memorial for his father. He has been extremely supportive and extremely helpful. He often comes to very sort of important events for the Institute, to kind of represent the Pauling family. He's kind of carrying the legacy of his father, and has made sure that it has a good place here at OSU. I haven't had a lot of interaction with him, besides when he's here to come to certain events. But in general, I have nothing but good things to say about him. He was a tremendous in supporting us, and we have had such a great relationship, through Steve primarily, because Steve and Linus Pauling, Jr. worked together very closely back in the Institute at Palo Alto. [1:30:03]

CP: So Linus, Jr. was happy to let you take charge once you moved to here?

BF: Right. Yes, yes. I think that's well put, that he kind of, "Okay, now I don't have to worry about it anymore, or not as much as I used to, because it's kind of in good hands." Not just because of me, but in general at OSU.

CP: How has it been for you to try to continue your research with this heavier administrative burden you took on once you became director?

BF: Yeah. It is a challenge. [Laughs] It still is. And I certainly—you know, I haven't worked at the bench in a long time, but that's not unusual for full professors. I don't have a lot of time to supervise my lab personnel, so I have some senior post doc, and I have a research associate professor in my lab, who kind of supervise people on a daily basis. And I don't take a lot of students, because I just feel I cannot do them justice, because of the administrative duties that I have. So my lab is not very big. We're still quite productive. We're publishing a good number of papers every year.

And research and science is what I really enjoy the most, so I don't want to lose touch with that, and I want to be involved with the research in my lab, and of course, in all the other labs in the Institute. And I don't want to move any higher up in the hierarchy. I don't want to become a dean, because then I—then I lose touch with my roots and where I came from, and what I really am most passionate about, which is science and research. I love to sit down with people in my lab and talk about results and science. So, it is becoming increasingly difficult, also with fundraising in particular. That's taking up more and more of my time, trying to keep the Institute afloat financially, which is a big challenge now with declining funding from NIH.

It's something that I enjoy enormously, meeting with donors, and supporters of the Institute. You meet a lot of very interesting people, very successful people. They all have a great story to tell, you know, how they came to support the Institute. Many of them still go back from investing in Palo Alto. So it's something that's very rewarding, and something that I enjoy doing, but it does take time away from the lab. And you know, you just have to balance all these things. I like the variety of my job, administrative, organizing things, running the whole Institute, but then also being involved with some basic research still, and meeting donors. So there's a lot of different things I do on a daily, yearly basis, but it's the variety that I enjoy the most, really, about my current position.

CP: Well, the culmination of a lot of fundraising, you mentioned, is this building here.

BF: Right.

CP: Tell me a bit about the story about how it came to fruition.

BF: Right. So in 1996, when the Institute moved from Palo Alto to Oregon State University, there was a memorandum of understanding that quite clearly spelled out kind of the expectations, and one of them was that the university would start a fundraising campaign soon to basically get a separate facility or building for the Institute. Now soon is a—is a relative term. But to the great credit of OSU, they did make the building for the Linus Pauling Institute and for the Department of Chemistry—they did make that a major, if not the major capital campaign project for the campaign that they have been running for the last seven years or so. So we were the biggest building project on that campaign.

When I first came here, Paul Risser had just become the President, and he actually was the one who had signed this memorandum of understanding, without really knowing what he was signing [laughs] I think, because he was completely new on the job. [1:35:01] That memorandum of understanding had been put in place by John Byrne, the previous President. John Byrne knew Linus Pauling very well, and he was also absolutely critical in bringing the Institute from Palo Alto to OSU. And John Byrne, just like Dick Scanlan, and some of the other people who were instrumental in bringing the Institute here, kind of considered the Linus Pauling Institute their baby. They very much cared about what's going to happen with the Institute.

So, John Byrne had negotiated this memorandum of understanding with the Institute in Palo Alto, but he was not the one who signed it, because he was on the way out. Or he may have signed it, but he obviously was not the one who had to implement it. So Paul Risser signed it. And Paul [sighs]—he was so busy doing a zillion other things when he arrived here, and he never quite embraced the Institute as much as John Byrne did, or Dick Scanlan. And so we didn't make a whole lot of progress, especially with respect to the building, and Paul Risser also didn't spend too much time on fundraising. I mean, he didn't start a capital campaign, like Ed Ray did.

So, once Ed Ray became President, things changed quite rapidly, and he was interested and supportive of what the Institute was doing. He always tells me that prevention is the future of medicine, and this is absolutely important, and it's kind of a signature area for OSU in general, that we are doing mechanistic studies, trying to understand mechanisms of disease and how to prevent it, versus the medical school who kind of treats disease or symptoms of disease with pharmaceutical drugs. We are trying to prevent it through diet and lifestyle, and to do that, you first have to understand mechanisms, and that's really what we're doing here at OSU, not only in the Linus Pauling Institute, but other departments as well. And there's quite a critical mass here of researchers who are investigating the role of diet and dietary components in disease prevention.

So he embraced the Institute, but also the work we're doing: medicine should focus much more on prevention than treatment, and that's what we're doing. And he put the Institute as a top priority on the capital campaign list, basically. So we started to look around for architects who we kind of liked to maybe build the Institute, this building here. And Steve and I visited a number of different architect firms, and the one that we liked by far the best was Zimmer Gunsul Frasca up in Portland. And they are world-class architect firm, and they have built many, many incredible buildings at UC Berkeley, and Cornell, and all over the United States. So, they built like a $350 million research hospital at National Institutes of Health in Bethesda. And they had a very long history of building state-of-the-art research buildings, and just beautiful buildings, and highly functional buildings, too.

So, we had kind of hoped that they would be the architect firm that gets picked. And we asked them to build a model for the Institute, and that I think really started the ball rolling on the fundraising, too, because once you had the model and you could show people, "Oh, this is what it's going to look like," and kind of the vision of what you want to build, people started to get more interested and supportive of it. So, Ed Ray was very successful in raising funds from the Valley Foundation, who had already supported many other buildings here on campus. And then also the Resers, and they also have supported many other buildings, in particular Reser Stadium. So the Resers had supported mainly athletics up to that point, and the Linus Pauling Science Center was really their first academic building that they supported, so I was very pleased that they would also support academia here at OSU.

And so that building came together fairly quickly after we got these big gifts, lead gifts from the Valley Foundation and from the Resers. Then we got the match from the state, [1:40:00] so it was a fifty-fifty match, $30 million from the Foundations, the Valley Foundation and the Resers, and some other gifts, and then $30 million from the state. Then we went out, had this RFA for the architects, and we had about—I can't remember—eight or ten firms that applied, and four that we interviewed, and lo and behold, Zimmer Gunsul Frasca was picked! [Laughs] It was a great experience for me,

because I was involved in the planning of the building, something that I've never done before—kind of a once in a lifetime experience, being involved in the design and seeing it then actually grow.

Now the final product, and having been part of it is really a fantastic experience. And the building came out just absolutely spectacular. I think it's a really beautiful building, and very functional, too. We are really, really happy to be in these state-of-the-art facilities, and know how spoiled we are. We used to be in Weniger Hall, which was very dark, and sometimes cold and sometimes very wet! [Laughs] Or too hot in the summer, and no windows in your labs. This is almost the complete opposite of that experience over in Weniger Hall. So that was a big achievement for us obviously, following through from the memorandum of understanding, and one of the big goals that we certainly are very happy to have achieved.

CP: You mentioned that you achieved just about all the goals you had initially. I'm wondering what the vision is for the future now, of the Institute. What do you hope to see?

BF: Yeah, that's a good question. We did actually start, about a half a year ago, a strategic planning process. So we said, "Okay, let's take a step back. Now that we have grown from one faculty in 1997, which was me, to about fifteen, sixteen faculty now, working in three major areas: healthy aging, cardiovascular diseases and cancer—and having achieved this building, where do we go from here?" We kind of have reached our first plateau, and gone quite a bit up from where we started in 1997, but it's a good time to take a step back and say, okay, where do we go from here? What's the next big thing for the Institute?

And so we're going through this strategic planning process. We hired a consultant firm in the Bay Area, and they are helping us with this process. What we want to do is build on the current strength. I mean, I don't want to re-invent the whole Institute, because what we have been doing so far has been working fine. Obviously, we were quite successful at the great achievements over the last seventeen years. So we don't want to just start from scratch, we want to build on our strengths, which are in research, healthy aging, heart disease, metabolic diseases and cancer. And then we have some outreach programs and public education programs, so we are just thinking of how we can take the next step for each of these programs. And it will require some adjustment of the overall focus.

What we really want to enhance now is this focus on health span. I mean, we have been doing this, in a way, already for the last seventeen years, but to bring that out a little bit more pronounced, and really focus more on that as a unifying kind of mission, or theme, of what we're doing. So, health span as opposed to life span is not only how long you live, but how well you live. And health span is the time in your life when you're free of chronic disease, but also free of what's called deficits of daily living. So it's not just absence of disease defined as health, but it's also optimum health: how well your whole body, all the systems in you body, are working. Like immune function—is that at the optimal level, and are you protected against infectious diseases as effectively as you can?

And then, how resilient are you? How well is your energy metabolism, [1:45:01] and all those things that you know, have different degrees of functioning well, or not so well, which is not manifested as absence or presence of disease, but being more vital, more fit, and having optimum health, not just good health. And so this time of optimum health and absence of disease is what we call health span. And what we trying to do is get the health span closer to the lifespan, so that the gap between when your health starts to decline, and you have certain daily deficits of living, and you also have signs of chronic disease, that this time, between those deficits and the diseases showing up in your life, to when you die—that gap is getting smaller and smaller.

The ideal world would be where your health span is equal to your lifespan, and you basically die of old age without having suffered before you die. That would be the perfect world. But unfortunately in this country, this gap between health span and lifespan is actually becoming bigger, because we are living longer, but we are not necessarily living better. You know, going back to Linus Pauling's book, *How to Live Longer and Feel Better*, so it's a long life, but you want to have a good life, too. And in the United States, and around the country, and around the world, we are living longer, but we are not keeping up with the health span, compared to the lifespan. So how can we close that gap? That's kind of what we are addressing in the Institute.

And a big part of that is prevention of disease, but another part is promotion of optimal health and quality of life. So the quality of life is what we are focusing on. How can you optimize that? How can you extend your health span as much

as possible, through diet and dietary factors, dietary supplements and lifestyle? And this obviously relates to aging, it relates to cancer, it relates to heart disease, and other disabilities and chronic diseases. So, we want to bring that health span concept to the foreground in what we're doing, and have our mission really focused on that, rather than just saying diet and dietary factors and disease prevention. It's health span, optimum health, that we want to focus on.

CP: Well, my last question then is, what do we need to do to live longer and feel better?

BF: [Laughs] Read Pauling's book. That's one piece. But basically, we have this "Rx for Health" on our website, and we keep updating that as new research becomes available. But that "Rx for Health" gives you kind of a recipe for how you can live long and feel good, and have a good quality of life. So it has three pillars: a healthy diet, a healthy lifestyle, and taking the right dietary supplements. Pauling put a lot more emphasis on the dietary supplements. Not that he said diet is not important, but diet and lifestyle are certainly very, very important, and then the supplements are kind of the icing on the cake. And they are there to fill certain nutritional gaps, and sometimes give you a little bit of an advantage, too, but, if you are eating a lousy diet and leading a very unhealthy lifestyle, you can take as many supplements as you want. It's not going to make a difference! [Laughs]

So on that "Rx for Health" we have different bullets of healthy diet, and it's kind of the known diet. Your mother told you to eat your fruits and vegetables; that's still true. Eat a lot of whole grain foods, eat fish, and go easy on meat and fat. But the emphasis is really more on again, the quality of your carbohydrates and the quality of your fats. It's really, whenever you eat something in amounts that are just excessive, you get too many calories, and that's a big problem in and of itself. So that's one thing; you need to pay attention not to eat too many calories, whatever these calories are, whether they're coming from carbohydrates or fat. And then the next important thing is to eat the right carbohydrates and the right fats, because there are healthy ones, and not so healthy ones. [1:49:58] So stick to the polyunsaturated fats, and stick to the whole grains, the carbohydrates that we know are healthy. And again, you can look that up on our website.

The other column then is the lifestyle, so obviously not smoking is a huge risk factor. More people die of smoking related diseases than any other cause of disease. It's still the number one killer in the United States. About half a million die as a direct consequence of smoking. That's by far the most modified risk. If people wouldn't smoke in this country, we would have five-hundred [sic] fewer deaths a year, basically.

But anyway, lifestyle, smoking, maintaining a healthy weight, and exercising. Those are the biggest ones. I think, you know, if there is a magic bullet—there is none—but if there is something that comes close to a magic bullet of how you can stay healthy, it's to exercise. Be physically active. You don't have to go running in the gym, or whatever. If you just have an active lifestyle, that can go a long way. Don't be sedentary. Don't sit in chairs for eight hours a day. Be just active. That can do a lot of good for your health. If you go running, or do some strenuous exercise, that's okay, too, that's good, too. That to me is one of the most important things you can do to stay healthy. And related to that, obviously, maintain a healthy weight. So, don't become overweight, or obese.

And then the third pillar is the dietary supplements. To me, absolute no-brainer, to take a multi-vitamin multi-mineral every day, because we know—if people would eat the perfect diet in this country, yeah, they would probably cover most, but not all, of their vitamin and mineral needs. You know, the government, the Institute of Medicine, comes out with certain recommendations: you should get so much of Vitamin C, and so much of Vitamin B6, and so much of calcium. But we don't meet these recommendations; almost nobody in this country does. Even if you would eat the very healthy diet, it would still be hard to meet all of the recommendations for all the vitamins and minerals. But the fact is that 95 percent in this country are not eating what we should. With the dietary guidelines, 95 percent of the United States is not following those.

So, we have a lot of nutritional gaps, so take a multi-vitamin multi-mineral to fill those gaps, and pay attention to some other vitamins. Like, Vitamin D is very important in immune function, and many other biological functions. I take an extra Vitamin D supplement. You need to pay attention to your calcium, to your magnesium, fish oils are important, so if you don't get enough of those from your diet, take a supplement. So there are a number of supplements that are very important. But again, it's just to fill gaps in your diet, first and foremost. So they are part of a healthy diet and a healthy lifestyle. But again, they are just icing on the cake. They are not the bread and the butter—or the fruits and the vegetables [laughs] of a healthy lifestyle.

CP: Thank you, Balz. It's been a lot of fun.

BF: Okay. Thank you. [1:53:37]