Joe Beckman Oral History Interview, September 15, 2015

Title
“A Leader in the Study of Neurodegenerative Disease”

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Location
Valley Library, Oregon State University.

Summary
In the interview, Beckman describes his upbringing in Pittsburgh and his family background, with particular emphasis on his parents' and siblings' experiences in the military. He also discusses his early interests in science and the outdoors, two passions that led him to enroll at the University of Colorado following his completion of high school.

As he recounts his bachelor's and master's studies at Colorado, Beckman focuses primarily on his academic progression, his research experiences, and the enriching scholarly milieu that existed at the university during that time. In particular, he notes his earliest exposure to the study of peroxidases and the ways in which this chance scientific encounter helped to shape the rest of his career.

Beckman next describes the means by which he came to serve for two years in the United States Army, and details both his work as an administrative officer in an Army hospital in Seoul, and his nine months as an executive officer at the Fort Sam Houston medical training center. From there, Beckman recounts his years of doctoral study at Duke University, noting in particular his shift in focus from plant pathology to biochemistry, and the beginnings of his interest in superoxide dismutase, stroke, and nerve degeneration.

An analysis of the sixteen years that Beckman spent at the University of Alabama-Birmingham comprises the next segment of the interview. In reflecting on that time, he recalls the differences in environment that one encounters when working at a medical school, his shift in focus to studying ALS, an important paper that he published on peroxynitrite, and two guest professorships that he held in Europe.

A major focus of the session is Beckman's tenure and activities at Oregon State University, with Beckman sharing his memories of his decision to leave UAB for OSU, providing his sense of the Linus Pauling Institute at the time of his arrival, and detailing the mission of the Environmental Health Sciences Center, which he has led since 2002.

Of particular interest is Beckman's description of the path that his research on ALS has taken since joining the OSU faculty. In outlining the evolution of this work, Beckman reveals that he and his collaborators have uncovered processes related to the interaction between superoxide dismutase and the human spinal cord that portend an exciting new understanding of ALS. This breakthrough is such that it may result in an effective treatment for what is now universally regarded to be a terminal disease.

As the interview nears its conclusion, Beckman shares his perspective on the ice bucket challenge, advancement and change at the Linus Pauling Institute, the legacy of Linus Pauling, and the impact of the Linus Pauling Science Center. The session ends with Beckman's thoughts on the current and future direction of OSU.

Interviewee
Joe Beckman

Interviewer
Chris Petersen

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

Transcript

Chris Petersen: Okay, today is September 15th, 2015 we are in the Valley Library with Joe Beckman, and we'll talk to Joe about his career in science and his association with OSU, but I'd like to begin at the beginning with a biographical sketch of your earlier years, and like to know where you were born.

Joe Beckman: So, I was born in Ann Arbor, Michigan, my dad was a student at the university shortly after the Korean War had largely ended.

CP: Is that where you grew up?

JB: At five I moved to western Pennsylvania, to Pittsburgh, grew up there, went through high school, left when I was seventeen, never been west, so I applied to the University of Colorado, went to the University of Colorado to see what the Rocky Mountains would look like, fell in love with them, and that's kind of why I ended up here, eventually.

CP: What were your parents' backgrounds?

JB: So, my dad was from the Midwest and he became a naval aviator at the end of World War II, my mom grew up in Connecticut, got a college degree, ran away from home to join the Navy, where she met my dad. So, she was one of the first naval woman officers. Then they left the Navy in '53, I was born shortly thereafter, and my dad went back to architecture school. So, I spent my first four years in the architecture school with my dad, even had Buckminster Fuller as a babysitter once.

CP: Really?

JB: Yeah. Two bald guys; one very short, one and a half year old, and Buckminster, walking around while the architecture students were building a new structure.

CP: Wow. So, your father became an architect, then?

JB: Well, he went on to become a city planner, which was a new profession at the time. So, he ended up being one of the first city planners in the city of Ann Arbor and then moved to Pennsylvania. That's where I grew up through high school, grade school years.

CP: Did your mom ever talk much about her experience as a naval officer?

JB: A fair amount. Not a whole lot, but she had a big influence on my sisters, so I have two sisters who made careers at the Navy. One sister went through officer candidate school in Rhode Island, and there she took down one of the pictures and had it duplicated; there was my mom in the first class ever to go through it. So, that was kind of cool. And then in the first Gulf War my dad called up one day and we were talking, he said "I never would have thought we're going to war, I have two daughters going to the war and two sons who are staying at home."

CP: So, it sounds like you grew up in Pittsburgh, then.

JB: Yeah, pretty much.

CP: What was that like? What was community life like for you in Pittsburgh?

JB: So, Pittsburgh had a reputation at the time of being a dirty industrial city, but actually it was going through a renaissance. And what was pretty amazing is I could take a city bus down, go to the Carnegie Museum and the Carnegie Library, so it, I think, facilitated a lot of interest in science. It was a huge technology center, and then the ability to go to a world-class library and a museum just made it so there was a lot of opportunities to see different aspects of things going on. We also, in high school, got to go to tours of Westinghouse Laboratories and different scientific facilities, which was a big introduction that a lot was going on. Fisher Scientific is located there. I would go down in grade school and high school and they would actually let me buy little pieces of equipment so I could try experiments. And these days the idea

that they'd sell a chemical to a grade school kid or a high school kid would be just impossible to fathom, but they were willing to tolerate us then.

CP: So, it sounds like science was a consuming passion from an early age.

JB: Yeah, I think part of it was I was in kindergarten when Sputnik went off and they started creating all these science programs, and so it was a huge opportunity to be involved in extra classes, and you got interest in it early.

CP: So, there was a teacher or teachers along the way that helped prod that.

JB: Yeah, there were a number of teachers, and there were also a lot of special summer opportunities or summer camps that were related to science that were being created at that time. And I think that actually created a whole generation of people interested in science, a much bigger impact than most people realize.

CP: Were there any that made a particular impact on you at the summer camps?

JB: Oh, I don't remember that much of a lot of them. One of them was I could identify just about any tree on the East Coast, because there was an arboretum that we could go to. The other thing I remember is going and doing dissections of different animals. So, I was amazed we got to dissect an earthworm that had been injected so you could see the circulatory system, and it was about a foot long, and I carried it home, I was so excited. It was wrapped up in paper towels and I walked in the door, my mom was on the telephone and I said "well, look at this," and she's deathly afraid of snakes and she screamed through the phone and the air. My mother's not one that panics easily, but a snake that she wasn't expecting to see just kind of set her off. And years later I was laughing and telling that story, a family friend was saying "yeah, it blew out my ear drum. I was on the other end of the line."

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CP: Well, speaking of your mom, I read a piece that you wrote where you mention that she gave you a copy of a textbook by Linus Pauling - *College Chemistry*.

JB: Yeah, so my mom went through college in the middle of World War II, her brother went off to the war and was killed in a few months, and she had high school chemistry, but because of the war effort, she went into—she got a job at U.S. Rubber and she was running a fairly large chemistry lab that was doing monitoring and standards. And when the war ended, her assistant, who was a male underneath her, was promoted even though he was incompetent, and she was fired. So, she always had a bit of an edge about opportunities and so forth, but she had a lot of chemistry that she talked about and she told me, basically, "you'd like chemistry." So, I do enjoy chemistry, but I've never actually studied chemistry or took that much in the way of courses.

CP: Were there other things besides science that you were interested in as a kid?

JB: Oh, it's long enough ago. So, really enjoyed running around in the woods of Pennsylvania. I learned to ski and cross-country ski and enjoyed the outdoors. There's quite a bit in the eastern United States, far more than people would think. So, it was basically outdoors things, and I actually thought I would be doing more ecology and working on trees than doing chemistry and medical science.

CP: What was school like for you growing up?

JB: I'm not a very good student; too ADD. I was also one of the youngest in any class and also one of the tallest, so I always felt inadequate or inept. And I was very fortunate in the fourth grade that there was one teacher that took me aside and gave me extra math problems and made me realize I could actually have some skills and move forward, so that made a big difference. But I was definitely a C, B- student for most things, but loved to read and would read encyclopedias and studied outside of the class. So, definitely it was not a great experience of benefitting from school itself, but rather the opportunities that were around it.

CP: Was there always an expectation of going to college, or did you entertain a different path?

JB: So, it was my parents were the first to go to college and it was kind of assumed we probably would. I remember when I was eleven or twelve that I didn't think I would get into college, and wasn't good enough, so I was actually looking at doing electrical engineering or alternatives, to have some sort of trade. I could repair TVs back in the days where there were vacuum tubes and hung around shops and learned electronics and what to do. But after a while I realized no, I'll make it to college. Similarly, I was a B, C student, but there were certain courses I did really well in.

CP: Well, we'll talk about your military service in a little bit, but is that something you thought about at that point?

JB: No, actually it really didn't have anything to do with the military. It was the Vietnam War and lots of different reasons not to think about it and I think I finally went into the military, or joined it, when everybody else was saying "oh, this is terrible, the wrong thing to do," and I realized it was a challenge and I really wondered if I could do that, to beat it.

CP: Well, you mentioned the decision to go to Colorado was based partly on the desire just to see a different place. Is that fair?

JB: Yeah. So, there was a—my parents took off on a vacation once; we didn't have a lot of money, but once a little bit came in, they went on a skiing vacation to Colorado and brought back all these pictures, and that was kind of like just a carrot hanging out there of this place of impossibly tall mountain and wilderness. So, that was a major part of it. So, I applied to Penn State and I got into University of Colorado. Some neighbors had moved to that area, and then it also had a strong reputation for molecular biology and a new program that had started there. And I knew that's really what I wanted to study as an undergraduate.

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CP: So, it was an easy adjustment, then?

JB: Yeah, it was just amazing; drive across the western United States and see these vast planes and suddenly you come up and you think it's a cloud and you realize no, it's a wall of mountains, and then right at the base of it is a really pretty city and a different climate. And college was different than high school, with so many more opportunities. And I discovered the Molecular Biology department had just moved. Most of them were—it just left Harvard and it was just getting organized and there was a lot of freedom, so they really didn't know that I was seventeen, and I managed to take courses that only seniors could catch, would be allowed to take, normally. So, you got into this research environment and being challenged to think about courses and read papers. I was in way over my head. But if I'm drowning, that's usually when I will start to swim.

CP: How did you identify molecular biology as something to study?

JB: So, it came when I was in the library of the high school and I came across a book on organic chemistry and started to see this is the structure of sugar, and I saw in a *Scientific American* article, articles on the structure of hemoglobin, myoglobin, which were determined just a year or two before, the idea of this is what a protein is, and that life is accessible. And then James Watson published his first edition of *The Molecular Biology of the Gene*. It had only been a couple years before that Nirenberg uncovered the genetic code, of how codons incorporate amino acids. And so, reading that book it was just like "this is a field that's amazing. Life is understandable, it's a science." And so, I really wanted to be part of that.

CP: You mentioned there were a lot of faculty there from Harvard?

JB: Yeah. So, Keith Porter, I'm not sure what happened, but he was famous for developing the electron microscope for biological samples, and he left for Colorado and he took along six or seven faculty. They built a new building, built a two-story tall electron microscope for—and there are a whole lot of faculty that were pretty young; they had been raised in the academic traditions there but were just as happy to get out west and enjoy life. And most of them went on to be very serious scientists, or strong reputations. But they were old men in their thirties then, when I was looking at them.

CP: You had the opportunity to do some research then, as an undergraduate?

JB: A bit, but it was really hard to get into labs. But one lab let me in, and that was a pretty amazing experience; a lot of challenges, a completely different way of looking at it. It was also funny, because the department was fairly loose. It was the end of the sixties, was the start of the seventies, and so there were a couple of graduate students that were in the lab that were doing different projects, and one of them was a guy named Pat O'Farrell, very quiet guy, and he was developing 2D gels. That became a huge method later on. But I had no idea, but it sounded really cool, and like you look at all the proteins in a bacterium. So, he could actually show that he could see a single mutation in E. coli, he could count about five thousand different spots and see where—in the E. coli they knew there was one mutation that was introduced, and he could pick out that protein by scouting it or spotting it.

So, he wrote up a paper and submitted it, he became very famous, and it's kind of a basis for a whole industry. And then he started to talk about getting his PhD and was in his fifth year; people said "but you never formed a PhD committee, you haven't done any of the things you're supposed to do." So, it was that kind of loose style that was possible there that gave a lot of freedom. And just kind of watching different people trying to develop labs, it was important too, because I would go sit in a class and I would learn about some technique. I remember going through recombination, and I could pass the test and I could tell you what it is and draw the structures, but I was sitting in a lab meeting and someone started to talk about it and the cutting of the DNA and it was like I suddenly realized I had no clue of really what was going on, and I took about five seconds of sitting and thinking of how it was a practical problem that the rest of the information came into play.

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And that's something I've tried to get across, and it's really hard to students now, is to talk about we teach a lot of things and it seems kind of pointless, but in fact there are a lot of reasons why it's really important, and if you are working on real problems, these are the things you run into. So, I'm hoping that years afterwards that some of the light bulbs will go off and say "oh, that's what he was trying to get across."

CP: What made you decide to stick around and get a master's degree at Colorado?

JB: Well, there were a couple of things that happened. So, I thought I wanted to go do molecular biology and work in E. coli bacterium and do lots of cloning techniques, and there was a course that was being taught in my senior year, and the first half was on population genetics and it was by a guy in a different department, and so the first day is he took all the good-looking women and went up into the mountains to collect pine needles and came back and chopped them up and then he was going to do—look for enzyme variations and genetic difference in pine trees using a technique called electrophoresis, but he couldn't get the dye that's used to detect this in the solution, and I had enough experience in the lab to know that it was hydrochloric acid, salt, so you add a little bit of base and it will go right in. So, it did.

And the first results were actually kind of amazing. If you went into the sunny, open north face, south-facing slopes of a mountain valley, there was one type of genotype; it was like they were all AB's, way more than it could possibly be if there wasn't selection. And if you went into the really cold shade, north-facing slopes, they were all homozygotes, they were all Type A and almost no Type B. So, it was a really startling result and I ended up staying on to work for this guy and try to track down what the basis of that was. And it was just that there was one enzyme that had any activity that came out of the pine needles, that was called peroxidase, and it uses something called hydrogen peroxide, and I didn't know what hydrogen peroxide was. It was before the days of Wikipedia, so you actually had to go to the library and look this up, and it was a form of oxygen radical.

And so, I got more and more involved in looking at what free radicals were and understanding what peroxidases do in plants, and that shaped what I did for the rest of my career. But at the time, I'd left the Molecular Biology department, I was working in an Evolutionary and Population Biology department, I was reading like mad to catch up and learn what was going on in ecology, and there were all new groups of students coming in which I became good friends with and still keep track of. But I still, my heart was basically more of a molecular biologist than a field biologist. And there's so many serendipitous discoveries. Serendipity is a big word in science which means a major part of science is being really smart, but a major part is being lucky, and most scientists, they say they'd rather be lucky than smart. And I had a lot of luck.

So, the peroxidases were one area that was a lot of luck. The other was that some of my friends who were climbers, we got involved in a project and we climbed Devil's Tower about the time that *Close Encounters of the Third Kind* was being

made. In fact, we were on top of it while it was snowing on us while all the trucks arrived with the movie set. But I stayed good friends with the two people I climbed with. And I had to leave shortly thereafter to go spend two years in the Army.

When I came back, or stopped through, one of my friends had gone to medical school and said "oh, I just heard a great lecture about peroxidases and white blood cells," and that changed my whole career, the direction I went in, and ended up getting me to work on ALS in the long run. But it was a windy road. But it was really driven by friends and interactions and people telling you "oh, I just heard about something." So, those are the parts of being lucky and making discoveries or finding things that reach across widely different fields.

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CP: Yeah. That's interesting. So, clearly Colorado made a big impact on you in a lot of different ways.

JB: Yeah. And it took the Army to drag me out of there. I think I would have been still there as a research assistant someplace, hanging around and going hiking on weekends or skiing, but I had the obligation to go into the Army and had to go to Texas, which at the time seemed like the worst place in the world to have to go.

CP: How did that obligation come about?

JB: Well, I had a roommate who was an Army brat and I grew up in the military and he said "well, I'm joining the ROTC in our sophomore year" and I thought about it and said "yeah, I'll join with you." So, I did. And it was towards the end of the Vietnam War and we were about the only three people that joined up in the entire university, or maybe in Colorado. It was a bit abusive. People would spit on us and they would harass you in lots of ways, you know, assume you're a baby killer for going off to do it. But it also turned out to be a pretty good choice, because there were no other officers joining at that time. There was a huge shortage of middle-grade officers.

So, I stayed to do a master's degree and took deferment going into the Army when I went in. I was a second lieutenant but I had a master's degree in pine tree genetics, but a master's degree. So, I ended up replacing a major, someone with fourteen years of experience. And so, I got this incredible administrative experience and opportunities to see how large organizations work and don't work, and immense amounts of responsibility for someone that was twenty-two years old at the time. So, that was a big growth experience, and it was a big shaping factor.

CP: So, my notes say your first appointment was in Seoul, is that correct?

JB: Yes. I went to Fort Sam Houston for basic training for two months, and my assignment was MECOM K, which I had to do a lot of calling and say "oh, you're going to Korea," and I was being sent to the last MASH hospital. So, where *M*A*S*H** was filmed was in Uijeongbu, and the 4077th was the 5088th, and it was still there. So, I was supposed to go become the administrative officer. When I got in, they had an urgent need for an officer more senior, so I got sidetracked into the 121 Evac hospital, and you hear about that in *M*A*S*H** too.

And so, suddenly I found out that I had thirty people working for me and I had several million dollars of different funds I was responsible for, and I'd be sent to these meetings where the most junior officer in the place would be a full-bird colonel, and there'd be three-star generals. They were talking about when Carter got out of office that they would—because we were supposed to be leaving Korea at the time, and it was clear they were defying the president, just planning to be there for a long time waiting for him to get out of office, and I'm thinking this is not the way it's supposed to work, but way too junior to say anything. Jetlag and room's full of smoke and I couldn't stay awake.

CP: Well, what were your duties while you were in Seoul?

JB: Oh, I was in charge of the hospital facility, which had major problems, and then also a lot of different construction for the different clinics around the medical facilities across the whole peninsula. We had like thirty different bases there and there were medical clinics in each of them that we had responsibilities for. And there was the other assigned duties, which for me ran to be thirty of them, including infectious disease control officer and the—what do they call it—the black market duties, which those just consumed an immense amount of time. So, it got me used to dealing with a thousand different things that had to be taken care of at once.

CP: It sounds like an extraordinary experience.

JB: The movie *M*A*S*H*, or the—it was still going on thirty years later, it was still crazy.

CP: Well, eventually you came to stateside and you were in Houston after that, is that correct?

JB: Yeah, I had nine months to go, so I was sent to Houston for Fort Sam Houston, which is the major medical training center, and I was the executive officer for a large training company that had five hundred people in it. Pretty tedious, but the beauty of it was there was a nice medical library next door to it. My friend had talked about peroxidases and I just kept reading on weekends about peroxidases and ideas of how these things might be involved, what they were doing. So, that was what I did with my free times, basically going to libraries and reading.

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CP: So, this idea about peroxidases was something that was consuming you, it sounds like, during the years in the military. And then you eventually went to Duke for your PhD, and I assume that that was something you were pursuing at that point.

JB: Right. So, the peroxidases we're doing something important, but no one really knew what they were, so I was trying to figure that out, and that's really the thing about being in sciences. You have a question and doggedly pursuing it trying to figure out every alternative and what—keep reading to understand why it would be that way. And I left, I went to Duke because they have a forestry school, but I ran into someone that just took what I had done with peroxidases and, in about ten minutes, pulled out his calculator, recalculated my data and calculated a free energy and said "well, that's not a very big effect." And it was like I had—it was another epiphany, because it was the same equations I had been taught as a freshman, you know, for the freshman chemistry unit in high school, but it never occurred to me to apply it that way.

And I figured this is the place I want to go. And it turned out that the man who discovered superoxide dismutase was a professor there. And we called him up at five-thirty and he said "sure, come on over," and he spent an hour and a half talking to me at five-thirty in the evening, as a prospective grad student. And so, that turned out to be a great move, to go to Duke. It was the center of free radical biology at the time.

CP: So, how did that spin forward for you, coming about your kind of progression at Duke?

JB: Well, it was in the Botany department. I was studying peroxidases in plants and trying to see do free radicals kill bacteria, which it turns out they don't, but I did have one other problem that arose, that Ronald Reagan cut budgets enormously in 1982. There was no money in the lab, and I got a letter that said "congratulations, you've been promoted to Captain," and I called up and said "I didn't think I was still in the Army," and they said, "oh no, you're still in until we let you go, if you're an officer." But you want to go on active duty, so I could make a lot more money in doing a couple weeks in the summer than I made as a graduate student all year long.

I got sent to Fort Sam, to Fort Gordon in Georgia, and I was assigned to inventory slide projectors in the hospital. I found out there's a research division, so I spent more time inventorying slide projectors there than elsewhere and started to talk to people about research. I ran into a guy that was interested in stroke and free radicals. I said "well, that's crazy, a stroke is you lose blood flow to the brain, so there's no oxygen." He said "no, there's reperfusion entry, and that's when the blood flow is restored and things get bad very fast then." So, he didn't know how to work with the enzyme superoxide dismutase, I did, and so I got us sent down there to do an assignment and suddenly found that SOD actually was very protective in stroke, and that's how I ended up switching from botany to working on nerve degeneration. So, it was a combination of being lucky, being in the Army at a time that was kind of a crazy transition and finding opportunities to look in different directions.

CP: Did this lead to a shift in your research at Duke, or did that come a little bit later?

JB: Well, I still finished my PhD, and my major advisor was pissed at me for switching fields, and I found someone over at the medical school, again a connection of a connection, who was willing to let me run as a postdoc. And so, when I started my postdoc, he managed to take the data I had generated in the Army to get a grant, which I did the work on and

he got the money and the glory. And then he got a job down in Alabama, so I followed him down there as a postdoc and I kept making progress there and eventually made it up to the rank of full professor, when I decided to move out here.

CP: So, this is the University of Alabama at Birmingham?

JB: Yes.

CP: You were hired into the Department of Anesthesiology, originally.

JB: Yes. So, the—at the time, anesthesiology would generate quite a lot of money. They were creating a research division, so they were trying to raise their profile, so they hired a number of people. And they had an amazing director of research, his name is Simon Gelman. He's a Russian Jew who was MD, PhD, who, because he was Jewish, was sent to Siberia, and when it collapsed he managed to make it out in the '73 immigration, when the Russians allowed a few Jews out. So, he went from Siberia, collapsed, being sent to Israel right at the start of the '73 war, so he got sent to the front and was running in the surgical theater, and then eventually came over to Cleveland without speaking any English and became one of the best-known people working on liver transplants, particularly the anesthesiology of it.

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So, it was really hard to go up and try to complain to him about how hard you have it. But we all did, and he was always very gracious about it. So, he was very forward-thinking and really wanted to get PhDs into the department, raise the caliber of the science and the direction.

CP: Well, what was it like for you being in a medical school? It's certainly a new fit.

JB: So, it was quite a transition, and you would think it would be a lot harder than it was. I was really pleased. You know, you worry about MD, PhDs, and the MDs were always very gracious, by and large. And the competition in medical schools, there's no—tenure doesn't really mean much; created some dynamics that were a bit odd. But it was just like a great learning opportunity. And you're taking something that you've got that looks very promising, you're trying to figure out how you can apply it clinically, and then you get to learn very quickly about what it's like being in medicine.

And it was kind of surprising to me, when I started to think about going into the field of stroke; it's at the time they were spending eight hundred million dollars a year working on stroke. I mean, there were a number of monographs written on it, and I found that after reading for about two months, I kept reading the same thing over and over again. There really wasn't much known. And so, it was a wide-open field with a lot going on. It started to advance after that and there were a number of directions, but it's still a wide-open area with lots to be done. And it wasn't that hard to make a transition. You had to learn new language, you had to go study a lot and keep an open mind, but it wasn't—it was fun to do.

And it was really fun to go watch how physicians work and what they're thinking, to seeing what they're problems are and realize just how primitive medical really is, how few things they actually measure and how little they can actually do. Just, even though it seems to be very sophisticated and you build big, elaborate structures, it's still the patients healing themselves and you're just trying to overcome a few little hurdles here and there. And stroke and working on ischemic heart disease, a lot of it's just thinking of the vasculature as a plumping system. And so, it wasn't that hard to learn about it.

CP: Is there a tension there between the medical practitioners and the scientists?

JB: Generally, no. There's always a tension, there's—it wasn't bad. It was actually there was a lot of respect. I have a lot of physicians that came and worked with me, and they were a lot of fun to work with, and they were, deep down, they had a lot of motivation. So, I ended up working a lot with pediatric intensivists, people who work on really sick kids in ICUs. And there was times they would come in just being really depressed and sad, and it was they had spent the last three days fighting for some kid and lost it.

And what I was excited about is we actually had, I think, pretty profound insights into why a kid could be going from perfectly healthy, running around, spikes a fever and then suddenly everything goes to hell and they die in three or four days, and we were the quaternary care facility for a lot of the southwest, southeast at the time, so we got a lot of those

cases coming in. They could save some, but some they couldn't. And then we were able to start to look at what was going wrong and why did it go so seriously wrong. And I still fundamentally believe there's huge advances to be made in medicine that we haven't quite tackled yet, haven't wrapped our heads around the right way to study it. That's what I've been working on now for the past twenty years.

CP: When you arrived, were your duties primarily research, or was there a teaching element, as well?

JB: Entirely research. And I really didn't do that much teaching there. I did some in bio chemistry and I would do a little bit of lecturing to residents, but not much. The teaching was for residents who wanted to do research. They would come over and you would work for them and that was pretty labor-intensive. But almost no teaching responsibilities.

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CP: That's a very different model from what I'm used to here, talking to academics at OSU.

JB: It's a different model, but we also were expected to generate our salary, too, so it was a lot more grant writing and we were a lot more aggressive about it. If you want to know what the tension was, it was trying to stay funded. The rest of it was trivial by comparison.

CP: So, you arrived and you were interested in stroke, but eventually there was a shift there, is that correct?

JB: Yeah. So, we started working with this molecule called superoxide dismutase, a protein that scavenges superoxide. Now, superoxide has this name that sounds like it's really dangerous, and it was given by Linus Pauling in 1927, but that was his impure chemical in water. It's actually not super-reactive. So, this was a problem. We had a compound that stayed in the circulation that really wouldn't get into the brain very much. It was very protective in a stroke. And there was already superoxide dismutase there, and it's working in the blood, has to be working on the blood-brain barrier of the vasculature.

So, why did it work? And so, I was puzzling with that, and what was superoxide reacting with. So, those were the things that you go around and you keep daydreaming about it and you don't have answers. So, I went to a seminar one afternoon for something called the endothelium-derived relaxing factor. I fell asleep in the first fifteen minutes and I woke up and said that this relaxing factor was protected by adding superoxide dismutase. That's when I woke up, because there's very few things that superoxide dismutase really would protect. So, here's something that's being released by blood vessels, and SOD was doing something that stabilized it in some way. So, it was a short-lived factor and it's really mysterious as to what it was. A lot of people jumped on the bandwagon, because it was a major regulator of blood flow.

So, about two years later I went through the library and there is a journal that had just come out and the cover was "EDRF is Nitric Oxide." So, it was basically this relaxing factor was identified as a molecule that's just a nitrogen and an oxygen atom. And I didn't know that much about nitric oxide, but having a botanist background, I knew something about the nitrogen cycle in nitrogen oxides. But I started to dig in and read more and more about it and it made perfect sense why it would react with superoxide.

And in fact, in high school, going back to Pittsburgh—it was actually in grade school—I went down; for a dime you go downtown and walk around, and there was this old used book store and I went into the far back of it and I bought a book on the inorganic chemistry for seventy-five cents, and I carried that damn book all the way to Korea. I never found it very readable and I just didn't get that much out of it. But it was my book, I had it and I trotted it all over the world. So, when nitric oxide was—this article came out, I pulled out that book to read the section on nitrogen oxides, and as I went down through it, my mouth dropped open, because there was a section on pernitric acids, and so nitric oxide and superoxide would reactive together and make a new molecule. And there was a paper cited from 1927 that said this thing broke down to give two really strong free radicals. One is nitrogen dioxide, the orange color in smog that burns your lungs, and the other is hydroxyl radical. It was like suddenly I said I can understand all of free radical biology. This makes immanent sense. Call up Stockholm, you know, I've just solved it.

But it really did make a lot of sense. And I was really fortunate to have that version of the textbook. It's a really famous inorganic chemistry textbook that was published. There's ten more editions. They stopped talking about that reaction in future editions, so it's back in now but only after the work we did in the past twenty years. So again, it's one of these

serendipity things. If you look in and suddenly there's a reaction that says, clearly states this thing is forming very strong oxidants, and that led to a lot of different discoveries from there, but understanding how superoxide dismutase, the protein we're using to treat the disease, interacts with nitric oxide and superoxide led to a lot of discoveries; markers that then we could go into the kids that died in the ICUs and show that their lungs were absolutely full of the products of that damage. An unbelievable amount. The pathologists that looked at our sections at first said "oh, that's an artifact, that can't be real," but it was. And so, there's a hundred different human diseases and this oxidative process occurs in every one of them. And now the problem is how do you cure it, how do you treat it, and that's why it hasn't taken off. It's not a simple drug that you can give, but there are treatments. It's just convincing people and understanding how to use it and when it will work and when it doesn't; just not simple.

So, we discovered this reaction, we know this enzyme's superoxide dismutase, we've been giving it to cure stroke and it works great. So, 1993 I went home early after a frustrating day, we had two kids, one kid at the time, got home early enough, I turned on the national news and Tom Brokaw announces there's a gene that's been discovered that causes ALS. And I really didn't know even exactly what ALS was. And it goes through the whole thing and I'm thinking yeah, there's another gene, it's like the Huntington gene, it's we have no idea what it is. At the very end of the broadcast he said "oh, and it's an antioxidant enzyme, so maybe taking antioxidants will treat the disease." And I looked at it and said "I think I know what it is," because I had discovered a toxic reaction that SOD had catalyzed. And so, that's when I switched and started working on ALS for the next twenty years.

And I've been trying to figure out how this protein that's normally so protective in every cell in your body can become toxic and cause this very selective death when you can be as old as eighty years before the disease starts. You have the protein in every cell in your body for those eighty years. So, all the different pieces we had been working on of this very reactive molecule, the nitrogen dioxide showing up on proteins as a marker, all of that has kind of come together to understand how ALS is driven by mutations to superoxide dismutase, and it's also a process that is hugely controversial. Most of what I've done for the past twenty years is dismissed by the ALS community as "well, we know that can't be right because we did this mouse experiment and it didn't quite work out the way you would expect." And I think we're going to be able to change that in the next year to two years.

CP: Wow. Well, I want to make sure I reference, there was a paper on peroxynitrite that is very important, I assume. This is a piece of what you are talking about. Was there something we should talk about more specifically about that particular work?

JB: So, I had a lot of trouble even getting time to work on the peroxynitrite project. My technical boss, Bruce Freeman—he was my postdoc mentor and he was the division person—said "you shouldn't work on it, you're wasting your time, this can't possibly be." So, I would come in at night to work, and then he came in one night and found me working late at night and he threatened to fire me, so I had to go talk to Simon Gelman, the Russian Jewish doctor, and Simon says "no, you just go do what you want, need to do." And I kept working on it. And so, when I finally got the paper accepted, Bruce of course had to be the last author, but that became a hugely cited paper, that I think it has ten thousand or twelve thousand citations. If you get more than twenty for a paper you're doing really well. This has really been the major citation.

It was not that complex of a paper, and we've published other papers after that that followed up, and for the first three or four years it was considered a kind of a crazy idea, an eclectic idea, this unproven hypothesis, if it turns out to—might be interesting. I think that the point where it changed is we realized—it was actually the experiment where I was close to being fired, the late night I was working the lab—I took the superoxide dismutase protein and I was studying a reaction where I thought there was an artifact, and I figured I'll throw in the protein as a control. And I was being lazy, I had a lot of the protein in the freezer, so I threw a ridiculous amount in. And I added the next reaction and the whole thing turned bright yellow. And that was completely unexpected.

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Well, I added acids and the solution went colorless, and now it's late at night, I wanted to leave, but I added base and it turned colored again. So, it was this yellow color that if you make the solution acidic it goes away, comes back. Couldn't figure that one out, and we did more experiments which showed it was on the protein. It turned out—the other thing I did was I played soccer, and have since high school, and there was a really good team, or league, in Birmingham that had lots of international people. I played defense; there was another guy who was much better than me, much faster, and we

played with each other for years. Finally we sat down and had a beer and it turned out he worked in the same building as I did. And he said "well, I can determine the structure of proteins very quickly, of things bound to proteins," and I said "well, I've got one. This protein, the structure's known, and it's turning yellow."

So, we did it, it took a year and he came up and said "the yellow color is not where you thought it'd be," you know, "it's out on a tyrosine, which is way out on the side." I couldn't figure it out and was walking around, something weird's going on. I had a surgeon, a Chinese surgeon that would come over, and he was helping me do these surgeries for stroke and he was studying to become an MD in the states. So, I'd walk him through the lab; he has a Chinese book of organic chemistry open that he's studying between the surgeries, and on that page is a diagram of a PH indicator called nitrophenol. It's a very common one, you'd learn about it in organic chemistry, and this lightbulb went off that tyrosine is basically a phenol group, and what we made was nitrophenol. And that was about one-thirty in the afternoon; by about eight that night we had done a hundred experiments or confirmatory measurements that proved this was absolutely what we have.

And that was important because you have this nitro group added to a phenol, and we made antibodies to that and now you can start to go track that in patients. And when we had a way that you could take a bit of tissue from any human or animal model and show that this process was occurring, that you were getting the additions of the nitro groups, that that's where you could show that this process is happening in hundreds of different diseases. And actually it was a pretty good marker for the disease process. So, there's a lot of different accidents that happen.

CP: Was that a game-changer for you, then?

JB: Oh yeah, and that summer we took it from being this unproven theory to everybody in the world wanting to get my antibody from nitrotyrosine. And we spent many, many thousands of dollars raising many, many gallons of blood for antibodies to be able to provide, meet the demand. And then dealing with the backlash of "your antibody doesn't work" and then going through "well, did you do this? Did you do that? How and where did you store it?" If you put it in a freezer that goes through a standard home type of freezer and a refrigerator, the auto frost will kill proteins. So, a lot of people killed a lot of antibodies by putting it in that kind of freezer. Just dumb things that you have to work through with each person.

CP: Well, before we move to OSU, I want to ask briefly about you did a couple guest professorships, one in Switzerland and one in Germany, if there's stories to tell there.

JB: So, the one in Switzerland was my friend Wim Koppenol, who actually was in Baton Rouge about the time that I published the paper, the highly cited paper, and he sent me a fax of the *Times* saying "thermodynamically, what you say is impossible." So, he's a Dutch physical chemist and we got into arguments, and we still argue about it, but it turns out his wife's brother was dying of ALS, and when we started to work on ALS, they would come through, we talked about it, and then he got a professorship in Zurich at the ETH, which is a very famous, high profile institute. So, I went over and spent the summer with him and just worked on peroxynitrite and toured a lot of mountains and had a great time with my family.

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And then I went to Konstanz, Germany, which is only eighty miles away. It's right on the border of Switzerland, gorgeous place, and worked with someone there on what are some of the implications of having nitro groups attached to proteins. So, both were great experiences, they were good to get away, and that was also, going to Konstanz, that was enough to convince my family and kids that moving to Oregon would be a good thing to do, because I did that the summer before I decided to move.

CP: So, let's get to that. It's after sixteen years, about, that maybe you make the switch to OSU. Give me the background behind that decision.

JB: Well, if you start as a postdoc in a medical center, you can hit ceilings. And I was kind of cornered where I was. I had lots of opportunities to move, but my father-in-law had had a stroke, and so I ended up staying probably twelve years longer than I planned. And it was a good opportunity. We did a lot of good science. But I was looking for another opportunity and Balz Frei had started the Linus Pauling Institute; he got a large endowment and was able to create an endowed chair. And I was looking at going to Harvard. Simon Gelman had left UAB and was a chair at Harvard and was

recruiting me up there, and there were a couple other places I could go to look at. But I liked the opportunity of coming out to Linus Pauling Institute. One of the people that was trying to keep me there said "you'll ruin your career if you go to Oregon State," and that was kind of what was the final thing that said yeah, this is the right place to go.

CP: Because—about something specific about OSU, or because there was no medical school?

JB: No medical school, OSU was not very well-known and the Linus Pauling Institute was brand new, and the reputation of Linus Pauling is sketchy in the medical community. He called himself the chief kook about the ascorbate part of it. And there were a lot of risks with coming here, because it is a smaller school, and at the time, it was just beginning to pull itself out of its low point from the cuts in state budgets. But I—and when I first came out the first time and I looked around, I said "no way." I'm not sure why, but after a couple days it seemed like it was—I liked the people and I liked what they were doing and I found of lot of eclectic people doing interesting things.

CP: Well, tell me a bit more about that. What was, I guess, your sense of the Institute, especially maybe the campus a little bit broader, as well?

JB: So, the Institute was housed over in Weniger Hall, which is ancient and falling apart, and they had recruited four or five people and three of them were quite young and they were just starting their careers, but bright people doing interesting things, and motivated. There was also a mass spectrometry core facility, and I had actually met someone named Doug Barofsky who ran that. And mass spectrometry was clearly going to be a really important tool. When I worked at UAB I helped get the money for the first mass spectrometer, but I was never allowed to touch one. I came here and they tore it apart and we put it back together. And I saw lots of examples of people being really innovative and a lot more flexible in what they could do.

So, that kind of intrigued me quite a lot. And then there was just being in Oregon and being out west. I'd really missed my time in Colorado and didn't want to spend my entire life chasing around a lab, and then, you know, what are you going to do, chisel my CV into a tombstone? So, the move was actually risky and I could have gone to higher profile places, sometimes I think maybe I should have, but by and large, actually it's been an incredible experience, and really fun to be part of making a place grow.

CP: And so, it sounds like Corvallis appealed to you as well.

JB: Yeah, I liked the small town. I was a bit worried about it as to how it would be, and also about bringing my family out, how they would like it. I think after about three or four years of—my wife said that she had a nightmare; she was born in Alabama and she said "I was really mad at you because you decided to go back to take a job at UAB and you didn't tell me." And so, I figured okay, we're okay, we're safe here, she likes it.

[0:55:31]

CP: Well, I'm particularly interested in talking to you about the Environmental Health Sciences Center. You became the director in 2002, what was the background there?

JB: So, OSU has a bit of a challenge even to this day of mid-level scientific leadership. So, the Environmental Health Sciences Center grew organically from the 1960s a lot. It has a strong—OSU has a strong tradition of working on the environment and health, farming and pesticides and the environmental movement of the sixties. And in fact, aquatic toxicology, the effects of pesticides getting in water, was really developed here in the Oak Creek laboratories. So, out of that when we were forming the National Institutes of Environmental Health Sciences, there was a strong cadre of people who were able to compete for NIH funding, and they created a core center.

The first director was [Virgil] Freed, and he was, as I understand it, he had been through World War II and lost an arm. And so, he was sitting in a meeting once where someone was saying "we need more one-armed scientists, because every time you ask them something they keep coming up and saying 'on the other hand," so he raised his hand and said "I'm your man." So, he's an interesting character. And then Don Reed had taken it over. Don then became the first director of the Linus Pauling Institute when it moved here. And Don was one scientist that I have met and had a lot of admiration for, one of the reasons I came here.

But I knew nothing about environmental health sciences, and they were trying to recruit a director, a big name from outside, and it seemed to be going fairly well, and then it came that oh, to get him here they had to have the laboratory that I was promised. And then it kept getting longer and longer negotiation that every time you thought you had an agreement, he would ask for more. It's a typical medical school play. And it turned out there was someone on campus who had been feeding him inside information about what to ask for, what to demand. Then he turned them down and they were going to lose this million dollar a year grant in a month unless they came up with a director.

There was an inside person who thought he would be the only person, the director who could do it, and he had offended all the deans. They were basically saying "just let it go. It's not worth it." So, Larry Curtis talked with Rich Holdren, who had just come here—Larry Curtis was the head of the Environmental Molecular Toxicology department—said, "well, ask Beckman." So, they came, and I'm looking at this hot potato of this big controversy over hiring people and everybody in the center and I have no clue what was involved, I didn't understand the science at all, but they were in a bind and there's like three million dollars' worth of funding, three more years of funding to go. So, if I took it, the worst that would happen is we get three millions of dollars and we have a big party at the end.

And I had to go to fly to Germany for a meeting. I was working with a drug company. So, I took the grant, which was that thick [holds fingers about four inches apart], that had been written, the proposal for what this center is, I went to the bookstore and went down into the undergraduate textbooks to find the textbook on what the hell is environmental health science. That's how naïve I am about the subject. And then when I was in the airport, I decided—I bought a book on executive management, which was by Drucker. I didn't recognize it, but it turned out that he is the guru of how executives should function, and it was a classic textbook. That was very readable and useful. I read them all on the airplane going over and coming back and then said "alright, I think I can do this."

And it turned out to be a great opportunity, because it's an unusual NIH grant, that a million dollars a year, not to do research but to support core facilities and to create your research. And it was a huge flexibility-giver to the center director of what you do, and you could leverage that by going and—because the deans, you know I didn't ask for anything to take it on, I said "just work with me." I had a fair amount of credibility with them that when we went and asked for different things, they would work with me, instead of having a shotgun held to their head, kind of a naïve university politics play that you just have to sit and hammer and scream for things, or else you'll never get anything.

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So, we were able to do a lot of really cool things, and one of the best was actually we had George Bailey working on trout models, but to be honest, it wasn't a great model system. You'd work for five years and you get one publication that nobody in the world can repeat, and yes, it's an accomplishment of doing forty thousand animals in an experiment, but nobody really cared that much about it. But to hire his replacement, he had this incredible young, energetic guy come through who wasn't appreciated at University of Colorado Medical School. His name was Robert Tanguay, and he looked around, he wasn't too sure about coming, and I said—I had a lot of fun talking with him, and I said "I don't know, but you can do things here, you can get things done, and I hope you come."

So, he came and it took an enormous amount of work, but he just created this phenomenal facility for working with zebrafish that's world-class. I'm really proud that we were able to make investments. We didn't do that much to help him with it, but we were able to provide enough money and leverage that it was seed funding. And we did that with Kim Anderson. I'm not sure if you're going to interview her, but you should. And she's doing an incredible job of figuring out what chemicals people are exposed to in the environment. And there are just hundreds of other things that we were able to help facilitate.

So, I've been learning more about going into business and creating businesses and learning about angel investing, which is as far from being an angel as you can. I realize I have essentially been able to be an angel investor in university projects for the past fifteen years.

CP: Wow, so that's sort of the crux then?

JB: Mhmm.

CP: Well, how about your own work on ALS? How has that progressed since 2001?

JB: So, when I came here—it goes in fits and starts, and I have a strong collaboration with the people in Uruguay, and the cell culture part of it works well. And I was hoping to get a lot of help with the biophysics of it, from moving to a real Biochemistry department, and that did happen. What became interesting was I'm trying to measure metals bound to a protein, so superoxide dismutase has a copper and a zinc atom, and I think what goes wrong in the disease is you lose the zinc atom but copper stays bound. It turns out nobody really knows how to measure proteins with metals bound to it *in vivo*, particularly when you're dealing with a couple of tiny cells in the middle of the spinal cord. And that's where the mass spectrometry core facility turned out to be useful. We ended up going down there, doing lots of different measurements. And we developed a method where we can take the entire protein, get it to fly into the mass spectrometer, and weigh it with a remarkable accuracy. And so, we can tell which metal is likely lots or how much is present in the spinal cord.

And as typical, your best theory is that we're losing zinc and it's the copper that's toxic, and when we look in the spinal cord, half the protein is sitting there and it's missing a metal, but it turns out it's missing copper and not zinc. So, I won't go through—we've developed enormous technologies, lots of different ways to look at these, study this work, but the problem is we have an animal model that's made by taking the human gene and putting them into a mouse. And that was created in 1994, and no matter what you do, the mouse dies in a hundred and thirty days, and a really good treatment takes about a hundred and fifty days. There's a million dollar prize if you get it to a hundred and sixty-three days. So, twenty years of work, expensive, working with animals and they all die of ALS, and you can watch patients die, I've gotten to know a lot of patients out here, and it would make no progress.

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So, one thing I've enjoyed is I've had a number of graduate students come through, and one of them is Blaine Roberts, who moved to Australia, and he's working at Melbourne and he would come back—or [in Australian accent] Melbourne—and he worked in lots of different laboratories. If an undergraduate's walking down the hallway, they might be shanghaied to getting to—and end up working for him. And he still is that way, you know; he comes back over and they all end up working for Blaine for a while. But, so a couple years ago he came back and there was a new compound they were excited about testing and it was extending the life of the mice as much as anybody had seen, but they were all still dying of ALS, and we were doing measurements of metals bound to proteins. We wrote a pretty good paper together.

Well, the other approach is if you can't improve it, how do you break it? So, I went back to a finding that someone had made. It's if instead of that—if you put in a second human gene that's related to SOD, the mice, instead of dying in a hundred and thirty days, they started dying at two weeks. So, it just makes this much, much worse. And we had a pretty good—our mass spectrometric methods told us what might be going wrong, that they needed copper. And the Australians have this compound that gave copper into the brain, so we synthesized it and put it on the back of the neck of the mice. The first mouse that we were looking at, it was, you know, it was ready to die within a few hours. And I came in to say "well, did the compound kill the mouse, or what happened?" They said "it's up and walking." And then that night it started to look sick again, so we dosed it again, it did better; next morning it looked pretty sad, we gave it again, and it got up and moving and then after about two or three weeks, the mouse looked normal.

Well, we then started a larger series of experiments, and the mice not only lived past that first two weeks, but then they hit a hundred and thirty days and they kept living. And we've—after atomizing the techniques, we now have the mice living out to two years. It's not quite their lifespan, but it's pretty close. Take the drug away, they get ALS and get really symptomatic. You can give the drug and stop it. So, we have a drug that works in mice, and remarkably well, and we'll hopefully begin to humans next year.

CP: Wow. So, that's the next step, then.

JB: Yeah. We basically have a drug that looks really promising; we're trying to figure out how to make it, improve it, and then just how do you give it to humans in the most appropriate fashion. And then I get killed at the reviews and at NIH on this drug, because any time you say you have that kind of improvement, everybody says "oh, it can't be," or, you know, "it's irrelevant" or "you're doing something funky." And maybe, but no one has ever seen a result like this, and it's pretty exciting to see when people are dumping ice buckets of water on their head saying "oh, we should do something about

a cure," and I'm sitting on the compound and we're just watching the mice go on and on, and you can't really say much about it until you get it published.

In the midst, in the basements of the animal facilities, we've done a really solid set of experiments and there's no question this drug works. Every mouse it's treated has made it way beyond any mouse ever. And then we've done lots of measurements. There's things that can go wrong in a mouse that are known in the field that create artifacts and there have been false claims before, but we've done all those controls; that's not what causes this. So, we're pretty pumped.

CP: Yeah. That's great to know. Well, I can't not ask you about the ice bucket challenge and your perspective on that.

JB: Well, I was in some ways excited to see it, and to be honest I didn't know it was happening. So, both my parents have major health issues, and I was back in Pennsylvania last summer, in 2014. They were both in ICUs at different ends of a major hospital and I spent morning and night shuffling from one end to the other. My wife said "you should see what your daughter's doing," so, and there's my daughter in a bikini on our deck dumping ice water over her head, and that's when I started to find out about this ice bucket movement. And it's exciting to see that the field has gotten this influx of money, and also the awareness about, you know, how many of the two and a half million videos actually understands the disease. It creates a huge challenge, because now there are all these expectations, and a hundred million dollars sounds like a lot of money until you try to do one single clinical study.

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So, it's, I think we can actually make a dent, and we can make progress in understanding the disease, and I'm hoping that this drug works, that it actually would say "you can tackle really serious diseases and you can make progress," you know. It's not hopeless. We've been working hard on it and people say "you've been wasting all this money for twenty years, why haven't you gotten there?" It's a problem that's worth working on for thirty years, until you get it.

CP: I want to ask about sort of how the Institute has evolved in your time here at the Linus Pauling Institute, and first to ask a bit about Balz Frei and the leadership that he's provided for the Institute.

JB: Oh, how to answer that. So, Balz is an extremely articulate and very thoughtful person, and I think he has enormous passion for the Institute. He would have many opportunities to go many different directions, and he stayed here. So, he believes in it and what it does. We've grown a bit as more people have come, and we've become, I think, a major source of recognition for the Institute—I mean for the university. I think Balz has done an incredible job of building the credibility of the Institute, of not going after "high-dose vitamin C is going to cure everything," but keep working on the science. And there's still a huge need for improving diet, and micronutrients are very important for your health.

There's a huge backlash, so science is actually a publicity contest, which is kind of sad to say, but if you want to get published in the *New York Times*, you basically say "vitamin E is going to kill you." And so, there are badly done studies, or using statistical methods that just don't make sense; that they weren't mathematical or not easy to defend or to pick out what's wrong, and when you ask the clinician that does it, he says "oh, well you'll have to ask a statistician about that problem. That's not my field." But that was the crux of the argument, was a bad statistical model.

So, I think we have a huge responsibility for saying there are a lot of things that you can do to improve your health through prevention, to extend your health span so you stay healthy as you age, and say there's a lot of credibility to it. Medicine basically goes by procedures, and so you make money by billing for procedures, so you don't get paid for doing prevention, even though that's by far a more effective way of improving health, and so that's why it's appropriate for us to do this kind of research.

The other thing is that our tools to do science have improved so enormously that we can do things that Linus Pauling only dreamed about. So, while he was doing the vitamin C research, people don't recognize that he was a leader in developing what is now known as. He and the people of the Institute really wrote the first papers on it. The 2D gels that Pat O'Farrell did were used heavily by the Institute to try to trap what are the changes induced. But they also were trying to use gas chromatography to analyze metabolites in urine. With the investments we made in mass spectrometry, particularly with the help of the Environmental Science Center and the Linus Pauling Institute together, we now have million dollar

machines that can analyze hundreds of thousands of compounds at once. So, we can actually start to track down what's really happening with these.

The science is beginning to catch up, and it comes back to the idea of it's actually pretty impressive how primitive medicine is, how few things you make adjustments. And people are aware of this, but now we're coming in with so many different measurements that no human being can possibly interpret all the results that a patient could present in a few days, using all the methods we have now. And so, we have a leadership position of trying to figure out what these effects are and trying to understand what are things that are natural products or things over the counter, or micronutrients, how they impact your health in ways that you can't really tell by the crude methods that are used by medical science now.

[1:15:23]

CP: What is your perspective on Pauling? I mean he's—you mentioned he described himself as the chief kook, and his vitamin C work was very controversial, to say the least. Your life was intersected with him at various points over the course of many years.

JB: So, I was pretty fascinated with vitamin C when I was an undergraduate and read about it, but in truth I was in the Army and close to heading off to Vietnam and there's this professor wearing a beanie, marching in front of the white house saying "no more war," and saying it's a lot more complicated than that, and yeah, you can come out of sunny California and walk around and chant, and I wasn't that impressed. I think when I started to look at the Institute and I read the biography of Thomas Hager going through the collection, I suddenly realized just how utterly inadequate I am as a scientist and how classed and what a remarkable individual he was. And it's not just as a scientist. The chemical bond; I didn't realize just how fundamental his contributions were to everything I had studied for all those years. But also his personal courage in the fifties of taking on the establishment, it was just remarkable. So, there are lots of movies made, but I don't think people really have done appropriate appreciation of what Pauling did to take on McCarthyism.

So, that was pretty cool. There are still things; Pauling was so persuasive that you can argue that he actually held back the field of inorganic chemistry quite substantially, and that's probably true, that his methods—Pauling was one of the few people that have the intuition they could make it work, and he downplayed what became the dominant method now. And yeah, you can make fun of some of the mistakes he made, of the structure of the double helix, but clearly he jumped a little bit too soon. There are other things, for instance the sickle cell anemia work; if it was anybody else, he would have had a Nobel Prize for that work. He should have had a third Nobel Prize, at least. He published more after he died than I published while I'm here, so a little embarrassed about that. It's amazing what his productivity was.

CP: Yeah. What has been the impact of the new facility for you and for the Institute?

JB: It's been an incredible place to advertise and show what you can do here at OSU. The biggest thing is a room that isn't shown in the public, but it's where we keep our animals. It's made my research working with animals much more secure. I like the open collaboration. But in truth, we're hurting a bit in these couple years, so it's really frustrating to see that science isn't valued anymore, and you can see that in the NIH budget; it's decreased by a quarter, which has made it much harder to get funding. And even the work I'm doing on ALS, that I have a drug that's keeping animals alive forever, but I'm not funded by NIH. So, for three years, I've been funding that, both by not taking salary and because there are donors to the Linus Pauling Institute. I would have been really in deep trouble at a medical school, whereas the donations that came into the Linus Pauling Institute let us keep going.

It's changing rapidly. I now have substantial funding to carry the work forward, but you need help getting through the gap years. I'm really excited about some of the core facilities there, and actually the connections with the Chemistry department, which has always been awkward, because of Pauling's reputation in vitamin C; chemistry was always a bit squeamish about dealing with Pauling. You know, great that he did all this, but that was a hundred years ago; what are we doing this week? But we've developed a lot of collaborations with people downstairs, and I think he'd be very happy to see that. And then the core facilities that are down on the first floor and the teaching are incredible. Our chemistry students now have an amazing educational opportunity.

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I think maybe one of the biggest things for collaborations is the Ava Helen Café, that I see lots of faculty, lots of students using that facility and enjoying it, and a lot of science comes out of inner connections. Most everything I've talked about, the serendipity was because I ran into someone at some point who said "well, I work on this" or "that's weird, yeah we can talk."

CP: Well, the last thing I want to ask you about is a question we're asking everybody for this project, and it's just to give their sense of where OSU is at right now, heading towards its sesquicentennial three years down the road.

JB: So, I think OSU has done an amazing job. I came in 2001 right as the first recession hit, and that was pretty crushing to watch more budget cuts, and it was really scary to say I arrived at this school and we had no idea how we're going to manage programs being cut by ten and twenty percent. When the recession came in 2008, I started to get depressed again, thinking oh, here we go. And then I realized wait a minute, we're going to start hiring faculty, and it was the capital campaign. So, the idea that we didn't have a capital campaign for so many years was partly being a state institution and supported reasonably well by Oregon for a long time, and we just weren't prepared for the change. But it was truly amazing to see how many people at OSU, alumni, really cared and how much they would contribute.

And it was great fun. I got—because I had worked with chemistry as well as the Linus Pauling Institute, I was one of the people that got to go out to present to the board about building the new Linus Pauling Science Center. And it was a pretty entertaining meeting of going out and saying "sixty-two million dollars," and you could watch jaws drop, of an unheard of money to go out after. They were telling me "well, what's your elevator pitch?" and it's like "what's an elevator pitch?" So, I have a lot of learning to do. But we had a lead gift that fell through. Balz Frei was about as depressed as I've ever seen him, and within two to three months, the Valley Foundation came through. Ed Ray got behind it and it was amazing; suddenly we're off and going. And when the recession hit, we started to hire faculty.

So, as an institution we're doing amazingly well. And you can see it in the buildings going up, the students coming, we're doing exceptional science, a wide range of it, lots of great new faculty. We have a lot of challenges. We have, as an institution, I think we need to understand it's not all about undergraduate student success, but lots of other things are important. To value research here is important. We are a very research-intensive university, but it always gets thrown in as the last in line and there needs to be more reinvestment in it. Everybody complains we need more money, and it's true, but you can still have a pretty good career here and balance things out. I think the future is pretty unlimited. We've just started to tap it. And you know, there's great resources and great opportunities here. A lot of my friends I have come out and visit from different things, kind of look around for a little bit and get a little wistful and say "is there another positional available?" And we could do, recruit a lot. We could do a lot of great things here.

CP: Well Joe, I want to thank you for this. This has been really interesting and I certainly wish you all the best with what sounds like some very promising research going forward.

JB: Yeah, it's a really exciting time. I didn't talk about all the things we're doing, either.

CP: Yeah. Thanks, Joe.

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