CHEMICAL HERITAGE FOUNDATION

STEPHEN L. JOHNSON

The Pew Scholars Program in the Biomedical Sciences

Transcript of an Interview
Conducted by

William Van Benschoten

at

The Home of Stephen L. Johnson's Brother
Studio City, California

on

25 and 26 September 2002

From the Original Collection of the University of California, Los Angeles

ACKNOWLEDGEMENT

This oral history is part of a series supported by a grant from the Pew Charitable Trusts based on the Pew Scholars Program in the Biomedical Sciences. This collection is an important resource for the history of biomedicine, recording the life and careers of young, distinguished biomedical scientists and of Pew Biomedical Scholar Advisory Committee members.

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UNIVERSITY OF CALIFORNIA, LOS ANGELES

Oral History Interview Agreement No. R110502L

This Interview Agreement is made and entered into this 5 day _____ of November, 2002 by and between THE REGENTS OF THE UNIVERSITY OF CALIFORNIA, a California corporation, on behalf of the Oral History Program at the UCLA campus, hereinafter called "University," and STEPHEN L. JOHNSON, having an address at Department of Genetics, Washington University, 4566 Scott Avenue, Campus Box 8232, St. Louis, Missouri 63110, hereinafter called "Interviewee."

Interviewee agrees to participate in a series of University-conducted tape-recorded interviews, commencing on or about September 25, 2002, and tentatively entitled "Interview with Stephen L. Johnson. This Agreement relates to any and all materials originating from the interviews, namely the tape recordings of the interviews and a written manuscript prepared from the tapes, hereinafter collectively called "the Work."

In consideration of the mutual covenants, conditions, and terms set forth below, the parties hereto hereby agree as follows:

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If to University:

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If to Interviewee:

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University and Interviewee have executed this Agreement on the date first written above.

INTERVIEWEE

X _____
(Signature)

Stephen L. Johnson
(Typed Name)

Department of Genetics
(Address)

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St. Louis, MO 63110

X Date 25 Sept 2002

THE REGENTS OF THE UNIVERSITY OF CALIFORNIA

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Date 5 Nov 2002

Pew Scholars in the Biomedical Sciences

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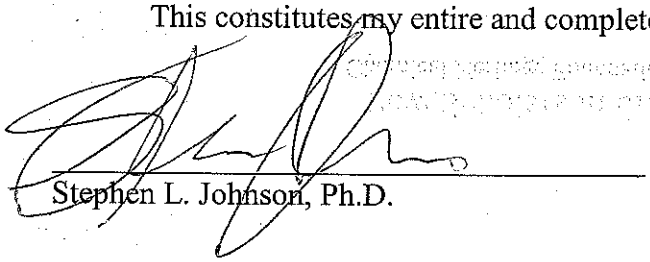

Stephen L. Johnson, Ph.D.

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STEPHEN L. JOHNSON

1960 Born in Cleveland, Ohio, on 26 December

Education

1983 B.A., Chemistry and Molecular Biology, Vanderbilt University
1991 Ph.D., Genetics, University of Washington, Seattle, Washington

Professional Experience

University of Oregon
1991-1996 Postdoctoral Associate

Washington University, School of Medicine
1996-2002 Assistant Professor, Department of Genetics
2002-present Associate Professor (with tenure), Department of Genetics

Honors

1979 National Merit Scholarship
1983 Eastman Kodak Chemistry Scholarship
1985-1986 Graduate School Recruitment Fellowship, University of Washington
1991-1992 Leslie V. Gates Young Investigator Award, National Neurofibromatosis Foundation
1992-1994 NIH Postdoctoral Fellowship
1997-2001 Pew Scholars Program in the Biomedical Sciences Grant

ABSTRACT

Stephen L. Johnson was raised in Nashville, Tennessee, the middle (with his twin brother) of four children, growing up in the pre- and post-Civil Rights Era. His father received his degree in electrical engineering and taught in that discipline at Vanderbilt University, though he also pursued a degree in divinity; his mother was a trained psychologist. Johnson partook in the normal activities of childhood, including Boy Scouts and music, but he had a very high affinity for and interest in writing. He matriculated at Vanderbilt University with the intention of becoming a writer.

After deciding against becoming a novelist, Johnson's interest in science was piqued while working in Lee Limbird's pharmacology lab, though he still had some trepidation about whether or not science actually suited him. Ultimately he decided to pursue science and was accepted into the genetics department at the University of Washington, Seattle, where he worked under Breck Byers on fusing Cdc4 and LAC-Z genes in yeast. While at Washington he was also fortunate to be mentored by Nobel laureate Leland H. Hartwell. Upon finishing his graduate studies Johnson decided to remain in the Northwest and began to work on zebrafish with James A. Weston and Charles A. Kimmel at the University of Oregon, Eugene. While there he worked on tissue regeneration mutants, pigment patterns, isometric growth, and genetic mapping, and he developed inbred strains and centromere markers for mapping the zebrafish genome. Johnson then accepted a position at Washington University School of Medicine to continue his work.

Near the end of the interview Johnson uses the topics already discussed in his oral history as a way to reflect upon his scientific development and the ways in which he mentors students and how he thinks about and practices science. The interview concludes with Johnson's thoughts on the role of technological innovation on his work; the advantages and disadvantages of competition in science; the direction of the national science agenda; the National Institutes of Health; gender issues; and the impact of the Pew Scholars Program in the Biomedical Sciences funding on his work.

UCLA INTERVIEW HISTORY

INTERVIEWER:

William Van Benschoten, Interviewer, UCLA Oral History Program. B.A., History, University of California, Riverside; M.A., History, University of California, Riverside; C. Phil., History, UCLA

TIME AND SETTING OF INTERVIEW:

Place: Johnson's brother's home.

Dates, length of sessions: September 25, 2002 (113 minutes); and September 26, 2002 (154 minutes).

Total number of recorded hours: 3.5

Persons present during interview: Johnson and Van Benschoten.

CONDUCT OF INTERVIEW:

This interview is one in s a series with Pew Scholars in the Biomedical Sciences conducted by the UCLA Oral History Program in conjunction with the Pew Charitable Trusts's Pew Scholars in the Biomedical Sciences Oral History and Archives Project. The project has been designed to document the backgrounds, education, and research of biomedical scientists awarded four-year Pew scholarships since 1988.

To provide an overall framework for project interviews, the director of the UCLA Oral History Program and three UCLA faculty project consultants developed a topic outline. In preparing for this interview, Van Benschoten held a telephone preinterview conversation with Johnson to obtain written background information (curriculum vitae, copies of published articles, etc.) and agree on an interviewing schedule. He also reviewed prior Pew scholars' interviews and the documentation in Johnson's file at the Pew Scholars Program office in San Franciscoincluding his proposal application, letters of recommendation, and reviews by Pew Scholars Program national advisory committee members.

ORIGINAL EDITING:

Carol Squires edited the interview. She checked the verbatim transcript of the interview against the original tape recordings, edited for punctuation, paragraphing, and spelling, and verified proper names. Words and phrases inserted by the editor have been bracketed.

Johnson reviewed the transcript. He verified proper names and made minor corrections and additions.

Squires prepared the table of contents. William Van Benschoten, senior writer,

assembled the interview history. TechniType Transcribing compiled the index.

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INTERVIEWEE: **Stephen L. Johnson**

INTERVIEWER: **William Van Benschoten**

LOCATION: **The home of Stephen L. Johnson's brother**
Studio City, California

DATE: **25 September 2002**

VAN BENSCHOTEN: Today is September 25, 2002. I'm with Stephen Johnson for the Pew [Scholars Program in the Biomedical Sciences] biomedical interview. We'll start with something fairly simple. What is your full name and when were you born?

JOHNSON: Stephen Lloyd Johnson, and I was born December 26, 1960.

VAN BENSCHOTEN: Okay. And where were you born?

JOHNSON: I was born in Cleveland, Ohio.

VAN BENSCHOTEN: Did you live there for most of your childhood?

JOHNSON: I lived there until I was about two.

VAN BENSCHOTEN: Oh, really? And then where did the family move?

JOHNSON: We moved to Nashville, Tennessee.

VAN BENSCHOTEN: Is that where you spent most of your childhood?

JOHNSON: Yes. I stayed there until I was twenty-five.

VAN BENSCHOTEN: I take it you don't remember too much about Cleveland.

JOHNSON: I don't remember anything about Cleveland.

VAN BENSCHOTEN: What was it like growing up— This is a big question, but were you in the city itself, Nashville, or you were in the suburbs?

JOHNSON: I was in the suburbs, out in the hilly part of the suburbs. It was, I guess you'd say, very isolated, no stores nearby, nothing really. You'd play on big lots and ride bicycles, but nothing to get in trouble with.

VAN BENSCHOTEN: Right. Tell me a little bit about your family. Maybe we can start with your grandparents.

JOHNSON: My grandparents. On my father's side, they're from the Southeast, Florida and Georgia. My grandfather [Lee Ensign Johnson Sr.], I didn't know. I think he died a year or two before I was born. He was an electrical worker, a lineman for the railroad. I don't think he went to college, and so very, I guess you'd say, working class. My grandmother [Sadie Duffy Johnson], I think she was a nurse, and maybe some education. She had gone to college. And then she died when I was eight, so I only vaguely remember her. So that's my father's parents.

My mother's [Donna Simpson Johnson] parents [Lloyd Simpson and Jewell Stanley Simpson Vick], her father died when she was something like eight or ten, and they were here in Los Angeles. And then her mother remarried, and my step-grandfather [Owen Vick] just died about two months ago, and he had moved back to Arkansas. He was, I guess you'd call him, an entrepreneur. He tried to develop businesses or do real estate and was sort of a loose cannon, and my grandmother kept him under control.

VAN BENSCHOTEN: In what way was he? Speculation?

JOHNSON: He would speculate, and he would give money away to his friends. He ended up, after my grandmother died, giving away or losing all of his money. And then he moved back to Arkansas and lived where he grew up, in the Ozarks, and lived in a trailer until he died well in— He was eighty-eight or something when he died.

VAN BENSCHOTEN:

JOHNSON: Yes.

VAN BENSCHOTEN: So your mother's mother?

JOHNSON: My grandmother, what did she do? She did go to college. She went to— Or did she? My grandfather had gone to [University of California] Berkeley. I don't know if she went to college or not. Maybe she did. She did some of the real estate business with him [Owen Vick], and she also ran a dress store. They started out in Los Angeles. During the war, she married my step-grandfather. They moved to Livermore when, then, he joined, I guess, the air force, but maybe it was the navy. And then after the war they moved to Tracy, California, and then she opened a dress store there.

VAN BENSCHOTEN: How about your parents? How about your father? What is your father's name, to get it on record.

JOHNSON: My father's name is Lee Ensign Johnson [Jr.]

VAN BENSCHOTEN: Tell us a little bit about him. Where was he born?

JOHNSON: He was born in a small railroad station where my grandfather was working on the railroad in Tennessee. I think it was Norris, Tennessee. But he grew up in Jacksonville, Florida. So born in the depression, and then they moved— I think they moved to where my grandmother's family had been in McDonough, Georgia, during the depression, and then they moved to Jacksonville during the war.

He's an electrical engineer. Let's see. He went to Vanderbilt [University] for engineering school, and he went on, I think, an ROTC [Reserve Officers' Training Corps] or some sort of thing with the navy, because after he graduated from school, he was in the navy for a couple of years. Then when he got out of the navy, he went back to Nashville and went to divinity school at Vanderbilt. I think he had always planned on being a preacher, but he paid his way through divinity school by teaching electrical engineering at Vanderbilt, and then he got to the point where he had to decide what he wanted to do, and Vanderbilt said, "Look, if you'll just go get a Ph.D., we'll hire you on full time." So he went to Case Western [Reserve University] in Ohio to get his Ph.D. and then came back.

VAN BENSCHOTEN: And is that what he did for the rest of his life, then?

JOHNSON: That's what he's— He just retired a year or two ago, and he's continuing to teach

a class or so.

VAN BENSCHOTEN: Did he see action when he was in the military?

JOHNSON: No, I don't think he saw any action. He was based in San Francisco, in a shipyard, so I think he just saw stuff about building ships, or whatever they do.

VAN BENSCHOTEN: How would you describe him? What is he like in terms of personality?

JOHNSON: He's very gregarious, much more than any of his kids, so he's much easier-going with strangers. Maybe that just came with old age, I'm not sure. [mutual laughter] What else is he like? He's very demanding.

VAN BENSCHOTEN: In what way?

JOHNSON: Just that either his kids or his students work hard and do well.

VAN BENSCHOTEN: So high expectations?

JOHNSON: High expectations.

VAN BENSCHOTEN: When you were growing up, did he have hobbies? Did he join groups?

JOHNSON: [laughs] Let's see. His hobby was to get from the library or buy books on warships and then read them and take notes on them. He's got massive collections of books on warships and collections of notes.

VAN BENSCHOTEN: That's interesting.

JOHNSON: Yes.

VAN BENSCHOTEN: Does he still do that?

JOHNSON: I don't think he still does.

VAN BENSCHOTEN: So he was an expert in warships. Let's talk a little bit about your mom. What is her name?

JOHNSON: Her name was Dona Simpson Johnson. She died in, I guess it was 1992, of breast cancer. She's from California, and she met my father when he was in the navy in San Francisco. I think they met through some church youth group. And she was the one who probably really wanted to be a preacher, but they couldn't be preachers back then— Or that is, women couldn't be preachers back then. So I think she felt like she was raised to be a preacher's wife. She had her undergraduate degree from College of the Pacific in psychology. When they got married and moved back to Nashville, she went and got her master's in psychology, and then started having kids. And then as we were growing up, she volunteered first with the school system and then went back to school herself and got her Ph.D. and then was a psychologist for the school system.

VAN BENSCHOTEN: How would you describe her personality?

JOHNSON: Now, she had high expectations. She was like my grandmother, very high expectations. So she's much friendlier. Like my father's gregarious, but doesn't have that many close friends; and my mother had lots and lots of close friends, but I wouldn't say was that gregarious.

VAN BENSCHOTEN: In what way did you know that she had high expectations? How did that show itself? For both of them, for that matter.

JOHNSON: With my father, it would be more him talking about his students and what bums they were. With my mother, it was just, you know, she could be very disappointed, and you would know it.

VAN BENSCHOTEN: What traits do you believe you inherited from your mother and father? Start with your mother. If any. Other than the genetic, obviously.

JOHNSON: I guess I have very high expectations of other people, or rather I tend to. Now that I've been running a lab of my own for about six years and employed quite a lot of people, I'm

getting much more realistic. What else do I— I definitely don't have the gregariousness of my father. I don't know what else.

VAN BENSCHOTEN: Could you describe— Again, this may be a bizarre question, but describe maybe the household as a whole. What was it like growing up in the Johnson household? Was it fairly regimented? Was it sort of show up when you show up? What was it like?

JOHNSON: I guess it was fairly regimented. We were out in a suburb without too many ways to get into trouble.

VAN BENSCHOTEN: No temptations of the city.

JOHNSON: They were very far. So until we could drive ourselves, there wasn't too much we could do. We could bike around a little bit, but our schools were all several miles away. So like until, I don't know, twelve or fourteen, it was really we played with each other or read lots of books or fought with each other, but we were there most of the time. It's not quite that bad. I mean, we did— Not that sterile. We all played musical instruments, and I imagine that meant we were running around quite a bit doing that. It was, you know, we were all at home for dinner.

VAN BENSCHOTEN: You say "our." There must be siblings in there, as well. Do you have brothers and sisters?

JOHNSON: So there were four of us. You saw my brother [Lee Ensign Johnson III]. I have a sister [Susan Carol Johnson], and I have a twin brother [Michael Owen Johnson].

VAN BENSCHOTEN: Talk a little bit about the siblings. Where are you in those four arrangements?

JOHNSON: I'm in the middle. Lee's the oldest. My brother [Michael Owen Johnson] and I are the middle, and then I have a younger sister [Susan Carol Johnson].

VAN BENSCHOTEN: Who did you tend to gravitate towards? I know, for instance, I grew up with two sisters, and the one who was closest to me in age, about a year, I guess, older than I was, we were always together, and the older sister tended to be sort of surrogate mom. She got stuck with us. My mom got tired of mothering periodically.

JOHNSON: Well, I guess, obviously, my twin, because we were, you know, physically there was just— We were doing all the same things.

VAN BENSCHOTEN: You mentioned biking, reading. Where those some of the main activities that you did, then, when you were growing up?

JOHNSON: Yes. As a kid, we would bike a little or play. I actually can't quite remember what we'd do at that age, but probably just riding a bike around the neighborhood or playing in the yard or reading. We all read quite a lot.

VAN BENSCHOTEN: What kind of books did you read? Or magazines or whatever.

JOHNSON: Let's see. I suspect a lot of science fiction and mystery novels and probably just about anything.

This will give you an idea about my mother. She was a psychologist. When we were about six, when I was about six, at that point I think she was volunteering a lot with the schools, so she had a maid come in once a week. So this was in the South, so it was a black maid; and this is in the segregated South, so that means that they were probably poor. I don't know if we understood that or not. And probably disadvantaged. And I think my mother made sure we understood that. So we would do practice books in math or things like that, and when we were done, it would go to the maid's kids.

I don't know if we ever really saw the outcome of this, but my mother always made it really clear that the maid's kids were doing better than we were. [mutual laughter] In retrospect, that's a little hard to believe, because we were a very talented group of kids, very smart. But a lot of that was because my mother just expected that, and she knew how to make sure that she got us to achieve. That's one example.

Another example is, at about that age we had a choice of reading— We had to read two books or two chapters of the Bible before we could watch television in a week.

VAN BENSCHOTEN: Was there a competition among the kids to sort of get this done, a friendly competition?

JOHNSON: I don't think among the kids there were. It didn't last very long, because we all read voraciously once we learned how to read. There was some competition between my brother

and me, the twin and me, and Lee. We learned to read when he learned to read, and I think we sort of goaded him into learning to read. He's two years older.

VAN BENSCHOTEN: You say that your siblings, you and your siblings, were very talented. In what way did that talentedness come through?

JOHNSON: I guess I just mean smart, maybe not talented.

VAN BENSCHOTEN: So does that mean, then, that you got good grades in school or that compared to other kids, maybe, that you were with, that you were fairly smart or smarter?

JOHNSON: You know, I don't think it ever really occurred to me when I was in school that we were smarter than other kids. I did know when I was a graduate student that I knew how to put together a whole program and others wouldn't. It's not until I'm at this position that I can look back and not see that, but see among my own students some are good and some are bad. I don't know if you really get that of your peers. Your peers are just your friends.

VAN BENSCHOTEN: When you mentioned the woman who came to help your mom, more or less, were you aware then of segregation? How aware, as a kid, of sort of racial politics, the racial situation in the South?

JOHNSON: We weren't very aware. Integration started when I was in the fifth grade. That was the first year of integration. I can remember like in the first or second grade some of my friends talking about—or maybe third grade—the possibility of integration, and they were saying ugly things. At earlier stages, like when I was five or six, I can remember hearing talk about colored people and being just so disappointed that they weren't colored. [mutual laughter]

My folks were very active in the Civil Rights Movement, and my father would occasionally preach in black churches. We would go to those churches while he's preaching, or occasionally there'd be meetings in Nashville and we'd have a bunch of black kids staying in the house. Initially, I don't think I understood that they were black. I think it wasn't until later. I must have been very slow. [tape recorder off]

VAN BENSCHOTEN: We usually ask about religion, but later. It seems very relevant now. What was the impact, do you believe, of religion on you and your family?

JOHNSON: I don't know what I want to say. We're from sort of a family of atheist Methodists.

My mother's brother [Stanley Simpson] did become a preacher, and he calls himself an atheist. Well, I don't know if that's right. He says he doesn't believe in an afterlife and things like that. Nevertheless, he calls himself a Christian, so that's sort of— And my father, too, is a very intellectual religious, but not an emotional religious person. My mother, however, actually, I think, was very much a believer and was very, you know, if we said things like, "Oh, God," then she would say, "You need to worry about that. You might go to hell for that," not in those sort of words, but you'd understand that she actually believed that. But mostly, religion in our house was more intellectual than emotional.

VAN BENSCHOTEN: Describe yourself as a young child. By that I mean, say, between five and ten. How would you describe yourself?

JOHNSON: Small, really unformed, just someone who was— I read a lot, but didn't do much. Yes.

VAN BENSCHOTEN: Was there any interest in science at that early stage? Were your parents buying you chemistry sets?

JOHNSON: No. My father's an engineer, but not a scientist. I don't think he got science. I wasn't really interested in science until after I graduated from college. My undergraduate degrees are in chemistry and molecular biology, but I did that because I was lazy.

VAN BENSCHOTEN: What memories do you have of your early schooling? You already mentioned integration in fifth grade, for instance, but what other things come up? Did you have, for instance, teachers who were molding or forming you in any way? Were there other fellow students who were important in your development? Activities? Interests? Subjects?

JOHNSON: Okay. I think until fifth grade I remember so little of it, because I think it was so boring. Okay? So I'd say there were two things that maybe helped develop me. One was, integration was really quite amazing. Because instead of having a bunch of really boring kids who were all the same, you had a lot of different people.

VAN BENSCHOTEN: Different classes, too.

JOHNSON: Well, there's an exception, but any exposure at that stage was better, because they pseudo-segregated us.

VAN BENSCHOTEN: Pseudo in what way?

JOHNSON: They took all the brightest kids and put them in the same classroom and kept us together for the next eight years.

VAN BENSCHOTEN: That's amazing.

JOHNSON: So that was both good and bad, because all of a sudden— I mean, we split a little bit as our neighborhoods had different zonings, and we would go away for two years and then be back together, and then all ended up in high school together. But by that time, we had a very intense peer group that, I guess I'd say, was competitive. We didn't sit there and say, "I'm smart and he's dumb." You'd just go, "Gosh, these guys are all exciting to talk to," about literature or algebra or things like that.

So in fifth grade, because it was the integrated South, the segregated South, they were reluctant to fully integrate the schools, and it was really quite obvious that brighter kids were being tracked together. In part, they did that—and I think a lot of the parents figured this out—by having all the kids who played stringed instruments had to take that course, and then that forced the rest of their schedule together. I think that's how they actually did it, how people get around these things.

So really, there's a lot to be said for having a really amazing peer group, and there's a lot to be said for having diversity. So I guess we had the best of both worlds, or at least we didn't have these horrible, boring suburb schools anymore, because we could see that people were different. We could see that, you know, if you're not careful, someone's going to beat you up and take your nickel.

We also started to see that you could, I wouldn't say break the rules, but the supervision wasn't actually always constant and there. This I remember vividly, because when they started integration, they integrated us into older city schools, and those were just amazingly fun buildings to roam around in. And then we could, because they just couldn't supervise us.

VAN BENSCHOTEN: That's very interesting. So you're hanging out, then, with this particular peer group, which is fascinating. You're exploring these old buildings, and you're learning quite a bit, no doubt, about your community, whether you're conscious of it or not, right, by this sort of half-hearted attempt at integration. I mean, what was the mood of your community?

JOHNSON: Yes, imagine all these lily-white kids running around these black neighborhoods—kids that they can't supervise because the music teacher didn't show up that day or something

like that.

VAN BENSCHOTEN: So what was the mood of your community about integration overall, then? I mean, obviously they're fighting— A certain segment is fighting this, which was not uncommon, as we know.

JOHNSON: Well, those guys left the school system. It was like the bad apples dropped out. All the rednecks—bang!—they're gone.

VAN BENSCHOTEN: So they're probably like-minded.

JOHNSON: I guess I wouldn't say like-minded, but I would say people whose parents didn't care enough or couldn't afford to put them in private schools, or kids with liberal parents, or people who thought, well, public education is still better than private education.

VAN BENSCHOTEN: Right. Now, were there incidents of violence around this?

JOHNSON: In Nashville at that time, no, there was no real violence around integration. That was long after the real violence of what you have heard about maybe ten years earlier.

VAN BENSCHOTEN: The period you're talking about, just to make it clear, is about, what, '72, '73?

JOHNSON: '72, yes.

VAN BENSCHOTEN: You said that your parents were involved in civil rights. I assume part of that was going to the churches, the black churches?

JOHNSON: Yes.

VAN BENSCHOTEN: In what other ways? Were there other ways they were involved?

JOHNSON: I think almost all the Civil Rights Movement was through the church in the South.

VAN BENSCHOTEN: Did they ever talk about race, have talks with you and your brothers and sister?

JOHNSON: About?

VAN BENSCHOTEN: About race. Or was it more teaching by example?

JOHNSON: Well, they'd talk about, you know— They'd just say, "This is how it is, and it's wrong. These people are equal to you, and there's not a difference."

VAN BENSCHOTEN: Getting back to school, other than this running around the school—I'm very interested in that; that's interesting—and, again, this peer group that you were with, what subjects were you interested in? What did you tend to do well at and enjoy?

JOHNSON: I liked math and history and English, and I was good at some of the sciences, like chemistry. I never took biology. I took one biology course because everybody had to take it in the ninth grade, but after that I didn't take it because I didn't think it was rigorous, and it was taught very poorly in the school that I went to. So mostly I liked the stuff that was fun or that— You know, most of it.

VAN BENSCHOTEN: As you sort of went on through middle school and high school, were you coming upon mentors or important teachers or new topics, new interests, or was school pretty much something you tolerated?

JOHNSON: See, this peer group of mine, we more or less taught each— You learn from your peers rather than your teachers, or at least that's what I learned. I had one or two good teachers in high school, but not many. When we learned, it was because sometimes the teachers could figure out that they could set us challenges and that we could meet them.

VAN BENSCHOTEN: How long were you with this peer group? Was it all the way through, then?

JOHNSON: Yes, from fifth grade to twelfth grade.

VAN BENSCHOTEN: Are you still in touch with some of these people?

JOHNSON: Yes, on and off, about every year or two.

VAN BENSCHOTEN: So in many ways, this peer group was the best part of your education, at least until you got to college?

JOHNSON: Yes.

VAN BENSCHOTEN: What were you doing, let's say, in school as extracurricular activities? What were you doing when you weren't with your peer group who were at these schools?

JOHNSON: I guess I had two extracurricular activities that took up a lot of time, and one was music and the other was outdoors. At eleven, you joined the Boy Scouts [of America], especially in the South, so I started camping then. By the time we were fourteen, I guess all three of us got— Of the boys. Girls don't join the Boy Scouts. But all three of us got our Eagle Scout, our Eagle Award, before we were fourteen, and then we joined the next group up, which was really no longer around community service or whatever military indoctrination the Boy Scouts do. It was just about camping or canoeing or caving or whatever. So from fourteen to eighteen, we essentially did something every weekend once older members, like my older brother, had access to a car.

VAN BENSCHOTEN: How important was the Boy Scouts, do you feel, in your development?

JOHNSON: I don't think the Boy Scouts was important, but I think the next step, which was this thing called Explorers, which is part of the Boy Scouts. But just being able to go out camping and being outdoors was very important.

VAN BENSCHOTEN: Do you still do that today? Do you still go camping?

JOHNSON: No, I don't have much time. I did some as a graduate student, but once I was a postdoc, I ran out of time.

VAN BENSCHOTEN: That's what often happens, unfortunately.

Let's talk a little bit about music, then. You mentioned it a little bit earlier, as well. How early did you start with your musical training?

JOHNSON: I think I started in the fourth grade, and I played the viola. My mother apparently wanted a string quartet, so she had two violins, a cello, and a viola. And I played that through twelfth grade, and then I have really not played since.

VAN BENSCHOTEN: How important was music?

JOHNSON: You know, it was really just the ticket into this peer group, because that was what got your schedule set so that all of these guys had the same classes. And maybe it helps to think mathematically. That's what a class of mathematicians would have said. I'm not sure. But I think the major thing was just establishing this group of people whose parents wanted musicians or wanted their kids in this pseudo-segregated environment who could feed each other.

VAN BENSCHOTEN: You haven't mentioned sports. You mentioned you were small. So I'm wondering, was sports important at all in your development, other than normal running and jumping would do, I guess?

JOHNSON: I didn't do any organized sports. I played basketball in the back yard or baseball in the back yard, but nothing organized. I think I weighed like a hundred pounds until I was—When I was sixteen, I weighed hundred pounds and was five feet tall.

VAN BENSCHOTEN: Really?

JOHNSON: Or something like that.

VAN BENSCHOTEN: So you wouldn't know that. I mean, nobody's going to know this from listening to the tape, but you're about my height. You're six foot, right?

JOHNSON: I'm 5' 11" and now about 190 or 195.

VAN BENSCHOTEN: Right. So it's hard to believe. So after sixteen, then you began to put on a little flesh?

JOHNSON: I grew. When I graduated college, I was about 125.

VAN BENSCHOTEN: In high school, how were you sizing up the future? What direction did you sort of think our life might go when you were about ready to graduate?

JOHNSON: I thought I might want to write, and, oddly enough, that's all I do now. But I thought fiction or maybe to be a historian, a scholar. I would not call myself a scholar now.

VAN BENSCHOTEN: And why not?

JOHNSON: Because that's actually hard work, knowing all the literature. In a very arrogant way, I'll say I prefer to lead and not really know. I'm maturing into being a scholar, though, because I'm finding it more and more fun to test hypotheses, which means you have to know the literature. So I'm joking when I say I'm not a scholar. But when I was a graduate student, or early in my postdoc, I just thought that I could develop the techniques myself.

[END OF TAPE 1, SIDE 1]

VAN BENSCHOTEN: We were talking about what expectations you had when you were about to leave high school, and we were talking about the difference between a scholar and what you are now, and you talked humorously about that.

You mentioned writing. Actually, I should let you complete it. You thought of becoming, maybe, a writer. Anything else? Any other routes that you thought you might take?

JOHNSON: Probably writing was what I thought I really wanted to do.

VAN BENSCHOTEN: And what kind of writing? You said fiction?

JOHNSON: Yes, fiction.

VAN BENSCHOTEN: Did you have models? Did you have authors that you were reading at the time that you thought you wanted to maybe model yourself on these people? [William]

Faulkner jumps to mind, but Faulkner may be too easy.

JOHNSON: Faulkner jumps to mind. In my freshman year of college [Vanderbilt University], I decided I wouldn't take any more English classes, and I just wouldn't do anything with that. I ended up having to take another one for distribution, but right from the start I got this horribly bigoted southern professor. How did this work? Somehow he decided that I was really evil, and he tried to fail me in this course. So I'd gone through like— These are the days before grade inflation, okay? So I got through two-thirds of the course getting As, and then I wrote a review, whatever, book report, but an analysis of a Faulkner short story, and I said something that apparently deeply offended him. So I got an F on this, and then I failed the exam, not just failed, but zero, so that he could give me a C.

And then, because my father [Lee Ensign Johnson, Jr] was on the faculty, he said, "Well, you know, you could fight it, but you shouldn't fight it." So I ended up not fighting it. And then I just said, "If that's what they can do in the field, if it's this arbitrary, then I don't want anything to do with it."

VAN BENSCHOTEN: And this was in your senior year?

JOHNSON: That was in my freshman year of college, my first semester.

VAN BENSCHOTEN: At Vanderbilt [University].

JOHNSON: Yes.

VAN BENSCHOTEN: Do you regret that decision at all now? Are you still—I guess what I'm asking—?

JOHNSON: No, because that didn't really keep me from— That just kept me from taking English courses or being that type of academic. I don't think I wanted to be an English teacher.

VAN BENSCHOTEN: But writing fiction, creative writing, did you still want to pursue that, let's say, maybe not academic teaching of English?

JOHNSON: Yes, I probably was still toying with this idea until I graduated from college.

VAN BENSCHOTEN: And that's about when, what, your interest in science began to kick off?

JOHNSON: So yes, my interest in science was really when I graduated from college and couldn't get a job for a long time. And then I finally got a job in a pharmacology lab at the medical school at Vanderbilt, and that was really a lot of fun. It was incredibly hard work, but then I understood what science was. It wasn't just knowing all these facts or being able to do all these calculations, which wasn't hard for me; it just wasn't interesting. What was interesting was asking questions and sometimes getting answers. So that was the first time I had ever been exposed to that. I had gotten absolutely no exposure to that in college.

VAN BENSCHOTEN: Before we talk a little bit more about that period, how did you decide to go into Vanderbilt, and were there other schools that you applied to? I know that your father went to Vanderbilt.

JOHNSON: And taught at Vanderbilt.

VAN BENSCHOTEN: Right.

JOHNSON: So that's the answer.

VAN BENSCHOTEN: Okay.

JOHNSON: I applied to two or three other places. [University of] Virginia. There's a liberal arts school out here in the east county.

VAN BENSCHOTEN: Occidental College?

JOHNSON: No. There are four or five of them together.

VAN BENSCHOTEN: Oh, Claremont College.

JOHNSON: Claremont [College]. And Pomona [College]. Those were the three that I ended up

applying to: Pomona, Vanderbilt, but really Vanderbilt.

VAN BENSCHOTEN: You've already described part of your experience in that first year, a dreadful experience with this English teacher. But what was that first year like other than that? What was that transition like? Did you leave your peer group or did some of them move along with you to Vanderbilt?

JOHNSON: I guess about half of them went to Vanderbilt.

VAN BENSCHOTEN: And was it still that group? I mean, were you still fairly close?

JOHNSON: Both. We did then get new friends. I think the people I was closest to did not go to Vanderbilt.

VAN BENSCHOTEN: Again, what was that first year like?

JOHNSON: Let's see. One, it was very hard, and I would hesitate to say I actually learned anything in college. But I had essentially taken the first year of college in my last year of high school, so I passed out of chemistry and taking the first year of calculus. So I was taking the second-year courses, organic chemistry and second-year calculus and I don't know what else. Boy, it was hard. And that horrible English class.

VAN BENSCHOTEN: How did you pay for college? Did you work? Did you have jobs?

JOHNSON: No, it was free. That's why I went to Vanderbilt.

VAN BENSCHOTEN: Oh, because of your father. That's right, yes.

JOHNSON: I'm sorry, that should have been explicit instead of implicit.

VAN BENSCHOTEN: And you say you didn't learn anything in college, or much. Why was that? Was that because of you? Because of the college itself? Was it timing?

JOHNSON: No. I guess Vanderbilt's a reasonably good school, and certainly I learned calculus, but not in a way that I ever will use again. You know, the chemistry, I learned lots of facts, but never really learned what the questions were. That's going back to this idea of the difference between facts and science. So it was a technical education rather than a question-asking education. So as far as science education goes, I am now deeply impressed how poor science education is in this country, that we do not teach students how to ask questions, what the nature of science is. We only teach them the nature of facts.

VAN BENSCHOTEN: Besides the science classes, did you have other interests? I know that you pretty much end your attempt to be an English teacher as a freshman, but were taking other liberal arts classes, maybe?

JOHNSON: I took other liberal arts classes. As an extracurricular activity, I joined the theater and did lots of backstage work, lighting or sound or stage construction.

VAN BENSCHOTEN: Did your older brother, Lee [Ensign Johnson III], did he also go to Vanderbilt?

JOHNSON: Yes.

VAN BENSCHOTEN: Did the rest of your siblings [Michael Owen Johnson] [Susan Carol Johnson] go, as well?

JOHNSON: We all went to Vanderbilt, that big, free—

VAN BENSCHOTEN: That's too tempting to pass up.

JOHNSON: We all tried to get enough scholarships to convince our parents that it would cost less, but in those days, there were no academic scholarships, or very, very, very few academic scholarships, so there weren't very many opportunities.

VAN BENSCHOTEN: How would you, then, sort of sum up your college education? If you had it to do over again, I guess, what would you change about it, other than, again, putting the sort of problem-solving science foremost rather than fact-finding.

JOHNSON: They're not problem-solving. Why don't I answer it this way. Since I don't know if I was to do it again— I mean, I love being a scientist. With retrospect, I would say, okay, let's do a better science education. I think a liberal arts education is also valuable, and I actually got a good exposure at Vanderbilt to some liberal arts. But I would design the science education that forced kids into lab settings earlier. I don't know how to do the other thing, and that would be to have small groups that could discuss it like you would sit around discussing a novel, instead of saying, "Here are the facts," "Here are the questions," or, "These are the ten other things I want to learn now that I've read this paper," and we don't do that. We even have a hard time doing that with graduate students.

VAN BENSCHOTEN: When you're near the end of your college education, you said earlier that after graduation you eventually join this pharmacology— Was it a company or was it a—?

JOHNSON: No, it was a lab at the medical school, as a technician, just someone who pipetted, things like that.

VAN BENSCHOTEN: What was your expectation when you did that?

JOHNSON: That it would pay my rent.

VAN BENSCHOTEN: How long did you do that?

JOHNSON: I did that for two years, and then I decided— Because I just went there because I had to have a job, and Mr. [Ronald W.] Reagan had made this terrible recession and there were no jobs.

VAN BENSCHOTEN: I remember that recession, unfortunately.

JOHNSON: So I had no intention of making a career out of that. I was just going to spend a few years paying the rent.

VAN BENSCHOTEN: We haven't talked about your social life at all at this time. Were you dating much in college?

JOHNSON: Yes.

VAN BENSCHOTEN: So you had a social life, which is saying something.

JOHNSON: Yes, I had a social life. I don't have one now, but I did then.

VAN BENSCHOTEN: You can look fondly back on it.

JOHNSON: Oh, that's what that is. [mutual laughter]

VAN BENSCHOTEN: When you are in this lab and you're sort of really becoming excited in science for the first time, what was the next stage for you? What did you decide to do?

JOHNSON: I decided that I liked doing experimental science. I liked the short-term questions, and I was thinking I needed to learn how to ask the long-term questions. I was working on human blood stuff, platelet coagulation, blood coagulation, and I actually didn't like doing those actual experiments. I didn't like working with people, because they were too variable.

VAN BENSCHOTEN: As people will be.

JOHNSON: And I said, well, you know, if we just had people that were all the same, the experiments would be better. They said, "Well, that's genetics." So I said I should learn to do genetics. That really was my rationale. "Maybe I'm interested in evolution and maybe my math is good enough that I'd be good at the quantitative biology, the population genetics," something I absolutely hate now.

VAN BENSCHOTEN: But it connected with mathematics, which you did enjoy.

JOHNSON: Yes. So I applied to a bunch of genetics departments, and I talked to a bunch of evolutionary geneticists. So the story I tell people is that I went to Stanford [University], I talked to [L.L.] Cavalli Sforza, who's a famous population geneticist there. He was in the middle of his work on migration effects in population genetics, and he was getting all of his data out of Italian telephone books.

VAN BENSCHOTEN: That's amazing. [laughs]

JOHNSON: So his office was stacked with Italian telephone books, and it just seemed like the craziest thing I'd ever heard. So I said, "This guy's crazy," and the rest of the department, just nothing attracted me.

Then I went across the bay to [University of California,] Berkeley, and I talked to one of their famous evolutionary geneticists, and I thought he was even crazier. He's now dead, so I won't say his name. But you can repeat this: Cavalli Sforza is just crazy.

VAN BENSCHOTEN: Okay.

JOHNSON: I later learned that he was one of the founders of molecular genetics who did this really beautiful molecular biology of recombination in bacteria, so he's got great credentials. It was just the [unclear].

So at that point, I had been accepted to the genetics department at the University of Washington. I had no idea that it was actually the best genetics department in the country at that time. I had just applied there because I said, "Well, it's the Northwest. If I have to move somewhere and then drop out, that's where I want to drop out."

VAN BENSCHOTEN: Really? So it was purely geographical reasons.

JOHNSON: After finding that I didn't like Stanford, didn't like Berkeley, I said, "I'm going to just drive up there and see what it's like." And I called them up and arranged interviews, and they said, "We thought you were interested in evolutionary genetics. Did you want to speak to Joe [Joseph] Felsenstein?"

I said, "I don't know where you got this idea I was interested in evolutionary genetics. I'm an experimental biologist." [laughs] I ended up really like Joe Felsenstein's work, but I never worked with him, which I don't know if that was a badness or not. But in retrospect, if I had started there instead of in the Bay Area, I might have ended up a population biologist.

VAN BENSCHOTEN: So you finally end up, though, at the University of Washington.

JOHNSON: Right. In Seattle.

VAN BENSCHOTEN: Describe at least— What was that experience like?

JOHNSON: [laughs] That was wonderful. I started working on yeast genetics, and it's like the perfect thing to learn how to do science with, to learn how to do genetics. The generation time is really rapid, so you can make a model that can be stupid as anything, but at least you've shown you're wrong within a couple of weeks.

VAN BENSCHOTEN: And what were some of the first projects that you undertook? How did they evolve?

JOHNSON: How did they evolve? Oh, god. So what actually turned into my thesis was what I actually started on, and in the middle was all my playing, okay? So the lab that I was rotating through, a large fraction of it worked on this gene called Cdc4, and presumably now we know a great deal about what it does. At the time, it was just a sequence gene in yeast that there were mutants for. The lab had its models of how it might work, and we wanted to know where in the cell it was.

So my job was to make a fusion of this protein gene to LAC-Z. LAC-Z makes a protein called beta galactosidase, which is great little enzyme that turns a store-bought chemical, cuts it in half, and you get a blue product. So that's one great thing about it. And then there are great antibodies to it so that you can visualize— You can take the antibodies against the protein to see where it is in the cell.

The gene I was working on was a very low-abundance gene. We knew it wasn't expressed very well, so we were going to need to have other techniques to find out where it was, just as a first initial question, not a hypothesis testing type of thing. So I made fusion proteins and overexpressed them, and found that when I overexpressed these truncated fusion proteins, the first one I made just took off a few amino acids, but it no longer worked. I later made fusions that were full length and then did work. But the first ones didn't work, and when I overexpressed them, they killed the cell with the same unusual phenotype that the loss-of-function mutant did.

So that was something we really had no background in, in the field, at that time. It's now a field that's routinely used, called dominant negatives. At the time we didn't have any experience with this notion, and I thought, okay, if I can overexpress this now functional protein and it gives the same phenotype, then I can use this as a really sensitive way to do a structural-function analysis. I'm not dumbing this down, am I? [mutual laughter] I can use it as a way to probe how the protein works, because different parts of it could then jam up the machinery and I can ask which parts are jamming up the machinery responsible for one phenotype or, it turns out, responsible for jamming up others.

So the first thing that got me hooked was when I overexpressed it and it did the same thing as if it hadn't been made at all. So that's what kept me going on that. In the middle, I

learned how to ask questions about other people's hypotheses.

VAN BENSCHOTEN: Who were the other people? Were there other people who were influencing you, teachers, mentors?

JOHNSON: Yes. My thesis advisor was a man named Breck Byers, and he was, I suppose, a great mentor, couldn't be more different than how I mentor people.

VAN BENSCHOTEN: In what way? How would you describe his style?

JOHNSON: He would listen to me. He would occasionally throw out ideas. Once a year he would beg me to do an experiment I had started but hadn't finished. If he was confused, he would just look at me and say, "Hmm. I'll bet you can figure this out."

VAN BENSCHOTEN: And then he'd walk away?

JOHNSON: Yes. So that was one. And from him I got more of this notion of you can actually explore deeply into a problem really without formal hypothesis testing. He wasn't, I would say, a formal hypothesis tester. He was an explorer.

The other mentor who I probably talked to five times in my research there was Lee [Leland H.] Hartwell. He's the guy who got the Nobel Prize, I guess last year, and the original mutant came from his lab. He was a very formal thinker and had developed many of the ways many of us now do experimental genetics, the way we think about our problems. So when I would think about my problems, I would think about it from those two men's viewpoints. What would Breck do? What would Lee do?

VAN BENSCHOTEN: Anything else about Lee Hartwell, though, about his mentoring style? I know that he did—

JOHNSON: I barely talked to him at all. He was sort of a mentor *in absentia.* He was down the hall. I'm sure he saw me running around all the time. One thing, once I wanted to use a— He had a lot of money. My lab had virtually none. But I had sort of learned from a previous experiment, the lab I had worked in after college, that if you're actually doing science, people don't mind you using their resources. So I'd just go down and use all their stuff.

And then one time I was thinking about using a drug that they had, that I didn't have

access to, but they had, so I had access to it, and I was starting to set up a fairly large experiment. I think he heard me ruminating out in the hall, "Okay, how am I going to do this?" And he actually came out and said, "Well, maybe that's a little expensive. We could tone it down first." That's like the only direct advice he ever gave me was, "Slow down first." So I wouldn't actually call that mentoring. But maybe.

VAN BENSCHOTEN: I'm interested, I guess, in listening to you now, you get accepted at, as you said, you know, the best program, one of the best, at least, in the country. You're going from a lab, a pharmacology lab. What was the work that you were doing in the pharmacology lab? In other words, describe, I guess, a little bit more that transition, because obviously that work must have made some impression upon these people at Washington.

JOHNSON: I don't think so. I suspect I had a letter that said that I had good hands and I could think. But I don't think they cared that I actually— They probably cared that I had achieved something that took some very difficult procedures and made them work reliably.

VAN BENSCHOTEN: So technically they were—

JOHNSON: So technically. And then I could take the data and analyze it in ways that the people who— My job was to feed the data to somebody else, my boss [Lee E. Limbird] at that time. And she wasn't— She's a very powerful scientist who I respect deeply, but she was in too much of a hurry. So she would look at her way of doing the analysis and say, "Well, this doesn't work."

And I'd say, "Wait a second. All we have to do is normalize this and normalize that and average this, and then we have results that are meaningful." So I think I impressed her that I could make experiments work that other people couldn't.

VAN BENSCHOTEN: Did you have much lab experience when you were at Vanderbilt? You didn't, did you? So what led to this sudden explosion of technical proficiency, I guess?

JOHNSON: Some people just have good hands. I no longer have good hands. [mutual laughter]

VAN BENSCHOTEN: You don't do much bench work anymore.

JOHNSON: All I do is breed fish.

VAN BENSCHOTEN: Breed fish and write papers.

JOHNSON: And write papers. I don't do any of the molecular biology anymore. But at that time, I think I developed really good hands.

VAN BENSCHOTEN: Was there a group of people, too, that you were communicating with that were helpful and sort of bouncing ideas off of, or was it just you, more or less?

JOHNSON: When I was a technician?

VAN BENSCHOTEN: Right. When you were at the pharmacology lab.

JOHNSON: No. No. I mean, there were very good people, but the types of questions that they were— I was really superficially interested in, how can I make my experiment give data, that someone else designed and asked the question for? How can I make it so the data works so that I'm productive instead of, I did the procedure, but it's garbage? If my technicians approached their work that way, I would be pleased. Many of them— No, they are alive. They might see this. I won't say anymore about that.

VAN BENSCHOTEN: [laughs] Okay.

JOHNSON: They still work for me. I can piss off big shots, but not the people who work for me.

VAN BENSCHOTEN: Was it a joint lab, Breck Byers' lab and Lee Hartwell? Did they share—

JOHNSON: They shared quite a bit. One of the rooms was shared. The initial mutation set that Lee Hartwell had developed, Breck had done the cytological analysis; that is, cutting the cells open and looking and seeing what they actually look like. So it was not a formal collaboration, but it was an intellectual symbiosis, because they had very different styles.

VAN BENSCHOTEN: If you would, describe, too, what was a typical day like for you? When would you come in? When would you leave?

JOHNSON: When I was in grad school?

VAN BENSCHOTEN: Yes.

JOHNSON: I would probably get there by eight-thirty and leave around six and go home and cook dinner. I even used to cook back then. And then I would read for a few hours, maybe three or four hours. So my typical day would be walking, pick up a cup of coffee, and start doing whatever.

VAN BENSCHOTEN: Did you work on weekends, as well?

JOHNSON: I would work one day or one and a half days on weekends. Maybe just one day. I had a social life in graduate school. [mutual laughter]

VAN BENSCHOTEN: Well, that's good. What was the general mood of the lab? How would you describe that lab, that joint lab?

JOHNSON: Both labs were great. The interactions were what you would make of them. Okay? So some people in Byers' lab wouldn't really go out of their way to interact with people in Hartwell's lab and others would. They were both really interesting labs because it was a great time to be developing ideas. Obviously, at that time Hartwell's lab was developing the really fundamental ideas on cell cycle control; not just the cell cycle genes, but what makes cells stop; not just what makes them go, but what makes them stop. And that was an incredibly exciting time. Even if you weren't in their lab, if you're nosy like I am, you're still paying attention and participating.

VAN BENSCHOTEN: You pursue the Ph.D. I don't have the date in front of me, but what was it, eight, nine years? I'm sorry.

JOHNSON: I started in '85, and I left in '90 and got my Ph.D. in '91.

VAN BENSCHOTEN: Yes, I'm sorry. And you eventually do your postdoc. Before we move on to that, though, what do you believe was your most important achievement in the Byers lab? I mean, several important articles come out of that, obviously.

JOHNSON: No, no articles came out of that.

VAN BENSCHOTEN: Really? So just your Ph.D. I mean, you contributed on certain articles, right?

JOHNSON: Breck doesn't publish very much. He hates to write. If I have one criticism of him, he can't teach science writing, so I did not learn science writing in his lab. And it's not his fault that I didn't learn; I could have learned somewhere else. But when I look at it, the chapters of my thesis, which could have been published, they were not written as science. They were written as technical achievements, and I don't think he was ever comfortable with that. We spent six months trying to write, and he was never able to tell me, "This is what's wrong with it." He would just say, "This isn't right."

My postdoc advisor actually taught me this, so that I'm actually now a fairly good writer. So we didn't get those papers published. A postdoc who had been in Breck' s lab needed that data published, and he ended up publishing it and putting me on the papers. It's fair to say I didn't get papers out of my Ph.D.

VAN BENSCHOTEN: Describe the transition then from your graduate work to your postdoc.

JOHNSON: In my graduate work, I was just sort of playing around and exploring, and then I decided that I wanted to study cell growth control, but in a vertebrate. Now that means cancer. Okay? Yeast has cell growth control, but it's not really the same thing as cancer. We can learn a lot from yeast, but once we learn from yeast, we need to start applying that to a vertebrate, something that actually does get cancer, and see what new things we can learn, that what we learned in yeast doesn't actually— What's missing from our yeast lesson.

So I decided that I needed to come up with a system that would let me do in a vertebrate what people can do in yeast, and I don't mean the molecular biology that's so incredible in yeast, but just the ability to manipulate it, find mutations, and then manipulate the physiology with those mutations. One of the great things about yeast is they grow out of a wide range of temperatures, so you can find mutants that work at one temperature, but then you heat the yeast up and that otherwise wildtype gene product falls apart and doesn't work. This is something we call temperature-sensitive mutation. That lets you turn the gene on and off at will. So once you found the mutants that are like that, they're really great for doing experiments with. You can ask when in the life cycle of the animal is the gene acting, or set up even more complicated experiments.

I wanted to ask, for instance, if you had tumors that you had— I haven't done this yet,

by the way. I hope to one day. If you have tumors that are induced genetically— We think tumors are induced genetically. That is, they're missing gene function, and then they progress to a tumor. So the key to that statement is tumors progress. They keep accumulating mistakes. They keep losing different gene functions and they get worse and worse and worse, and then they really take over the body and kill you. So I want to be able to find mutations that caused cancer, but then be able to, in my experimental system, add back gene function and ask, is that tumor still bad or have I caused it to be a normal tissue again? And once I have things like that, can I ask how long can the tumor progress, and eventually, what other problems does that tumor accumulate, do the cells in that tumor accumulate before it can no longer be fixed by adding back the causative gene, the gene the loss of function was causative of tumorigenesis.

So that was the experiment I wanted to do, and I thought, okay, so I need a system that is really a flexible-growing system. You can imagine, yeast grows as a colony, and even though it's individual cells that you can think of as organisms, you can think of the whole colony as the organism, and it's giving you views of that organism at different times in its development. Okay? It's a very simple way of thinking about development.

So I wanted something like that, but in a vertebrate. So you could think maybe like if we had a worm that was growing by adding segments. Okay? Worms aren't vertebrates, by the way. Some of my colleagues would read that and go, "God, Steve never did get biology." [mutual laughter] But you could imagine then doing a genetic manipulation, like changing the temperature, while it's making this segment, and it continues to go on. And then you restore it, and you've both got the old segments to look at that were developed wrong and then the new segments that formed after that.

So that's what I wanted, except vertebrates aren't worms and they're not yeast. And mostly vertebrates grow up. They make an embryo and then the embryo sort of just enlarges, and there's not much you can do about it. But some vertebrates, you can amputate tissues and they'll regenerate, so that gives you multiple views at the same tissue within that organism, sort of like replica-plating in bacteria or yeast. You can challenge that organism at one condition, ask what happens, then cut off that fin and let it grow back again, cut off that limb and let it grow back again under a different condition. So I wanted to do that, and I saw that zebrafish would regenerate their fins. And at that time people were just starting to show that you could develop it as a genetic system. So that's what I went to do.

VAN BENSCHOTEN: That's what you proposed?

JOHNSON: That's what I proposed to do. I mutagenized some fish and I cut off a lot of fins and looked for mutants, and I never really found the mutant I was looking for. But that was my transition, was trying to test that hypothesis.

VAN BENSCHOTEN: I'll ask you the same questions I asked about the Byers' lab. What was

it like working in that lab?

JOHNSON: So this, again, was an amazing environment. I was in Jim [James A.] Weston's lab. Well, I have to give you a little more background. Over the years, you've probably talked to Marnie [E.] Halpern.

VAN BENSCHOTEN: Right. Right. We have.

JOHNSON: And you've got several other zebrafish people coming. A guy named George Streisinger had started the ball rolling in the seventies. So this was like fifteen years before any of these postdocs show up. And he just decided he wanted to develop genetics in a vertebrate. He wanted, I think, to study eye development and physiology and perception, and he was going to use the zebrafish because it had these clear, beautiful embryos that develop external to the mom, and his contribution was then developing ways of manipulating the sperm and the eggs, how to make mutants and then how to look at them. And then he died in the eighties. So while I'm a graduate student, there's all this talk about what George had done, and, oh, wouldn't it be great if people could actually do this, but George is dead.

So George was a geneticist, a classical geneticist, but he left behind him people who were interested in what he was doing who were developmental biologists, So Chuck [Charles A.] Kimmel and Judith [S.] Eisen and Monte Westerfield, and then Jim Weston, who actually never worked on the zebrafish himself, but put together the big program project grant to pay for the zebrafish.

So even though I was in Jim's lab and Marnie was in Chuck's lab, we had pretty much equal access to everything. Not precisely, but we had equal access to the ideas. Some of us had more crazy ideas that we were pursuing, like me, like Marnie was pursuing very precise, beautiful ideas. We talk about it now in retrospect, and she says, "Well, you had freedom that I didn't have," but then I had a lot of risk, too. But it was an amazing place, because everybody talked to everybody, we really did.

VAN BENSCHOTEN: So there was much more interaction then.

JOHNSON: Yes. It was like the yeast group in the Seattle, but now the fish group in Eugene, and it was just amazing. So even though I was doing my really half-baked idea, I was learning embryology from the work of people like Marnie.

VAN BENSCHOTEN: This is sort of backing up a little bit, but had you applied to other places other than the University of Oregon?

JOHNSON: For a postdoc?

VAN BENSCHOTEN: Right.

JOHNSON: Initially, I only applied to do zebrafish at Oregon, and I had initially talked to Chuck and Chuck had said, no, he's full, which meant, "This is a harebrained idea." He said, "But maybe Jim Weston's interested in actually starting a zebrafish lab, and he's interested in hare-brained ideas." He didn't quite say it like that.

So I went and talked to Jim, and Jim said, "That's really hare-brained. If you can get money for it, you can join my lab."

So I spent a year trying to get money, writing this precise thing, and finally I did get some money. And then I ended up getting two grants, one that was something Jim was on the board of, so I think he manipulated it. But that was okay. And then I ended up getting an NIH [National Institutes of Health] grant, and I manipulated it so that I had four years of funding, which actually did give— Most postdocs grants are up to three years. So it gave me a lot of freedom.

I forgot what your question was, though.

VAN BENSCHOTEN: Had you applied to other places for your postdoc.

JOHNSON: So I spent a year applying for funding, and the third to the last one said no. This is like twenty grants, and the third to the last one said no. I started applying to other labs, and like two or three weeks after that, like one thing. I had thought of a really great yeast chromosome instability lab, and I had written them and said, "I really wanted to do zebrafish for this reason, but I can't. Chromosome instability is very similar to what I'm interested in, and can I work in your lab?" This is someone who had worked with Breck Byers in another one of the yeast labs himself as a graduate student.

So then he called to get the references, called Lee Hartwell, and Lee Hartwell was talking to me in the hall. He said, "I just got a call from Tom [Thomas] Petes, and he wanted to know if you were really interested in this postdoc."

And I was opening this letter at the time, and there was my money. I said, "You know, I'm not." [mutual laughter]

VAN BENSCHOTEN: Deal done.

JOHNSON: So no, I only looked when it looked like I couldn't get money for zebrafish, and then I did.

VAN BENSCHOTEN: We're near the end here. Let me— [tape recorder off]

[END OF TAPE 1, SIDE 2]

VAN BENSCHOTEN: We were talking about the transition from graduate work to your postdoc and how you got eventually to the University of Oregon.

Describe the [James A.] Weston lab. You already mentioned that there was a lot of interaction, a lot more than in the earlier lab. But what was his mentoring style? How did he handle his students or his postdocs?

JOHNSON: Jim's mentoring style was to stay in his office and talk to us when we had a paper to write or he had a grant to write.

VAN BENSCHOTEN: Really? So hands-off, fairly?

JOHNSON: We would have lab meeting once a week, and his only meaningful contributions would be, he would force us to start our talks with what we're interested in so that we weren't too diving into the technical. So he was very interested in style, and I think he assumed we would solve our experiments one way or another.

VAN BENSCHOTEN: How big was that lab?

JOHNSON: When I was there, it got up to six postdocs and one student.

VAN BENSCHOTEN: I'm sorry, I should have asked this earlier. How big was the [Breck] Byers lab you were in?

JOHNSON: At one point it had as many as four students and three or four postdocs.

VAN BENSCHOTEN: Did you continue to come in at eight-thirty? Did you have pretty much the same routine in the Weston lab that you had in the Byers?

JOHNSON: No. One thing I've learned is that where the postdocs and graduate students have a cohort, like we were in Eugene, can be really great, the technicians can be really awful. And these are people I do dearly love, but by awful I mean awfully stuck in their ways. So they had ways of breeding fish that I just quickly found were too slow.

The big fish facility there really was Chuck [Charles A.] Kimmel's facility, and they found space for me and then I built my own facility. So when we started procedures in the main facility, the fish would wake up at nine-thirty. That's just crazy. So except for the breeding procedures that required extra equipment, like the half-tetrad, the early pressure parthenogenesis, or heat shock, I would do all my breeding up in my own facility. I had a desk where I could sit and I could squeeze my fish. And then I set my clock to eight o'clock. So I was there when the fish were there, and I probably bred fish five days a week for the first five years.

VAN BENSCHOTEN: That's amazing. In reading some of the letters of recommendation that were sent in to Pew [Scholars Program in the Biomedical Sciences], they mention, for instance, the risk involved, first of all, in setting up this system, and some of them were very impressed with that effort, too. But part of that, alSo was probably because of the funding, too, that you felt you had time, therefore, to set this up?

JOHNSON: I think that I was naïve. It was probably a bad decision. I probably should have focused earlier on some discrete questions; and I didn't get pushed that way by Jim Weston, but I did get pushed that way by Chuck Kimmel. He strongly encouraged me to look at pigment pattern.

VAN BENSCHOTEN: Talk a little bit about Chuck Kimmel then, and what was it like working with him.

JOHNSON: Chuck is absolutely great. He's amazing. He knows no molecular biology. I mean, he picks up what he needs a little bit. And I don't think he cares. He's really interested in what cells do, and he has an intuitive understanding of how to use genetics. He doesn't have the formal rigor that Lee Hartwell had, but he understands the formal rigor. But he also understands that it's not that we don't study genes; we study what happens when genes don't work, to understand what cells are doing. And that's really what he is so amazing for, and that he picked up later in his career. Initially, he picked up just how to do morphology of development.

Okay, now, for me, coming from a yeast genetics background, where you know what a cell is doing, it's growing or not growing, but it doesn't go from here to there and then play ball with these guys. And in our current generation, many developmental biologists don't actually think about the complex nature of the organism, that it's a lot of cells that have to coordinate, and as they're coordinating, they're doing a lot of amazing things.

So Chuck is, I think, the best morphologist in the business, and he's really accessible with people. He can look at your data and come up with ideas, and then you go, "Wow, I can come up with ideas like that, too," because it's fun when you hear them. So yes, he leads with his incredible imagination, and he can actually put down the law, too.

When I joined Eugene, he was not in Eugene; he was on sabbatical. When he came back, he heard people saying, "Oh, Steve Johnson wants to mutagenize with ethylnitrosourea," and no one does that and everyone's scared, and I suppose they should respect it.

But, you know, he sat down and talked to me, and he said, "Well, I understand that you want to do all these things, and that's great, but you have to work with my people or I'll have to ask you to go."

VAN BENSCHOTEN: Give us an overview of the research that you did for your postdoc then. Here we do have many articles.

JOHNSON: Yes. Here I knew I had to publish. I worked on, I guess I'd say, four different ideas, apart from that one that we discussed that just didn't work. One was, okay, just how does a tissue regenerate? So if you cut off a fin, it regenerates, and one way to study that is to find mutants that don't regenerate, and try to figure those out. I found some mutants, and we made a little bit of progress on those. Well, one of those mutants is now becoming interesting, but only recently. So that was the most of the work that I probably did there, so it was the least productive for the time.

I picked up working on pigment pattern, because as I was cutting off all these fins, I noticed that they regenerated the stripes on the fins, too. There was some very ancient literature that suggested it was very precise, and I could replicate that, and then I found one of the mutants that [George] Streisinger had found many years ago that I just happened to have in my hands for some reason. I don't remember why I had it. When I amputated it and asked it to regenerate its pigment pattern, it did it in a remarkably weird way. It didn't make cells when I thought it should. Then I've been pursuing— That's the major part of our biological program, is understanding the insights into melanocyte stem cell biology that that first observation was suggesting. That's one.

I started working on— And we have made no major insights into just— Because I was working on melanocytes, I picked up stripes, why stripes are this far apart [indicates two fingers spread apart] instead of this far apart [indicates two fingers pressed together] or why they're

stripes instead of spots, and we're still trying to clone those genes.

Another thing that I started working on as a postdoc was the notion of isometric growth control. This is the type of project that I just did because it was easy to generate a little bit of data, and then both Jim Weston and Chuck Kimmel strongly encouraged me that it was fundamentally interesting. And that is why, when fish grow, do they grow proportionately isometrically. That is, when they grow, they grow everywhere at the same time, and yet we have mutants that overgrow their fins. So I made some progress there, but I don't think I ever published any of it. And then about half of my lab works on that project now, and we're having a lot of fun with that.

VAN BENSCHOTEN: And we'll talk about that, too, your current research.

JOHNSON: And then I worked on developing the map, the genomic resources.

VAN BENSCHOTEN: What was that like? I mean, we've just recently seen sort of a carnival surrounding the human genome and sort of the race, you know, in terms of money, personalities. You know what I'm talking about. Talk a little bit about the effort to create this genome for the zebrafish. What was the project? How was it set up? Who was the—

JOHNSON: Yes, I guess it is a carnival. It's sort of amazing how genomics is what brings out the worst in scientists, I think.

VAN BENSCHOTEN: Right.

JOHNSON: When I moved to Eugene, my understanding with Jim Weston and Monte Westerfield was that one of the things I was going to work on was how to develop maps for zebrafish. Clearly, we needed genetic maps to organize our data and eventually get us to cloning our genes.

At that time, other people were toying with other ways of doing it, which turned out to be better, and, thank God they did it. For instance, Mark [C.] Fishman had hired people to use these methods of SSLPs, simple sequence length polymorphisms, CA repeats to develop maps.

But at the time, shortly after I got to Eugene, John Postlethwait had an undergraduate student who showed that you could use a random oligotenmer— This was first showed in plants by other people, but then we found we could do it in zebrafish and get bands, and if you looked at a haploid cross— So that's real easy to look at, because from your diploid parent, you have this allele or that allele, but not both. You could see that they were segregating; they had this

one or that one. And if that was the case, it would be a very cheap way of developing maps.

So I looked at that and saw that I thought the data would be good, and convinced Jim and Chuck to spend their money on this program in Eugene instead of donating some money to this project that was going on in Boston. And so then we developed that.

VAN BENSCHOTEN: What was your role in that, other than, of course, helping to get the ball rolling?

JOHNSON: When they had a whole bunch of data and didn't know how to analyze it, I sat down with the data and turned it into a map. That was the first map, which was actually useless, because it wasn't based on inbred strains and most of the markers were not reproducible from fish to fish. But that was a *Science* paper. Go figure. And then I was able to use that to map the first mutants in zebrafish too, so it wasn't completely irreproducible, but largely.

From doing that, I learned there were things that I wanted to figure out how to do. I wanted to figure out how to use centromere markers for mapping and I wanted to do it reproducibly, so I needed inbred strains. So I developed inbred strains, and then I repeated the map on inbred strains and mapped the centromeres, and then developed the way of mapping with centromere markers that we now use.

VAN BENSCHOTEN: I'm a novice at this. What's the advantage of using a centromere marker?

JOHNSON: Oh, okay. I'll see if I can do it without drawings. You know, in meiosis there are four— Well, in a diploid cell there are two chromosomes, one that you got from Mom and one you got from Dad. In meiosis, those are duplicated, so you have two of Mom and two of Dad. So those are the four chromosomes, and that's what we call the tetrad. Later on, when they form the gametes, you have the four products of meiosis, each have one of those chromosomes. In female meiosis, for instance, typically only one of those turns into the egg and the other three are destroyed. Okay?

What happens, then, at the four-strand stage you get crossover and recombination. But then they're segregated by tugging. The cell apparatus tugs at the centromeres. So if you have crossover, it will give crossover distal of the centromere. But the centromere, Mom's centromeres are pulled in one direction and Dad's in the other, because you can't have crossover between the attachment site and itself. Okay? So that's the first meiotic division. And then the second meiotic division, which we call equational, segregates those from each other, and then that becomes the gamete. Okay?

In what we call zebrafish early-pressure parthenogenesis, we let this occur. That is,

that's what the fish does for us before we can get the egg, and they're arrested at that. And when we add the sperm, it proceeds to do this, and it does that in the first six minutes. We can cause it to fail to do that by putting it under very high pressure.

VAN BENSCHOTEN: When you said "this," you separated your finger.

JOHNSON: The second division. Oh, I'm sorry. We can prevent the second division with high pressure in the first six minutes, and then it'll package one half of that first division as the female pronucleus. That's the gamete. Okay? Now, that's got to be homozygous at the centromere. All right?

VAN BENSCHOTEN: I think I'm following you.

JOHNSON: Okay. Now, let's say you have a mutation. Let's say it's a mutant that makes the melanocytes pale instead of dark. One sits way out here, so there's going to be a large probability of getting a crossover. So if you looked at any individual chromosome, it's likely that it's recombinant between the centromere and that mutation. Okay?

But now we're going to look at our half-tetrads, our parthenogenetic embryos. They're homozygous at all their centromeres, and a small fraction, somewhere between 5 and 50 percent, depending on how far this mutant is from its centromere, will be homozygous at that mutant location; that is, they have two copies of the mutation. Okay? Most of the time, the majority will be heterozygous for the mutation because there's been a crossover. Not strictly a majority, but oftentimes we find the majority of the half-tetrads have one crossover, so they're heterozygous. And then some others are no crossovers, but they're homozygous wildtype. We're going to ignore those. We're going to only pay attention to the ones that are homozygous mutants. So homozygous at the centromere; homozygous at the mutant locus.

We can't—we can, but it's a complicated event—have crossovers have occurred between the centromere and our mutant. So now, essentially no matter how far away we are, no matter on average how often we'll get crossovers between these, we can ignore them. We've taken a statistical subset, but we know which subset to use if it's non-recombinant. And now, instead of having to screen an enormous number of markers to find out what chromosome this is on, we just use one marker per centromere.

VAN BENSCHOTEN: I see. I'll play this over again so I'll understand it better, but it seems to make sense.

JOHNSON: So that was— I think this was a trivial result from classic tetrad analysis, and

people could have told us this in the thirties. We just didn't understand it. George Streisinger understood it, but he didn't tell it to us. After he died, Chuck Kimmel and Ira Herskowitz wrote his manuscript, but it didn't actually say this, because I didn't get it out of that manuscript. I didn't get it until the fish showed it to me.

VAN BENSCHOTEN: So it had to be rediscovered.

JOHNSON: Or re-intuited. I should have known this as a yeast geneticist, but I didn't. And all the yeast geneticists, when I had them read the paper for me before submitting it, they all go, "Well, you know this is trivial."

I go, "I know it's trivial. I can't believe I'm just now understanding it." But it was very important. Maybe it was most important in that I figured out how to explain it.

VAN BENSCHOTEN: So you play an important part, then, in the mapping of the zebrafish genome. Are we forgetting any other important development? You've already mentioned four projects, and a couple of those, obviously, you carry over into your PI [principal investigator] work, as well.

At the end of your postdoc, you eventually end up at the University of Washington, as you know.

JOHNSON: Washington University [School of Medicine].

VAN BENSCHOTEN: Washington University. I'm sorry, yes. How do you get there? Why there rather than another place?

JOHNSON: So I mostly applied for jobs blind. I was invited to apply to one place that was looking for a melanocyte worker. But mostly advertisements. Zebrafish was just starting to take off. A lot of people thought maybe they needed a zebrafish worker.

I got a lot of interviews. I got two, and would have had three, but I ended the search job offers, and of those I went to Washington University because I didn't really want to teach undergraduates. So between the biology department at Michigan [University], where I probably would have had to do a lot of teaching, and in the med school, my teaching responsibility is virtually nothing. I do lots of one-on-one mentoring, but very little organized teaching.

It wasn't clear that Michigan could have come up with the fish facility I wanted, and it was clear that Washington University could do what they said they would give me, because I

knew they had the money. The genome guy, Rob [Robert H.] Waterston, if he says he's going to do it, I knew he could do it.

VAN BENSCHOTEN: What was the set-up package at Washington University, other than having the mechanism in place to produce these zebrafish?

JOHNSON: What was the second set-up package? Like how much money did I get?

VAN BENSCHOTEN: Yes.

JOHNSON: What guarantee of my salary?

VAN BENSCHOTEN: Yes.

JOHNSON: I don't know what guarantee of my salary. Essentially, my salary was, and is, guaranteed whether I bring anything in, because everybody in the med school's salary is guaranteed. Though after you have tenure and you don't continue to produce, they'll start to cut it back, but they can't, and won't, fire you for that.

I was given $300,000, which was a lot, but not outrageous at the time, for the lab, and then another— Gosh, how much did it cost? I think it cost $200,000, or a little more than that, 240[,000], to set up the fish facility.

VAN BENSCHOTEN: What was the hardest part about setting up your lab?

JOHNSON: Setting up the fish facility.

VAN BENSCHOTEN: How long did that take?

JOHNSON: About six years.

VAN BENSCHOTEN: Oh, my god. [laughs]

JOHNSON: I would argue we're not done. The water in St. Louis is different than the water in Eugene. So I tried to replicate what I was doing in Eugene, but it wouldn't work. And after about four years, we tore it all apart and replaced it with stuff that other people were using very successfully, some commercial stuff that's now available, and we're now learning how to use that.

VAN BENSCHOTEN: So a very long, difficult process.

JOHNSON: But before I had fish, it took about nine months.

VAN BENSCHOTEN: You've already mentioned a little bit about the research that you carried over to your position at Washington University, but tell us a little bit about your current research, and again in terms— And you've done really well so far. I want to compliment you on that. But in terms, again, that a non-scientist can understand, how you sort of extended those projects that you already mentioned.

JOHNSON: Okay. Let's do genomics, because that's the easiest to explain. NIH[National Institutes of Health] has decided that it really wants zebrafish to be an important model system, and therefore they decided about six years ago to begin to develop the infrastructure for zebrafish genetics and genomics.

I took advantage of being at Washington University, with its amazing Genome Center, to propose to do everything they wanted done. They decided not to let me do everything, or not to give me money for everything. I proposed to identify all the genes, map many of them, find single nucleotide polymorphisms on those between my inbred strains. I guess that was the initial proposal.

Then I was asking them to let us build the physical map from *BACt* clones. Then they gave me money to find most of the genes, and then over the next few years, as we didn't have enough money to do all the gene discovery we wanted, they continued to give us money to do more gene discovery; that is, the EST project, expressed sequence tag. That's where you take a cDNA and you sequence a little bit of each end, and that gives you an identifier. Okay? Oftentimes that's enough to even tell you what the gene is, comparing it to human or mouse or fruit flies. So we've been very successful at that.

And then they gave us some money to map genes. That is, radiation hybrid mapping panels had been developed, two of them, and we took our ESTs, designed primers for them, and then typed them on a radiation hybrid panel. So we did that both ourselves, and then we coordinated several other labs. So in order to limit redundancy, we did the gene distribution. We said, "You guys are doing these, and you guys are doing those."

In part to limit redundancy, we needed to find when we got a tag, is that tag an independent gene or is it just an old gene, so that we don't sequence the same gene over and over— Map the same gene over and over again. So we have been developing informatics in my lab to cluster the genes together where they have direct overlap, or when they are from different ends of the same cDNA, associate them. And that sounds really trivial, but it's not, because oftentimes there are errors, and they may be associated. So then we developed techniques to find when there are probably errors in the data submission so that we don't associate them.

So we're just wrapping this part of the project up, and we found 25[,000] to 26,000 genes, which is about right. I'm sort of guessing, of our predicted genes, about 4[,000] or 5,000 of them are actually cloning artifacts, and then the others are real genes. We've got, I think, 7,000 of those mapped. We've been able to draw, I think, fairly significant insights into the relationship of the zebrafish and human genome. For instance, when we were going into this project, we thought there'd be really big stretches between zebrafish and human that were un-rearranged, and we're now finding from our mapping data that it's probably the stretches are quite small, two or three or four genes, and then there's a rearrangement breakpoint. So evolution has really scrambled these genomes.

That's leading me to think that the next projects that I want to do aren't data generation. I'm sort of tired of that. But now that we've got all this data, we can ask, if there's a breakpoint every three or four genes, is that actually generating new genes? If you break a gene in the middle and recombine it with another gene broken in the middle, you've got a chimeric gene. So now I think we have enough data in zebrafish to ask, is that playing a significant role in the evolution? We can't ask this functionally, but we can ask, how many can we find? Or similarly, is the evolution could not be because you're making new genes, but you're changing promoters, the part of the upstream that causes it to be regulated. So can we begin to come up with ways to identify when the promoter is chimeric and shows expression characteristics of two ancestral genes. So that's sort of where I want to take that, one of the places I want to take that.

We're sort of done with this massive production of data. The SANGER [System-Wide Information Network for Genetic Resources] Center in England is going to do the sequencing, thank goodness, or I would have gotten dragged into that, and that really would have killed my biology career.

VAN BENSCHOTEN: And the mapping. The mappings are a third done, then?

JOHNSON: Of the genes, a third of them are done. But the important thing about that isn't that the genes are mapped; it's that we now have places on the map. That is, we get genome sequence, we can anchor them to our map. So as the SANGER Center generates data, they know where they fall, and then they can do more targeted experiments to try to link up the things that we think map together.

VAN BENSCHOTEN: So you're, in a sense, a coordinator of all these efforts?

JOHNSON: Well, no. I'm not the coordinator of the SANGER effort. I'm just providing a resource that they will use. They speak such a different language, that I can't coordinate what they do.

VAN BENSCHOTEN: Okay. So there's this stuff. And then what other [unclear]?

JOHNSON: So this initial observation of, when you cut off a fin in the *sparse* mutant, it doesn't make melanocytes, we are following that up in a lot of different ways. One, we made temperature-sensitive alleles of *c-kit.* The gene was a gene called *c-kit.* That's an old famous mutant from mouse, also called dominant spotting. That's the receptive tyrosine kinase. In mouse, if mice are mutant for this, they grow up without any melanocytes, and we think— In the literature we think that they don't have melanocytes because they make their stem cells, but they die in the embryo. Okay? So if you don't have your stem cells and your hair falls out, then you make a new hair, but you don't have a stem cell for it, then it does this, it's gray. Okay? And then that mouse is all white because it lost its stem cells in the embryo. That's the mouse notion.

So we decided to test that in the zebrafish by asking, if we made a temperature-sensitive allele of *kit,* that is, one that grows normally at a low temperature, but without gene function at the high temperature, could we use that to ask, is it acting early or late? And we made the allele. We made several alleles, and we showed that it acts late, after amputation, in the process of recruiting stem cells back into development. It has no role early in establishing the stem cell lineage. So that was nice. That's making us, and I hope others, rethink this mouse result. There are a lot of things that are hard to resolve, still. But that was a fun result.

Now, the next step is, when these *sparse* or *kit*-dependent melanocytes don't develop, we'll that's not the whole story. They wait about a week, and then other melanocytes develop. So we call those secondary regeneration melanocytes, and these are really interesting melanocytes that are going to tell us a lot about how tissue integrity is maintained, because you want to know— I know you want to know this. Why do you continue to have blood? Because your blood cells are dying all the time, yet you keep having blood. So somebody's paying attention in there. Or why, if you nick yourself, does that heal right? Something's paying attention who knows the right form or tissue and makes it, and we think that's the job of the stem cells, that they're actively surveilling their environment and saying, "Oh, there's a problem here. We're going to make new cells."

For instance, in this *kit* mutant, when it doesn't make these melanocytes, after a week new melanocytes are made. Now, new melanocytes are always being made in the distal-most growing part of the regenerating fin. This is all a regeneration experiment. But in the *kit* mutant, when it begins to make melanocytes, it's making them in a very old part of the regenerate, a

week older than where they're typically being made. So it's making them in the wrong place; that is, after a week delay.

We know if we look at a wildtype fish, they're just not being made there, or very, very few are being made there. However, we can do experiments to reveal some role for late cells. We can look for holes in the stripe. These stem cells, the idea is that they're surveying the environment for defects in the tissue that they're responsible for. So we looked for holes, did lineage experiments to see how those holes are fixed; and, in fact, they're fixed from new cells, not from old cells. Okay. That was confirming our notion. So we want to know, how do those cells survey their environment, and this is a great opportunity for it.

VAN BENSCHOTEN: What's the feedback loop?

JOHNSON: What's the feedback loop? We did a mutant screen; and, in fact, when we did a mutant screen, we didn't get mutants in the feedback loop. We got mutants in the first part, which is presumably when we amputate, a stem cell is recruited to divide. You know, all this is inferential. We've got only the briefest glimpse of a stem cell after it's divided. We haven't seen a stem cell. This is sort of like nuclear physics before they've seen neutrons, but they're inferring them, okay, or whatever particles that they're still only inferring. But we want to see those cells.

But we can still do these experiments to make inferences on those stem cells. We think you cut them—the stem cells recruited to make new cells. It then allocates some of the cells to remain stem cells, and it allocates others to immediately differentiate as a melanocyte. Okay. Then we looked for mutants that didn't make this regulatory population in a *kit*-mutant background, so we're looking for double mutants that don't make it, and then we add back that first gene *kit*, we found something really striking, and that is, it now makes way too many of that first population of melanocytes. So that suggests to us that in this allocation project, or problem, it's allocating most of its daughters to make melanocytes and very few as stem cells. So that's going to be a fundamental insight into how stem cells are maintained so that you can continue to have blood or skin or all these other parts of your body that are maintained by stem cell populations.

VAN BENSCHOTEN: That's fascinating.

JOHNSON: Yes, it is.

VAN BENSCHOTEN: What are the sort of long- and/or short-term applications for your work? I mean, obviously one of them is cloning and whatnot, but expand a little bit on that, if you would, both real and potential.

JOHNSON: Well, the short-term application of our genomics work is it will let people clone their genes more rapidly. That's a very fundamental technical problem, advance. Our work on melanocyte stem cells is going to get us insights into how stem cells behave in the adult organism, because even in us, and in mice, the adult stem cell is something that we don't really have a solid handle on, so we're going to get insights into that. And if we begin to get insights, we'll be able to learn how to manipulate them.

VAN BENSCHOTEN: Any others?

JOHNSON: When we clone long fin, we're going to be able to introduce into other fish and make them equally pretty. [mutual laughter] The real answer is, this is part of the proportional growth thing. We're going to begin to understand what the growth control mechanisms are systemic in the body and local in the tissue that are coordinating growth. Some of our overgrowth mutants— If I starved you, you'd quit growing, right? But if you had a tumor and I starved you, your tumor would continue to grow. Okay? If I cut off your fin, your fin would regenerate, even though you were starving. So this is a fundamental problem of nutritional— We call it nutritional surveillance, how do tissues pay attention to the nutritional status of the individual and decide to grow or not grow. Tumors lack much of this. Regenerating fins or limbs in animals that do that bypass this. We have mutants, overgrowth mutants, not regeneration mutants, some of which pay attention to nutritional surveillance, and others bypass it. So we think we're going to start to get some of a fundamental understanding of nutritional surveillance, and maybe that'll tell us something about cancer. I'd be surprised if it didn't.

VAN BENSCHOTEN: We're almost at five, and we're at the end of this tape, so this may be a good place stop today.

JOHNSON: Okay. [tape recorder off]

[END OF TAPE 2, SIDE 1]

[END OF INTERVIEW]

INTERVIEWEE: **Stephen L. Johnson**

INTERVIEWER: **William Van Benschoten**

LOCATION: **The home of Stephen L. Johnson's brother**
Studio City, California

DATE: **26 September 2002**

VAN BENSCHOTEN: Today is September 26, 2002. I'm with Steve [Stephen L.] Johnson again.

Before we get back to the question set, I had a few follow-up questions which I thought I'd throw at you. What do your siblings do? You mentioned them; you mentioned their names. What do they do, and where do they live? I know that Lee [Ensign Johnson III], the oldest, we're here in his house, so he lives in L.A. But what does he do?

JOHNSON: He works in the movie industry, in the stage part of it. I think you'd call him a best boy.

VAN BENSCHOTEN: And how about your twin?

JOHNSON: My twin [Michael Owen Johnson] is in Nashville. He is an electrical engineer. He automates factories. And my sister Susan [Susan Carol Johnson] is a psychologist, and she's at Stanford.

VAN BENSCHOTEN: When you were growing up, did your family happen to have subscriptions to magazines and journals that you can remember?

JOHNSON: I think we had subscriptions to magazines like *Newsweek* and *Atlantic [Monthly]* and *Harper's [Magazine]*.

VAN BENSCHOTEN: And did you read those? Is that something that the whole family read together?

JOHNSON: Yes, I suspect everybody read those.

VAN BENSCHOTEN: You talked about the Boy Scouts [of America] and becoming an Explorer, and you also said it was very important to your upbringing, being an Explorer, when you reached that stage. In what way was it important?

JOHNSON: It gave us a lot of freedom. It was the way we got out of the house, going out camping and things like that most weekends.

VAN BENSCHOTEN: So a sense of freedom.

JOHNSON: Yes.

VAN BENSCHOTEN: The pharmacology lab at Vanderbilt [University], who did you work under in that lab?

JOHNSON: The lab PI [principal investigator] was a woman named Lee [E.] Limbird.

VAN BENSCHOTEN: And how big was her lab?

JOHNSON: Her lab was about, at any time, about two graduate students and two postdocs, maybe three postdocs, and two technicians.

VAN BENSCHOTEN: You'd said that science didn't interest you that much till after a B.S. degree, and really when you joined this lab, and this changes when you work in the pharmacology lab. Why? What did science mean to you at that point? What made it different?

JOHNSON: Well, before, it was just an accumulation of facts, but not really an appreciation that science is asking questions and learning how to get them answered. And actually working in a lab, I've learned how to ask the questions, the importance and the fun of asking your questions and getting them answered.

VAN BENSCHOTEN: What can be done to improve the state of U.S. science education? Because you had talked about how poorly that science education was, for you at least.

JOHNSON: Put students in research labs.

VAN BENSCHOTEN: So let them do research right from the get-go?

JOHNSON: Yes.

VAN BENSCHOTEN: You also talked about literature. You said that students should be dissecting *Science* articles in the same way that, say, literary or literature majors would dissect a great novel. Am I paraphrasing that right?

JOHNSON: Yes, yes, I think you are.

VAN BENSCHOTEN: So basically group activity, analyzing, working together?

JOHNSON: Yes. You know, most places, almost to a fault, have something called journal clubs, but in journal clubs they present the data rather than actually discussing what's going on, so many of these are really dreadfully boring.

VAN BENSCHOTEN: Just a point of fact, are or were you married?

JOHNSON: No.

VAN BENSCHOTEN: [James A.] Weston helps you with your science writing, you had mentioned, and through him you learn how to write journal articles. What was the article-writing process in the Weston lab?

JOHNSON: Article-writing process was, you would decide to write something or he would say, "You know, I think it's time for you to write something." And then you'd write it, and then together you would make it make sense. So he was very good for me to learn how to start with topic sentences that summarize everything so you don't have to read the rest of the paragraph, and it helps write the paragraph.

An important part of learning to write from him was, he actually can't write that well. He writes clearly, but he can get really lost in the details. So when I got there, I helped him a lot.

I think I helped out; I don't know if I helped, writing his grants on subjects I just didn't understand at all. So I had to work with him and say, "You know, I don't understand this, so how can your reviewers understand this? And if we did this, it might be comprehensible." So instead of working on my stuff, we were working on his.

VAN BENSCHOTEN: How did you work this? Was he looking over your shoulder while you were writing these grants or you were writing your own articles? Are you passing drafts back and forth? He's giving your corrections?

JOHNSON: Correct. Paper corrections.

VAN BENSCHOTEN: No papers were published from your Ph.D., you said. Papers are critical, as you know, practically every stage of the way. I don't need to tell you that. You get a postdoc at the University of Oregon, working in a pretty amazing lab, the [Charles A.] Kimmel/Weston lab. Your experience seems, therefore, to contradict sort of the conventional wisdom about papers. How do you explain your own particular trajectory? Is it that your recommendations were just so glowing that they bypassed that route?

JOHNSON: I didn't see my recommendations, so I don't know. I think several things. One is, there aren't that many scientists out there, and most of us will take a chance on most of the postdocs. I will take chances on postdocs who don't really have publications, but I have to talk to them and see them speak first. So that's one.

I think that I was able to convince Jim that I had some interesting ideas that could be tested, that possibly could be tested but would be fun to explore. His idea was that if I could convince someone to give me money, then I could come. So it wasn't really his decision.

VAN BENSCHOTEN: Getting a postdoc with cash in hand, too, is really nice, probably. What is your own advice to your students and postdocs about the publication of their work? What is your philosophy on that?

JOHNSON: My philosophy is they have to publish a lot, because most scientists won't really trust their own judgment, so they want to see the paper trail.

VAN BENSCHOTEN: And finally, in grad school you said you were socializing more than you were as an undergrad. In what way?

JOHNSON: No, about equivalent as an undergrad, more than as a postdoc, where all I did was work.

VAN BENSCHOTEN: All right. That brings us back to the question set again. We talked yesterday, as you know, about your family and upbringing, and you talked us through your education, college at Vanderbilt[University]. And then we spoke about your research as a tech, grad student, and postdoc, and then we finally ended up with your current research and possible applications of it.

We'll turn now to sort of a different part of the question set about duties as a PI, and there are several of those. What do you spend the bulk of your time doing as a PI?

JOHNSON: I think I spend most of my time thinking about the projects in the lab and talking to the students about what they're doing, or technicians about what they're doing, or helping write papers.

VAN BENSCHOTEN: You mentioned last time, too, in our last session that you don't get to do a whole lot of bench work either now, do you?

JOHNSON: No. I do no real bench work. I have a couple of strains of fish that I'm trying to turn into robust, viable inbred strains that have both boys and girls, so I'm introgressing genes that bring the sex ratios into something acceptable into these lines.

VAN BENSCHOTEN: You also mentioned that part of the attraction to going to Washington University [School of Medicine] was that there was very, or no teaching. Is that true? So you have no teaching lab whatsoever?

JOHNSON: I do lecture or two a year.

VAN BENSCHOTEN: And the teaching you do is not classroom, then? It's one-on-one with the people in your lab, I assume.

JOHNSON: Most of it is, what I'm doing now, mentoring my lab or taking students through their preliminary exams.

VAN BENSCHOTEN: Do you believe students have changed very much from your own day?

I know that makes you sound very old, but I don't mean to make it sound that way.

JOHNSON: But I am. I don't know if I know. Many students aren't quite adventurous enough, as I would have viewed myself and my peers, and it's hard to know how to compare that.

VAN BENSCHOTEN: Another duty that you have is travel. On average, how often do you travel?

JOHNSON: I probably make about ten trips a year.

VAN BENSCHOTEN: How do you feel about job-related travel?

JOHNSON: It's something I have to do. I have to give seminars. I don't go to many meetings, just one or two a year. I have to go to those or the lab work would become invisible, because most visibility seems to be from meetings rather than from the written articles.

VAN BENSCHOTEN: And how about administrative duties? By those I mean things like search committees, research or doctoral committees.

JOHNSON: I'm on the Graduate Admissions Committee, initially for development and now for genetics, and that actually takes a fair amount of time. The recruiting is very labor-intensive. I'm on a search committee with the biology department right now. Currently we don't have any active searches in genetics, but I'm often— We bring people in, and everybody has to talk to them. I do a fair amount of preliminary exams because I'm on our coordinating committee for both genetics and development, and we put people from the coordinating committees on the exams. So I do a fairly heavy load of that. I'm not on very many thesis committees.

VAN BENSCHOTEN: If, let's say, there were an imaginary pie chart out there, what percentage of time do these administrative responsibilities take up, do you think?

JOHNSON: I suspect those responsibilities are about 10, 15 percent of my time.

VAN BENSCHOTEN: Do you have tenure now?

JOHNSON: Yes, I just got tenure.

VAN BENSCHOTEN: Congratulations.

JOHNSON: Thanks.

VAN BENSCHOTEN: What does tenure mean at Washington University [School of Medicine}?

JOHNSON: It means a pay raise.

VAN BENSCHOTEN: That's nice.

JOHNSON: A different title, So to associate professor. And really not much else.

VAN BENSCHOTEN: What was the process there to get tenure?

JOHNSON: The process there is, the chairman decides that he thinks he can put you up for tenure and you would succeed, and then he does it. And that's based on do you have enough grant support and papers and, presumably, respect. If he thinks you've got that, he asks you to suggest— [tape recorder off]

VAN BENSCHOTEN: All right. I'm sorry.

JOHNSON: We were talking about tenure. The chairman then asks you to come up with a list of people who are prestigious in the field, to write letters. They do that, and that takes a while for him then to accumulate those letters. And then he calls a committee, a tenure committee in the med[ical] school, which is some chairmen and some senior faculty, and then they evaluate this package that they put together. And then they pass that on to the executive faculty, which is all the chairmen of the medical school, and then they either accept or reject the recommendation. But I guess they usually accept the recommendation.

VAN BENSCHOTEN: How long, from beginning to end, is that process?

JOHNSON: Gosh, I think that process is about a year.

VAN BENSCHOTEN: Let's turn to funding, another responsibility. That can put gray hair on your head. How secure is your funding, do you feel, right now?

JOHNSON: I have a good level of funding that's secure, and then I don't yet have— So that's about two-thirds of the money that I think I need right now is secure, and I need to find the next third now.

VAN BENSCHOTEN: So you're writing grants now?

JOHNSON: Yes.

VAN BENSCHOTEN: What is the grant-writing— I mean, how long does that usually take, the grant-writing process, and how much time does that chew up?

JOHNSON: Obviously, it takes many, many months of pondering and then a few weeks of writing.

VAN BENSCHOTEN: Some Pew [Scholars Program in the Biomedical Sciences] scholars have said that the grant-writing process, however much they don't look forward to it, nevertheless, allows them to sort of crystallize in their heads what they're doing and where they may or should go. What does the process do for you? Is it just sort of an onerous task?

JOHNSON: That perception's right. It forces you to critically write down things you may not have written down and then see whether they make sense. Is it an onerous task? Yes, but—

VAN BENSCHOTEN: A necessary onerous task.

JOHNSON: Many are necessary. But my best ideas have never been in grants.

VAN BENSCHOTEN: What are the sources of your funding for your lab right now?

JOHNSON: For my lab now, I've got one RO1 to study melanocyte stem cell development, part of a program project grant to study fin overgrowth syndromes as part of from child health. It's part of a program project on overgrowth in model organisms in humans. I still have some money on the zebrafish genomics, but that's winding down. And then one of the postdocs, who's a physician, is bringing in an extra something like $75 [,000] or $80,000 worth of spending money.

VAN BENSCHOTEN: On a scale of one to ten, how much concern do you usually feel from day to day about your present funding, about getting that third, let's say? I guess what I'm trying to get at is, is this something that really hounds you or is this something that's sort of another pressure among many other pressures of your job?

JOHNSON: It's not that high on my worry. I know that I have maybe three things I could sit down and write a grant on and get, so now I just have to settle down and do it, or at least do two, though I'd have a hard time spending that extra money if I got two.

VAN BENSCHOTEN: How much does the source of your funding inform the projects that you do?

JOHNSON: I should say absolutely, but then I have to remind the readers that in an RO1 grant, investigators actually have extended authority— It's like I'm reading a lawyer's statement. And we can really spend that money any which way we want, as long as it's in the general idea of the proposal, and I would never have a problem casting a new idea within the general idea of an old one. So the answer is yes and no. How is that? I think I'm safe. [mutual laughter]

VAN BENSCHOTEN: You've described the writing process in the Weston lab. Describe the writing process in your own lab for journal articles.

JOHNSON: Most of the writing is done by the postdocs and graduate students, and I am now writing my second paper that I wrote since I've been there. I hate writing papers myself.

So the process for them is, they write a draft. I usually try to get them to prepare an outline first as they're doing the project. We will then say, these are the things we want to ask and present in a paper, and then focus the last experiments towards that. Then they'll write a draft, and I will, on that, write comments and suggestions about how to state things. We'll go through that one or two times, in some cases eight or nine, and then it'll get to a point where I think it's okay, but everything else is style. And then we'll sit down at the computer and we'll work through sentence-by-sentence style, but then that's when I'm typing.

VAN BENSCHOTEN: Let's talk a little bit about your lab management style. What kind of boss are you? Ideally, of course, we should ask the people who work under you, but since they're not here.

JOHNSON: I think I'm pretty demanding. I give the scientists the ability to work on very, I hope, interesting problems that other people are not doing so that it's exciting. I then expect them to work hard on it.

I try to talk to most of the scientists in the lab two or three times a day just to see how they're making progress. I probably overmanage here, but on experimental details, I really don't like to see them wasting too much time not doing the right controls. I don't know if that's the best for their training.

VAN BENSCHOTEN: How do you decide on projects? If you have a new person show up in your lab, do you have a protocol that you go through, deciding what they're going to do?

JOHNSON: No, I don't have any formal protocol. I think about what is bothering me, on one hand, and what I think they're suggesting they're interested in, on the other. So if someone comes in and says, "I want to work on a particular aspect of melanocyte stem cell development," then I would say, "Well, you're working on that." They come in and say, "I want to work on fin regeneration," I say, "Maybe we should work on pigment cells," because we can develop really good hypotheses with the pigment cells and test them. But with fin regeneration, most of the work, until very recently, has been very fuzzy and really hard to work with, with the students.

So I find something that I think we can do, and it may be something that I know we have to do because I can see that it just has to be solved, a detail that has to be solved. Then I'll try to get them started on that, and then hopefully they will take it from there.

VAN BENSCHOTEN: When you started your lab, how well prepared do you think you were to set up your lab?

JOHNSON: I think I was fairly well prepared to set it up scientifically and start people on projects. I'd done a fairly long postdoc, and I'd certainly been directing a lot of undergraduates on various aspects of my interests. For management, I don't know if I'm prepared.

VAN BENSCHOTEN: What do you believe is your greatest strength as the head of the lab?

JOHNSON: My greatest strength is I'm really great at generating ideas.

VAN BENSCHOTEN: Was that an ability that you had when you first took off in science or was that something you've cultivated? I know that you mentioned, for instance, [Charles A.] Kimmel and how important he was, I think, in generating ideas. I think I have the right person.

JOHNSON: Well, I think all of those really important mentors—Kimmel or Weston or [Breck] Byers—have been really great at generating ideas, but I don't know. Since early as a graduate student, I found I could generate a lot of ideas. I look at my students now, and some of them are really afraid to come up with models. As a mentor, my job is to train them to come up with models, and that's probably the hardest thing, and perhaps they rely on me too much for that.

VAN BENSCHOTEN: Where do your ideas come from?

JOHNSON: They come from the data. I don't know, they just—

VAN BENSCHOTEN: They show up one day on your doorstep. [laughs]

JOHNSON: Wrapped in a bow. They come from really being immersed in thinking about what's going on and letting your mind wander.

VAN BENSCHOTEN: So in a sense, permitting yourself to sort of play with the data and to sort of dwell on the data.

JOHNSON: Yes, but not get caught up on data. But you have a model and you generate data, and it can partially support or partially fail to support your model. And then you have to then think about how to further explain the data.

Certainly, I see now in younger graduate students, they are pretty good at saying, "The data doesn't fit the model." They're not very good at saying, "Well, I have explained this much of the model, and now I need to come up with more of a model." That's what I think I'm good at.

VAN BENSCHOTEN: How do you get them to generate these ideas, to go the rest of the way?

JOHNSON: I don't know. I'm not good at that.

VAN BENSCHOTEN: You also provide services for the professional community, and by "professional community," I mean things like study sections and editorial boards. What are your own duties in that regard?

JOHNSON: I guess I've sat on three study sections, maybe four. I did a site visit. That's sort of like a study section. And I review grants. You know, sort of standard, is this scientifically sound and interesting? I review papers, and I'm on the editorial board of *Genome Research,* and I get papers from about a dozen journals to review. So I probably do one to two papers a month. And I honestly think that many editors use me as a way to reject papers. They say, "This one's terrible. Let's see if Steve can put it in a way that we can reject it."

VAN BENSCHOTEN: And why is that?

JOHNSON: Because I usually reject papers. [mutual laughter]

VAN BENSCHOTEN: How much time does that usually take to do all these activities?

JOHNSON: It usually takes me a couple of days to review a paper, as I have to make sure I understand it and then I have to make sure I know whether the data is sound or not and whether it addresses what they claim it addresses, and then I have to figure out how to write what I've said, what I've concluded. So I guess I do twenty papers a year. That's like forty days of work. That sounds about right.

VAN BENSCHOTEN: If you would, describe a typical workday, from the time that you get up in the morning to the time that you go to bed.

JOHNSON: So I typically wake up fairly early in the morning, and then just sit in bed and listen to the news for about an hour.

VAN BENSCHOTEN: NPR [National Public Radio].

JOHNSON: Yes. And then I might get up between five-thirty and six-thirty. I feed the cat, and I then I drive to work. I pick up a cup of coffee, and if I didn't drink orange juice at home, I get orange juice, too. And then I go in and start reading stuff or working on— If I'm working on my own paper or someone else's or whatever, and I might do that for a couple of hours and then go out into the lab and start talking to people.

VAN BENSCHOTEN: When do they begin to show up?

JOHNSON: So I typically show up between six-thirty and seven-thirty. I have one technician who shows up at seven, and she's the lab manager, and another who shows up at seven-thirty. The postdocs and graduate students show up between eight and ten, depending on if they're breeding that day. I try to get everybody there by eight, because I just think you have to show up early if you're going to work.

I typically stay until around six or six-thirty, and then I go home. Then I eat something and read. More often now, I read novels or spy books or things like that for a few hours, and then I go to sleep.

VAN BENSCHOTEN: Are you going to be able to do any reading on this trip?

JOHNSON: This trip, I have three manuscripts, and I went through two of them on the plane, or one and a half on the plane. I have my own manuscript. I have like three paragraphs to write, so that'll take me about two more weeks. My writing is really slow. So I think I'm going to get that actually done. I mean, I probably could do my writing on this trip. And then I'm doing a little bit of reading. I picked up a book in the airport that looked like it was going to be on when the culture of the Jewish culture and Christian cultures actually split and recognized that they were different. That's something that I'm completely mystified by. But I don't think this book is going to tell me that.

VAN BENSCHOTEN: Do you usually go out on the weekends?

JOHNSON: I usually spend about a day on the weekends. I just, a year ago, bought a cabin about forty minutes out of St. Louis. It's on a river, on a bluff over a river. It's actually quite peaceful there. So I often spend about a day out there, just listening to the birds and reading.

VAN BENSCHOTEN: That sounds great. And I've got to get this in, since I'm a cat person myself. What is the name of your cat?

JOHNSON: My cat doesn't really have a name. A previous owner gave it a name, but I think that's private between them and the cat.

VAN BENSCHOTEN: [laughs] All right. What do you do for fun and leisure? What do you do when you want to sort of decompress?

JOHNSON: So I read a lot. That's my major activity now.

VAN BENSCHOTEN: Assess your efforts so far in achieving your professional goals.

JOHNSON: You know, I haven't cured cancer. [laughs]

VAN BENSCHOTEN: Yet.

JOHNSON: My professional goals are pretty good, I guess. I have a solid enough base of funding that I know the lab's not just going to fall apart in the next five years. So I can only enhance it, but I don't think I can destroy it. I've got tenure. I've got seven scientists doing very, very different things in the lab. I mean, we're all focused on pigment cells or fin growth, but incredibly different aspects of that in those tissues. And I think that's really where I wanted to be, because it's a lot of fun. I hope they think it's fun, too. So really, that's where I wanted to be, and I think I'm pretty close.

VAN BENSCHOTEN: Where do you see your lab going in the next five years?

JOHNSON: We're starting some work— I think I described the nutritional surveillance yesterday. So we're trying to develop rapid assays to see this instantaneously in the fish, whether they know they're starving or not. And then if we can do that, we're going to do mutant screens and try to understand nutritional surveillance. If we can develop those assays, that will become a large part of the lab.

We're continuing to work on melanocyte stem cell problem. For the last ten years, most of my work's been on fin regeneration. I'm using the fin regeneration assay from melanocyte stem cells. We think we've shown that we can get melanocytes to regenerate in embryos without otherwise damaging the fish. We found a drug that we think is killing the melanocytes, and then they recover. We've got ways now to laser-ablate all the melanocytes in a single fish for fifty embryos at a time, and that'll let us do mutant screens. So embryos are incredibly much

easier to work with than adults, so I think we're going to have a lot of fun when we gear up on embryonic assays for this stem cell regulation that we're interested in. So those are the two major things I see us doing.

VAN BENSCHOTEN: And how about in ten years?

JOHNSON: Hmm. I don't know.

VAN BENSCHOTEN: Okay. The next set of questions is about biomedical research in terms of ethics, technology, and public policy, and then we'll head back and finish up with the composition of your lab, as well. Do you have any patents?

JOHNSON: No, I don't have any patents.

VAN BENSCHOTEN: All right. And do you believe patents are good for academic science?

JOHNSON: I guess in general, I think the idea is good. I think that in today's environment of patenting, way too much letting the lawyers work it out, it's not good.

VAN BENSCHOTEN: Do you see that as a trend that's growing or a possible danger? For instance, as you know, the patenting of gene sequences and their applications—is this the direction that we should be going?

JOHNSON: So patenting of gene sequences is clearly a problem, and I think that that's going to be resolved. I suspect it will be resolved. Clearly, the Patent Office didn't know what they were doing when they started to allow just sequence to be patented. But, you know, the way we do medicine in this country to develop products to market, which actually do some good, and recently we've seen amazing progress. The first substantial progress in people using their knowledge to develop new ideas that bring drugs to market, I see a lot of that happening, and that's not going to happen without patent protection. So it's really annoying in academics, but it's essential if we're going to actually make progress. Or we could socialize every aspect of medicine in this country, but that's not going to happen, nor would it work.

VAN BENSCHOTEN: I was just reading an article in *The Scientist* about how, I think, two-thirds of the R & D [research and development] now in the U.S. for biomedical research comes from private sources now. How do you feel about the rise of industry labs and sort of the

increasing privatization of scientific research?

JOHNSON: I think I actually have thought about this. I have no problem with companies trying to develop ideas into drugs, into therapies. I have problems when companies— And when they do that, they have to protect their ideas, and, you know, as a scientist, we have to have open flow of ideas, but that's a different set of rules. I have problems when they try to play both sets of rules and they try to say, "Okay, we are doing science, and we'll publish a little bit, but not enough, and you don't actually have access to this. What we've published is really just a news flash so that we can get more stocks."

VAN BENSCHOTEN: So either no disclosure or full disclosure?

JOHNSON: Let's not sew it up so tightly. None of us disclose all of our data. It just can't be done. We have to decide what's interesting, and we can tell in a story now and what has to wait.

VAN BENSCHOTEN: Right. Well, I think part of the fear, just to take an example, for instance, with stem cell research, is that with the growing privatization, maybe, of that, there's going to be less oversight. Whether you agree that oversight should exist or not is another thing. [mutual laughter] But the fear is—

JOHNSON: [laughs] Boy, if it could get me out of [unclear], I would jump to industry.

VAN BENSCHOTEN: Have you ever been tempted, by the way, to jump to industry?

JOHNSON: Not to jump to industry. But some postdocs who aren't in my lab at Washington University are starting a company, and I'm joining them in it as their scientific advisor. The notion of the company is regenerative medicine, is to do genetic analysis like we do in our melanocytes on all variety of stem cells, and then from the analysis, develop therapies. And we don't have any patents, so I can't say any more.

VAN BENSCHOTEN: [laughs] Smart.

JOHNSON: But if we had a patent, I could tell you the kernels of the ideas.

VAN BENSCHOTEN: A question about the history of science. First of all, did you take any

history of science classes in your education?

JOHNSON: Gosh, did I? I don't think I have taken a formal history of science course.

VAN BENSCHOTEN: How useful do you believe to your work and research would be knowing something about the history of science, say at that earlier stage, but even now?

JOHNSON: You know, gosh. Who would you say was the first scientist?

VAN BENSCHOTEN: That's a good question. It'd probably be some Greek.

JOHNSON: Yes. I guess I might say I didn't believe they were scientists, though they were mathematicians. What I call science, really making up models and then testing them, experimental science, to me, it's someone like Galileo. When you read about him, you go, "This is real science." He would flourish today, and he would recognize— If we went back to then, many of us modern biologists, we would click just like that. It would be amazing. And it's so fun to read about how he does, how he approached his problems. I think it would be really important for a lot of people to read more of how did Galileo develop his ideas, how did other scientists develop their ideas. This is essentially what you guys are trying to do for some modern cohort. Obviously I believe it's important, or I wouldn't be here.

[END OF TAPE 3, SIDE 1]

VAN BENSCHOTEN: Do you want to add anything else to the history of science, its importance to the development of science, scientists?

JOHNSON: No, not now.

VAN BENSCHOTEN: What effect has technology and technological innovation have on your work?

JOHNSON: It lets us peer deeper and work faster, so that's what we all want to do. We say technology drives science. A lot of people say that. I think that that's wrong. I think that science drives technology. It's when people have questions that they then go off and develop better ways to answer their questions.

VAN BENSCHOTEN: As you know, the development of technology is sort of rushing along. It's very difficult, I think, to stay up. How, for your own work, do you handle that problem of sort of a growing obsolescence of technology and this constant—

JOHNSON: [laughs] Well, I still use the same word processor program that I used when I converted to [Apple] Macintoshes in 1991. So I guess I could tell— Well, I just stick my head in the sand. But that's a trivial example.

The things that will actually help the research, like microarrays or better methods for mapping or better ways to see individual cells in the fish, I explore as hard as I think I can. So the lab's going into microarrays now. We're developing single-nucleotide polymorphisms for most of the genes in fish between my inbred strains. We're going to try to develop an efficient way to identify promoter regions for driving GFP [green fluorescent protein] fusions for making transgenic fish. We're going to combine the genomics of zebrafish and fugu to do that. Zebrafish have large promoters that are hard to manipulate, but this other species of fish, it's not too far distant evolutionarily. It is a fish, so presumably the promoters are going to recognize many of the same things and respond and express in many of the same cells. Those promoters are quite small, so we're getting ready to take advantage of all of our databases on zebrafish genes in whatever available sequence we have to then automatically start culling promoters so that we can make our transgenic fish from that. So we try to use relevant technology and push it in my lab, but on irrelevant technology like what word processor we buy—

VAN BENSCHOTEN: You often hear about a biomedical revolution taking place, even a biological revolution. From where you stand, do you believe there's a revolution under way, say, in the last ten years?

JOHNSON: No, not the last ten years. I think we're starting to reap the benefits of the revolution in genetics from the sixties and seventies, but that was when I think the revolution was, when we really understood how to do genetics.

VAN BENSCHOTEN: What do you believe is sort of the next great challenge, the great challenge for biological research?

JOHNSON: We still have to cure cancer, so that's clearly a challenge. And a lot of people are interested in it, so let's not discuss that. There are all sorts of cognitive challenges, how the mind works, and I'm not at all qualified to think about that.

For my field of biology, one of the questions that really I don't know how to solve yet,

so I'll say it is the next big mystery, is how do cells know their current status and their neighbor's status? Or even how does the stem cell know that if it's all in the stem cell? So that when some cells die or disappear, they can be repaired, and repaired with cells that know the appropriate positional information. Okay?

We know that cells have positional information. Exquisite knowledge of their positional information from ancient—not so ancient, because the woman who did this is still alive, but regeneration work in newts, where they found that you can— These are very difficult experiments to describe. But they could get evidence by putting cells of different presumptive positional values next to each other, the growth and regeneration would, instead of just regenerating from here on, they would [have] intercalatory regeneration to fill in all the presumptive missing values.

So presumably, cells that look to us identical know precisely one's here [indicates a place near his wrist] and one's here [indicates a place near his elbow], and if we put them together, they know that difference and then fix it. So how do they know that? And that's all part of this idea of how do we maintain the integrity of our bodies? What is the actual memory that cells have, both for themselves and for their community? That's the mystery. That's sort of getting mystical, too.

VAN BENSCHOTEN: Well, it's interesting you say that, because many of the early scientists had gotten much knowledge from alchemy and early chemistry, too. So it's interesting, the sort of interplay between so-called magic and science, at least in the early stages of the scientific revolution. I'm thinking of the work of Mario Biagiolli and others.

That philosophical digression aside, competition in science. Is competition, from your point of view, generally good for science?

JOHNSON: Well, sure. Competition's always good.

VAN BENSCHOTEN: Always?

JOHNSON: Well, within reason. But, yes. It's clearly abused. There are clearly scientists who don't generate their ideas. They look for "How do I get the next *Cell* paper?" Or *Science* paper, and then work for that. And that's a terrible aim. But the solution is much easier than eliminating competition. It's eliminate *Cell*, *Science*, and *Nature* and journals like that. Easy. Let's do it.

VAN BENSCHOTEN: Right. [laughs]

How competitive is your own field in which you work?

JOHNSON: So there is competition in genomics. The other fields, pigment pattern and fin growth and fin regeneration, there's really no competition. We have three or four labs in zebrafish pigment pattern, and we all have to talk to each other just to make sure that we're not overlapping too much. We really do share reagents and see that each other's work is valid, replicable, but we come to agreements, formal or informal, not to work on each other's stuff. So I guess competition's good as long as you don't have to do it. In fin regeneration and fin growth, it's the same thing. There are really three or four labs, and we're all talking.

VAN BENSCHOTEN: So a lot of collaboration?

JOHNSON: Cooperation rather than collaboration.

VAN BENSCHOTEN: Okay, because that was my next question, the importance of collaboration, and collaborations in your own lab. Do you have collaborations going on?

JOHNSON: You mean, outside my lab?

VAN BENSCHOTEN: Yes.

JOHNSON: I have collaborations in genomics, because that's a big, integrated field, and it takes lots and lots of people to generate the data.

In pigment pattern, I don't have any collaborations. We go off wherever we think we're interested, but we don't collaborate. We have a physician [F] who we're formally collaborating with, because she's taught us how to use a laser. So I guess that's collaboration. But that aspect of it's over, and we just have to write the paper.

In fin regeneration, I'm collaborating with some people who, they came to my lab, did a mutant screen, learned how to do mutant screens and work on zebrafish, and they got some mutants. And now we continue the collaboration, but it's about to end, this formal stage is about to end, of analyzing the mutants that they got. They've done a great job of analyzing and cloning some of these mutants, and after that we won't have formal collaborations. We're going to continue to talk to make sure we don't step on each other's feet.

I think I find I personally prefer to follow directions that other people aren't doing, so I don't collaborate much.

VAN BENSCHOTEN: Some have argued that before, let's say, you receive tenure, that if you collaborate too much, that can endanger the process. What's your own view on that?

JOHNSON: What I tell postdocs leaving my lab, and that sort of depends on the job, that really they don't want to be seen as continuing to collaborate with me, because they need to be viewed as independent. So the first postdoc who successfully left, he wrapped up a couple of papers after he left, but really he's completely on his own. We just now agreed, but he'll be on his own for three years before this happens, to write a review together. That's not collaboration; that's just a review.

I have another postdoc who's leaving next month, and she's not as strong. She's going to a teaching college, and they don't view that she has to be completely independent. They just view she has to be productive, and we will probably have to collaborate for several more years on projects to finish them up. Because of her position, I don't feel it would hurt her to have my name on her papers, where the first postdoc, it clearly would have hurt him to have my name on his papers. So that's half of the answer.

The other is, so if I was collaborating with people who weren't my mentors before I got tenure, would that hurt me? They clearly want to see independence. So you can collaborate with people as long as you show that you're clearly leading in some of your fields. If you're only a follower, it's not going to fly at a place like Washington University [School of Medicine].

VAN BENSCHOTEN: The next question gets back to competition. Have you ever been scooped?

JOHNSON: Oh, yes. So the first time I was scooped was when I was trying to take somebody's published data and draw conclusions from it, and I did. It was the identification of the neurofibromatosis 1 gene. So they had published part of the gene. This was actually their second publication of part of the gene in *Science.* And they didn't know what they had, so why it was a *Science* article was beyond me. But from their sequence, I could tell what the gene was, because a database that I had access to had identified it in yeast; and from its yeast function, we knew what it was doing. And so from that, just this extra hundred or two hundred bases in this *Science* report, we could tell the whole story.

So I wrote that up and sent it to *Cell,* because *Cell* at the time was the only place that was doing this sort of homology grabbing. The editor, Ben [Benjamin P.] Lewin, sat on that for two weeks, published the group that— There were two groups that were intensely collaborating on it, and each of them managed to get a little bit more of the sequence of this horrible gene. It was quite difficult to clone. And then they got the same story. So whether I got the same story before or after, I'm not sure, but I do know that I got scooped because the editor of *Cell* sat on

this for two weeks, until it was safely in press, before he then wrote and said, "I'm not accepting this," when if he had immediately rejected it, I could have sent it to *Science,* and someone else did that several weeks later. That's one.

Another was, one of the guys that I worked with at [University of] Oregon I started— And this doesn't bother me so much, because his paper was so bad. I had started a project on difference between male and female meiosis, the difference in recombination rates along the chromosomes. I had been collaborating with him as I was a postdoc. He ran the mapping lab. He clearly knew that I had started this stuff at Oregon, and I had presented to the group there, the fish group there, that I was working on this project. And I was even ready to write up some of this when I was at Oregon and put him on the paper, and when I did it, he said, "Well, I don't want you working on that project because I just hired a postdoc to do that."

I'm going, "What the hell is this? He's taking my ideas."

So many years later— I continued to putter on this. Many years later, which means this spring, they finally published this incredibly bad paper showing maps of male meiosis in zebrafish, with no conclusions of what it meant. So I don't know if I'm mad that I was scooped or mad that I was scooped with such a horrible job.

VAN BENSCHOTEN: The next set of questions deals with biomedical research and ethical considerations. We have dealt with, clearly, some ethical considerations. Given the limited resources in your lab, and in every other lab, for that matter, in the U.S., and the strings that are attached to those resources to a certain extent, what criteria do you use in determining one research project over another?

JOHNSON: Gosh, I don't know how to answer this. Whether we can actually achieve it, what we want to do.

VAN BENSCHOTEN: That's feasibility.

JOHNSON: Whether it's feasible and whether it's interesting.

VAN BENSCHOTEN: What criteria— This is sort of taking it up another level, outside of your own lab. What criteria should we be using nationally to determine the direction of science? Or is the present system fine? Don't fix it if it's not broken.

JOHNSON: The present system has a lot of great points to it. We have this notion of investigator-initiated research funded by the NIH [National Institutes of Health], the RO 1s, and

the idea there is that if an investigator is incredibly interested in an idea and willing to pursue it and can convince people that he's going to do a good job and it's going to be sound, then it's worth funding, because, you know, we do self-select what we're going to study. We don't sit there and study incredibly stupid things, no matter what some of the popular press says. It may appear stupid if you give a humorous slant to it. And this process has been an incredibly valuable way of doing science.

What I find doesn't work very well is when the NIH tries to say, "This is where we need to put resources," and then they put out program projects or RFAs [request for applications]. And I'm guilty of participating in both of these and have benefited quite a bit, but I think that it ends up putting resources on not quite as good science and science that otherwise would have been done, but with more flexibility by an individual researcher.

VAN BENSCHOTEN: Have there been recent projects like this, that you know of, that bear out what you just said?

JOHNSON: Yes. I'm going to get into real trouble with zebrafish workers. The last big round for zebrafish— So zebrafish is benefiting from the NIH really targeting zebrafish work. Their first big effort was the genome resources, and possibly we would not have, quite probably we would not have done as well as we had done. I would not have written grants to quite as big a project as I had done. I might not have done any of it, and then maybe nobody would have done it. The type of gene discovery EST [expressed sequence tag] project that we did, you have to be associated with the Genome Center to really do this well, and I'm the only zebrafish worker really associated with the Genome Center. Okay. So perhaps that was successful, though I'm not quite confident that we, and they, always spend the money in the best way.

The next thing was, some of the zebrafish workers were complaining that they could not get their grants funded that were based on mutant screens. So we had a special RFA for mutant screens in zebrafish, and I really disagree with this. I think that any— I find that I can write a mutant screen based on a hypothesis and it will get funded. It will do very well in study sections, and the ones that don't do well, it's because they don't have a hypothesis. They haven't demonstrated that they know how they're going to study these mutants. They're just saying, "I'm going to do a mutant screen looking for embryonic mutants that are missing something or other," but we don't know what they're going to learn, and they don't do well. But all grants don't do well if they can't give some hint at what they're going to learn.

So I think we actually wasted a lot of money there. The good mutant screens were going to be done one way or another. They would have been incorporated into fundable grants.

VAN BENSCHOTEN: It would have taken care of itself.

JOHNSON: And it would have taken care of itself.

VAN BENSCHOTEN: What causes these projects to be funded, then? I mean, is it politics, then, that's behind this?

JOHNSON: So we're both guilty, both the zebrafish community has learned to be a pretty good lobbying group, and the other is the structure of the bureaucracy at the NIH. So they have an intramural budget that both does their own research on that campus, but then they have program officers that are trying to develop their own research programs without getting their fingers wet. So they think that they can direct a project through an RFA and have a bunch of projects doing something for them. This is actually a very dangerous trend that we're doing much more of in NIH now.

VAN BENSCHOTEN: There was a recent article; I believe it was in *Nature.* We talked a little about the NIH and how it operated, and that suggested that there should be a major overhaul of it to sort of trim it a little bit, even though it's budgeted, and I think it's growing by 3.5 billion this coming year. I think altogether now there are twenty-seven centers and institutions. I know that Harold [E.] Varmus is very important in trying to push that, as well. What is your own view about the NIH and how it's configured? You've already talked a little bit about that. That's why I've thrown this in.

JOHNSON: So the "different institute" argument of Varmus I don't quite understand. We have a lot of institutes. Many of them are focused on organs instead of mechanisms. What we will learn in melanocyte stem cells will be, presumably, applicable to every organ system. So for basic biology, the organ system-based institutes don't help. But we have an institute for that, general medicine, and general medicine, I think, is probably the crown jewel of NIH. But clearly there's a need to study the organs in the same way that the doctors treat them, so I don't think I have a clear problem with it.

VAN BENSCHOTEN: Again, this is connected with the question about who should be signing off on projects, research agendas, at least the national science agenda. Take, for an example, stem cell research. As we know, there's a great brouhaha about who should have oversight of that and what the government's role should be. What is your own view of stem cell research?

JOHNSON: I think I have some qualifications. So in basic research, we can do the experiments in animal systems with no need for any additional oversight. There's nothing new here, except the knowledge that we're going to gain. But there's no new ethical dilemma occurring in animal work.

Clearly, there will be ethical dilemmas working with people, and we would love to be able to— So I've cast this argument as the very conservative, okay, maybe there is this thing in adult stem cell, which is what I work on, so I'm very uncomfortable being on the side of the conservatives in Congress, and that all we need to be able to do is understand and take advantage of adult stem cells, and we don't need an embryonic stem cell. Perhaps that's possible, but it's very shortsighted. The promise of being able to isolate something like an embryonic stem cell that in mouse ES cell work has proven very, very powerful for being able to generate many different types of cells and reconstitute types of tissues suggests that we really have a good chance of learning how to reconstitute tissues. If we could then reconstitute a tissue and put it back in you to replace your kidney and you didn't have to be on drugs the rest of your life that otherwise debilitated you, that would be a fantastic thing. A little surgery, snip, snip here, and you put back in the kidney.

So to do that, we need a large number of different haplotypes of the molecules that the immune system recognizes. I don't know, I think someone suggested to me, when I asked them this question, perhaps 16,000 different combinations of the immune system would cover most of the human populations. So we need a lot, so we can't really be limited to one human stem cell or six human stem cells could then do it. We're going to need quite a few if this is working. So we can't let the government back us into a narrow opportunity when the opportunity could be really amazing. That's my view.

VAN BENSCHOTEN: You know how the debate worked itself out. Who should have oversight on this decision to do this?

JOHNSON: Well, actually, I have no idea, because I'm not interested in the day-to-day manipulation of human biology. Who should have oversight?

VAN BENSCHOTEN: [President George W.] Bush set up a council, a Council of Ethics, a sort of science advisory committee, obviously. But ideally, if, let's say, there were this imaginary commission, who should be on that commission, not only to make decisions about stem cell research, but other critical decisions, you know, genetics?

JOHNSON: [laughs] Gosh, not politicians. So the issues are making sure— Because to get stem cells, we have to have embryos, and that's a real issue. The next issue is, are we going to modify stem cells to make people, not organs, but people? I would come down firmly that that's just wrong. Anyone who's thinking that they're going to genetically modify and make new people, just the experimentation that would be involved before we could do it is mind-boggling, how much suffering that would cause. And then the notion of the— Now we really are controlling our evolution. Those are both, I think, insurmountable obstacles. So there shouldn't be oversight committees for that. It should not be an issue.

Where embryos that are used to generate stem cells come from is clearly something that is a problem, that there are two viewpoints that are both right; and therefore there need to be committees that solve this, and I think almost anybody is qualified for that question.

VAN BENSCHOTEN: A question about public policy, and it's connected with this. As you know, the Pew [Charitable Trusts] has started up a new program to clarify what it considers to be the true issues in biomedical, in especially genetic research, and how they might be addressed, where there's a little bias and maybe as little political heat as possible. Should scientists like yourself be involved in matters of public policy regarding these controversial issues, and if So in what capacity?

JOHNSON: Scientists should be involved because they have an interest and they can express it. People who do have interests should be involved, and then people who have expertise should be involved, but it shouldn't be the exclusive area of scientists if it's an ethical issue.

VAN BENSCHOTEN: What should that role be and how should it be embodied?

JOHNSON: I don't know.

VAN BENSCHOTEN: Does your own institution encourage you and other scientists to participate in public policy debates like the ones we've just talked about?

JOHNSON: Does it encourage us? No. I think that we have the freedom to do whatever we want, but they're not sitting there saying, "Here's this ethics council in Washington, and we want to make sure someone from Wash U's involved." They don't do anything like that. I don't know if anyone does that.

VAN BENSCHOTEN: With regard to public policy and informing the community, what is the average scientist's responsibility? We've already listed your duties, the average PI's [principal investigator's] duties. Should this be one of them?

JOHNSON: Oh, should it be a responsibility? No.

VAN BENSCHOTEN: So it should be entirely voluntary?

JOHNSON: Yes. It's not science, public policy. Telling people our results is an essential part of science, but formulating how science is used is what the community has to do; and scientists then have a different responsibility as a member of the community, but not as a scientist.

VAN BENSCHOTEN: Let's shift gears a little bit. Talk a little bit about your lab, questions about gender and about ethnicity, as well. How many people are in your lab, first of all?

JOHNSON: It's close to twenty.

VAN BENSCHOTEN: And how many women are there in the lab?

JOHNSON: Right now I have— I'm going to divide this. I have seven graduate students and postdocs, and two of those are women. Let's make sure that's right. There's a rotating student, and she's a woman. So then the others are obviously men. For technicians or other technical, everyone who's not a graduate student or postdoc, I have one, two, three, four, four women, and one, two, three, four men. I think that's right. That's not quite twenty. I'm not counting undergraduates.

VAN BENSCHOTEN: And what is the ethnic breakdown in your lab?

JOHNSON: I have a graduate student and a postdoc from Taiwan. I have one black technician. And I think everybody else is Anglo-American, American.

VAN BENSCHOTEN: In your own department, how many women PIs are there? You don't have to give us an exact number, but sort of a ball park.

JOHNSON: I think we have seventeen people on the tenure track, and we have three of them are women.

VAN BENSCHOTEN: Given your experience in grad school and throughout your science career as PI, as well, do you feel the playing field is level between men and women who are pursuing biomedical research?

JOHNSON: For pursuing biomedical research, yes. For life, no. I think women have more opportunities.

VAN BENSCHOTEN: Women do?

JOHNSON: Yes. It's easier for them to say, "I don't want to do this. I'm just going to do something else."

VAN BENSCHOTEN: Are there any other benefits that they have, that you feel?

JOHNSON: No. I honestly think the opportunities in science are just about equal, or at least in biology.

VAN BENSCHOTEN: Do you believe women do science differently than men?

JOHNSON: No, no.

VAN BENSCHOTEN: African American and Latinos are two, at least, underrepresented groups in science, as you know, especially at the PI level. How specifically do you believe might these underrepresented groups be encouraged to become more a part of biomedical and biological science?

JOHNSON: Well, we work very hard trying to encourage these minorities into the academic track. It's going to be very hard, and it's going to be very hard for a long time. In part, it's going to be because as science is essentially a middle-class and upper-class endeavor, and very few poor people get into science from any ethnicity. If you're poor and can come up and have the ability to achieve, then it just seems that you go into something that's going to make money. So I suspect that's the problem, that when we can recruit minorities out of the lower class, science isn't their first choice. That's how I perceive the problem. I don't know how to fix it.

VAN BENSCHOTEN: What is the best part about being a scientist?

JOHNSON: Exploring ideas.

VAN BENSCHOTEN: And what is the least pleasant part?

JOHNSON: Of managing. Because now I'm a lab manager, and I have a lot of people. That's the least pleasant.

VAN BENSCHOTEN: What one or two measures would help improve the quality of science in the U.S. today? We've already mentioned some of those, I think, at least how the NIH might be improved.

JOHNSON: To improve the quality of science. It's going to start in science education. We need to do a better job of teaching the facts in high school so that in college we can start teaching them how to ask questions, because we still have a remarkable number of investigators who don't know how to ask questions. You know, there aren't going to be very many systematic solutions.

VAN BENSCHOTEN: Let's talk about the Pew [Scholars Program in the Biomedical Sciences] grant. What were the consequences in your lab of the Pew grant?

JOHNSON: It gave us some more money early in developing my lab, and that was really important. That's not going to be for all the Pew people. Some of them get them several years into their career, but I had one essentially right away. So as I got my first RO 1, I also had a Pew, and that was very useful. It gave me a lot of flexibility. That's one.

Two, they're sort of like the stamp of approval. All of a sudden, a lot of very prestigious people said that I was worth watching, and that was very important. I could see immediately that that was having an effect. I don't know how, but I could.

It got me to the Caribbean for a week every year, and that was important. I don't really take much time off. I think that's it. And I'm not joking when I say it got me to the Caribbean. I thought that was an incredibly important contribution of the Pew.

VAN BENSCHOTEN: I want to return to the gender question. Some would argue that there is still in science, and in biological science, this "old-boy network." Do you sense that that still exists in science?

JOHNSON: I don't see it as a gender problem. There is an "old-person's network," and it can be men, women, or both, and it's clearly there. Is it really a problem? It's a problem if you wanted to publish in *Science.* It's got to go through this old-boy network, which that's not a gender term as I use it. So no, I just don't see it in my field that gender is an issue.

VAN BENSCHOTEN: Maybe the better way to say "old boy" would just simply be the science establishment then.

JOHNSON: Yes.

VAN BENSCHOTEN: Other people would say, too, though, that women, once they become PIs and if they choose to have children, are at an inconvenience, a disadvantage, than, say, males, that the clock's still ticking tenure-wise, that when they go to conferences, let's say, accommodation is not made for children. Nursing rooms, for instance.

JOHNSON: So that would be so easy to solve. Sure, accommodations like that should be made. They're incredibly easy to solve. The idea that women aren't getting tenure because they may need to take it a little slower sometimes to have a baby, I don't think is right. I think that, one, most people do get tenure, though people I've known who haven't gotten tenure— We've had two women in my department who did not get tenure who were up for tenure. One of them withdrew before she was coming up. She decided she really didn't want to be in a medical school. She wanted to teach. She probably wouldn't have gotten tenure. But she didn't have kids. She didn't pursue research. She didn't have a well-funded lab and lots of papers. The other woman was single, no family. She just wasn't a good scientist. It had nothing to do with family.

[END OF TAPE 3, SIDE 2]

VAN BENSCHOTEN: As I said, we've gone through the question set. Is there anything that you'd like to add to the record?

JOHNSON: No.

VAN BENSCHOTEN: All right. Thank you very much for allowing me to sit down with you. I appreciate it.

JOHNSON: Okay.

[END OF TAPE 4, SIDE 1]

[END OF INTERVIEW]

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