CHEMICAL HERITAGE FOUNDATION

TOSHIO TSUKIYAMA

The Pew Scholars Program in the Biomedical Sciences

Transcript of an Interview
Conducted by

William Van Benschoten

at

The Fred Hutchinson Cancer Research Center
Seattle, Washington

on

24 and 27 October 2003

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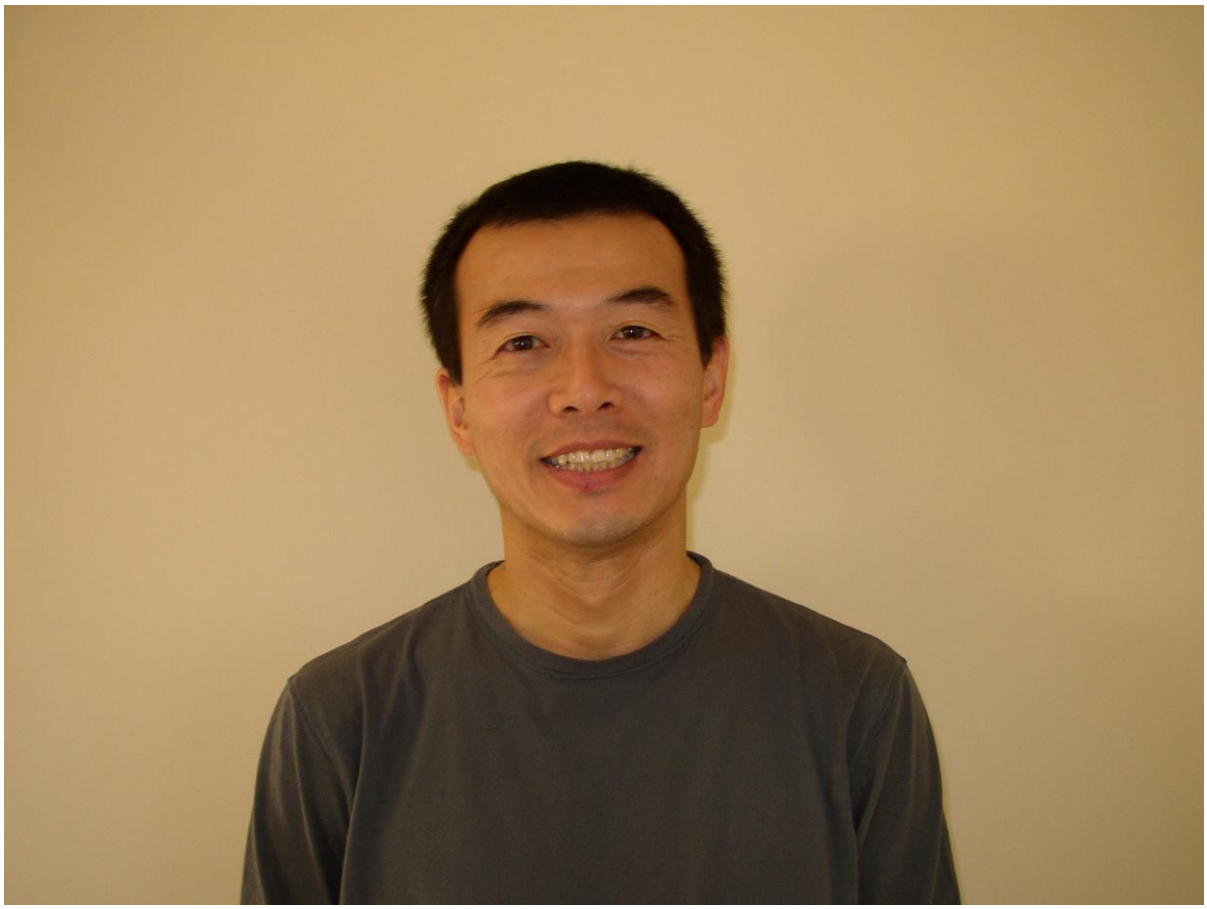

Toshio Tsukiyama

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D.V.M., Obihiro University of Agriculture and Veterinary Medicine
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Professional Experience

National Institutes of Health
Postdoctoral Fellow in the laboratory of Carl Wu

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Selected Publications

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ABSTRACT

Toshio Tsukiyama was born in Chiba, a prefecture near Tokyo, Japan, the second of two children. His father began as an engineer in a company that built chemical factories, but he eventually became an executive. His company exported its factories, so Toshio's father travelled outside Japan a great deal. For that reason and because he was, as Toshio describes him, a typical Japanese male, the family did not interact much with him, and he did not discuss his work at home. Toshio's mother was a housewife and the children spent part of each summer visiting grandparents.

Toshio's sister wanted to be a veterinarian and wanted to get away from home, so she enrolled at a vet school on Hokkaido, the northern-most island of Japan, Japan's last frontier. Influenced by her, Toshio also went to Hokkaido, but to a different school, Obihiro University. His sister's college turned out to be better in basic science, and she switched to biochemistry. Again influenced by her, Toshio decided to go into scientific research. Also, one of their aunts was a chemist and an uncle a physicist, so they had been exposed to science for a long time. While in vet school Tsukiyama met the woman who is still his girlfriend; she currently lives in California, and she and Toshio take turns visiting each other.

While at vet school, Toshio read an article he found very interesting, and he decided he wanted to study with its author, Ohtsura Niwa, at Hiroshima University. He met Niwa and persuaded him to accept him as his student. Niwa had obtained his PhD from Stanford University, so he was familiar with the American course of study; he made Toshio read and present books and articles, something the Japanese did not do. He also influenced Toshio to come to the United States for his postdoc, which he did at Whitehead Center for Biomedical Research at Massachusetts Institute of Technology. There he worked on chromatin remodeling in Carl Wu's lab.

The Fred Hutchinson Cancer Research Center in Seattle, Washington, hired him as an associate member. He also has an affiliate assistant professorship at the University of Washington. He continues his research in molecular biology on the regulation of chromatin structure and its effect on cellular processes. He likes to read, to do outdoor things with his girlfriend (currently gardening), to teach, and to think about—though to leave to others to adapt—the practical or clinical applications of his research. Upon hearing that Toshio was going to the United States to study, a friend told Toshio that he would not come back to Japan, and Toshio is still here.

UCLA INTERVIEW HISTORY

INTERVIEWER:

William Van Benschoten, Interviewer, UCLA Oral History Program; B.A., History, University of California, Riverside, 1990; M.A., History, University of California, Riverside, 1991; C.Phil., History, University of California, Los Angeles, 1995.

SETTING OF INTERVIEW:

Place: Tsukiyama's office at Fred Hutchinson Cancer Research Center.

Dates of sessions: October 24, 2003; October 27, 2003.

Total number of recorded hours: 5

Persons present during interview: Tsukiyama and Van Benschoten.

CONDUCT OF INTERVIEW:

This interview is one in a series with Pew Scholars in the Biomedical Sciences conducted by the UCLA Oral History Program in conjunction with the Pew Charitable Trusts' 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 Tsukiyama to obtain written background information (curriculum vitae, copies of published articles, etc.) and agree on an interviewing schedule. He also reviewed documentation in Tsukiyama's file at the Pew Scholars Program office in San Francisco, including Tsukiyama's 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.

Tsukiyama did not review the transcript. Therefore, some names remain unverified.

Carol Squires prepared the table of contents and TechniType Transcripts compiled the guide to proper names.

TABLE OF CONTENTS

INTERVIEWEE: **Toshio Tsukiyama**

INTERVIEWER: **William Van Benschoten**

LOCATION: **Fred Hutchinson Cancer Research Center**

DATE: **24 October 2003**

VAN BENSCHOTEN: This is tape one, side B. I am with Toshio Tsukiyama. Did I say that right?

TSUKIYAMA: Yes.

VAN BENSCHOTEN: Good. Today is October 24th, 2003. What is your full name?

TSUKIYAMA: My full name is Toshio Tsukiyama, and, of course, in Japanese it is pronounced just a little differently, but that's how it goes in English.

VAN BENSCHOTEN: Where were you born and when?

TSUKIYAMA: I was born in Chiba prefecture, which is right next to Tokyo, on October 15th, 1962.

VAN BENSCHOTEN: So you recently had a birthday. Happy birthday.

TSUKIYAMA: Yes, thank you. Forty-one. People say I don't look like it.

VAN BENSCHOTEN: You don't.

TSUKIYAMA: I still get carded when I buy beer, occasionally.

VAN BENSCHOTEN: Tell us a little about Chiba. Where is it located, and then what is the local economy?

TSUKIYAMA: So, Chiba is basically—especially the area I was raised—a big satellite city for Tokyo. A lot of people will commute to Tokyo, because in Japan it's so expensive to buy houses, especially around Tokyo area. People tend to commute more and more and more, and even though it takes easily an hour or two to go to Tokyo, a lot of people live there to commute. My father [Yasuo Tsukiyama] was one of them, even though he was not going to Tokyo, only maybe halfway to Tokyo.

Local economy—I don't know—it's like a newly created town. So right around the time we moved to the town when I was five or six years old, basically that town was created. So it was a very strange situation that almost all the neighbors had kids about similar age. So I knew all the kids around my place, and almost all the families had children about our, my and my sister's [Kyoko Kohara's] age. So it's basically a bed town. I don't know if this is [an] English expression, but people come here, come back to that place to sleep.

VAN BENSCHOTEN: Bedroom community.

TSUKIYAMA: Yes. That was it.

VAN BENSCHOTEN: Did you spend then most of your childhood and your adolescence there in Chiba?

TSUKIYAMA: Yes. Well, actually, I was born in Chiba and moved—I don't know—a few miles to that new town when I was five, and I was there until I finished my high school. I left that town when I was eighteen, so I basically grew up there.

VAN BENSCHOTEN: Let's talk a little bit about your family. If you could, maybe start with your maternal grandparents.

TSUKIYAMA: So my maternal grandfather [Sueshi Katsuki] was a teacher in a school that's almost like junior college in this country. He specialized in—let's see, I actually don't know—engineering, I think, and so he was sort of a semi-academic person, more into teaching than research, I believe. My maternal grandmother [Shizue Katsuki] was staying at home, I think, just supporting my grandfather.

They had five children. My mother [Misako Tsukiyama] is the second child. The oldest is the only son they had. He was a professor of physics in Japan. And then my mother, and my mother's next sister is a housewife. Then the other, the second youngest one, is a professor or lecturer—I don't know—right now, maybe an assistant professor, in chemistry, but she's doing more teaching than research, I believe. The youngest one died of a heart

attack recently, but she was into pottery. So it's a little untypical family, I'd say. I had a little bit of exposure to an academic setting from that side.

VAN BENSCHOTEN: Are they both still alive, those grandparents?

TSUKIYAMA: My grandfather died a while ago. My grandmother is still alive, doing well, living alone. She is ninety-something years old. Next March I will be visiting Japan, so I will see her.

VAN BENSCHOTEN: Good. How about on your father's side, the grandparents?

TSUKIYAMA: On my father's side, both have died already, but my paternal grandfather [Moichi Tsukiyama], he was already in bed. As far as I remember, he'd been in bed for a long time, because he had tuberculosis really early. So I actually don't know what he did. I'm sure I heard this from my father, but I don't remember the details.

My paternal grandmother [Haruyo Tsukiyama] was raised in a family that had been medical doctors for a long time, for generations, basically. She tried to convince my father and his siblings to be medical doctors, but my father didn't want to see blood, so he refused. So that tradition is gone, basically. I didn't have a lot of interaction with either of them, so in terms of academic connection, not much was there.

My father was the youngest kid of three, and the oldest sibling is a brother, I think, and he was working for a company. I actually don't know the details of his job. His older sister was married to another typical Japanese businessperson. Nobody in the line is in academia, I don't think.

VAN BENSCHOTEN: So, of the two grandparents, you saw your mother's parents much more then?

TSUKIYAMA: Right, because my father was just like a typical Japanese male; he was a workaholic. So in summer if we had to go to see my grandparents, they were actually living very close, but usually it's Mother who took us to the place, so naturally we would stay like a day or two with my paternal side, then like a week or two with the maternal side. So I was more familiar with the maternal grandparents, then.

VAN BENSCHOTEN: What did you children do during these visits, especially the week?

TSUKIYAMA: I don't remember details, although actually there were bookstores, rental bookstores right next close to my grandparents' place, so we used to go there all the time, rented comic books. We also did a little fishing. My sister was a real tomboy. She was very, very active. So we did all sorts of things that boys would do together: fishing, swimming. It was real fun, that's all I remember.

VAN BENSCHOTEN: It sounds like it. Now, is your sister older than you or younger?

TSUKIYAMA: Yes, two years older than I am.

VAN BENSCHOTEN: Okay, we'll get to her. We'll talk a little bit about her as well, hopefully.

Let's go back to your father, though, and talk a little bit about him. Talk a little bit maybe about his work and his character, too, his temperament, I guess.

TSUKIYAMA: Sure. So this is very typical—Japanese tradition—the job and private life are completely separate; people don't talk about their family at work much at all. On the other hand, once they come home, they don't talk about their job at all. So I actually don't know exactly what my father was doing, but I know his company was specializing in building chemical plants. They exported those plants. So my father used to go abroad very often. I think he's been to like fifty different countries or something. So he'd go to East Germany, or China, India, Russia, Iran.

And I think his job description changed quite a bit. He used to be on the engineering side. Then he got promoted. At the end he was one of the executives for the company, so he was doing negotiations with the government of the foreign countries—their clients—something like that. Basically, they would build plants for fertilizers or something like that. So, very often he was absent from our place for more than half a year. The longest was for India and China.

This was not that uncommon in Japan, I don't think, but I didn't get along with my father that well originally, partly probably because I didn't get to see him that much, but also it's not that he didn't care about kids, but I think he thought it was Mother's job to take care of the kids for everyday things. We did do baseball together and that kind of thing, but I think I had a lot more distance between myself and my father than with my mother. As I said, it's not that uncommon in Japan, and in Japan the relationships between parents and children are probably a lot more formal than in this country.

One thing that surprised me when I came here is that grown-up adults call their parents Mom and Dad, which sounded very strange to me, because something like that is not common in Japan. It's a little bit more formal.

VAN BENSCHOTEN: Is there an equivalent in English or in American for how the children would address parents in Japan, the father and mother?

TSUKIYAMA: Yes, *Oto-san, Oka-san,* would be father and mother, and there are people who call their parents Papa and Mama, because English words are very common in Japan. We used to call our parents in that way, and one day I and my sister decided this was too childish and decided not to use those words. I don't remember when it was. Maybe I was five or six at the time.

VAN BENSCHOTEN: It sounds like you were very close to your sister.

TSUKIYAMA: Yes, we are very, very close. Actually, the reason why I become scientist is probably mainly due to her, because she was always ahead of me. She's a scientist, too. She graduated from the vet [veterinary] school, and I was graduated from vet school. It was a different school, though. So I was influenced a lot.

VAN BENSCHOTEN: We'll talk more about that.

Your father, you didn't meet him very often when you were growing up. When you did meet, did you do any activities together? Did he have hobbies that you shared with him?

TSUKIYAMA: Yes, we would play baseball. We'd go to batting cages or play catch ball, because my father loves baseball. One thing that might be funny is that my father likes drinking a lot, and in Japan drinking is a lot less strictly regulated than in this country. For example, when I was five or six, I used to go to the liquor shop and buy sake for my father. Nobody cares about it. You can even buy those things from vending machines.

So when I was—I don't know—three or four, probably, my father started to train me in drinking, because he wanted me to be able to drink with him as early as possible. So when I was in junior high or high school, I was allowed to drink with my father during dinner; sake and beer.

I remember one day I was preparing for university entrance exams, which is a real big deal in Japan. A lot of people think that's the biggest goal of their life, or in their lives. I was studying, and in Japan parents would not do anything to disturb their kids when they are studying because it's such a big deal. My father came back, wanted to drink with me. I said, "I'm studying." My mother stepped in and said, "Oh, just a few drinks. Just have it." I was like, "Oh, what parents I have."

But so that was his hobby, I think, to drink with me. When he came home with his colleagues, usually they had been drinking. They were already drunk, usually, but he almost always invited me to join them, sort of showed off me drinking, because I was able to drink quite a bit when I was in high school. So that was definitely something he enjoyed, and I liked that, too.

Even though I was mentally a little bit far from my father, as I grew up more, I think I got closer to him, because I guess I'm in a similar situation. I understand more why he didn't have time to spend with us. Also, I started to appreciate that he was an interesting personality.

VAN BENSCHOTEN: I'm wondering about drinking in Japanese culture. Is it a part of the culture of the Japanese?

TSUKIYAMA: Yes, I think so. It's a very, very big part of it, and definitely big differences, I think, between this country and Japan. One is that it's publicly accepted to get drunk in public, and if you go to Japan in party seasons—end of the year or something like that—in train stations you see company executives completely drunk and sleeping on the floor and things like that, and people really don't care about it.

The other thing is people take pride in drinking, so if you are able to drink much more than the guy next to you, you feel superior. It's childish, but it's very strong. I heard it's changing a little bit, but at least when I was in, say, college, if you were asked to go for a drink by your friends or something like that, you were supposed to go. And if you're asked to drink up your glass, you're not supposed to refuse. That kind of thing.

Now I heard that younger generations are changing that. People just say, "Oh, I have family waiting for me. I'm not going to go for drinks," something like that. Actually, I don't know how true that is, but they definitely have their culture.

VAN BENSCHOTEN: How about where you drink? Where does this mostly take place, in the home or outside of the home or both?

TSUKIYAMA: Until I became drinking age, I was told by my parents, "Don't drink outside," because I would be in trouble, not because they didn't want me to drink more, just so that I wouldn't get caught. So until I graduated high school, I didn't drink outside much, even though I did drink with my friends occasionally. Even though drinking age is twenty in Japan, it's socially accepted as soon as you get into the college, which is at the age of eighteen you can start drinking.

VAN BENSCHOTEN: Does the custom apply also to women?

TSUKIYAMA: Yes. And my college was one of the worst drinking schools in Japan.

VAN BENSCHOTEN: Really. [laughs] Then you picked the right college.

TSUKIYAMA: That was not the reason why I went there, but it was good match.

VAN BENSCHOTEN: Yes, sort of the [University of California] Santa Barbara of Japan.

TSUKIYAMA: Yes.

VAN BENSCHOTEN: When people hear this, I'm sorry; I apologize for slandering Santa Barbara. [laughs] Let's talk about your mom. Again, maybe talk about her education and her work.

TSUKIYAMA: Okay. So she stayed home. I think she was a housewife when I was growing up. But for women of her age in Japan, it was not very common to work outside. It's a social thing, and I don't think it's reasonable, but it was probably a matter of pride for men, I think. The fact that their wives were working outside implied—used to imply, I should say—that the men were not bringing enough income home. So that was a trend, I think. Even in my generation it's not true anymore, so actually I don't know the details.

But my mother was a little exceptional, so she went to a junior college and got a license to teach in elementary school, I think. Well, she taught for a few years before getting married to my father, then quit her job, I think. At the time, getting married was almost equal to quitting a job. All the women were supposed to stay home after getting married.

But one thing was really clear. She was the second oldest in the family, and at the time I think that her family was not that rich, so I think she was forced not to go to full university. That's why she graduated the junior college. And it was very clear that she didn't like that, and I don't think she complained about it or anything, but it was very obvious to both of us. So I could feel that she strongly hoped that we could get as much education as we could get, because of her experience.

Then they got married and had both of us, myself and my sister. Then when I was in, I don't remember, junior high, I think, she started teaching again, not in formal schools. But in Japan—actually I don't know how it's called in this country—after kids come back from school, they very often go to private schools for an hour or two a couple of times a week. They usually specialized in something like math or English or something like that, to get

extra education, so that they do well in school.

She was one of those. I think the formal reason why she started that was because my sister was struggling with math and as it got more and more advanced, it got harder for my mother to teach her—my sister—the math. So she wanted to be able to get training, I think, how to teach my sister the math. That's how she started this, but part of that was probably because she used to be a teacher and she missed something. I don't know the details, actually. So she was doing that for about ten years, I think, and I could see she enjoyed it quite a bit. Yes.

So I don't know how much influence I got from her in terms of the decision to be a scientist, but maybe part of that came from my mother, because it's very clear that she looked up to education or educated people.

VAN BENSCHOTEN: Was that because she was saying that? How did she convey that to you?

TSUKIYAMA: I don't remember any single incident, but I think the way she talked about her brother, who was a professor in physics, or about education in general sent us message. Even though when we grew up—I and my sister—it was pretty common to go to college, so it was almost expected. I think something like 80 percent of the people went to college in Japan.

VAN BENSCHOTEN: That's a high percentage.

TSUKIYAMA: Yes, it's very high.

VAN BENSCHOTEN: How about your mother's temperament? How would you describe her as a person?

TSUKIYAMA: She's very gentle, even though I was a very bad kid. I made her upset very, very often, but when, for example, every semester I had to have meetings with teachers at schools, and almost every time they commented how gentle and nice my mother was and things like that, and that was a pretty common thing. And she's very liberal, I think, politically and also socially. That was probably the tradition of her family. I could tell very early that my paternal and maternal families are very different in terms of how liberal they are, especially socially.

VAN BENSCHOTEN: So by "liberal," you mean more interested in political parties that

want to change?

TSUKIYAMA: Or, say, in Japan, the society is very conservative, and also it's a little hard to describe, but it's very clear, depending on your social status, what you're supposed to do. So you get pressure if you're a student or if you're a professor, you're supposed to do this; you're not supposed to do that. Or because you graduated this school, you're supposed to go to this kind of company. There are a lot of unwritten rules that society expects you to do, and if you're out of that, you're considered a dropout. I'm exaggerating a little bit, but that's how it is like. So that's why people spend so much time and effort to try to go to the best college possible, because that sort of sets up the path for the rest of their lives.

But my maternal grandparents were not quite that strict on those things. That's what I meant by liberal. For example, my youngest aunt [Sanami Katsuki], who died of a heart attack, she didn't have a real job. She was doing pottery, which is not that common in Japan. So the two youngest aunts are not married, which is also not that common, and usually when a woman hits an age of twenty-two to twenty-six, they usually get tremendous pressure from their parents to get married, because it's shameful—supposed to be shame—for their parents that their daughter is not married, I think. It's a social thing, which I don't think makes any sense, but anyway. But I don't think they got any kind of pressure like that, so in that sense very, very liberal. People can live any way they wanted; that was pretty clear.

And the reason why my mother couldn't go to college was not because of her parents, but her grandparents, who were alive at the time. They were very strict. So they were great-grandparents for me. Then they died, and then I think the family got a lot more relaxed. So my mother had that kind of a tradition, pretty strongly, I think, very liberal.

VAN BENSCHOTEN: I'll ask the same question I asked about your dad. Did she have hobbies? Did she have interests?

TSUKIYAMA: When I was a kid, I don't think she was doing anything on a regular basis. Maybe she was too busy. If you ask me, maybe teaching was part of it. Those were the only extra things that she was doing other than normal household stuff.

Now, after both I and my sister left the house, she's been doing horseback riding quite a bit, which is a very unusual hobby for Japanese. I don't know why she chose that as her hobby, but she goes and does horseback riding a couple of times a week, even now, I think.

VAN BENSCHOTEN: How often do you see her? How often do you go back?

TSUKIYAMA: The last time I went back to Japan was four or five years ago. I'm not a very good son. I go back to Japan only when I'm invited to a meeting or something, when I have

reason to go back home, probably because I don't want to leave my lab. Especially after I moved to the West Coast, it got, obviously, very close to Japan. And my father retired from his job, so they visit me once a year at least, in summer, partly to see [the Seattle] Mariners games. It's a big thing for my father.

VAN BENSCHOTEN: Mariners had a good season until the very end, didn't they?

TSUKIYAMA: Yes, two years in a row they didn't make it in the playoffs, but that's okay. We always have next year.

VAN BENSCHOTEN: Right. I want to ask another question about the family. Was it a family that met at prescribed times, had meals together? What was the general feeling of the family?

TSUKIYAMA: So it was clear that my mother wished we could eat together all the time, but it was not practical, because my father was commuting for such a long distance and he stayed late. I'm sure a lot of that was basically drinking with his colleagues. So he often didn't come back until ten or something like that.

So almost always, except for weekends, I and my sister had dinner together, and my mother would eat a little bit, just to be with us, I guess. Then she would clean up; we helped. Then she would wait for my father to come back. Then they'd eat together again. That was for dinner.

For breakfast, I think my father left home earlier than we did, so I think they had breakfast together, and I and my sister would eat together again, and so we didn't eat together much at all. Then because of that, probably, on weekends my mother insisted we had to eat together, so that was about it, and that is pretty typical, I think, in Japan now. Especially because it's so difficult to live close to the workplace, fathers tend to eat alone or with their wives.

VAN BENSCHOTEN: Let's talk a little bit about your sister, and then we'll get to you. You've already mentioned that it is partly her example that made you interested in science and to go to veterinary school.

TSUKIYAMA: Right.

VAN BENSCHOTEN: Talk about her a little bit. What were her interests? Talk about the relationship that you had growing up with her.

TSUKIYAMA: Right. So, as I say, we were pretty close, and until you're like ten years old, actually, girls develop faster than boys, so on the top of that, she was two years older than I was. So she was the one to protect me when I was kid, and she was pretty strong. For example, when we played catch ball, she could throw harder than I did, and she was like the number-three hitter and the pitcher on the softball team, so she was very athletic. So I basically grew up looking up to her, and I was the kind of kid who would come home crying every other day. I was not very strong or anything, and so that's how I grew up.

Then in school, she did quite well. We grew up reading a lot of books about animals. We both loved animals, so getting a dog was a huge deal for us. We constantly talked to our parents for—I don't know—maybe five years until we finally convinced them to have a dog.

VAN BENSCHOTEN: That's a long lobby.

TSUKIYAMA: Yes, so we worked really hard.

One day I remember I and my sister had a family gathering with another family. The father of the family was my father's colleague, so we were pretty close. We had sleepovers and things like that very often. One day we had this party, and we wanted to convince our parents to buy a dog. So I and my sister decided to hide somewhere and wrote a letter—a threatening letter—which we thought, saying that we abducted your kids. "If you want your kids, buy a dog." [Van Benschoten laughs.] Obviously, that's a kids' idea, and we left the message and hid somewhere.

A few hours later, we came back, and my parents said, "Okay, if you want a dog so much, we'll buy one." And that was when we were in—I don't remember— tenth grade or something like that, I think.

So we did a lot of things together, and of course, when we went to junior high, we went to separate high schools, and then we also got busy on our own stuff. But until then, we were pretty close.

Then when she was in high school, she decided she wanted to be a vet because she liked dogs so much, and there are not so many vet schools in Japan. There's an island in Japan that's in the most northern part of Japan. It's called Hokkaido. Hokkaido has this special image for a lot of Japanese. It developed only a hundred years ago, so it's a very new place; frontier, if you will. Maybe something similar to the image people have of Alaska here, probably, that it's very different. And, as I said, Japanese society has a lot of different restrictions, but those restrictions tend to be lighter in Hokkaido, because people haven't been living there for a long time and because they have to live really a difficult life. It's a very cold place, people are more open-minded. Anyway, that was the image. So I think that was a big attraction for her. The other thing was to be away from our parents, of course. So

then she went to vet school there in Hokkaido.

Then two years later, I also wanted to be a vet, but I did not want to go to the same school, so I went to another vet school in Hokkaido, which was five hours away, probably, by driving, from her school. So being a vet was one thing, and I'm pretty sure I was strongly influenced by her decision. I always wanted to be a vet, seeing how much she enjoyed her school when I was in high school.

In Japan, you go up to vet school straight from high school, so it's not like this country. You apply to vet school when you're eighteen, and then if you're accepted, you're in vet school right away. When I was preparing for exams, she already had started taking anatomy and physiology and so forth, and I heard those stories all the time, and also the interesting college life she had. So I'm pretty sure that was a big reason why I went to vet school.

Then I wanted to be a vet, of course, when I went to vet school, and how I changed to basic research is also very strongly influenced by my sister. Actually, though, I never asked her why she decided to study or to go into basic research, but anyway, her school was stronger in basic research, actually, than for animal practice, maybe that's part of it, and she started working in microbiology.

So at the time I was already in the vet school, and one day I and my friends visited her, and I saw her working in the lab doing a microbiology experiment, and it was pretty impressive. I still remember that visit, because I never saw my sister being that happy, while doing experiments. Also, a lot of people were excited about their research. We went out for drink together, and I think that was probably one big reason why I wanted to do basic research.

Of course, my background—that I was exposed to my uncle and aunt also in academia—I'm pretty sure affected me, but probably the biggest influence came from my sister.

VAN BENSCHOTEN: Until that time, had you been in a laboratory at all?

TSUKIYAMA: I don't think so. I had been to my aunt's [Kazuko Katsuki] chemical laboratory, but—as I said—she was doing more teaching than real research, and I'd been there maybe a couple of times. So I don't think I ever saw a real laboratory until I visited my sister.

My uncle was a theoretical physicist [Shinichi Katsuki], so I don't think he had a real lab setup. He used to tease me that biology is for dumb people.

VAN BENSCHOTEN: That's inspirational. [mutual laughter] What does your sister do

now? What is her research?

TSUKIYAMA: She's working on viruses, and I think she's mainly interested in translational control of viral genes. She's in Japan in Tokyo University, sort of an assistant professor job right now, and her husband is in a separate institute studying hepatitis C virus.

Both of us ended up being basic research scientists, so my parents have to take their dog to another vet. They used to claim that that was a failed investment, because we were useless as veterinarians. [mutual laughter]

VAN BENSCHOTEN: All that money and education.

TSUKIYAMA: Right.

VAN BENSCHOTEN: Now, I have to ask this question, because I am a pet lover. What was the name of this dog that you finally got, and what breed was it?

TSUKIYAMA: Oh, it was called Muku. That was the name of the dog. So it's a Japanese dog. In Japan, it's called a Hokkaido dog, but I don't know if this is an internationally recognized name, because there are only a few Japanese dog names that are internationally recognized, like Sheba, Akita. But this was bred in Japan for a long time, and it's from Hokkaido. People used to use this kind of dog for bear hunting, so it gets big.

Actually, retrospectively, it was not a good decision to buy that kind of dog at the time, because we were still very small, and this was the kind of dog that decides that only one person is a master per family. So obviously, he chose my father as a master, so he didn't listen to us very well. As I grew up, I finally became able to control my dog a little bit, but that's not a good dog for a family like that, I think. But it was a really lovely dog.

VAN BENSCHOTEN: You read books. We were talking about how your sister and you read a lot of books. What kind of books did you read?

TSUKIYAMA: We read all kinds of books. A lot were essays. There was our favorite writer who was not a vet, but who wanted to live like a vet and wanted to be around animals. So this guy ended up opening a very big ranch, I think, in Hokkaido, that had a lot of different animals, tens of dogs, tens of cats, tens of horses, and he even had a bear, and he lived with this bear for a while.

He's a very strange person, but a lot of young people who looked up to his kind of

lifestyle used to go there and live together. He wrote a lot about his life there—his life with animals—in essay style. So we read his books a lot, and I bet that was part of the reason why my sister wanted to go to Hokkaido, because this writer was in Hokkaido also.

I don't remember. I read a lot of books. I'm still like this, but I always have to be reading something when I'm in bed or something. So I read anything. I used to read a lot. When I got into junior high school, I got into bicycling. Then I started reading a lot about bicycles, and other reading went down quite a bit. No, that was in high school. Sorry.

Then when I got to college, I started reading about cars, because I got into cars, automobiles. So then reading went down a little bit, but throughout my life I've been reading a lot, and I read basically anything. Now I like reading histories, reading about histories, but that's a recent trend, I think.

VAN BENSCHOTEN: What was the last book that you read, or what is the book you're reading now?

TSUKIYAMA: Two days ago I bought a book; it's a mystery. There's a favorite writer that I discovered recently, that's this thick [gestures], which I shouldn't have started reading, and I couldn't stop reading. I was really sleepy yesterday because of that. It's just a light mystery, just easy to read, nothing special.

I also like reading about food. I have a lot of books about food. I especially like old people who have their strong opinions about how things should be done. So for those, I don't actually necessarily care about what's written, but I'm more probably enjoying the style or the claim they're making, rather than how to cook things.

VAN BENSCHOTEN: So sort of Julia Child.

TSUKIYAMA: Yes, probably like that, yes.

VAN BENSCHOTEN: A master.

TSUKIYAMA: Yes, I've seen her a few times on TV.

VAN BENSCHOTEN: How would you describe yourself? I'm getting sort of a general picture, pieces of the picture. How would you describe yourself as a child and young adolescent?

TSUKIYAMA: Okay. So, of course, I cannot help being opinionated. As I said, when I was a kid, I was not one of those strong kids. I was not a leader.

VAN BENSCHOTEN: If I could interrupt you, I'm sorry, we're near the end.

[END OF TAPE 1, SIDE 1]

VAN BENSCHOTEN: This is tape one, side B.

You were in the middle of describing—giving a portrait of—yourself as a young adolescent.

TSUKIYAMA: Okay. I grew up as a child who was active but not like a leader in a classroom or anything like that. The school I went [to] was a local public school that basically everybody goes to there. I was never a top student in terms of academic accomplishment, I don't think.

The size of the classes was typically something like forty to forty-five. This is, again, Japanese style. Very often for midterm exams or other kinds of formal exams, they give you a rank, where you are kind of thing, which I don't think is a good idea. Anyway, it's a very, very competitive society in that regard. I don't think I've ever been in the top three in any of those tests in a class. Maybe I was in top 10 percent, top 20 percent, something like that, and I never thought—even now—that I'm very smart.

So it may not be very typical, in a sense, and I did not think I was going to be a scientist, and I'm pretty sure if I met with my friends from elementary school, junior high school, and said that I'm a researcher, they will be surprised. They'd be even more surprised if they're friends from my high school, because in high school I was one of the very bad students. My girlfriend [Riri Shibata] still accuses me. There's an album of when we graduated, and she can point out my friends one by one, because we all [were dressed] in a strange way. So in Japan, if you're a bad boy, you were supposed to wear a certain kind of look: long uniform, and hairstyle should be this way, and so on, so forth. We were all typical like that. So she can tell: "They must be your friends."

That was supposed to be one of the very good high schools, but there were four hundred students, and in tests I probably was one-hundredth in the school. Every single person knew my name, probably, because I was a cheerleader of the school. It's probably very different from this country. Cheerleaders are supposed to be the drop-outs in Japan. Yes, we did a lot of drinking and escaping from school and smoking and gambling with my friends. So I'm pretty sure my father [Yasuo Tsukiyama] was disappointed about me when I was in high school, because I was not clearly doing well.

VAN BENSCHOTEN: But you didn't drop out?

TSUKIYAMA: No, I didn't. I was not doing that badly, and I knew that I wouldn't do that. But part of that, too—it's childish—but I did not want to be what my father was hoping me to be, I think, and it's very clear that my father wanted me to go to the best school possible as a college. At the time, I was very strongly negative about that kind of thinking, so I wanted to be different from what my father wanted me to be, I guess. That was part of it.

VAN BENSCHOTEN: What was the craziest thing you ever did?

TSUKIYAMA: Craziest thing? So even though I was a bad child—bad boy—in high school, I had a policy not to do certain things, like threaten people to get money, steal things, do illegal drugs. I was not doing those things. I don't know the craziest thing.

This might get a little long, but anyway. So one day most of my classmates and I were very late to a class in high school because there was something real fun outside, I think. So we all came back late, and the teacher of the class happened to be the one that we all hated, because he was very nasty and unfair. He liked punishing students.

So usually at the beginning of the class, the teacher called the names of students one by one and marked whether that student was in class or not. He started doing that. He knew exactly who came in late. Then he started skipping those people who came late. So, "Okay, Mr. Suzuki, oh, he's absent." He's there, but because he knew that we all came late, he started skipping those. We didn't make any points that he's ignoring us. So we started to get pissed off.

When he came to my turn, he forgot I was late, so he called my name. I said, "Oh, Mr. Tsukiyama is absent." I said that, and people cheered for me. Then he went on. He was embarrassed, but then he kept going.

Then after class started, I got up. I said, "Oh, because we're absent, we should just, you know, go outside." Well, we first started sweeping the floor, just to make noise, because we were not supposed to be there, and we did the cleaning while he was doing teaching. Then we all went outside, but we declared we are going out because we are not supposed to be there. And that was quite popular afterwards, because we all hated him. That's one thing I remember.

I don't know. I don't think I did a lot of crazy things. When I was in junior high school, we all carried—I don't know—a teacher's small car into a corridor of the school. That kind of thing we did a lot.

VAN BENSCHOTEN: So, lots of pranks?

TSUKIYAMA: Yes, yes. I was one of those that did those things a lot.

VAN BENSCHOTEN: Looking at your socks, was, maybe, another thing wearing clothes that didn't match?

TSUKIYAMA: Oh. [laughs] Because I live alone, I hate matching socks, and after I wash my clothes and dry, I dump that thing [with clothes] onto the floor of my bedroom, and I decided not to care about matching socks. So to save a few minutes every morning, I just pick whatever is close to each other. Yes, I know. People are used to it.

VAN BENSCHOTEN: Yes, I should just say, because people are not going to notice from the tape, but one sock is red, white, and blue; it has stars on it and sort of a nice little hem there. Then the other one is green—light green—and flesh-color toned. Anyway.

TSUKIYAMA: The thing is, yes, I like colorful socks. So if I don't care about matching socks, there are three ways to go. One is to buy the same socks, so that they all match. Number two, don't wear socks. Number three, just don't care about matching socks. I decided to take the third path, I guess.

VAN BENSCHOTEN: I think I've gone the first route. I buy socks that are all the same color, more or less, and then I don't have to worry and just mix them all.

TSUKIYAMA: Is that right? Yes. Maybe that's a good idea. But I already have really a lot of colorful socks, though.

VAN BENSCHOTEN: You do. These would be much easier to match up, in fact, as long as you didn't lose one.

All right. We were talking about your temperament. We were talking about your character as a young boy. Anything else that we should know besides that you were a bad kid, as you said?

TSUKIYAMA: I don't know.

VAN BENSCHOTEN: You weren't scholastically shining at this point?

TSUKIYAMA: Not really, not at all. I liked math, I liked physics. I hated chemistry, organic chemistry. I hated biology even more, and I really, really hated English. English classes in Japan are awful. It's all grammar. "I have a pen," convert this to past perfect tense, or something like that. So I really hated it, and I started to like English in vet [veterinary] school, because I met a really wonderful teacher. So that was the turning point for English, I think.

VAN BENSCHOTEN: What was the schooling like? Now that you look back on it, what was the quality? You've already mentioned that the school had a reputation. Did you feel you got an adequate education, better than average?

TSUKIYAMA: In high school?

VAN BENSCHOTEN: Yes.

TSUKIYAMA: Well, adequate in standard, I think. Well, of course, yes. I don't know. I think it was a good school. It was reasonably liberal in the Japanese standard, I guess. We had pretty good teachers. Especially, I liked my math teacher.

Oh, that reminds me. One crazy thing I did: I threw a firecracker at the school principal at the graduation.

VAN BENSCHOTEN: That's definitely different. How did he take it, by the way?

TSUKIYAMA: He didn't even stop his speech. I was extremely impressed.

VAN BENSCHOTEN: Just ignored it.

TSUKIYAMA: Yes.

VAN BENSCHOTEN: Apparently that was a strategy that many of your teachers appeared to do and did.

TSUKIYAMA: But that was not something that's typical for a Japanese student to do. My parents were freaked out that I did it. I just remembered.

But anyway, it was a good school, and I think I got a pretty reasonable education. Whether what I learned in my high school really helped me being a scientist, I don't know. It helped me getting into college, that's for sure. But I did have a good time.

VAN BENSCHOTEN: Now, it sounds as if some of your pranks, at least with your fellow students, they went over really well. Did it make you a popular figure on campus? You said you knew almost everybody, or they knew you.

TSUKIYAMA: Everybody knew me because I was a cheerleader. I think I was reasonably popular. I got along with a lot of people. Unfortunately, the school was pretty far from my place. It took me ninety minutes to go to high school, so I couldn't stay around to be with my friends after school—after classes—very often. So it's not like I played around with my friends a lot, but, yes, I had a very good time, and socially it was very fun. I was enjoying it a lot.

VAN BENSCHOTEN: You mentioned a math teacher. Were there any other teachers that were important at this phase in your education?

TSUKIYAMA: I don't think, because of the way I was living myself—my life in high school—I had quite a bit of distance between myself and my teachers, so I don't think I got a lot of influence from my teachers when I was in high school. No.

VAN BENSCHOTEN: You did mention the math teacher. What was special about the math teacher?

TSUKIYAMA: One thing that was special about him was, it was very clear that he loved math and he loved teaching mathematics, and that was the biggest thing, I think. To see someone really enjoying what he does was very refreshing to me, because most of the teachers were doing their job because that's the way they make money, I think. So, yes, that was it, I think. Of course, he was good at teaching, but just seeing him enjoy teaching was a pretty good experience for me.

VAN BENSCHOTEN: Yes, something unique.

Were there any special projects or presentations that you did throughout your

education that stand out, that you're proud of, or maybe a few monetary?

TSUKIYAMA: Oh, in high school?

VAN BENSCHOTEN: Yes.

TSUKIYAMA: Oh, that's probably very different from American system. In Japan, we don't do that kind of thing much at all in high school. So we go to school, get classes, six classes a day or something like that, and go home, and there's not much. We don't get training in presentation at all. We also don't have a lot of activities to encourage that kind of things. I believe in this country, a lot of students who are interested in research, for example, take extracurricular activities. But it didn't even exist as an option in Japan. So just taking classes, and that's it.

VAN BENSCHOTEN: I was going to ask you, too, the differences between the two systems. Of course, you never went through the American system, but looking at it now, are there any other important differences? For instance, I actually teach at the community college level, and I know that the big program is critical thought, having the students question. How important was that in the system you went through?

TSUKIYAMA: In Japan, zero. There's no discussion, number one, believe it or not. There's no discussion in class. They give you the lecture, and it's basically how much you can memorize. Of course, for math or physics, you just cannot memorize everything. But basically, they explain how you should think, I think. But I do not remember any single class that we had discussion among students about how to think about something.

We had zero training for presentation, which I thought was a big drawback for Japanese people coming to this country to do science later on. Yes, so now, looking back, it's surprising I received that kind of education, really. Of course, you know, when I was in Japan, because everybody's the same, I didn't really even question it, because I didn't know your system.

VAN BENSCHOTEN: We're going to talk, too, about your time in college, but to skip ahead, at what point does that discussion and that critical thought come in, then?

TSUKIYAMA: In my case, that was in graduate school. Even in college, I don't think we got much of discussion at all, and that was after I got affiliation to a laboratory and started doing research and doing journal club or data presentations on a regular basis. That was probably the very first time that I got any presentation.

Oh, in junior high school, there was one teacher teaching—I don't even know how to translate—things like economy and sociology, I guess, who asked students to study books and present. There was a theme at every class, for example, economy in this period in Japan, or something like that. And people would look up books and write down what they found on a blackboard and explain in front of class what they found. That was quite unique in terms of style of teaching. That was about it, I think.

VAN BENSCHOTEN: Were you participating in extracurricular activities at this time?

TSUKIYAMA: Which now?

VAN BENSCHOTEN: Sports or clubs?

TSUKIYAMA: In high school?

VAN BENSCHOTEN: In high school, yes, or junior high.

TSUKIYAMA: No, partly because my school was so far away, I didn't have time. But also I was doing cheerleading things; so before a big sports event, we'd get together and practice. That was about it. Every day I came home and walked my dog for an hour. That was a big part of my life.

VAN BENSCHOTEN: I wanted to ask, too, you talked about the competitiveness. How did the competitiveness show itself in school? I assume it was there, the ranking system.

TSUKIYAMA: Yes. So there were probably different ways that students dealt with it. Most people don't like to show that they care about those things, even though everybody cares. It's sort of not cool to worry about how you do all the time. So especially when you're younger, people are not brave enough to say, "I really care about my tests." So most people pretend as if they don't care about it, but it's obvious everybody cares about it.

In high school we started seeing people who'd just sit, even during break, and flip through cards to memorize equations or English words or something like that, preparing for exams. And, of course, I was at the other end of that thing, because I was a bad boy and my pride didn't allow me to show that I'm studying in front of others, even my friends. So that's one typical thing.

But people talk about, especially in high school, as I said, getting into college is a big, big deal. So as soon as we got into high school, teachers started talking about the entrance exam for college, and that was the thing that's over your shoulder all the time throughout high school. You cannot *not* think about it at all; so it's a huge pressure. I mean, there are people who kill themselves from that pressure and things like that in Japan. So it was very clear.

I still remember the first day in high school, the teachers mentioned the entrance exam, and I said, "Whoa."

VAN BENSCHOTEN: How did you handle it, then, throughout high school? How did you handle this pressure? One, to disguise the fact that you were studying for the exam.

TSUKIYAMA: Yes. So I was actually studying reasonably hard, not really hard, but I was studying on a regular basis at home. But I don't know. My girlfriend describes me as a person who doesn't have a receptor for pressure.

VAN BENSCHOTEN: That's a clever way to put it.

TSUKIYAMA: So I probably didn't feel a lot of pressure. I don't remember, at least, being pressed. I was aware, of course, I was not doing that well. I wouldn't be able to go to Kyoto University or Tokyo University. That was clear. I didn't even think about it. I was very clear that I wasn't going to be able to go to medical school, but not that I worried about it.

I don't know. Of course, at the time I had no idea I was going to be a researcher. The only other thing I think I was clear on was I did not want to work for a company like my father did, because I could see clearly how stressful it was, how little he could do to the organization, and he had to say yes to things, orders that he didn't like, kinds of things. Even though he rarely talked about that kind of thing, it was very clear.

I wanted to be able to do something that I had more control over in my life, and that's probably one of the reasons why I went to vet school, because I thought if I became a specialist like a vet, maybe I could have more control about my life.

Now, that's what I think now. It's not really clear that's exactly what I thought, but I still remember that I hated life as a company man like my father, work for a company and just cannot say anything, cannot say no to the orders. Yes.

So, regarding the pressure to do well in school, probably I didn't really care much. But I think at one point I realized that I was doing too poorly at school, so I started studying reasonably hard when I was in the last year of high school, I think. It's three years in Japan, so that was something that I suddenly decided one day, "I have to study a little bit harder,"

and then I started studying in a more systematic way. And it showed. I started doing a lot better in exams.

VAN BENSCHOTEN: I know that in the U.S. [United States] system, at least that part of it that I'm familiar with, a lot is based on GPA [grade point average], whether you get into college or not, and that's cumulative over time. It seems in the system you're describing there's this monumental exam, and it's almost as if regardless of what you did before the exam, what you do on that exam determines where you're going to go and the opportunities you'll probably have.

TSUKIYAMA: Right, right. So you have a letter from your teacher, but unless something really bad is written, I don't think it's a big deal. How much it counts is not usually discussed. Actually, I don't know, but I don't think it's a big part of it. You take two exams, usually. One is a national standard test, and then each university or college has its own exam, depending on the scope of the study. For vet schools, one of the big reasons why I chose that school is because there's no English test, because I hated English so much. So, yes, so even if you're doing really poorly, if you do well in those two tests, you can go to any school, basically.

VAN BENSCHOTEN: How did you do on this exam?

TSUKIYAMA: In the first national one, I did quite well, actually, and I could have gone to many good schools, schools that were supposed to be better than my school I ended up going to. So my mother got excited and she started saying, "You should go to this and that and that," but those schools didn't have vet schools, so I said no.

In the secondary test, I think I did well, too, and I actually had the best score of all the students in the year, so I was a representative at the ceremony. What do you say?

VAN BENSCHOTEN: Yes, to celebrate that.

TSUKIYAMA: Yes. At the first of the school year, all the freshmen got together and I was the one who had to go up to the stage and receive something from the dean or something like that.

VAN BENSCHOTEN: What was the second test focused on? What did it test for?

TSUKIYAMA: So, math was one, I remember. Then you could choose one out of three; that

is, chemistry, physics, or biology. And I took physics because I liked that the most. Those two, I think. It was one of the simplest tests around. That was another reason why I chose that school, I think. I didn't have much background in biology. I really didn't like biology when I was in high school. I didn't know what DNA was when I got into college, believe it or not.

VAN BENSCHOTEN: What do you put that down to: bad teaching, just lack of information?

TSUKIYAMA: Part of that, maybe, I don't know. I think big part of that was just my own problem. I thought physics was the easiest because it's so logical, and there are not so many things to just memorize. I remember the time I started hating chemistry, for example, was when we moved on to organic chemistry, because then I had to remember a lot of things, this bond, this bond, and ring and everything. I just hated memorizing things.

And biology was even worse, at least in Japanese high school. You have to remember a lot of technical terms. If they explained phenomena first, and how fascinating it is first, then it would have been a lot easier for me to remember those terms. But in Japan, they start from the terms, so you have to remember all the technical terms first before looking into phenomena. So I just hated those things.

Physics, if you know the basics, you can actually think about things and come up with solutions, and I think I enjoyed that part of it a lot.

VAN BENSCHOTEN: It's interesting, because it seems that in math and physics that they give you a means—a tool—to move from one part to the next, and it's not all rote, for one thing, and it's problem solving.

TSUKIYAMA: Right.

VAN BENSCHOTEN: All those three things.

TSUKIYAMA: Yes, I liked that more than the other things, so my mother was quite surprised when I told her I wanted to go to vet school, because she thought I'd go to engineering or something like that.

VAN BENSCHOTEN: You were never tempted, though, to?

TSUKIYAMA: I thought about being an architect. Even now I really like looking at big buildings or to see how buildings are built. And engineering also. I'm reasonably certain I would have been happy if I'd decided to be an architect. How successful I could have become, I just don't know, but I still like that aspect, you know.

VAN BENSCHOTEN: Just recently, [Walt] Disney [Concert] Hall opened. It opened yesterday. I was wondering, have you heard or know anything about the hall? Have you seen photos of it yet, by any chance, Disney Hall in Los Angeles?

TSUKIYAMA: No.

VAN BENSCHOTEN: I was going to ask you what you thought of it, but it's made a big splash in L.A., as you might imagine.

TSUKIYAMA: I see.

VAN BENSCHOTEN: So you've taken the exam, and you eventually go to—and I may mangle this—Obihiro [University of Agriculture and Veterinary Medicine] University.

TSUKIYAMA: Right.

VAN BENSCHOTEN: And you chose that because?

TSUKIYAMA: Because there's a vet school that's big. Another big thing is it was in Hokkaido where I really wanted to live. Another reason, I think, was because it's not the school that my sister [Kyoko Kohara] was going, and that was it, I think, and the entrance exam was simple.

VAN BENSCHOTEN: Describe that first year. Was it what you expected?

TSUKIYAMA: Yes, I think so. I knew that people drank a lot, because I'd read about that school. In Japan, because the entrance exams is such a big pressure, usually—well, very often—the first couple years students don't study much, because they're sort of relaxed too much, because the biggest goal of their lives is accomplished. So the school is basically the same.

The first couple of years, the classes are boring because usually the first couple years they mostly teach general things: math, chemistry, and so forth. They didn't do much of specialized teaching such as anatomy. Those things didn't start until second year. That aspect was not that great, but it's the first time for me to live alone away from my parents [Yasuo and Misako Tsukiyama], and it was very exciting. I had to cook my meals. I could do anything I wanted. I could read while I was eating, which I couldn't do.

VAN BENSCHOTEN: Simple pleasures.

TSUKIYAMA: Yes. And it's a very, very, very cold place, so it gets something like minus forty degrees Celsius in winter, which I'd never experienced, and all the roads get frozen. Just living there was big deal, and it was unbelievably fun.

Then I joined the club that started when I was in second year, I think. So that didn't belong to the university formally, but we formed a group that tried to protect sea seals from fishermen. They're a kind similar to harbor seals in Japan, because it's the other end of the Pacific, the same kind basically that exist on the East Coast of this country. A lot of them get drowned by fishermen—fishing nets—so we wanted to protect them, because this is the only kind of seal that would breed in Japan. So that group was really fun, the activity was fun.

One thing we did was a census. So twice a year, in June, that's because it's breeding season, and in August, I think, we'd take a week off from school and go to different breeding sites, and from sunrise to sunset, every thirty minutes we'd count the number of seals and take pictures of them. Depending on the pattern, we actually recognized each seal, and we had family trees. Because we'd count at the same time, we knew exactly how many seals were living in Japan. That was summer activity.

In winter we would go out on a fishing boat. There was a fisherman who was very understanding of the situation. So we would stay with fishermen in winter and get onto the salmon fishing boat and help them get the fishing net up and count them [seals] eating fish—salmon—and also if we found seals that were drowned, we would cut them out and take organs for studies; such as, by counting follicles in the ovary, for example, we could tell the age of the female because they have certain number of follicles per year after reaching sexual maturity, and also measured bone size and everything. And that was a lot of work.

We would take turns during fishing season, and so I visited those places several times. We got to know fishermen, also, personally, and it was a very interesting experience. While we were there, we didn't succeed in protecting seals under law. I heard recently they succeeded.

But it was so different from what I used to do in high school. You sit in classroom, you receive everything; whereas this one you go out and think about what you can do. It was a really interesting experience. And we would report. We even had a grant. We'd write grants and apply to foundations, and we were run by our own grant, which we were very proud of.

VAN BENSCHOTEN: What were you learning about yourself and maybe about science that you didn't know before?

TSUKIYAMA: When I was in vet school, I was just at the transition phase that they were switching from a four-year education to a six-year education. So because of some strange bureaucratic problem, I think, it didn't go smoothly. Only for four years or so there was a transition period, which both my sister and I went through. It was a lot easier for the Japanese government to change so that after four years you graduate first, then go to master's degree, then graduate, instead of making it six years straight. I don't know why that was. So both my sister and I had to get master's degrees before graduating vet school. Now it's six years, so people don't have to do it.

Because of that, some schools didn't take it seriously, because it's just not a real master's because you had to go to a master's course. But my school—some laboratories—took it seriously, so some people had to do real research for that. Because after my visit to my sister's laboratory, I was interested in basic sciences, I decided to go to the lab that was best in that school for basic research, which was also doing microbiology. So that's where I was exposed to science for the first time, I think, and I was surprised that I liked it. [laughs] That's how I changed, I think. I was there for three years. Then I was pretty much decided after that, that I wanted to do research.

VAN BENSCHOTEN: What was it about research? What were you finding in the lab that drew your attention?

TSUKIYAMA: Yes, so that was actually the only lab that was doing really competitive research, publishing papers in English journals, so in a sense I didn't have a lot of choice if I wanted to do research. Other labs were doing more clinically oriented research like reproduction or like blood type of cats or something like that, for example. So that was the reason.

The professor I worked for [Tetsuhiko Shinagawa] was a very, very good scientist. Even now, looking back, I think he was a pretty good scientist. The other thing is just like the math teacher in my high school, it was very clear he just loved work doing experiments. That was probably the biggest thing he showed me: how important or how great it is to enjoy work. It was very clear he just loved doing experiments. So that was very good.

VAN BENSCHOTEN: What kind of work did he do? What did you study in his lab?

TSUKIYAMA: So because it was vet school, we needed to use animal viruses, which is

strange. So at the time, one of the popular things was the oncogene, the genes that could cause cancer. Early stage was in DNA viruses. At the time, I think things like retroviruses were not there yet, and adenovirus and SV40, those viruses were very popular as oncogenic viruses. In Japan, the research trend is probably five, ten years behind the Americans. At the time, maybe, in this country retrovirus might have been a little more popular. But anyway, back then in Japan, adenovirus was still very popular.

A lot of people were using human adenoviruses to study genes that can transform cells to malignant cells, and the theme I got was screen first for a few different animal adenoviruses to see if they can also transform cells from normal to malignant. Then I found that one of them—canine—dog adenovirus Type 2, has produced strong oncogenes. So, the rest of my research in the master's course was to map and identify [the] transcription unit that's responsible for this transformation. So, very basic.

VAN BENSCHOTEN: What was the name of the man whose lab you worked in?

TSUKIYAMA: His name is Dr. Shinagawa. S-H-I-N-A-G-A-W-A.

VAN BENSCHOTEN: Just a few questions that have no real logic. Were there other mentors that you were finding at the vet school or maybe other fellow students also while you were doing these various things?

TSUKIYAMA: Yes, there were several people there, but I was the only person who was working on that particular project, and my girlfriend [Riri Shibata] now, who is a year junior to me, took over the project after I graduated.

VAN BENSCHOTEN: That was going to be my next question, because you had told me before that you've known her for twenty-one years now.

TSUKIYAMA: Twenty years, yes.

VAN BENSCHOTEN: So you met at this school?

TSUKIYAMA: At the vet school, yes, in that group protecting the seals. I'm pretty sure that's how I met her.

VAN BENSCHOTEN: What does she do now?

TSUKIYAMA: She's a scientist for a company called Gilead [Sciences] in San Francisco right now; Foster City, actually. She's sort of biology group leader over there.

VAN BENSCHOTEN: Let's take you through to your Ph.D., the beginning of it, at least. You go to Hiroshima University.

TSUKIYAMA: Yes.

VAN BENSCHOTEN: Why that university?

TSUKIYAMA: Let's see. Why? In Japan, a lot of people stay in the same school from undergraduate to Ph.D., actually. It's a bad thing to do, but it's common. But in my case, I didn't have a choice, because my school did not have a Ph.D. course. So I started looking for places I could do a Ph.D. course.

I was reading through review journals looking for interesting things to work on, and this article written by my future supervisor [Ohtsura Niwa] was extremely interesting, so that was big thing. And also, I don't know, maybe I still had this school mentality from high school that somehow I did not want to go to a mainstream school like Tokyo or Kyoto or Osaka University. Oh, that's very probably the reason why I went to my vet school, which was also very small school compared to the school my sister went. I was sort of anti-mainstream, I think, for childish reasons, probably.

So that's another thing. So he was in Hiroshima University at the time, which is a good school, but not topnotch. He was doing good research there. That's probably part of the reason why I was attracted to his lab also. Yes, other than that, I really can't think of anything.

Then I wrote him a letter asking if I can apply to the program there, and he was a little bit reluctant. Later, it turned out that he was thinking about moving to Kyoto, because he was not very happy in Hiroshima. But I met him in Hiroshima and had drinks together, and I really liked him. Later, after I joined the lab, he told me that, "I told you not to come. Why did you come?"

I said, "Well, did you say that? I didn't get the message." And we laughed, but it worked out great. He was great, great person, so.

VAN BENSCHOTEN: We're near the tape.

[END OF TAPE 1, SIDE 2]

VAN BENSCHOTEN: This is tape two, side A.

We were talking about going to Hiroshima University and while you went there. Your mentor [Ohtsura Niwa], I should get his name down.

TSUKIYAMA: Ohtsura Niwa.

VAN BENSCHOTEN: Describe the management style that he had. How did he run his lab?

TSUKIYAMA: So this is unique. Well, it's quite a bit different from U.S. [United States] style, actually. In Japan, so he was an assistant professor at the time, and there was a full professor, and basically assistant professors work for full professors. So it depends on the school or depends on the lab, but in many labs still assistant professors don't have real independence in research.

I was, though, exceptional in that I applied to him directly. Again, I was not either aware of the system or I didn't think it was important, I don't remember. I didn't even think about it, I think. But anyway, the professor at the time was a reasonably understanding person, so he said, "Okay, you know, you came to Niwa's place, so you are not my student; you should be directly studying with Niwa," which was very unusual for that laboratory.

I was the only student he had at the time, and I was the first—very first—real student for him, so we worked very close together throughout my education. Part of his work was actually to do work for his boss, the full professor of the laboratory, and 50 percent of the time he would do research for his own interests. So this guy took over that part. That was a research institute, and he did not have to do teaching much at all, so he was in the lab all the time. That was good. We had a bench, back to back, and he was working at the bench a lot of times.

He was a little unusual in a sense. He had a lot of influence on me coming to the U.S. because he did his Ph.D. at Stanford [University], which is very unusual for someone at his age. When he was in graduate school, I think there was a very strong student movement, and there were a lot of schools that were shut down and so on, and he didn't like it. I think he thought about quitting research, so he came to the U.S. and was a technician for a year, then enrolled in the graduate program at Stanford. Then he got the degree there and then went back to Japan to take [a] research position.

In Japan, usually graduate school does not provide any education—believe it or not—so there's no single class I took. It's very common. It might have changed a little bit, but

because there're no postdocs [postdoctoral fellows] in Japan almost, graduate students are the main workforce in Japan, so they are used as cheap laborers. What people do, basically, is come into the lab and do their own experiments all day and go home. That's it. No teaching, no classes to take. They don't do teaching either. They don't do teaching assistance.

They come out, no experience of teaching, no lectures to receive. So depending on your mentors, the level of knowledge you can get could be completely different. In some laboratories, students basically are used as parts of a big factory, so in an extreme case, you might have a Ph.D. who probably had been doing cloning or one type of experiment for four years.

What was fortunate for me was because Dr. Niwa had an education in Stanford, he knew the system; he know how important it was to have broad knowledge, so even though I didn't have to take classes, we had pretty strict reading assignments. So, for example—I think I have it in here—this is a famous textbook for molecular biology called *Genes.* It's written by Ben [Benjamin] Lewin, who used to be an editor for *Cell,* and it has something like eight hundred pages. We needed to read that in eight weeks, which is a lot for a Japanese who is not used to reading English. We had to read in English, of course. Not only that, we had to explain it in front of him. So just reading for yourself versus reading and explaining is completely different. You need a lot better understanding. So that was a huge training. It was hard, but I didn't want to give up, so I did that.

After that, he gave us a similar assignment reading a journal called *Trends in Genetics,* which was hard because it deals with all sorts of different problems from plant genetics to *E.* [*Escherichia] coli.* I mean bacteria genetics to human genetics. So it doesn't matter; we had to read all the articles and present that in front of him. That was good training, I think. So he was very high on training me.

And there was another fellow student who was there for the professor, but she joined the reading assignments, so we did that. It was good training. I'm very thankful that he did that with me.

VAN BENSCHOTEN: Yes, it sounded very rigorous.

TSUKIYAMA: Yes. Because he had left his family in Kyoto, he was living alone, so he pretty much had a life like I'm having right now, so he would come in late and stay until midnight or one o'clock. So we were there for—I don't know—maybe fourteen hours a day together, every day, and very often after both of us were done with work, we would just drink together in the office and talk about all kinds of things. It was very good training, one-to-one, basically.

Then the professor retired, and he was promoted to be a full professor. Then after, about the time I left, he got three or so graduate students, so he's having more people right now with him. And he moved to Kyoto, finally, to be with his family, and he's very happy

over there. So his style was very special, I think. That's not very typical—one-to-one—and very thorough training.

VAN BENSCHOTEN: Given the closeness between the two of you in those six years, what was the focus of your research, and then what was its evolution?

TSUKIYAMA: Right. So one thing about him, my mentor Dr. Niwa, he's really, really smart. And smart means in this case very fast in picking logical flow, for example. Someone talks about something, he will say, "Oh, that's logically incorrect because of this and that," or if he has to write about something that he's not really working on, he can go through journals and write the review about it in a couple of weeks. He was really good at those things.

One thing that he was not very good at—maybe you could say he's so smart— is to stick with one thing and keep working with something for long time. So he's interested in ten different things all the time, and I don't think he ever worked on one thing for a long time in-depth, but that was his personality. Very often he'd get too excited about something easily without thinking really in detail. He just starts working on something that sounds sexy, but things get stuck very often.

So initially, the project I was assigned—or I agreed to work on, I should say—didn't work out, because the assumption was too naïve, I think. But anyway, the general interest at the time was why early embryos are so multipotent. So basically, one cell becomes the whole body. And we knew until ten-twenty divisions are done in the mammalian system every cell can differentiate into every tissue. So that means that those cells have potential to differentiate in any way, but it's suppressed.

How that specificity is defined was the center of the question. I should say, how that multipotency is kept in our embryos was the interest for us, because the way those tissues' specific information is kept should be reversible, because those cells should be able to differentiate in every tissue. But yet the suppression should be pretty strong, because if you start pretty much early differentiating, you can end up with having body without head or hands or whatever. So that was the biggest interest.

Let's see. To make the long story short, basically we wanted to find a magic key regulator in this early embryo that's doing suppression, and if my student came up with that idea right now, I would laugh, because there's no proof that there's a key regulator. But it was a really good, cool idea. So we came up with a way to screen for that regulator, and I spent a year—a full year, I think—trying to isolate this regulator. Went nowhere, of course, so we stopped doing that.

But instead, we didn't change direction completely, but decided to use a different model system; that is, we knew that a lot of viruses adapted to grow in differentiated tissues, because they infect bodies, not embryos. So consistent with that, those early embryos that can differentiate into any cell type are completely resistant to viruses, because most of the

viruses just cannot grow at all in early embryos. So we decided to use one of those viruses, retroviruses—mouse retrovirus—as the model system, and decided to look for factors that repress gene expression of the virus. I did find a protein repressor for this virus transcription unit, and that was my thesis, basically.

Later, a competitor in North Carolina identified the same factor and showed that this factor is required to make male. If you knock it out, all the progeny become female. That's pretty interesting. So I enjoyed that work a lot.

So that was the first, I guess, of my research in gene expression. It's funny that I'm still working on repression, not by choice, just ended up working on it. But it looks like I'm doing some of the same things even now.

VAN BENSCHOTEN: Talk a little bit about your typical day in that lab. When would you usually come in? You said you worked fourteen-hour days.

TSUKIYAMA: At the time. I used to show up somewhere between ten and noon, and I usually stayed there until one or two. So I would get up and wash my face and eat something, and then go to the lab. I always live close to my lab so that I can go to the lab quickly. So it was something like five minutes to the lab.

Then I would go to the lab, do some experiments, have lunch, and work, then have dinner and then work, and then I go home and sleep. That was it. [laughs]

VAN BENSCHOTEN: Simple and direct.

TSUKIYAMA: Yes. And a year after that, my girlfriend [Riri Shibata] decided to go to graduate school in Kyoto, which was two hours by train. So we started commuting on weekends; every other week, actually. So only on weekends I would go to either Kyoto or she would come to Hiroshima. But she was a year junior to me, so for about a year I was in Hiroshima, she was in Obihiro, so we met like twice or something like that.

VAN BENSCHOTEN: In this lab, were you learning anything about the running of a lab, about the culture of science; not so much, let's say, discovering repressors and whatnot, but how to actually run it?

TSUKIYAMA: [laughs] At Hiroshima?

VAN BENSCHOTEN: Right.

TSUKIYAMA: So I laughed because that was a horrible lab in terms of organization.

VAN BENSCHOTEN: How not to run a lab.

TSUKIYAMA: Yes, I learned a lot about what not to do. So as I said, my supervisor [Dr. Niwa] was a wonderful person, but this professor was a very messy person, even though he was nice to me personally. So he had some political power for unknown reason at the institute. So even though usually in Japan—in Japanese labs—it's one full professor, one assistant professor, and a couple of research assistant professors, and usually those three work for the full professor. That lab had four research assistant professors, for unknown reasons. They were about the same age. At the time they were like forty, forty-one, something like that. They were all competing with each other. They hated each other, and it was very clear that nobody was getting along, and there were a lot of personal conflicts.

Believe it or not, there were incidents that one would sneak into someone's tissue culture and contaminate the tissue culture with bacteria. Because it happened so frequently, the one who was suffering isolated bacteria that was inoculated, and sure enough, there was plasmid in it that was used in the laboratory. So it was pretty clear that that was done on purpose, even though, obviously, that person was not nice either in other aspects. So it's not like someone was good and someone was bad or anything; everybody was having trouble.

Then everyone had independent projects but—I don't know—there were a lot of troubles, which later caused a huge headache to my supervisor when he was promoted to full professor. And a lot of them actually had left the lab already, so it ended up with this being okay.

What I decided to do is to be fair for science. So if I was asked for something—reagents or protocol—I helped people as much as possible, no matter what my relationship with them might be at the time. Other than that, I didn't do anything. That was my position. So I helped a lot of people, I think, and I didn't really get help from them.

Every lab, of course, has some problems, but it's not a problem for me. I've seen the worst, probably. [laughs] So in a sense, it was not bad training. It was a part of training—I should say—that I was in such a horrible laboratory. I was a graduate student, and there were more senior people who would come to me, one by one, saying bad things about the other faculty members. What can I say? I would just ignore them, and it was very clear that they hated each other. Yes, that was not the most pleasant environment, but, again, because my supervisor was a nice person, that was fine.

VAN BENSCHOTEN: Did you do anything outside of the lab? Did you have any moments where you had sort of leisure activities?

TSUKIYAMA: Basically, my life had only two aspects, either science or with my girlfriend. So every other weekend I would spend some time with my girlfriend. We both like hiking and bird watching, so we did that kind of thing a lot. I didn't have a car at the time, because it's very expensive to have a car in Japan. So we had to rent a car to go birding or long hiking, but we did that. Also, every year, at least twice a year, we would have a camping trip, so that was fun. That was about it. Life was very simple at the time. Even now, actually.

VAN BENSCHOTEN: Just out of curiosity, why was it so expensive to have a car there?

TSUKIYAMA: Oh, parking space. You have to pay something like—now I don't know—I would just say something like five hundred to a thousand dollars per month for a parking spot in Japan.

VAN BENSCHOTEN: Oh, my god.

TSUKIYAMA: And taxes are high, and you have to have your car checked up every other year, and that costs like a thousand dollars.

VAN BENSCHOTEN: You mean like de-smogged?

TSUKIYAMA: No. They check details. It takes one full day, usually, and they check brake fluid, gears, tires, and everything. They always find something wrong, and you have to pay for that. The gas is three times more expensive than in this country. Everything is expensive, so just having a car is a luxury. But that's the way it should be, because the whole country is the size of California, basically, and the population is half of this country.

VAN BENSCHOTEN: That is amazing.

TSUKIYAMA: Yes, there shouldn't be a lot of cars, in my opinion.

VAN BENSCHOTEN: A question maybe I should have asked earlier. How did you pay for college?

TSUKIYAMA: Oh, that one. So I applied for scholarship, but I was not qualified. They

refused to tell us the reason. I think it was because my father's income was too high. That's only because my father believed that, you know, grown-up adults should pay for education, at least partly. So he asked me to apply for it for college, and I didn't get it. So he said, "Okay, fine, I'll pay for it." So my father paid for it.

And in Japan, it's rare, extremely rare, for students to pay for their education at all. Most of the time, parents pay full. And in grad [graduate] school it's the same. In Japan, you have to pay to be a grad school student; you don't get paid. I always tell this to my students. "You guys are getting paid to do research. I paid." And of course, I didn't have time to have a second job to pay for my life, so I was supported by my parents for a couple of years. Then I started receiving this fellowship, which basically paid all I needed. So I still have a loan back in Japan, which I'm paying like a hundred dollars a month. I'm paying back that loan, but it's no interest, everything. So it's a pretty good deal. I was receiving that loan and a fellowship from Japan, Japanese Society of Promotion of Science, or something like that.

VAN BENSCHOTEN: You get your Ph.D. in 1991. What was the next step? How were you seeing the future?

TSUKIYAMA: So, at the time I was pretty clear I wanted to come to the U.S. for a postdoc , and—as I said—a lot of that was probably influenced by Dr. Niwa. He told me repeatedly how great his experience was in the U.S., and he still comes to the U.S. often for meetings and things. I was pretty firm that I wanted to come to the U.S. as a postdoc. I didn't think about after that, though. I usually don't think much of my future in detail.

So that was clear, and I, of course, talked to my girlfriend about it all the time, and she also wanted to come to the U.S. because for women, even now, it's not easy. It's probably easier to come to the U.S. to do well, to be respected, I guess, and she had no problem coming to the U.S. to do research. Everyone in the lab where I was doing my Ph.D., knowing my character, personality, said, "Once you go to U.S., you won't be back to Japan."

VAN BENSCHOTEN: They pegged you.

TSUKIYAMA: They were right, yes.

VAN BENSCHOTEN: So what were the postdocs that you were considering?

TSUKIYAMA: So that probably shows you how I am indifferent about my future. I actually didn't think much about it. So, first, let's see how to start.

When we started thinking about doing postdocs, my girlfriend already had a place she

wanted to go at the NIH [National Institutes of Health], because her supervisor had a sabbatical with Dr. Malcolm Martin at NIH and had a very good experience, and they were still working very closely. So she wanted to go to the place, and Malcolm's lab was one of the good labs and he already mentioned to her supervisor that he would take her. She was extremely productive as a graduate student, and there was no problem finding her a position.

Obviously, I could have looked at places at NIH, and NIH is a huge place. It's easy for two people to find a job. But also I wanted to look for other places. When I was thinking of postdocs, I was doing a lot of molecular biology using the mouse model system for embryos, but I was very aware that we hit the wall, really, at the end of our research. The reason is because we were not into development much. We were using cell lines. Number two, we couldn't do any biochemistry, so it was very hard for us to go into the mechanism. We just couldn't do it, so it was very frustrating for me.

I thought there are two ways to go to do postdoc. One is to study mouse development, rather than tissue culture cells. The other is to do biochemistry so that I can go deep into the mechanisms if I want to. Originally I thought going to do mouse work was higher priority, so I contacted a few labs that I was interested in. One of them was Hal [Harold M.] Weintraub, who was here [Fred Hutchinson Cancer Research Center] at the time. He immediately wrote me a very nice letter saying that basically the lab was completely full, "So I cannot take you." I didn't know at the time that he was always having this many applications. He was such a nice guy.

Also contacted a couple of people in other places than NIH, and I didn't get a good answer immediately because I happened to choose really famous labs at the time. Then there was one lab at NIH was doing mouse work, and that person told me I could come. So I thought it was set, and then—not that I actually read a lot about her or not that I read her papers much—I was a little bit unhappy about our contact; that is, I was trying to apply for fellowship, and I'd write to her. At the time, there was fax; e-mail was not there. I would fax her something, and she would not get back to me for like two weeks, usually, and I was a little unsure. I didn't know at the time that at NIH you really don't have to bring your own money because money is so abundant, but I wanted to make sure that I got funding just in case. Maybe that's why she didn't think it was important. Anyway, she didn't explain that to me, so I was a little bit concerned.

Then—I still remember this—the whole lab at Hiroshima, we went on a trip for leisure purposes, not for science or anything, and I woke up at night and I thought about the not very pleasant interaction with this person.

Then [I] came up with the notion that there was another place I could apply. At the time I was in collaboration with another lab in Japan, because the factor I cloned from mouse embryos happened to be a homolog of *Drosophila,* a fruit fly gene that was isolated by another researcher in Japan. That guy just came back from Carl Wu's lab at the NIH. He was one of the first postdocs for Carl, and I was hearing from him how great his experience was with Carl.

Then suddenly it occurred to me, "Oh, maybe I can go to Carl's lab." You know, I was not thinking about Carl's lab because he was using *Drosophila* as a model system, and I was thinking about mouse work. And Carl is still a very good biochemist, so maybe rather than going to embryos—going to one particular system— learning biochemistry so that I can do mechanism work later on might be also fun.

Then I just basically decided that night that I want to go to Carl's lab, and I wrote a letter, and Carl said, "Okay, come on." Later it turned out it's very rare for him to take anyone without even meeting, but because he knew Hitoshi, who was my collaborator, who was a postdoc with Carl, and Hitoshi recommended me to Carl very highly, he took me basically without seeing me. So that's how I decided to go to Carl's lab.

So right now my student is looking for a postdoc position, and when he asked me how he should look for a job, I say, you have to think about this and that and that, but then at the end I have to say that, "By the way, I didn't do it the way I said you should. I just basically decided in one day."

The way I chose my graduate lab was basically the same thing. I read one piece of paper and just, "Okay, I want to go to this place." It's been working. [laughs]

VAN BENSCHOTEN: Yes, apparently. Before we get you to Carl Wu's lab and talk about how very productive you were, and a lot of good papers came out of that, I wanted to get to the transition from Japan to America. Had you been to America before?

TSUKIYAMA: Once, yes, for a meeting, a Cold Spring Harbor [Laboratory] meeting, and I and Dr. Niwa and my girlfriend came to the meeting. I think at the time we already knew we were coming to the U.S. as postdocs, so it was a year before we came or something like that.

We flew to New York and attended the meeting. We both presented posters. We didn't understand what people were talking about. The funny thing is my poster was reasonably popular, and there was a guy who was real interested in my work and he asked me really detailed questions about it. I answered all the questions. He stayed there, and other people started asking me questions which I didn't understand. So this guy started answering questions in my place.

VAN BENSCHOTEN: He was your interpreter.

TSUKIYAMA: Yes. So I still remember that. So that was only real trip to U.S. before that.

VAN BENSCHOTEN: What was your impression of America on the first trip?

TSUKIYAMA: It was intense. It was real fun. Of course, you know, being in a place that you not completely comfortable about, language is really intense.

VAN BENSCHOTEN: How was your English then?

TSUKIYAMA: It was okay. I could speak, but not very fast, and the vocabulary was obviously not there. But grammar-wise, I was okay, I think. So when I wanted to say something really slowly, it was okay, especially to scientists, because they are used to foreigners' English. But hearing was horrible, because we learn English on paper, basically, so you know how it's written, how to read. It's completely different. So it was very hard to pick up what people said, but it was okay. It was really enjoyable. I had a great time.

On the way back to Japan, we actually stopped by in Seattle, because, since it's a big trip for us, we wanted to have a little bit of extra stay. I actually don't remember why we chose that, but we decided to go to Rainer, Mount Rainier, and believe it or not, we rented a car at Seatac [Seattle-Tacoma] Airport and drove to Rainier, and we made it. In Japan we drive on the other side, like in Britain, and also we didn't understand what the lady at the counter was saying to us. But she gave me a key, and we drove.

It was intense, though, because we never drove the freeway in this country and the road to I-5 [Interstate 5] is not that clear. Actually you have to take a ramp that's really narrow. It doesn't look like it's a major way to go to any freeway. But we somehow made it and stayed in a lodge that's right in Rainier, which is wonderful. And we just happened to see a scientist from Tokyo who was there for a different meeting. We didn't know each other, but he was staying in a lodge in one of the high places at Rainier. And he invited us for dinner, and we had very memorable dinner there. Then we flew back to Japan. That was really, really fun.

VAN BENSCHOTEN: That'd be great.

TSUKIYAMA: Yes, that was quite an adventure, actually. On the way back to return the car, I once made a wrong turn and went to the wrong side of the road, and I saw cars coming to me. I turned around. We didn't have a big problem.

VAN BENSCHOTEN: That's pretty terrifying. That happened to me today, by the way, too. A motorcyclist was coming at me. I was downtown. It was one of those one-way street things. That skinny little ramp that you talked about that doesn't seem to be going to the [I-]5, I also took that today, so this is all resonating quite well.

When you come back again, though, a year later, had your English improved in that

time?

TSUKIYAMA: No. I didn't take any classes. Oh, maybe a little bit, actually. In Hiroshima in the graduate school, there were a couple of foreign students. One of them was from Bangladesh, and the only language we could communicate in was English. So I talked to him a lot, but not like every day, basically. So it might have been a little better, but not significantly, I don't think.

Though, I think, my English was okay from the beginning, because I remember, the first day I showed up in the lab, I was told to go to the secretary's office, and I got an explanation about the keys and blah, blah, blah. And then Carl showed up, and Carl was expecting that I wouldn't be speaking English much at all, I think. So the secretary said, "Carl, this guy speaks English."

I saw Carl's face, and I could tell he was very embarrassed, because the secretary told me basically that Carl already told her, "Don't expect this guy to understand or speak English." So I was not very fluent, I don't think, but I was functional.

VAN BENSCHOTEN: And this is in Bethesda, right? You're in Bethesda, Maryland?

TSUKIYAMA: Right. That's correct.

VAN BENSCHOTEN: How about American culture? How were you adjusting to that?

TSUKIYAMA: I actually didn't have any problem at all. I don't know. Maybe because it's not that different, I don't think, from Japan. Well, at least the modern part of Japan. Or maybe because I stayed in the lab all the time; I didn't do much else. But I did not feel like I wanted to go back to Japan even a single time, I'm pretty sure.

VAN BENSCHOTEN: That's amazing.

TSUKIYAMA: Yes. I've been very happy. I mean, I've been happy basically throughout my life, as far as I can remember. It's not that different. But I think people were right when they said that "You won't come back to Japan." So I can't complain. [laughs]

VAN BENSCHOTEN: All right. Let's get you in the lab again, in Wu's. Again, I'll ask the same question. What was the focus of your research from that point? You obviously were making a key transition, it seems, to another model system.

TSUKIYAMA: Right, right. So I changed organism. I changed the technique from molecular biology to hardcore biochemistry, and I changed subject. I also changed language. So that was quite a bit of an adjustment, I think.

Carl was one of the first persons who described in 1980—early eighties, I think—that when there's an active gene, that region of chromatin becomes open, more accessible. So my subject of study was to reconstitute that in the test tube. The reason is because a previous postdoc, who left like half a year before I joined the lab, had established one of the first in-vitro test-tube systems to assemble chromatin-like structures in test tubes. So he wanted me to use that system to reconstitute what happens in cells, which is a very dangerous, high-risk, high-return kind of project.

I knew that from the beginning, and when I told other colleagues in Carl's lab what my projects were, some people said, "Ooh, do you think it's going to work?" But I didn't really care.

One thing I may not have told you is in both vet [veterinary] school and graduate school, the projects I had were new to the lab, so I had to establish a system from scratch in all the laboratories I was in, so I felt comfortable starting something new in the lab, and that was probably one of the best education training I got throughout graduate school, I think: to establish new system. So because of that, I didn't have a lot of hesitation in trying something new in Carl's lab.

VAN BENSCHOTEN: Well, it's funny, in reading some of the Pew [Scholars Program in the Biomedical Sciences] documents they give us on the Pew [Scholars Program in the Biomedical Sciences] scholars, there're letters of recommendation in there, and I like reading them, because certain themes do come out. And one of the themes that came out repeatedly for you was being a quick study, being able to pick up these systems quickly and adjust and find your feet and move on. That came up again and again.

TSUKIYAMA: I see. That's interesting, because I consider myself slow in picking things up.

VAN BENSCHOTEN: So you felt, in other words, in familiar territory, having to start from scratch, even though it was all in another country now, in another language.

TSUKIYAMA: Yes.

VAN BENSCHOTEN: So you picked it up, and how did the research go?

TSUKIYAMA: So in Carl's lab, he gives difficult projects to everyone. It's almost expected that you struggle. As a result, some people burn out and quit science. But he publishes in very good journals, and my project was not an exception. In the first full year, basically, I spend time getting reagents ready to do experiments. So I couldn't even do the experiment in the first year.

I joined Carl's lab in '92, I think, April, then the time I started real experiments was in early '93, I'm pretty sure. I didn't just have reagents that I could use, because that in-vitro experiment I mentioned is real high maintenance. A lot of things need to be right, so you need a lot of different reagents, all in working condition. If one stops working, it takes weeks to figure out what's wrong. So to keep the system running, it was a lot of work. It was a struggle at the beginning, but I really didn't care.

I think that's of the reason why my girlfriend says I don't have the receptor, seriously, because I really didn't worry about my experiment or anything. I was having fun. It was really good.

Six weeks after we arrived here, we had a huge accident, and that slowed me down a little bit. But other than that, not much was happening.

VAN BENSCHOTEN: May I ask, what was the accident?

TSUKIYAMA: Yes. I was turning left. It was Sunday, and it started to rain, so a lot of people were rushing home. Again, the turning left is a small turn in Japan, but it's a big turn in this country. So I didn't pay attention to the car coming straight. I was turning left, and then the car hit the right side of my car.

My girlfriend later found out that she cracked four ribs and her pelvis, and she got unconscious. I got scared. It could have been a lot worse, though, because the rescue needed to cut out the door to get her out. Fortunately, she didn't have any bleeding at all, internally or externally, so she could get out of hospital in ten days. But it took her a while to be able to walk normally.

And it was like six weeks after we came to the country, so we barely spoke English. That was scary. We didn't know the system at all, and the hospital billing system is completely different, and I didn't understand why I got so many different bills from different doctors. I had to get into an ambulance, and the police came to me and explained.

[END OF TAPE 2, SIDE 1]

VAN BENSCHOTEN: This is tape two, side B.

You were in the middle of explaining a horrible accident, unfortunately. But the key thing I think you wanted to stress—I don't want to cut you off—but that this set you back in your research quite a bit.

TSUKIYAMA: A little bit, yes. I was going to the lab every day, but that was a really big distraction.

But other than that, we got back to the lab quickly, and my girlfriend [Riri Shibata] went back to the lab after maybe ten days. So we were back to normal. And she was also doing new things herself. For both of us, the first year was a struggle, essentially. But we didn't really have problems having fun. It was exciting to live in a different country.

VAN BENSCHOTEN: I asked you about the lab management style of your mentor earlier. How about Carl Wu? How did he run his lab?

TSUKIYAMA: Carl was quite different. At the time, he would have five or six postdocs [postdoctoral fellows], and he was not doing experiments anymore, because NIH [National Institutes of Health] is very bureaucratic, he needed to do to a lot of things and he needed writing and everything.

But, again, he would come late and he used to stay until eight, nine, something like that. I actually didn't know what he was doing every day. He was in the office very often, but also he wandered around a lot, and he would look over our shoulders and say, "Oh, what's going on? What's that band? What's that gel?" So we started hiding our data until I digested our data before talking to Carl. But he was pretty close to the lab in a sense.

We were jam-packed into the laboratory and that was the time that lab was most productive, I think. Then later, he was promoted and the lab was divided into two levels, and then people who were on the same floor with Carl were okay, but people who were left behind, I think felt like they were left alone a little bit. So that made it a little harder for people. That's how I learned, you should be close to the lab all the time, that's why I wanted to move to this space that's closer to the lab, even though I've not been in this office much at all.

So he's a big-picture person, so he would give us the general direction of the experiments. You know, this is the direction I'm excited [about]. But for everyday experiments, he was not on the top of it. He didn't know the details of the experiments we did, because he had been away from benchwork for a while. So we needed to figure out everything. Troubleshooting, basically, was up to us. So that might have been hard for some people who are not good at troubleshooting.

VAN BENSCHOTEN: How was it for you?

TSUKIYAMA: I actually like troubleshooting a lot, and, again, I was the only person doing that kind of experiment in the lab or anywhere else, basically, and Carl had no idea how the experiments were done, so I didn't even expect him to say anything about the details. I basically did troubleshooting all by myself. It was good, actually, good experience.

For example, one night I decided to purify this factor NURF. I never had real experience with chromatography or protein purification, so I asked him, because he's a good biochemist, "What should I do?"

And his answer was, "You just have to try." That's a typical Carl answer, which is true. But, you know, you have to try because every protein is so different; there's no simple rule. Yes. But that answer is very, very typical of Carl. So he's supportive and everything, but he doesn't give you details.

VAN BENSCHOTEN: Right. He wants you to figure out the details.

TSUKIYAMA: Right, right. I think he's good at doing those things himself, so he cannot think that some people can't figure things out by themselves. There were people who quit science after me, several of them. So, part of that is you have to be lucky, but part of that is you have to have the right personality to be in Carl's lab, I think.

VAN BENSCHOTEN: How about the general mood of the lab?

TSUKIYAMA: It changed a bit. In the first half when everybody was in the same room, and at the time everybody was having a pretty productive time, so it was great. I didn't see any problems. People got along reasonably well, and we were all excited about our work, and it was really good.

In the second half after the lab was split and some people moved on and a few people who came in got a little unhappy about how their projects were going or some people didn't get along with Carl, which was very rare, but that happened. So after I left, three people quit science, I think, within a year or so. Maybe four.

So the last one or two years in Carl's lab, I could feel the atmosphere was not as good as the first half. Not that I cared much, because being a postdoc, it's really easy to be selfish. It's all about your experiment. You have every control over your project. And it's nice to have colleagues who are doing well and happy, but at the same time, if somebody's not doing well or not very happy, it's not your problem, in a sense. So I could shut off myself and just

concentrated on my work. And, as I said, it's nothing compared to my graduate lab—I mean my Hiroshima lab—so it was nothing to me. Some people complain about atmosphere, but I told them my experience in Hiroshima and laughed about it.

I was having a very good relationship with Carl. I don't think I ever had any problem, and I still maintain that with him. To me, he was and has been a great mentor.

VAN BENSCHOTEN: Did you continue the routine that you had adopted in grad [graduate] school? Did you come in around maybe ten or twelve?

TSUKIYAMA: Yes, I wanted to, but the problem is at the beginning we lived a little far from NIH, and parking at NIH is really bad. That's one thing. Finding a parking lot after nine is a nightmare.

And number two, we couldn't afford more than one car at the time, and also my girlfriend likes to go to the lab early. She goes to bed really early, so basically I had no choice but to get up early, earlier than usual, and go home a little earlier. So I think I used to go to the lab at eight-thirty to nine, and stayed there until seven or something like that, seven, eight. Then I would have dinner. She doesn't like to work after having dinner because she gets sleepy, so it was rare to go back to work after dinner.

VAN BENSCHOTEN: Correct me if I'm wrong, you have two *Cell* papers, and you have a *Nature* paper that comes out of research that you do in this lab.

TSUKIYAMA: Right.

VAN BENSCHOTEN: Talk about that, the chromatin-remodeling experiments that you did.

TSUKIYAMA: Okay. So that finding came out of nowhere, actually. It was a surprise. As I said, originally the aim of the project was to reconstitute the open chromatin structure in [the] test tube, and from genetics we knew the DNA-binding protein called GAGA factor, because it binds the GAGA sequence, is required for establishment of this open chromatin structure. John Lis at Cornell [University] had transfected a piece of DNA into flies with and without binding sites for this GAGA factor, and showed that only when GAGA-factor binding sites are present can you get open chromatin structure. So that was the biggest aspect for a factor that's necessary for opening up chromatin. Whether that's actually doing the job was not known at the time.

So what I decided to do was to take plasmid template containing that promoter of our interest and purify this GAGA factor that's expressed in *E.* [*Escherichia] coli* recombinantly,

and add it to the template and then assembled chromatin with and without this factor, basically, to see how chromatin structure changes. Because if GAGA-factor binding induces open chromatin structure in the test tube, this did prove that this factor is responsible for this reaction.

So I did that after a long, long, long, long struggle to get this assembly system working and the GAGA factor. It took me a year, basically. Then after that, I got results that said addition of GAGA factor indeed establishes open chromatin structure, which is very exciting, because nobody had done that before.

I don't remember who proposed it; I think it was Carl's idea. So as a biochemist, if you see something really interesting, next thing you do is to purify the system to basically disassemble the system and identify the minimum components required to observe what you saw at the beginning.

One thing that I didn't tell you is, to assemble chromatin in [the] test tube we were using crude extract from frozen embryos; it has millions of different proteins. So then we were not sure that GAGA factor alone could open up chromatin, because we already knew that it's analytically very expensive to change position of a nuclear cell, so to change the structure of chromatin.

So we suspected there was some co-factor in chromatin-assembly extract that was helping GAGA factor to do the job. So that's why we decided to fractionate the chromatin extract, a simple extract.

Then first thing I tried to do was basically to purify chromatin—assembled chromatin—out of the chromatin assembly mixture, because it has a ton of other proteins. So then after that, I added GAGA factor. Nothing happened. Okay, so this was good, because then I could tell that GAGA factor alone was not sufficient, even though it was required for opening up chromatin structure. That meant there was something that was missing after purification of chromatin.

Then I immediately thought, "If I find what it is, it's a big deal." Now, originally I thought that, and Carl thought, it's something in the chromatin-assembly mixture, because it has ton of different proteins. Then I added protein, but nothing happened. I thought, "Oh, this is strange."

Then I realized that for the chromatin-assembly reaction, I added ATP, because the chromatin-assembly process is very ATP dependent. But I hadn't added back ATP because there was no reason to believe that this process was ATP dependent. So then instead of assembly extract, I added back ATP alone. Then, here we go, we got chromatin transition. So that was the very first discovery actually of ATP-dependent chromatin remodeling. So to date, I think this was the biggest contribution I made in science, the discovery of one new biological phenomenon. If I can get something bigger than that before I retire, I'll be happy.

So that was how it was discovered, and I'm pretty sure Carl doesn't remember this

now, but he didn't believe my result at the beginning. I showed him data, and he says, "Aah, you know, maybe," which is not his fault, because this was not described anywhere before and the data—quality of data—was not that great.

But I didn't care at the time, because I was very confident about my result, and I had to change the protocol to purify chromatin to get cleaner results, but at the end, we got the result, and that was the *Nature* paper.

So then it was easier next time. Then after that I decided to go after this. Later, I also showed that it's not just ATP; there's a factor that utilizes ATP to do chromatin remodeling, so I decided to purify this Factor X in chromatin-assembly extract that helps GAGA factor to change chromatin structure. That's basically those *Cell* papers.

VAN BENSCHOTEN: Correct me if I'm wrong, but looking at your CV [curriculum vitae], you're in his lab from 1992, then, to '97.

TSUKIYAMA: That's right.

VAN BENSCHOTEN: And the last two years, you're there as visiting associate.

TSUKIYAMA: Right.

VAN BENSCHOTEN: Is that basically a title that allows you to carry on your research?

TSUKIYAMA: Yes. I actually don't know why I was promoted. Oh, I know that. What was the first title?

VAN BENSCHOTEN: The first title was visiting fellow.

TSUKIYAMA: Visiting fellow. That's right.

So I think we needed to do that to get my visa status changed. I came with a J1 visa, which is an exchange visa, and people who come to the U.S. [United States] with J1 visa have an obligation to go back to their home countries and stay there for two years before revisiting this country for an extended period of a time.

Carl wanted me to stay there for longer than a J1 visa would usually allow, so we started the process. Then for doing that, he needed to promote me, because NIH rules didn't

allow a visiting fellow to get a visa changed.

This is kind of an interesting story. I think Carl wanted me to stay there as a scientist also. He actually offered me [a] job when I was in the job market, which is not very typical in this country. But he was just promoted and he had a few slots to fill. So, it's a little bit delicate. He indicated that if I applied for [a] job in his department, there was a good chance that I would be—well, he said—considered seriously. But also he indicated I'd have to also look for a job outside, because NIH is the only place I know in U.S., and also it would not look good for him to hire someone who cannot get a job outside.

So maybe I'm ahead of the schedule, but when I was looking for a job, I was— in a sense—not that serious about looking for a job, half knowing that there was a good chance I would get a job at NIH. It was a little bit more like, "Oh, let's see how it is like outside."

So I think that was his long-term plan. He didn't say at the beginning, but that's how he promoted me to fellow, I think. Then I got an H1 [visa], which would have allowed me to stay in this country for a longer time.

VAN BENSCHOTEN: How important, do you believe, were the papers? I guess what I'm getting at is that there's a debate that's going on about the overreliance sometimes—or the overestimation—of journal articles to promoting and advancing people in their careers, pro and con on that. In your own case, in your own experience, how important do you think the two *Cell* papers and the *Nature* paper were?

TSUKIYAMA: In getting job here [Fred Hutchinson Cancer Research Center]?

VAN BENSCHOTEN: Yes, in getting a job here, or just being heard, I guess.

TSUKIYAMA: It was probably very important. Not necessarily because they were published in those journals, I don't think, but if I published those papers in—I don't know—*Genes and Development* or something like that, I think I would have gotten the same job.

Of course, if, let's say, after I evaluate someone when we do [a] search here and if I have to evaluate someone outside of my field, it's very hard for me to say how good the research is. So it's understandable in some places people put heavy weight on where papers are published, because people with much to consider, you know, to get paper published in *Cell, Nature,* and *Science,* you have to have high standards, which is not necessarily always true. We all know that. But it's a convenient way of measuring things.

But it, I think, depends a lot on the department. One thing I was very intrigued after joining the "Hutch" [Fred Hutchinson Cancer Research Center], was the first search we had after I was hired, there was a candidate who had like eight papers in *Cell, Nature,* and

Science. We didn't even give this guy an interview, because we felt that this person was at the right place at right time, and we didn't see creativity. So what this place, especially the basic science division, values most is whether or not the person has established new concepts or new ways of figuring things out; how creative that person is, is the most important thing. So there were people who were hired out of two papers, basically, two papers not in *Cell* or *Nature* or *Science,* but something really new. And, of course, this person may be exceptional. I know this is a really, really good place to do science, and a lot of people have broad interest, maybe that's why we can do it, and this is a small division.

So it depends on the place, I think. In some places I know people count numbers of publications and places or names of the journals. They'll be sad, because that's almost like making confession that they cannot evaluate science. This place is different. They're not like that. I feel it's fortunate that I'm in that environment.

VAN BENSCHOTEN: You bring up the question of creativity, and thinking back now to your chromatin-remodeling research that you did, what were the ingredients that you needed personally to make that discovery, which you've admitted if you can do another one like this, again, you'd be very happy. What were the conditions that allowed that?

TSUKIYAMA: Do you mean personal side or experimental side?

VAN BENSCHOTEN: You mentioned creativity, so I'm trying to get at the heart of what allows certain discoveries to be made. So it could be all of these things. It could be personal or it could be typical or any of that.

TSUKIYAMA: Scientifically, I was extremely lucky. One is that a previous postdoc, Peter Becker, had established this new in-vitro chromatin-remodeling system that didn't exist before, and not much was done using that system, so a lot of things were basically up for grabs. So I was in at the right place at the right time. That's a big part of it. If I didn't have that system, or if I joined a lab ten years later after even a lot of interesting things were done using that system, it would have been hard to do the same thing. That's one thing.

The other thing probably might be what my girlfriend calls this insensitivity to pressure on my side. When I decided to take this project, and especially after the *Nature* paper, I decided to purify this factor, which takes three days of nonstop working to do the assay for chromatography fractions, and it's not something most people would do. It's doable, but just too much work. But I didn't care about it, because I knew it was important work.

I might have told you repeatedly, I don't think really about details of my future. If something's interesting, I just do it. My girlfriend mentioned to me that she would not have done that, even tried that, knowing how risky the project is. So that might have been part of

it.

So it can be either you're insensitive like me, or you can be brave or you can be smart enough to know. Whatever it is, sometimes you have to take risks, and that's probably very important to find and do something new. You either need to be very confident or very insensitive, I think.

VAN BENSCHOTEN: Was that insensitivity to pressure and to the future and making all these things pay towards a nice career in science, where do you think that comes from? Is that just simply a part of your nature?

TSUKIYAMA: I think this came from my father [Yasuo Tsukiyama], I'm pretty sure. He's like that. Yes, partly, he's a little indifferent for things. Yes, he's very insensitive to a lot of things. Yes, that would be part of the reason why I didn't get along with my father when I was younger. In finding out the same character within me was an interesting experience, but I'm pretty sure a big part of this is coming from my father, because my mother [Misako Tsukiyama] is a pretty careful and nervous person. I have to be thankful to my father.

And I think I have been on purpose trying to be insensitive because it's easy for me to live in that way. So I try not to think about my future much because it doesn't help, usually.

VAN BENSCHOTEN: The logic, too, is that if you just continue to do good work— follow your inspiration or whatever—it's going to pay off.

TSUKIYAMA: Right. Hopefully. The important thing is to do good work, and just worrying for the sake of worrying just doesn't do anything good. If that's the case, it's probably better not to think about it and just do what you want to do. That's been my philosophy and it's been a good plan.

VAN BENSCHOTEN: I only have about two more questions and then we probably should wrap up. How did you know when to end your postdoc? When the money ran out?

TSUKIYAMA: Oh, no, no. So this was also very strange situation, very untypical, probably. So I did interviews in the winter at the beginning of '97, I think. Well, from the end of '96 to the beginning of '97. And I immediately fell in love with Hutch. I knew I was going to come. I got an offer at the end of March, I think.

Then this place is extremely flexible for everything. There's no teaching, so Mark Groudine, the division director, told me, "Okay, you can come tomorrow or you can come a year from now, it doesn't matter. Whenever you feel like, just come in."

And Carl had plenty of money. His lab is extremely well funded. So he told me, "You can leave soon or you can stay around, whatever you want. If you're going to stay, stay as long as you want." That's what he told me.

Then at the time my girlfriend didn't have a job yet, so she started looking for jobs. I was going to wait until at least I knew where she would be going. Then she decided where to go probably in summer. Then I decided to move. But at the end, basically, I was spending half of my time doing service for Carl's lab, doing experiments for other postdocs, and spending half of my time doing yeast experiments, knowing that I would switch to yeast. Carl said, "Do whatever you want. I know that you are going to take that with you. You can do your experiments." He was extremely generous in that sense.

So I was also trying to return his favor by spending half of the time doing experiments for the lab, and I basically gave up all the fly projects. I left everything to the lab, so I didn't touch anything about the flies. As a result, it worked out quite well, so he kept publishing good papers with my name on them, even after I left, because of that. It worked out quite well for both of us. But I'm extremely grateful for how supportive he has been. It's a little unbelievable.

I think I decided to come here, probably, because I really wanted to start. But I could have stayed there longer if I wanted.

VAN BENSCHOTEN: When you were doing your graduate work, I asked about the culture of science and what you had learned, and it was mostly what not to do, how not to set up a lab, perhaps, in some respects. You learned a lot, obviously. But under Carl Wu, did you make any further progress in learning how scientists keep their labs together, article writing, grant writing, recruiting?

TSUKIYAMA: Yes. So let's see. What was the most significant thing? He's [Carl Wu's] a very good writer. I definitely learned a lot about writing. Of course, doing everything in English was a challenge. I remember the first *Nature* paper I wrote, I wrote something, and when it came back from him, I didn't even see the structure that I wrote. For *Cell* papers, I could tell exactly what I wrote. The main structure remained. I was very proud of it. That was pretty big, so that's something I must have learned.

Grant writing, because people don't write grants at NIH, I didn't learn anything. I didn't even know how it looks. That's something I really needed to learn from scratch when I started my job here. Maybe I can talk about it on Monday. It was really funny. I was very, very naïve.

Again, Carl is a person who really loves science, and, yes, just like the other two mentors [Tetsuhiko Shinagawa and Ohtsura Niwa] I had earlier, it was pretty important for me to see how much Carl likes science. That was pretty big. And how fair he has been; I

learned how important it is to be fair to people. Let's see. I tried that hard. Of course, I can't be perfect. Oh, one thing I learned from Carl, I think, is to be optimistic. He's unbelievably optimistic. I think it's quite common among good scientists, because we cannot avoid having ups and downs.

The first mentor of mine, Dr. Shinagawa, he was in very hard, tough conditions many times in the past. He was very optimistic. Dr. Niwa, my Ph.D. advisor, was very smart, but not that optimistic, actually.

Carl was probably the most optimistic, maybe probably because he was the most successful scientist, and it's probably easier to be optimistic. But he was very, very, very positive all the time, and I think I learned that from him, even though I think I'm a positive person to start with. But it was great to see him being upbeat all the time. Just by being upbeat and fair, I mean, you're almost half done to be a good mentor, I think. So that was a big thing.

VAN BENSCHOTEN: There's a saying, I think, "Well done is half done," or something along that line.

TSUKIYAMA: Yes, and he doesn't complain much. That's another good thing. So I seem to have learned a lot about personal sides from my mentors than practical scientific things, but I've been very fortunate, I think, in terms of mentors.

VAN BENSCHOTEN: When we pick it up again on Monday, we'll talk about the current research you're doing, and then we'll move to more public policy issues, patents, and other theoretical and philosophical issues.

[END OF TAPE 2, SIDE 2]

[END OF INTERVIEW]

INTERVIEWEE: **Toshio Tsukiyama**

INTERVIEWER: **William Van Benschoten**

LOCATION: **Fred Hutchinson Cancer Research Center**

DATE: **27 October 2003**

VAN BENSCHOTEN: This is tape three, side A. This is October 27th, 2003.

I had a question about religion. We hadn't talked about that question. I was wondering what impact, if any, did religion have on you and your family when you were growing up.

TSUKIYAMA: Okay. So just like the vast majority of Japanese, our family, my parents [Yasuo and Misako Tsukiyama] are particularly Buddhists, but it doesn't mean much, actually. It's more social than anything. For example, Buddhism probably might have something to do with your life only for your funeral or wedding, probably. So, for example, I never visited temples for religious purposes, so the impact of religion to my life is probably next to zero. Yes, that's just probably the simplest answer.

VAN BENSCHOTEN: What was the startup package that they gave you here [Fred Hutchinson Cancer Research Center, the 'Hutch']]?

TSUKIYAMA: The startup package this place gives is a little bit different from almost all other places that I was offered a job. Most places say, "Okay, we have this much funds that you can use any way you want," but here I was asked to submit a list of heavy equipment that I needed, such as chromatography machines and so on, so forth. Then they guaranteed that they would buy anything we wanted, we needed. Then they also guaranteed that they would pay my salary, as well as the salaries of two people, one technician and one postdoc [postdoctoral fellow], usually, or a student, until we got a major grant, that is either an NIH [National Institutes of Health] grant or NSF [National Science Foundation]. That's the standard for the Hutch, so depending on how soon a faculty member gets the grant, it can be very cheap or very expensive. It's an open-ended offer, and that's what I got. I, fortunately, received an NIH grant in the first round, so I'm sure I was not very expensive for that division.

VAN BENSCHOTEN: If you would, talk a little bit about your current research.

TSUKIYAMA: Sure. So my research, the center of interest of my research—the big-picture, I should say—in the long-term sense, is to understand how chromatin structure is regulated and how regulation of chromatin affects other processes inside cells, such as transcription, recombination, repair, and replication.

As a junior faculty member, I had to concentrate on a small number of things, so we initially focused on a couple of factors that are known to regulate chromatin structure, and we are trying to understand what they do and how they function inside cells. That's been the major focus of my work in laboratory.

VAN BENSCHOTEN: Let me back up a little bit. We were talking about your lab. What was the hardest part about setting up your lab?

TSUKIYAMA: Hardest part? It's not that I had a hard time. I wouldn't say it was easy. The first couple years, looking back, I would say were the hardest. Probably the most difficult thing was to see whether or not we were, as a lab, on the right track in science terms.

So it's kind of strange that I started to think about it more seriously as a PI [principal investigator], but as a postdoc student, I should have had the same kind of thoughts. But I never had a trouble. I was always happy just working as hard as I could to do research, and I did have situations that I had to make decisions on the direction, and I didn't have any problem with that. I always took the most logical—to me always—path, no matter how hard it was, and I never had trouble convincing myself that I was on the right track.

After being a PI, I had a few occasions that I woke up at night and really got this feeling that I was not sure if I was on the right track, and I had to really think about it: go one by one, what we have, what we know, what we are planning to do, then convince myself that we are on the right track, then falling asleep. It had never happened to me, so that was probably the hardest—if you will—thing, even though I didn't feel like it was very tough for me.

But it was a little strange that after becoming a PI, I started thinking about that kind of thing, because as a PI or postdoc, you always have to be—want to be, anyway—on the right track, and I never thought about it.

VAN BENSCHOTEN: How do you run your lab? How do you set it up? In other words, journal clubs or meetings?

TSUKIYAMA: So, currently we have weekly lab meetings. My laboratory is not very big. That's the way I like it. So every other week we have a group meeting that is an internal lab meeting. We pretty much know what we're working on, so this is an opportunity to let everybody know what kind of technical problems we have, what kind of directions we are

trying to go, so it's very informal, and people jump on each other freely.

Every other week, we have a joint lab meeting. I took the idea from one of the senior investigators here. His lab prefers to do one round of joint meetings with another lab, and after one round, it's over, and then maybe come back and do the same thing in a year or two. By doing this, you can get feedback from people who usually don't think about that kind of thing, so you can get fresh ideas, and it's semi-informal, so it's good training for students also, and you don't have to listen to the same kinds of things over and over again, because it's just one round at a time. My students just really like that, so we're doing this. This week, actually, we are going to start a joint lab meeting with another lab that has similar interests. After this group meeting, probably I'll look for another partner.

At the end of each lab meeting, we have two things to do. One is one week we will do a so-called two-minute journal club. This, again, was taken from the same senior principal investigator. The aim of this is to give students the habit of going over a lot of journals, so not just papers of our interest, but in a more broad view. So people would go through the tables of contents for many different journals, including *Nature, Science,* those journals that have very broad aspects of science, and people in two minutes—every single person—introduces one paper in a quick way, so people don't have to read in detail. And they can be physics or chemistry or math or social thing. So some people talk about some crazy discovery someone made, or it can be, in an extreme case, from the news if it's about science or it can be science policy. Basically, the idea is it can be anything interesting, and to me this is an aid for the students to have a habit of going through a lot of different journals on regular basis.

Every other week we have a more regular, formal journal club. So one person picks up a paper or two and we go into detail. That's all we have for regular things. I don't want to take away a lot of bench time from my students, so I try to limit that to once a week. [tape recorder off]

VAN BENSCHOTEN: All right. We're back. Does your research have an overriding aim or goal?

TSUKIYAMA: Overriding?

VAN BENSCHOTEN: Yes, do you wake up in the morning thinking, "Okay, in three years I've got to hit this, and then I'm going to move on in that and go to this"?

TSUKIYAMA: Yes. I think a lot about not three years, but five, ten years. As I said, so this is the dilemma I think a lot of people have. For junior faculty members, I was told, and I agreed, that it's very important to focus on a small number of things, because the lab isn't established yet. Everybody is inexperienced. So if you delete too much, it's hard to get things

done.

So that's what we have been doing. We have been focusing on these two factors, basically, for a long time, and I know this line of work will be fruitful— productive—for the next few years. But I also know that I have to start thinking about expanding—if you will—our area. Because if you keep working on one thing for a long time, what's going to happen—what can happen, I should say—is it gets too deep, more and more and more into detail, and at the end, nobody cares because there's so much detail.

So I like to keep an option open. Ideally, I want to have two things going on in the lab, so that if one is not doing well, the other can help. So, yes, in a short answer—it was a long answer—I do have something like that in my mind.

The center of my interest is still chromatin, and I came to realize what kind of researcher I am, so it's been my learning process. What I think I do well is to come up with one big project, a big problem that's hard to solve, and stay with it and keep attacking until something happens. So in that sense, I have been looking for something big—big problem—to work on, and right now I'm mostly interested in chromatin assembly and how it's regulated. And I think that's going to be our second branch, hopefully.

VAN BENSCHOTEN: What are the long- and/or short-term applications of your work, whether real or potential?

TSUKIYAMA: Application. You mean clinical?

VAN BENSCHOTEN: Yes, clinical.

TSUKIYAMA: Okay. I know this sounds odd, but there can be a lot of applications. For examples, the class of factors I'm working on are known to be abnormally regulated in some kinds of leukemia, and the research we're doing might give us some hints on how activity of those factors can be regulated, and that can give us some clue to how to deal with this type of leukemia and so on and so forth.

And chromatin assembly itself, if that line of work pans out, it's involved in many different things, including cancers. I'm pretty sure that kind of application can follow from our work. Though for everyday work, I am not thinking about that kind of thing. It's not like I'm against applying our work or anything like that, but what I'm trying to do is to think from a biological point of view the most logical thing, the thing that's most interesting for us.

So, of course, when we write a grant, we emphasize how useful our work can be, but I wouldn't say we're lying, but for doing everyday work, I really don't think about it that much. Of course, given that we are using taxpayers' money and also we are living by doing

what we like to do, it would be great if we can pay back some to society. But it's not something—to be honest—I think a lot about every day.

VAN BENSCHOTEN: Let's talk a little bit about your responsibilities. We'll go to a different part of the question set now. You have a lot of different responsibilities. What do you spend the bulk of your time doing as a PI?

TSUKIYAMA: Probably it's fifty-fifty between my own research and helping my students. Because of the way it's set up, I can still work at the bench. I work a lot and probably I work as much as some postdocs at the bench, which is good and bad. I know that, because as a PI, probably the most important thing is to make sure that all the people in my lab are happy and get support. So I spend a lot of time talking to the students and postdocs and technician, even though I've been pretty fortunate that all the people in my lab are pretty good. I've been very, very picky. So most of people I don't have to babysit at all. So with senior grad [graduate] students, probably I talk in detail once a week, once every other week, kind of thing. When something comes up, of course, we sit down and talk in detail, or when we write papers, we do that a lot. But on an everyday basis, it's not a lot of work for me.

With my technician, it's a little different. I work with her a lot, because she's not very experienced, and with the postdoc, it's even less. We talk to him occasionally, and he wants to be left alone, which is understandable. I was like that. We sit down and talk in detail maybe once a month, something like that.

Other than that, we have a lot—a little bit—of teaching. Well, I say a lot, because teaching is coming soon. But actually compared to outside, it's nothing. I know that.

The other thing that takes up a lot of time is reviewing papers for journals, and sometimes we get a lot of time consumed on committees, even though Hutch is very good at keeping junior faculties out from heavy committee duties, so it's not a big part of my life.

VAN BENSCHOTEN: How much teaching do you do?

TSUKIYAMA: I'm in charge of one-half course since three years ago. This is about chromatin and transcription. This is a five-week course, so I have to be there twice a week, ninety minutes each, I think. And also I teach one third of that. Then I'm responsible for grading. So it's a little bit less than two months, basically in November, and from end of October to the beginning of December, it's hard to do anything else, because it's Tuesdays and Thursdays and I have to be in class all the time. But I do not notice, because I enjoy teaching quite a bit, so it's not too bad.

VAN BENSCHOTEN: Part of your responsibilities is to travel as well. How often do you

travel during a year?

TSUKIYAMA: Yes. I actually don't go to meetings as much as I should, probably. I think a lot of people have this dilemma. On one hand, it's good to go to meetings and sort of advertise what you do so that you can recruit good postdocs and so on and so forth. On the other hand, a lot of people want to stay in the lab and get the research done, and it's a big dilemma for a lot of junior faculty members.

I go to one or two big meetings in summer. Other than that, unless I'm invited, I don't go. So probably I go—I don't know—I average two or three meetings a year. In addition to that, I occasionally get invited to seminars, so I travel, though I'm pretty sure I travel less than five, six times a year for that kind of thing. It is increasing, though, so I'll probably have to do that part a little bit more.

VAN BENSCHOTEN: You mentioned benchwork and doing it. Most of the people I speak with don't do benchwork anymore. What's the secret? How do you still continue to do it?

TSUKIYAMA: A lot of that is actually because the way Hutch is set up. For example, this place, it's very clear that science has the highest priority, so the administrative duties are unbelievably light. For example, faculty meetings for administration are once a year, or twice a year probably at the most. I think that's because people know we won't go if it's more frequent. A lot of things are done by chat or e-mail or telephone, and that's it.

And teaching—as I said—is a little bit over a month a year. Some people don't teach, so even senior PI's are doing experiments at Hutch. Though not so many people do experiments as much as I do; part of that maybe because I live like a postdoc. I usually show up to the lab between ten and eleven and stay here until midnight or one, and very often when I come to the lab, students have something to talk to me, and I sit down and do troubleshooting with them, and then go through e-mails, then do other stuff, or when I have a rotation student, I have to work with them very closely.

Very often I can do big experiments only after everybody is home, so after dinner. From seven to midnight is my free time. Very often I run chromatography columns or I do time-course experiments in that time. So otherwise, if, say, I had a child and I had to go home at five, there's no way I could have done this. Or if I have to go home at eight or ten, that would have been hard.

VAN BENSCHOTEN: I want to make clear, too, that your girlfriend [Riri Shibata] of twenty years lives in San Francisco. I think we might have mentioned that earlier as well. And you don't have any children.

Was there a two-body problem, though? Was there a time when you were trying to

get in one place together, or did you just come here?

TSUKIYAMA: No. When we were doing job hunting, we were doing it together, and we had three places that we had joint offers, including here. My girlfriend got two offers at the University of Washington as assistant professor, and she didn't take them because she just didn't like the job. Over twenty years is long enough for me to learn that whatever I think or do has nothing to do with what she does. [Van Benschoten laughs.] So she does what she wants to do, and I'm perfectly fine with that. She might come to Seattle [Washington], move up to Seattle sometime, or it may never happen. Either way, I'm fine. As long as she's fine, she's happy.

Throughout this period, we lived together for some years and then lived separated for some years and so on and so forth, and it's not really a problem. It would be horrible, I think, if she had to live in Seattle just to be with me, and if she stayed home unhappily, I'd probably run away. I just can't live like that. If she has to live in—I don't know—East Coast to be happy, I'd be happy with that. Right now it's the same time zone and everything. I can't complain. I'm very happy.

VAN BENSCHOTEN: You've mentioned administrative responsibilities already and some committees. Could you tell me maybe precisely what committees you're on?

TSUKIYAMA: The committees I have been on, one of the big ones was the admission committee for graduate students. In that we have to read like four hundred applications in detail and rank them all, then get together and rank them all again and come up with some consensus and decide how many students we offer graduate school positions. That basically wiped out one week of my time, because I had to read all of those applications and rank them, including their own research interests, recommendation letters, and so and so forth.

Others are not that big. This year I will be helping with training-grant evaluations for graduate students. For this one I probably have to, again, read some letters and research interests and interview students and so on and so forth. It won't be too bad.

Other things, we have graduate students' symposium once a year. There's an award that's established after Harold [M.] Weintraub was one of the founding members of this basic sciences division, and basically top students from all over the countries are invited here and have [a] one-day symposium. I was serving as one of the faculty committee members there for a few years involving selection of candidates.

VAN BENSCHOTEN: Funding. What are the sources of your funding right now?

TSUKIYAMA: The biggest funding comes from NIH, and about the time the Pew [Scholars Program in the Biomedical Sciences] ran out, I started investigating funds from Leukemia

and Lymphoma Society, also, which covers basically most of my salary, so that freed up some money from NIH. So those two are my current major fundings.

VAN BENSCHOTEN: You got an NIH grant right from the start.

TSUKIYAMA: Right.

VAN BENSCHOTEN: What do you attribute that to? Had you done much grant writing before then?

TSUKIYAMA: No. So I came to the U.S. [United States] to NIH straight, so I didn't even know how grants look, how thick it is, or what should be written. Then when I read my first grant application, it was not very well written. I don't think I'm a good grant writer.

The reason why I got funding, I think, was largely because of what I did as a postdoc. It was written and critiqued that this grant—it doesn't say it's not very well written—it's very ambitious and blah, blah, blah, but because this guy has done quite a bit as a postdoc, maybe there's the benefit of the doubt that this guy will probably do fine. That was what was written and I'm pretty sure that was the big reason.

Grant writing was a lot of work, actually, and one thing that was very good for me was, a few senior investigators here volunteered to read my grant and give me very straight, honest criticism. That was great help. Especially one of them, Dan [Daniel E.] Gottschling, sat down with me over two hours, just basically crossing out everything bad that I wrote. That, I'm sure, helped my grant a lot.

VAN BENSCHOTEN: Right. Besides being very humbling. How secure is your funding now?

TSUKIYAMA: I'm actually just done with the first competitive renewal, and I got an okay number. It's not spectacular. The problem is right now to feel safe, you have to have a spectacular number, the top 10 percent or something like that. I'm not there yet. So I talked to my grant officer at the NIH, and I was told unless something outrageous happens, I should be fine. I should be able to get renewal. So I'm not rewriting it.

If something happens, though, another great thing about the Hutch is that this place has a system called interim funding. So for one year I can get the exact same size of grant money from Hutch, so I don't have to fire anyone. And as long as I get the money back in a year, which is easier after you get critiqued, and if the score is not too bad to start with, just by incorporating some of the criticism you can easily raise your points. So I'm not that

worried about that right now. So Hutch—I actually don't know if this is the case for every division, but—the support, I think, is just unbelievable.

VAN BENSCHOTEN: It sounds like that's an incredible safety net to have.

TSUKIYAMA: Right.

VAN BENSCHOTEN: And it allows you, of course, to concentrate on what you're there for.

TSUKIYAMA: Right. Otherwise I'd have to rewrite just to be on the safe side. I was asked if I wanted to do it, but then also he said, given that it's likely you'll get funded, maybe it's a waste of time. So I didn't bother doing that. The senior investigator said, "Oh, don't worry about it." A lot of even senior people rely on this, so it's not like getting this is going to hurt me or anything like that.

VAN BENSCHOTEN: Like a black mark or anything.

TSUKIYAMA: Right.

VAN BENSCHOTEN: On a scale of one to ten, how much do you concern yourself day to day about funding? You have a lot of different concerns, obviously, floating in and out.

TSUKIYAMA: About funding, I don't think about it at all, usually. Once a month I get a report of how much money we have spent, and that's only the time I care about money. I know I have to write another grant sooner or later, so in a sense, I probably worry about it a little bit somewhere deep down, but on an everyday basis, I don't. I try not to think about it, because it doesn't help. So I don't know, maybe one or two.

VAN BENSCHOTEN: Another part of your job is writing articles. Describe, if you would, the writing process in your lab for journal articles. How do they originate, and then how do you get them through?

TSUKIYAMA: So for students, my postdoc has not written a paper yet, but for students, I ask them to write the whole thing first. We, of course, sit down, I ask them to give me a frame, first, introduction, and especially the results section, how to order data. Of course,

before that, we talk on a regular basis and sit down. "Okay, maybe you need this and that," to wrap up a story.

Then students write, and I sit down and correct them, and I try not to actually write the sentences so that they just convert what I write. Instead I try to point out, say, for example, this part is not logical, or this is not clear, you have to rewrite, and let them think, which is more painful and takes longer time. But this is part of training, so I have to do that.

But so far, I have been pretty fortunate that students have been pretty good about writing. And when I write, because I'm not a native speaker, I ask students to check my writing, I mean grammar, very often like that or a singular and a plural or tense is not matching within a sentence or something like that. So it's been pretty easy. That was a concern, though, to appear as a foreigner writing. I knew writing was a big part of it, and I knew I'd have to correct the writing of American students, and I was not sure if I could do it, and it's a lot easier than I thought.

VAN BENSCHOTEN: Why do you think that is? Because of your own knowledge of English, it seems to me you speak it very well.

TSUKIYAMA: I think my writing got a lot better after I wrote the NIH grant. That was big. That made a huge difference. I could write short sentences, of course, but to write logically or to—I don't know— write in a way that would push a paper from one journal over to another, I don't think I'm there yet. But fortunately, in science, you don't have to write to move people. The most important thing is to be logical and clear, and that I think I learned during writing my NIH grant. I think it made a huge difference, actually.

Right after that, I had to write something, some small book chapter or something, and I sent it to my previous boss, Carl Wu, and he said he was surprised that my writing improved so much. And I was pretty sure that was due to my NIH grant writing.

VAN BENSCHOTEN: You've described the lab management styles of some of your mentors. I was wondering how would you describe your own lab management style?

TSUKIYAMA: I think it's pretty laidback. So one thing I decided is I'm not very good at pressuring people, so it's rare. I haven't done anything except for one case to tell people that they're not working hard enough.

So there are, I think, two ways to go. One is to keep pressure constantly. But this way, you have to do it constantly, otherwise it won't work. And it takes up a lot of energy, and I knew I wouldn't be able to do that. So what I'm hoping to do is to keep encouraging people, so when something good happens, tell them how great it is.

Of course, everybody goes through good and bad times, so you cannot do that all the time. But it's very clear for students, the first couple of years maybe are a bit hard, but once they commit themselves into projects, they can sort of gain the state that this is my life, this is part of my life, a big part of my life, I really want this to be done. My goal is to get every student to that state, and once they get to that state, it's easy, because all I have to care about is how to talk to them and decide what the best way to get things done might be. I've seen a couple of students reaching that state. That's probably the biggest pleasure as a PI to see. So I'm hoping that this works for most of them. We'll see.

VAN BENSCHOTEN: I know that PIs very often say that they are not trained as managers. They do a lot of benchwork.

TSUKIYAMA: Right.

VAN BENSCHOTEN: Was there anything here at the Hutch or any other aid that helped you become a better manager, or is helping you become a better manager?

TSUKIYAMA: I don't think there is anything, though, because, as you know, I like to talk. I very often talk to other senior PIs, other PIs, about lab management, and one thing that sort of relieved me was a lot of very good scientists said, "Oh, I made huge mistakes in the past." They're very honest about it. They are talking about it, actually, and that was fun.

Also, here, it's sort of irregular, but once a year or so, the division pays money for junior faculty members to get together and exchange gossip or whatever, see how things are. I think that started a few years ago, and that maybe is a form of help, if you will.

There's a thing called mentoring system, so I have a few senior full [faculty] members who are my mentors, and they're supposed to get together with me once a year and see how things go. But because I talk to them all the time or they're on committees of my students and so on and so forth, I don't have anything formal. But I know if they think there's a problem, they actually sit down and talk to the junior faculty members in a real detailed way, so this is a no-news-is-good-news kind of deal. So I know that I'm not having much of a problem from their point of view in that sense.

Sometimes when someone is trapped in the wrong direction, in an obvious way, those mentors actually suggest changes in direction. Of course, nobody can force any PIs to change directions, but they make suggestions and things like that. It's not a big part of what I've been getting so far, I think. But it's probably a good thing to have, even though I thought it awkward that even though we are junior, we are principal investigators, and if you have to rely on mentors, you are not independent.

So I remember when Mark Groudine, our director, asked me about a mentor, I said,

"Mentor?" And he said, "Oh, let's talk about it later." So I didn't have mentors until late, but I think it's probably not a bad thing to have.

VAN BENSCHOTEN: Yes, if people want it.

TSUKIYAMA: Right.

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

TSUKIYAMA: Strength. I'm not very good at saying what's good about me, but I think I'm reasonably good at being patient when I have to be. And the other might be I'm very honest, because I know I cannot lie. So I just don't even try to lie or hide something. I try to be honest to students. That may be a good thing. I don't know. Probably I'm good at being positive. Yes, that's about it, I think.

VAN BENSCHOTEN: You provide several services, I assume, to your professional community, things like study sections, perhaps, or editorial boards. Do you do any of those things or other services?

TSUKIYAMA: The study sections I was asked to do a few times, but when I was really junior, and I said, "Sorry. I'm just trying to establish myself," so I haven't done that. I'm ready to do ad hoc things, and I haven't gotten anybody contact me, so I haven't done that. I heard doing an ad hoc study section is actually a very good experience, so I'm ready to do it.

For journals, I'm not on editorial boards on any journal, but I review a lot of papers, and it's increasing, probably several per month. I usually have some paper I'm reviewing all the time, and that takes up quite a bit of time. But at the same time, it's good for us to know what's going on, because papers are from similar research areas and it constantly asks students and postdocs to review papers, so it's a good experience for them also.

VAN BENSCHOTEN: Just a few other questions on this part of the question set. It's not really a responsibility, but you've already talked about your girlfriend and carrying out this long-distance relationship. How do you negotiate the demands of work and family life?

TSUKIYAMA: Oh, we actually don't. I do whatever I want to do, and she knows that for me science comes first. And it's a little bit hard to explain. She's the most unsocial person I know in my life, and she's not that interested in the outside world, and I'm included in the outside world, even though I'm in a special position. She doesn't want to be cared for too

much from me, so if I take care of her too much, she will run away, I'm pretty sure. She wants me to be around, but it's not like she wants my attention all the time. She's like a cat, I think. [Van Benschoten laughs.]

So for example, when we go for vacation, because I don't work, I have too much energy and I take care of her too much, like second day or first day sometimes, she said, "You should never retire, because I just cannot believe living together all the time. Don't stay around too much."

So because of that, it's really easy. For example, when she comes here to Seattle, it's usually Friday night, and she stays until Monday morning, and I work full day on Saturday and part of the day on Sunday. And she does whatever she wants to do, gardening, basically, usually, and she's perfectly happy that I'm not around. When I go there, of course, I'm around all the time. So I never had trouble finding a compromise between private life and science.

VAN BENSCHOTEN: Do you find that you go to her or that she comes to Seattle more often or is that fairly equal?

TSUKIYAMA: We take turns, even though when I go there, it's usually I take the last flight on Saturday and stay there full day on Sunday and fly back on Monday. Whereas when she comes in, she comes in on Friday night, so one more day. And because she's in a company, it's easy to do it that way.

VAN BENSCHOTEN: Let me flip this over.

[END OF TAPE 3, SIDE 1]

VAN BENSCHOTEN: This is tape three, side B now. What do you do for fun and leisure? How do you relax?

TSUKIYAMA: So, right now, because my girlfriend's [Riri Shibata's] so much into gardening, I usually help her doing gardening. But what we like to do includes birding and hiking, and in winter we like skiing a lot. Also, in San Francisco [California] in summer we often go to beaches and read books and just have a nap on beach. And once a year at least we have a camping trip for week or so. We have to sleep in a tent for a while every year, otherwise we are going to go nuts, I think.

VAN BENSCHOTEN: How did you get into birding?

TSUKIYAMA: Oh, she started that when we were both in vet [veterinary] school in Japan. I actually don't know why she started it, maybe because there were so many birds around, and also in Hokkaido, which is in the northern part of Japan, you can see a lot of birds that you don't see in any other places. I was dragged into birding by her.

VAN BENSCHOTEN: And where do you hike around? Do you hike around here?

TSUKIYAMA: Yes, so one great thing about Seattle [Washington] is, after—I don't know—thirty minutes' drive you can go to reasonable mountains, so we take I-90 [Interstate 90] very often and hike up. In winter, last year, we discovered snowshoeing, which is very fun. We do that, too. Or sometimes we do cross-country skiing. So those are things that we really like to do.

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

TSUKIYAMA: Okay. So I get up at eight or nine, and it takes me a bit of time to be sort of conscious. But then I take shower and eat breakfast and come to the lab and usually talk to students or the technician who have technical troubles or something like that. If not, I go straight to my computer and check my e-mail, and write responses. If nothing else is there, I usually start doing my experiments right away or talk to students for the experiments.

Then I don't eat lunch, usually, so I work through afternoon, and go back home for dinner between seven and nine. I usually come back in—I don't know— somewhere between forty and sixty minutes. Then I stay here until midnight or one o'clock. Very often I do a lot of thinking and reading at night when I'm not doing experiments. Yes, that's about it. It's very simple.

And in the meantime, if I have things to write, for example, when I'm writing a paper or writing a grant, I do a lot of writing at night, because I'm alone usually.

VAN BENSCHOTEN: Is this the time, too, at the end of the day when you read, you have that pile of books beside your bed?

TSUKIYAMA: Oh, yes. After I go home, I read every day. I have hundreds of books at home, so then I usually fall asleep reading something. Then I get up, start the cycle. It's a real simple life.

VAN BENSCHOTEN: Assess, if you would, your efforts so far in achieving your professional goals. How are you doing?

TSUKIYAMA: I think I'm doing all right. The first couple of years, maybe three years, I was publishing, but I was not that happy about what we were doing. It's not that I was unhappy, but I knew what we were doing was not at the level I wanted it to be. We were basically doing very simple things, knock out some genes and see phenotypes. There's no creativity there.

But I knew that that was something we had to do to come to the next level. So the last year or so, we have started doing the kinds of experiments I wanted to do, so I'm pretty happy about that. In that sense, I think we are doing reasonably fine, even though I really hope that the new direction I was talking about will pan out. And that was my summer project, and I am getting some interesting results, so I am very hopeful about that.

VAN BENSCHOTEN: Again, assess your efforts so far but in achieving your personal goals.

TSUKIYAMA: Personal goals. So that's a tough question. I actually don't have real set goal; I just want to do good science, and I want to be happy, and in that sense I'm doing fine, I think. I don't talk about this kind of thing when I'm not drunk, usually.

VAN BENSCHOTEN: We can accommodate you. I can go out and get some sake or something. There you go. [laughs]

TSUKIYAMA: So science is what I like to do, and I'm very happy to do it. I don't know how to say. Yes, this is the best job, I really like it, but my real goal that I set a while ago when I was in—I don't know—I was doing the postdoc [postdoctoral fellowship] or I don't remember when I set this goal, personal side, is to be a person who can be completely free from prejudice or what society wants me to do or something like that. So I want to be a person who can judge—make decisions—on everything I do in my life. And I want to be a person who does everything in the way I think it should be done, because whatever we do is influenced by other things: prejudice or information—wrong information—that I get from outside, whatever. Of course, it's impossible to be like that, that's why it's a good goal to have, because once you have achieved the goal, your life is done. In that sense, I don't think I'm there yet at all. So I still have to work on it.

VAN BENSCHOTEN: It sounds like total freedom, but freedom from both external and internal restraints.

TSUKIYAMA: Hopefully. Or, well, internal is fine, I think. If I want to do the things that I think are right to me, but I want to rely on my own judgment to do anything, or I want to be the person who can judge things, I should say. Not because this news said this or that or not because my neighbor said this or that; to have some internal standard for a lot of things that would be the kind of person that I want to be.

VAN BENSCHOTEN: You've already mentioned more or less where you want to take the lab, I think, or where you see the lab going in the next two or three years, but how about in ten years? Do you still yourself as a principal investigator?

TSUKIYAMA: Yes, I think so. I'll be a little surprised if I was not. I cannot think of another thing to do. I can be a teacher, I think. I found that I liked teaching quite a bit. But there is joy—pleasure—I get from research is so strong that it's a little bit hard for me to think about me doing anything else. In case I don't make it here, to be full member, maybe I'll find other job somewhere that I can do research, pretty sure.

VAN BENSCHOTEN: That brings up the question of tenure. Does Hutchinson [Fred Hutchinson Cancer Research Center] have something like tenure here?

TSUKIYAMA: We don't have tenure. Actually, we got rid of it about the time I joined. Not because I joined as a faculty member. So one thing that was outrageous, I thought, is that they took away tenure from people who already had it, which is unheard of, because everybody voted for it.

So basically, this place is a five-year renewal thing. So even after being promoted to full member, you have to have an external evaluation every five years. It's basically supposed to be as strict as a full member evaluation, and I don't know of a single person who needed to be out because of that, but I think that's what they decided to introduce to keep this place active. And I think it's only fair, because we do so little other than research, so we don't really provide any service. It's not like a state school where people can actually teach and so contribute to the university by teaching.

So in this place, if you don't do research well, you shouldn't be here. I thought it was a good idea. Even though I was not a part of the voting process, I would have voted yes strongly if I were there. But you have to be promoted to full member by your tenth year or end of tenth year, I think, something like that.

VAN BENSCHOTEN: So you're on your sixth year, then, here?

TSUKIYAMA: I am on the sixth year, right, and I was promoted to associate member about almost two years ago, I think, or year and a half, something like that, so maybe in a few years I have to go through the process. [tape recorder off]

VAN BENSCHOTEN: All right. That does that question set. Let's turn to public policy questions, and there was a question on patents. Do you have any patents?

TSUKIYAMA: No.

VAN BENSCHOTEN: What is your own view of the patent issue in science? I know that there are a group of people who feel that it blocks or it hinders the flow of information in science. Other people feel that it's a completely valid way for people to recoup some of the investment made on their research.

TSUKIYAMA: Yes, so I have mixed feeling about it. Traditionally, I was against making money out of research. I'm influenced by a Japanese tradition that a scholar is supposed to be pure and poor. I mean, they're not supposed to go after money. I still have that feeling, but at the same time, because of that, I know research in Japan has suffered because industry and academia are separated so much. In this country, big part of drugs comes from collaboration between industry and academia or from industry themselves.

So in Japan, they tried to integrate this collaboration between academia and industry, and, of course, that brings things like PIs discovering something, establishing a company, or selling that right to companies and make money out of it. If I discovered something, I'd be happy if the money is used by the Hutch to help this institute. I'm not sure I'd do anything else. It's not that I look down on people who do it, but for myself, I don't want to be bothered by money, I don't think.

But I do understand some people want to make money out of their discoveries because they work hard, but then the fact that they are usually supported by public funds helped to make it, it's a gray area. Of course, if there were no NIH [National Institutes of Health] or NSF [National Science Foundation] grant, most of the people probably couldn't have come up with that.

I actually don't even know what the system is, so it would be totally ideal if there's a system that they pay back a little bit—part of their income—to the funding source. Then they can take some either for themselves or for the institution they belong to, any way they choose, and how much should be returned to the institution is something that probably someone has to come up with.

VAN BENSCHOTEN: I read recently where about two-thirds of the biomedical research, R&D [research and development] comes from industry now. Do you feel that's a good or a bad trend? It's a fact, regardless, but is a good fact?

TSUKIYAMA: I don't know. Let's see. So if that reflects lack of funding from public institutions, it's a bad thing. If that's because industry is so wealthy that they are willing to invest money for research, that's a good thing. I'm not really answering your question, I think. But from my point of view, NIH funding, it can go up or down, but has been quite good. So I think it's probably closer to the second case, that it's not due to lack of funding from NIH, and, to be honest, it's a little bit hard for me to imagine NIH will keep increasing this scale of funding right now.

So if that's the case that a lot of researchers can get all kinds of funding from outside, it's not necessarily a bad thing. Of course, all the fundings from industry have strings attached, so how strict that is, how much that affects their research, I just don't know the details.

So having funds is good thing as long as it doesn't disturb the research, because I believe strongly that the basic research—the knowledge coming from basic research—should be freely shared by other researchers. If you cannot do that because there are strings attached, it's a bad thing, no matter how much money is available. Of course, I understand you cannot make it freely available to every single person, but that's one thing we have to be extremely careful about.

VAN BENSCHOTEN: That's where maybe those collaborations would be useful, when you give—I think this is happening—information, say, in industry, selectively, to certain universities that you have some agreement with or whatever, that might work.

TSUKIYAMA: I think the big issue came when Human Genome Project—I mean sequence—came out, and I know some people resigned from science, because science accepted the paper without guarantee that the human genome sequence would be freely available, and that was unfortunate that it happened. You cannot just take advantage of the system without sharing the standard in the community. So that's the biggest question for me: availability of information.

VAN BENSCHOTEN: When you mentioned strings attached, you were talking about, I think, industry grants, let's say, but I was thinking, too—this is a question I should have asked earlier—with the grant that you get from the NIH, does the source of your funding inform or shape the kind of research that you do?

TSUKIYAMA: Oh, you mean whether we are restricted to what we write in the application?

VAN BENSCHOTEN: Right. How closely do you cling to that?

TSUKIYAMA: Yes, in theory it should be, but we know how to handle that flexibly, because everybody knows it's hard to predict what we would be doing in five years. So we come up with the best ideas or the ideas that sound best.

In reality, NIH does not like to fund projects that are too risky, so when we write an NIH grant, we try to come up with experiments that sound interesting but also doable. In reality, we get excited about something and we come up with crazy experiments, sort of home run or strike out kind of experiments, and we do that often. If you happen to have a hit, that can change direction completely. The good thing about NIH is then if you actually change direction quite a bit, you can say that in an update on your report, that because of this we decided to change our direction, and it's usually accepted. So it's not too bad at all.

VAN BENSCHOTEN: Where do your ideas come from?

TSUKIYAMA: Hmm. I don't think it comes from one place. Very often I come up with ideas when I am talking with other people, other students, or the PIs. Sometimes it just happens. I can be—I don't know—taking a shower, I can be reading something, maybe when I'm hiking. It just happens. It's hard to say. But it's easy to think things straight when I'm explaining something to people, and that happens a lot. I'm explaining something to my student, then come up with one experiment.

Another thing is when I'm preparing for my talk—presentations or seminars— I have to think about my project from the beginning to the end, and then sometimes that probably activates some part of my brain that I come up with some new experiments. That happens a lot. Or when I go to meetings and talk to other people and from exchange of ideas or sometimes I get ideas from other people's presentations, that also happens often. I cannot tell which one happens to me most. Yes, it's really hard.

VAN BENSCHOTEN: Can scientific creativity be cultivated?

TSUKIYAMA: I think so. Here, for example, at the Hutch, it's very clear that people don't count the number of papers. So when we were trying to hire someone, it was very impressive that people repeatedly asked whether this candidate had come up with something new, new ideas, or a new method or new something, how creative that person was, and it was great. I mean, it's scary and good, I think.

If it's very clear that all the senior faculty members only care about number of papers,

probably junior faculty members get pressured to publish a lot. And unless a person is extraordinarily good, it's probably difficult to be creative and write a lot of papers at the same time, because to do creative experiments, you very often have to think a lot and the experiments tend to be hard and high risk. So it's rare that things go very fast.

Knowing that people care only more about creativity than the number of papers we have and knowing that is the culture of this place, we have the luxury of doing that kind of work, and that's definitely influenced by the culture in this place. I think it's possible to create a system or environment to facilitate creative work.

And of course, having creative colleagues help us, too, because once a week we have this faculty meeting, Friday, and it's all science, no administration, and everybody talks and gives a one-hour talk once a year. You exactly know what's going on in the other labs. And if a lot of people talk about creative work, you also, number one, get pressure to do creative work, and also you get stimulation. So that's a good thing. Unless you are truly creative, you probably have to make an effort to do creative work, so that helps.

VAN BENSCHOTEN: Did you take any history of science classes when you were going through?

TSUKIYAMA: No, no. I like to know about history, so I sometimes read books about history of sciences, but I don't think I took anything formal.

VAN BENSCHOTEN: Do you think that history of sciences classes or a class would be beneficial to upcoming scientists?

TSUKIYAMA: I think so, yes. I wish I had something like that as an option. You know, yes, I guess so, to see how personal science can be or what it takes to have breakthroughs, for example. That may be [an] interesting thing to go through. [It] may be hard class to teach.

I know that our graduate program a couple of years ago tried to set up our journal club in that way: Come up with two papers that are five to ten years apart. First paper predicted some future, and second paper sort of followed-up that to show students history within one field. It was believed in this way five years ago and then after that, this happened, kind of thing. I thought it was good idea.

VAN BENSCHOTEN: A question about serendipity. What is the role of serendipity in your research?

TSUKIYAMA: I'm sorry. I don't know the term.

VAN BENSCHOTEN: Serendipity. Chance, I guess, chance discoveries. So what is the role of chance discoveries?

TSUKIYAMA: It's big, I think. Of course, you have to be prepared to make the discovery, because I'm sure we all miss those chances. So you've got to be prepared to grab that chance, but, for example, my discovery I made when I was a postdoc, ATP-dependent chromatin-remodeling factor—as I said—I don't think I could have done that one if I was there two years before or two years after that. So something like that happens, I think. So it is big. But if you constantly try hard, it's something that you can get once and not later.

VAN BENSCHOTEN: Yes, the odds improve, be able to get in your favor.

TSUKIYAMA: Yes.

VAN BENSCHOTEN: What effect has technology and technological innovation had on your science?

TSUKIYAMA: Oh, it's big, especially because I do work in yeast. It's been sort of the model organism for molecular genetics, so I took full advantage of the genome project first, and then I've been taking advantage of the things that followed-up on genome projects, such as DNA micro-array or systematic genome projects. I'm using [a] robot to introduce my mutants to the collection of mutants that was made in the genome project. So there are a lot of experiments we are doing right now which would have been impossible ten years ago.

In biology, I strongly believe that technology is a big part of it, even though it's sometimes necessary but not sufficient, obviously, to do good science. Of course, if you are caught up on technology too much, you can miss something, and there are a lot of experiments that still can be done. So sometimes you can get too excited about techniques and forget about thinking. But I do think that technological advancement is a big part of science.

VAN BENSCHOTEN: Some people have talked about a divide, because technology is becoming more and more expensive, between those labs that can afford that technology and those labs that can't. Do you see that divide in your work when you talk to people and go to conferences?

TSUKIYAMA: Yes, I think so. So I have been pretty fortunate that this institute [Fred

Hutchinson Cancer Research Center] has been extremely good at catching up with new technologies. But there are labs that cannot do, for financial reasons, the kind of experiments we are doing. But part of the reason why we can do what we do is because, number one, the institute works very hard to get funds for those new techniques. But also, we share a lot of things. So we don't have to each buy everything, because the door is always open, and our robot is used by five or six different labs, and I use other people's equipment freely, more or less.

So there is some room for improvement, even if funds are limited. Hopefully that would facilitate collaboration more than leaving some people out. But I know in reality there are people who don't have access to a lot of the new techniques. Yes, so I can see that happening.

VAN BENSCHOTEN: In the new technology, do you find that you have the time and you have the staff to learn these new technologies?

TSUKIYAMA: Yes.

VAN BENSCHOTEN: I know that you do a lot of benchwork, so I think your situation is maybe a little bit different than theirs.

TSUKIYAMA: Well, even for me, there are some experiments my students are doing that I don't know exactly how things are done in a practical sense, but I like new toys, so that helps, and my students have been pretty good at learning new things. I think it's probably also fun for many of them. As long as I convince them how important those experiments are, I think it's not a big problem. I never have problem convincing my students to do new things. They are pretty brave in a sense, I think. So, yes, I'm sure there are times that things are so complicated that we need to hire someone or work with someone who has technologies, but we haven't done that recently.

VAN BENSCHOTEN: We often hear that there's a biomedical revolution afoot. Do you believe that there is? Are we in the midst of a revolution?

TSUKIYAMA: Biomedical revolution. Like?

VAN BENSCHOTEN: Like a complete overhaul or a change or a transformation of a field, say, from this point to maybe ten, fifteen, even twenty years ago.

TSUKIYAMA: Hmm. I don't necessary believe that. I think some people might say that because of the genomics. To me, genomics are giving us a lot more data to deal with, a lot more things to think about. Whether a lot of experiments will be doable in cell cycle in the near future, I doubt that, partly because I know most of the things, at least in our field, that are done in genomics have not discovered anything new.

If you look at a lot of DNA micro-array paper, very often they describe something that is already known, so it's easy to publish proof of concept. And when they come across something that's not expected or new, they don't have an explanation usually, because they're not doing traditional experiments to figure out what it is. So then they end up with on the waiving argument usually. Now, whether that continues forever, I don't know. Maybe someone will come up with more revolutionary ways to deal with it.

One manuscript I'm aware of is by Rick Young at Whitehead [Institute for Biomedical Research], at MIT [Massachusetts Institute of Technology], that they got together a lot of cell-cycle gene expression regulation data and predicted how cell-cycle regulation of transcription is done, and proved that their predictions were right for some genes. So they came up with a network of transcription during cell-cycle progression, but that was pretty new.

Whether that kind of thing is applicable for everything, maybe someone will try that. Whether that changes everything, I doubt it. I still believe that, if we want to go deep into the mechanism underlying some observation or disease, whatever, we probably have to take things one by one and figure things out. So to me, genomics are providing us with a new branch of research, not necessary changing everything altogether. That's my feeling. I can be wrong, though.

VAN BENSCHOTEN: In this particular system of science that you're a part of, American science, to use a short phrase for it, competition is very important. As you know, it's a big part of it, whether you're writing articles or applying for grants. Is competition a good element in that system?

TSUKIYAMA: I think so, in general, as long as it's fair competition, because I'm lazy. If there's no competition, I'm sure I wouldn't work as hard probably, at least not all the time. And because of the sense of competition, we try to the maximum, I think, to work as hard as we can.

Of course, competition sometimes means that it's hard to do long-term experiments. But the reason why I think it's good is because I know the Japanese system, which is a lot less competitive, and I even know full professors who don't write papers for years, but once they get the position, they won't be fired unless they commit some crime.

In theory, the Japanese system should allow people to think in long-term and do experiments that U.S. [United States] scientists cannot do that may be high risk or may take

too long a time for NIH to support. They can even do experiments that take twenty years if they want to, because their job is guaranteed, basically. Their salary is guaranteed by the government, so they don't have to have grants to be paid. So they can live without ever receiving any grant, no problem, if they don't have to do expensive research. But in reality, I know almost nobody does that kind of work, because if they don't have to work, they don't work. So I know competition is necessary in a sense.

Whether this is too competitive, I don't know. But still, there is some room to do research that not so many people are doing, so I don't think so. So I think it's about right, right now.

VAN BENSCHOTEN: Without mentioning names, do you know of instances where facts were fudged or papers were maybe published too soon because of a competitive attempt?

TSUKIYAMA: I actually had recently a situation that I talked about our new stuff, and someone came up to me that, "Oh, one of my colleagues has the same story." That was in Japan. And this turned out to be pretty good, so I talked to that guy. I e-mailed him, and he called me, and he was very open about how he came up with this project. It was very good reasoning; it's not like he jumped on it. And we had our own reason to work on it. He even sent me a preprint, and he told me the paper was under review. And later he told us this is in press.

But then I got back to him saying, "Maybe you should change this and that." He took many of those. And I asked him to cite and publish [that] while in preparation we also discovered the same propanes, and he agreed to do that. And I also cited his paper in our paper and sent him our preprint, and then the particular paper is under review. Of course, if we didn't know about his paper or if his paper was not coming out, we probably wouldn't have written it up at the time and tried to make it bigger story. We needed to publish that because his paper was coming out. So in that sense, it was a little unfortunate.

But as far as I can tell, everything was done in as fair a way as possible, and I'm pretty happy that way he has been honest about it and how we communicated. I ended up having a new friend because of this, which is probably a little untypical. But if competition is like this, I won't complain.

The next step, we do our own stuff, and he made it clear that his lab is not following up on this. So I also now have a few competitors, so when we meet at meetings, we know we're competing and we try not to reveal everything. And I expect them to do it, and they know that I'm not telling them everything. But we also try not to overlap completely, because we know roughly what kind of direction the other labs are going. So it's not been too bad in a sense.

VAN BENSCHOTEN: You talked a little bit about collaboration, then. That's sort of the

flip side of competition. Are you doing collaborations now with scientists?

TSUKIYAMA: We're doing some, though I prefer not to worry about other labs all the time. So when I'm asked about the reagents, I usually give them the reagents and just let them do whatever they want to do. If there's stuff we receive or requested and it was not published, we ask them [if they want us] to put their names on. And if those reagents are published, I say, "Don't worry about it. Just acknowledge us."

When we get some stuff from other labs, depending on the author, and sometimes they request to be a collaborator, which is not the way it should be. Once it's published, you should be able to use it. But anyway, some people want to be co-authors. In that sense, as long as it's not outrageous, I say yes. We are having that kind of collaboration.

And for another project we requested something that we knew was not published, but this person is a friend of mine, and he was nice enough to send those things, so we have done collaboration on that. And we keep informing him what kind of results we get, and this is doable because our interests and his interests are completely different, not overlapping right now.

[END OF TAPE 3, SIDE 2]

VAN BENSCHOTEN: This is tape four, side A.

Another question, moving down the public policy side of this question set, is about labs, your lab's scientific agenda. I know that earlier you [Toshio Tsukiyama] talked about maybe where you see the direction of your lab going in the next two or three years, maybe more long-term than this question is asking about, but given the limited resources in your lab and in every lab, what criteria do you use to choose one project rather than another?

TSUKIYAMA: So that has a lot to do with what I think is good science. So what I think is good science is a kind of science that has impact on [a] broad range of people. So the more generic effect it has, it's better. Obviously, it's a positive effect. For example, if your discovery changes people's thinking about something really fundamental in biology, that's really good work.

I want every student in my lab to have an opportunity to write a big paper. A big paper means a paper that has high impact. So that's one big thing about me in choosing the project. But also I know everybody has preferences. Some people are very good at biochemistry but hate looking at cells, so those people are no good at genetics, and vice versa. So I ask them what they like, and we choose from there. Sometimes I can tell clearly this student is good, better at this kind of work than the other, and then I sort of arrange it in that way.

I never tell them, "You should do this and that." Rather than doing that, I try to come up with consensus. But if you do well, you can sort of guide them to the direction you want to, usually. I never had a problem with that. So potential for big impact and what kind of research the students might fit well, so those are two things that I care most.

VAN BENSCHOTEN: We know that on the national level, too, the criteria that are used to determine what projects are undertaken at different labs can be affected by many different things, like 9/11 [September 11] and the surge of bioterrorist research. Recently there was breast cancer research, for instance, too, and that was, I think, initiated from PACs [Political Action Committees] and some community groups, but then it also was pushed by the Senate. So, politics plays quite a bit in determining the direction of U.S. [United States] science. You have celebrities who play a part of it.

In your mind, what is the ideal criteria? What would be the idea criteria for determining how this sort of limited amount of money that the NIH [National Institutes of Health] has and how that money is spent and allocated?

TSUKIYAMA: That's a very big issue.

VAN BENSCHOTEN: It is.

TSUKIYAMA: I know from politicians' point of view, they have to have something that they can be proud of. "We accomplished this and that." In that sense, it's probably inevitable for them to come up with those things. For example, [William "Bill" Jefferson] Clinton came up with AIDS [Acquired Immune Deficiency Syndrome] vaccine, and he declared that it should be done in ten years, and NIH built a huge institute for that. Nobody talks about it now, though, and it's been ten years, I think.

So, on one hand, I would say it's understandable, though I'd prefer that that kind of thing wouldn't take up too much money, because I think we're not clever enough to say—to predict—what would be most useful. History says that. It's very clear that a lot of discoveries that change society came from unexpected directions.

So ideally, I think if we can support as broad science as possible, that's the best way for the future to come up with research that would impact our society. So, focusing on one thing limits that, especially by taking out funds, and the things that are supposed to be not very exciting anymore turn out to be something really exciting because of one discovery. This happened a lot of times in the past. So I think it's ideal if NIH can support as broad range of science as possible. And if politicians want to have their own stuff—very focused research—I hope they would come up with additional money for that, rather than taking out money from NIH. We should all realize that we are not smart enough to predict what's going

to be useful.

VAN BENSCHOTEN: So spread the wealth, hedge your bets.

TSUKIYAMA: Right. And also, I know from my experience, we cannot do good research unless we're excited about it, so I'm hoping that I don't have to change the direction of research due to government funding. I know it sounds pretty rude, but the ideal situation is to do the research that we are excited about most, and regarding that, I'm pretty sure we can be very honest and we can work as hard as possible. If everybody does that, someone's research will be useful as a result. But it cannot be the goal, I think, because we just cannot predict what's going to be useful. So that should be the result, not the goal. That's what I think.

VAN BENSCHOTEN: Do you think that that breadth exists now within the NIH, the money?

TSUKIYAMA: I don't think so. I think NIH—at least what I heard—is NIH is getting a little bit more focused or shortsighted, that "This is an investment. We want a return." So I'm a little bit worried. At the same time I know this goes up and down in waves, so probably it's going to come back sometime. I have quite good trust in that sense. History, at least, tells us that it's going to come back.

VAN BENSCHOTEN: It will be interesting to track budget crises—national budget crises—in this trend that you're talking about, because there might be some linkage to that.

TSUKIYAMA: Right.

VAN BENSCHOTEN: The Pew [Charitable Trusts], as you know, has an initiative to try to better understand the connection between science and society, or to make the communication between the two, to facilitate that a bit more. What do you feel is the average scientist's responsibility for communicating what science is about, what their research is about, and why the public should be interested? Or do they have a responsibility to do that?

TSUKIYAMA: I think we do, because I think it's good that the public is interested in science. It's a lot more prominent in this country than in Japan, actually. I'm surprised how much people are interested in science, and I think that's a big part of why science is strong in this country. And because of that and because we are getting public funding, I think we have an obligation to return some of our knowledge to public. It's definitely a good thing for people to be interested in science; otherwise, good students won't come to science. So, yes, I

think it's a positive thing.

VAN BENSCHOTEN: What would be an effective way to do that, though? In other words, how do you improve the science literacy of Americans?

TSUKIYAMA: For example I know at MIT [Massachusetts Institute of Technology] researchers have obligations to go to local high schools and give talks or interact with students. Maybe a lot of students are too shy to come out and talk in front of their classmates. Maybe we can have programs that every lab receives a high school student who's interested in science. Something like that would be good. I actually like having young people working in my lab, because they get excited about just running a gel or making one plasmid, and it's really refreshing to see those. And it is a lot of work from our side, but something like that might be. If a lot of labs do that, I think definitely that changes. If one person, a class or one person from one year of one school falls in love with science in that way, I think that's something positive we can do to the society.

Politically, I actually don't know anything about what we do and what scientists do in recommendation to government or devising science policies and so on, so forth. That part, I have no idea. But I think it's very important for us to make efforts to keep the public interested in science, and it's a good idea to start from schools, I think.

VAN BENSCHOTEN: Have you participated here at the Center [Fred Hutchinson Cancer Research Center, the "Hutch"] or elsewhere in any of these public policy debates or questions?

TSUKIYAMA: No, but this place has a program called SEP, Science Education Partnership, so every summer, I think, secondary students have the opportunity to work with local high school teachers and set up some experiments. And they come here for over eight to ten weeks with graduate students and do experiments, and Hutch loans the equipment so that those teachers can go back to the schools and use the equipment in class.

Sometimes those students work in the lab, so I had some high school students a couple of summers, first couple of summers, and I talked to them. That's always fun. And those students actually go to high schools and give talks also.

VAN BENSCHOTEN: We have reached near the last part of that question set. It's mostly about your lab and then questions of gender and race. How big is your lab now?

TSUKIYAMA: My lab is composed of seven people including myself: four students, a postdoc [postdoctoral fellow] student, technician, myself, yes.

VAN BENSCHOTEN: Has it stayed at that level, more or less?

TSUKIYAMA: No. It's expanded recently. At one time my lab had only two people; myself and the technician. That was the smallest I ever had. And then we got three, four. So last three years or so, it's been between four and eight.

VAN BENSCHOTEN: And what is the makeup of your lab in terms of nationality?

TSUKIYAMA: They're all Americans, which is a little surprise for a person who came from NIH. We had only one American in my lab that I did graduate work. No postdoc work. Excuse me. So it's interesting. I think that's partly a Seattle [Washington] thing. This program has a lot of Americans, not many foreigners, and the city is very American also. Well, that's probably not true. There are a lot of Asians, though they are Asian-Americans, so, yes.

VAN BENSCHOTEN: How about the makeup in terms of gender? How many women and men?

TSUKIYAMA: So we have three women and four men, I think, but I actually don't care much about gender. As long as a person is good, I will hire the person no matter what. So I won't be surprised down the road if my lab becomes all female or all male transiently. Because the size of the lab is small, you can have the fluctuation, and whoever is good will come.

VAN BENSCHOTEN: How about how many postdocs and graduate students?

TSUKIYAMA: I have one postdoc, one technician, and four graduate students.

VAN BENSCHOTEN: Given your own experience in graduate school—and now we're talking about Japan as well—do you feel that the playing field is level between men and women PIs [principal investigators] in biomedical sciences?

TSUKIYAMA: In Japan, no. In grad [graduate] school, actually, I'm not in a position to be able to say that, because my boss had only one student; that was me. But my girlfriend [Riri Shibata] was in Kyoto, and I don't think she was treated different because she was a woman.

So up to the graduate school level, I don't think it's a big deal.

In Japan, a lot of times students, grad students, are hired directly to be sort of research assistant professor equivalent. At that level, I don't think it's equal to men and women. I think the women have a big disadvantage, and I can say that because my sister [Kyoko Kohara] tried to look for job for a while, and I'm pretty sure she would have gotten a job more easily if she were a man.

VAN BENSCHOTEN: Where does that come from? Where does that discrimination originate?

TSUKIYAMA: I think it's a social thing. It's a more male, chauvinistic society, that's for sure, and the people who are in power are old men, and probably a lot of people are afraid of women taking over power, and it's easy for them to keep it that way because they're in power right now.

It's changing, slowly. But, for example, my institute [Hiroshima University] had a female full professor who was the first female full professor in a Japanese national university, and there were—I don't remember—twenty labs or so, but she was the only female professor in university. But the institute was so proud of her being a female professor. So that tells you how rare it is.

Again, it's changing slowly, but I think it takes time. And, obviously, up to graduate level, it's not that obvious, I don't think. And if you're in real society, as soon as you try to get a job, I think a lot of people hit the wall in Japan. But I can only guess, because I never had a real job in Japan. But that's my feeling.

In this country, it's obviously a lot less prominent. Hmm. I actually don't know, really, whether or not women are equally treated, probably because I have a very limited life staying in my lab all the time. From looking at my girlfriend, even, I don't think she has been treated in an unfair manner because she's a woman; I don't think. I've never heard her complain about it, but, of course, she's from Japanese society, which is a lot less respectful of women, so maybe her standard is lower than an American woman. I wouldn't be surprised if she's not as sensitive to that matter as people here. But as far as I can tell, I don't think she had any trouble—being treated in unfair manner—because of her gender. So I'm pretty happy about that.

VAN BENSCHOTEN: How many women do you find in PI positions in your department here at the Hutchinson Center?

TSUKIYAMA: In this department, Susan, Cecilia, Linda, Linda, Sue, Susan. I think it's six or seven out of thirty.

VAN BENSCHOTEN: Out of thirty?

TSUKIYAMA: Yes. So Hutch, I know, had a reputation of being male chauvinistic. I know that this division tried to hire senior female faculty members for quite a while, and that can be a little tricky, because if you hire someone only because a person is a woman, it's sort of reverse discrimination. Or even worse, if someone is promoted or hired only because that person is a woman and if the Hutch or division decided to lower standards for that, it's really bad for them and the women, I think, because then people will say, "Oh, okay, they have a double standard." I don't think that's a way of respecting people.

In that sense, I think we did a very good job of hiring someone who's very, very good, and I'm very happy about that. Again, just like what I said, for my own laboratory, I really don't care much about gender. As long as someone is good, that person has to be hired or promoted, and that should be only the reason for evaluation.

VAN BENSCHOTEN: Where do the bulk of your female students go? Do they go into industry? Do they become PIs?

TSUKIYAMA: I have only had one student graduate, who went back to medical school. I actually don't know, but I expect most of them go and do a postdoc after here.

VAN BENSCHOTEN: Do women do science differently than men, in your opinion?

TSUKIYAMA: I don't think so. As far as I can tell, individual difference is bigger. I mean, the difference between men and difference between women is bigger than just men and women as a whole. I don't believe that.

VAN BENSCHOTEN: Another issue is ethnicity. African Americans and Latinos, for instance, are two of several underrepresented groups in science, maybe underrepresented here in Seattle, I don't know. I haven't looked at the demographics.

TSUKIYAMA: It's hugely underrepresented. So I came from D.C. [District of Columbia] area, and, of course, D.C.'s a city with black people, and because NIH is a government institution, they have to have a certain population, I think. So there are a lot of black people at NIH. And one thing I feel is a little strange here, is that we just don't see black people at the Hutch and even in the city much at all, and there are not so many Latino people, either. So I miss that ethnic mixture a little bit that I used to feel at the NIH. But I mean, it's not like

Hutch is discriminative or anything; it's just the city just doesn't have a lot of black people and Latino people, and I wish it was a little bit more mixture.

VAN BENSCHOTEN: In science, generally, though, those groups are underrepresented as well. What, to your mind, can be done to bring those groups into science? That's another big question.

TSUKIYAMA: Yes. Of course, so that comes to things like affirmative action, I think. So, regarding affirmative action, I also have mixed feeling. On one hand, you know, there's a group of people who are underrepresented; why don't we help? I understand that. At the same time, if people can get into a school at the lower score only because a person is from a certain ethnic group, it's also just as I said for the gender problem, not really the way we should treat people with respect; because if there's a black person who got into school because that person was smart enough, people might say this person got in because he's black or she's black.

Ideally, if we don't have to have affirmative action, that's a great thing; we have a situation we don't have to worry about. But the thing then, under the situation that a certain ethnic group is underrepresented, it may not be bad thing to have. So when to get rid of it, I think, depends on the local society, and it's something that local society has to decide.

I actually don't know personally anyone, but my girlfriend's ex-technician used to be a person who's from Ixtlan [Mexico]. He's a Latino; he has a Latino background. One thing he told her is that the biggest problem in the society he grew up in is that people think there's no hope. People just don't know that there are ways to get out. That's the biggest problem, not anything else. So just by letting people know there are ways to get education, that can change quite a bit.

So how to do it, I actually don't have a clear answer right now, but because a lot of times people don't have anyone, people don't know anyone who has been through schools and got education, if there are people like that close by that kids talk to on regular basis, that probably changes a lot. Or if in school people can teach, there are ways to get education or invite people who are from the same kind of background and [who] went to school and got education and changed their lives, that might change.

So letting people know on a regular basis, not just once or twice a year, that there are ways to get education, if things change from there, that's probably a lot better than having affirmative action and trying to fix things at the end in an artificial way. But for a short fix, if that needs to be done, it's okay. But at the same time, long-term solutions should be done, I think, to offer more opportunities or let people know that there are ways.

VAN BENSCHOTEN: Comes down to information again; getting the word out.

TSUKIYAMA: Right, I think so, yes.

VAN BENSCHOTEN: I know the Japanese is a very different society. It's homogeneous. But are there any connections in terms of ethnicity and discrimination in Japan?

TSUKIYAMA: Yes. So it's one thing that I'm not very proud of. I think it's because—as I said—the Japanese society is very homogeneous, people tend to be very insensitive about discrimination because they don't have to think about it. So I think people need to be a little bit more aware of that.

I had this situation that someone I don't know, a Japanese researcher, came to NIH to give seminar about AIDS patients, and I don't remember the details, but basically his seminar upset a lot of people because of the lack of respect about some of the AIDS patients, I think. That's not because he's really a bad person, but because he just doesn't have the habit of thinking about those things. So it's just a system.

I don't know. Japanese society is becoming more and more open to foreigners, so it might change in the long term, but it will probably take a lot of time. So in that sense, I think it's a good idea for as many Japanese people to visit foreign countries, not just U.S., just to see outside.

VAN BENSCHOTEN: We haven't talked too much about comparing the two systems of science, Japanese and American. You did mention, though, that the American system tended to be more competitive and that the Japanese system could maybe use more of that. Are there other differences, though, or similarities?

TSUKIYAMA: The biggest difference, I think, is the age, ideas on age. So, in Japan—this is an Asian thing, I think—you have to be old enough to be respected. So I'll give you one example. I used to receive a lot of phone calls from Japan offering jobs. So right after I got a job here, I got a telephone call from Japan from someone I didn't know, and that person basically wanted to offer me a full professor job in Tokyo. I didn't know this person. He didn't know me.

The first thing he asked me was my age. And I said, "What?" Then, I said at the time I was thirty-five or something like that. And he just stopped there, and I could tell immediately he was thinking, "Oh, no, this guy's too young."

Then I said, "Oh, I know other people who are old enough," and I gave him other names, which was so funny that I used to tell this to other people a lot.

So what this is telling me is that if you are too young, you just cannot be independent.

As I said, unless you're a full professor, you're not scientifically independent. By the time you become full professor, you are usually pretty worn out. You have been serving two full professors as a servant, almost; you expect your assistant professor to do the same thing to you, unless you are like angel. So that's a bad tradition.

So I think, you know, in our thirties and forties that we can do most productive, creative work, and it's almost impossible to be a full professor around that age in Japan. I think that's the biggest problem.

VAN BENSCHOTEN: It's odd about the story you tell is that it's a story about age discrimination. When people tell stories about age discrimination in American, usually it benefits the young, and in this case it benefited the older.

TSUKIYAMA: Yes, right. So I know a lot of Japanese PIs go back to Japan after they become old, because then they don't have to do much. So in this country, the higher you go, the more you have to work. But it's the opposite in Japan. You have more power and you have to work less. So get a job in this country and retire—sort of, halfway retire—in Japan is probably the best way to go.

VAN BENSCHOTEN: What is the best part about having the job that you have, being a PI?

TSUKIYAMA: The best part of having this job is probably to be able to work with young people whom you like, on something that you are very excited about, and share that excitement. That's one big part, I think. It's not something that you can buy no matter how rich you are, to work with someone who is really interested in something that you are also very interested in. I, of course, didn't know this part of science until I became a PI, and this is really fun.

Another big part is more pure science, I think. When I discovered this ATP-dependent chromatin remodeling when I was a postdoc, I knew I was the only person on earth who knew about it for a while. Of course, I told this to my boss immediately, and he didn't believe it at the beginning. But that feeling was incredible. Sometimes I was so excited when I put my film into x-ray developer, my body was shivering, and that's probably the biggest reward I got from science. Once I learned that feeling, it's was very hard to think about anything else to do in my life. So that's more for a person who does work in his or her hand, I think.

But as a PI, as I said, working with people, young people, who share interest is a big thing, and also to see students growing up—becoming better at science—is also another thing that I found is very fun. But in terms of pure pleasure, nothing is even close to the feeling I had when I discovered something exciting. Even now, sometimes students find something really exciting, I get so excited I cannot sleep, or I keep talking about what we can do or what

we should do with the student. That's probably the best part.

VAN BENSCHOTEN: The best type of insomnia, right?

TSUKIYAMA: Yes.

VAN BENSCHOTEN: That situation. What is the least pleasant part of your job, though?

TSUKIYAMA: Least part, least pleasurable. I would say I don't like writing. [laughs] Writing grants. I know it's a good thing, so it's like taking exams. You know it's a good thing for you in the long term, but it's not like you want to do it. That's my own thing.

The worst kind of feeling you can have as a principal investigator, I think, is when you feel like you care about someone in your lab's project more than that person. So it happens, I think, to a lot of people, even if that student was a postdoc, or whoever it is, is good, because young people tend to have shorter span of interest, or they have their own life.

So, for example, I had a situation that someone had to leave the lab to move on to another job, and we had a big paper submitted. The person was very, very good, but also he knew he was leaving, so he was not 100 percent into the story. But we only had two months to respond to the reviewers' comments, and it was a big, big paper for us, first big paper from the lab. So I really, really wanted to make this happen. But then, that person had to go to somewhere, had to go to a concert or something. Then sometimes I left out in the lab feeling that, "Oh, he doesn't care about this as much as I do." So that's like the worst thing you can have as a PI, I think.

But then I remember I did exactly the same thing to my PI when I was a student. I had a softball game or something in the middle of preparation for a paper. It's even a really, really similar situation. And my boss got really upset at me, which is understandable, so after I remembered that, I just laughed, and then it became a lot easier for me. And it's not like this person really doesn't care, but he has so many different things, and he just doesn't know how to separate things. And after that, it's not a big deal. But it was an interesting experience.

VAN BENSCHOTEN: It was good that you had that memory. It gave you a certain balance and perspective on it.

TSUKIYAMA: Yes, because it was such a similar situation, you know, such a good parallel. So I just had to laugh.

VAN BENSCHOTEN: You got the Pew [Scholars Program in the Biomedical Sciences] grant in '97. What were the consequences on you and your lab of getting the Pew [Scholars Program in the Biomedical Sciences] grant?

TSUKIYAMA: Oh, it was great. So I think the biggest thing about Pew [Scholars Program in the Biomedical Sciences] is it's very flexible, so I could use it in any way I wanted. Because I immediately got the NIH grant and because what I do is not very expensive, I kept—accumulated—my grant as much as possible. I carried over almost to the maximum every year.

At the end, I wanted to really use Pew [Scholars Program in the Biomedical Sciences grant], my financing, in the best way; that is, doing crazy experiments I wouldn't be able to do otherwise, rather than buying consumables or something. And because of the way we were funded, we could do that. So that's why I bought that robot, and there's no way I could have afforded it if I didn't have Pew [Scholars Program in the Biomedical Sciences] funds. I knew that it would be very useful in the long time, and it will be not only for our lab, but for the other laboratories at the Hutch, not even just our division. And it's something that I knew would extremely— strongly—facilitate our research; that would enable us to do experiments that we wouldn't be able to do otherwise. So I think that was the biggest thing. Of course, I used it for some other things—smaller purchases—but in that sense I think I made good use of that money.

VAN BENSCHOTEN: I'm curious, how much did the robot cost?

TSUKIYAMA: That whole thing cost about $100,000.

VAN BENSCHOTEN: Yes, that is. That's a big chunk of change.

Assume, maybe, that the Pew [Scholars Program in the Biomedical Sciences] people were here. They're interested in improving the program. You know that it included the annual meetings, five-year anniversary meetings, networking, all of that. Is there any way that perhaps the Pew [Scholars Program in the Biomedical Sciences] could improve that program and make it even a better grant?

TSUKIYAMA: Make it ten years. No, I'm just kidding. Give us more money.

One thing I wish I did more, probably, was to talk to people in advisory committee more, because they're obviously all very good scientists, and I wish we had time. I don't know what to do. One thing, for example, one kind of meeting I really like to go to is the Gordon [Research] Conferences. The reason is because it has a lot of free time. It's held in middle of nowhere and has a lot of free time in the middle, so people stay around and talk a

lot.

In Pew [Scholars Program in the Biomedical Sciences], we have a lot of scientific sessions, which is fun, but also we have ton of extracurricular things, which is good. But maybe we can leave out some time for not going anywhere, just people stay around and chat for hours, and that might help. And make sure that people don't go back to their room and do writing.

VAN BENSCHOTEN: Lock their doors. [laughs]

TSUKIYAMA: Yes. And with and without alcohol, it doesn't matter.

I did become good friends with many people only in the last couple meetings, and I wish I did this a little bit earlier. First couple of years, people tend to be shy, and it's even more the case with the advisory committee, advisory board members. So, if anything, if we had more opportunities to talk to people, that might be a good thing.

VAN BENSCHOTEN: Another big question. I've only got three more left. What one or two measures would you believe help improve the quality of science overall that's being done in the U.S., besides having billions of dollars more for research from the NIH?

TSUKIYAMA: Yes. Let's see. That's tough. I think obviously the best thing is to keep attracting the best students to science, because people come first. I heard people worrying about it, that the best students tend to go to different directions. If that's the case, probably we have to make a serious effort to attract the best students to science. I don't know if it's going to improve or just to keep science at a level high, but that's probably the most important thing, how to keep young people's interest in science. I think is probably the biggest thing.

VAN BENSCHOTEN: Do you have any ideas about how it might be done?

TSUKIYAMA: Hmm. I think one thing, again, is give enough information and opportunities to people for learning, because there are people who are interested in science naturally, and if they're assisted, they can take advantage of when they want to do something about science, it's there. Then that only helps, I think. Just provide more information and more opportunities to young people that they can actually experience science.

VAN BENSCHOTEN: As of today, what is the most important lesson that you've learned as a lab manager and as a scientist that you wish you had known when you started down this

path so many years ago? Any great truth that you could pass on to a budding scientist?

TSUKIYAMA: Management. I think the best tool for me is to be positive. So, for example, I have a policy that I don't talk to students if I'm upset. I wait until I'm calmed down and talk to them, and I try not to say things like, "Don't do this because this is no good," or, "I don't take you because you're not good enough," something like that. No negative things. I try to say, "You'd better do this, because this is good for you," or, "You'd better take alternative path, because it's likely that you're going to be more happy in that way."

Of course, I cannot say from their point of view, but I think it's working positively so far. We'll see. But that's one thing, I think. And I try not to say much about negative things. I don't know if they are going to stay in this way forever, but other than that, I think that's about it.

VAN BENSCHOTEN: Final question. Is there anything that we haven't covered or anything that you'd like to clarify, any topic we haven't brought up that we should before we end?

TSUKIYAMA: I don't know. It's been pretty thorough, I think, and fun.

VAN BENSCHOTEN: We try to make it thorough.

TSUKIYAMA: Yes.

VAN BENSCHOTEN: I want to thank you for allowing us to come here, allowing me to talk with you and to take your time.

TSUKIYAMA: Sure. It's a pleasure.

VAN BENSCHOTEN: Thank you.

TSUKIYAMA: It's fun.

[END OF TAPE 4, SIDE 1]

[END OF INTERVIEW]

INDEX