CHEMICAL HERITAGE FOUNDATION

SHI HUANG

The Pew Scholars Program in the Biomedical Sciences

Transcript of an Interview
Conducted by

Helene L. Cohen

at

The Burnham Institute
La Jolla, California

on

19-21 January 2000

Shi Huang

ACKNOWLEDGEMENT

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Interviewee agrees to participate in a series of University-conducted tape-recorded interviews, commencing on or about January 19, 2000, and tentatively entitled "Interview with Shi Huang". This Agreement relates to any and all materials originating from the interviews, namely the tape recordings of the interviews and a written manuscript prepared from the tapes, hereinafter collectively called "the Work."

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Attention: Director

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La Jolla, California 92037

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

INTERVIEWEE

Signed release form is on file at the Science History Institute
(Signature)

Shi Huang
(Typed Name)

Burnham Institute
(Address)

La Jolla, California 92037

Date 1/19/2000

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10/06/2021
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SHI HUANG

1961 Born in Dalian, People's Republic of China on 26 October

Education

1983 B.S., Fudan University
1988 Ph.D., University of California, Davis

Professional Experience

University of California, San Diego, Department of Pathology and Department of Medicine
1989-1992 Postdoctoral Fellow

Burnham Institute, La Jolla, California
1992-1998 Assistant Professor
1998-present Associate Professor

Honors

1993-1997 Pew Scholar in the Biomedical Sciences

Selected Publication

Buyse, I.M. et al., 1996. Physical mapping of the retinoblastoma-interacting zinc finger gene *RIZ* to D1S228 on chromosome 1p36. *Genomics* 34:119-21.

Mock, B.A. et al., 1996. *RIZ* maps to distal chromosome 4 near genes involved in tumorigenesis and nerve degeneration. *Mammalian Genome* 7:637.

Mock, B .A. et al., 1996. The B-lymphocyte maturation promoting transcription factor BLIMP1 maps to D6S447 on human chromosome 6q21-q22.1 and the syntenic region of mouse chromosome 10. *Genomics* 37:24-28.

Liu, L. et al., 1997. The retinoblastoma interacting zinc finger gene *RIZ* produces a PR domain-lacking product through an internal promoter. *Journal of Biological Chemistry* 272:2984-91.

Buyse, I.M. et al., 1997. In vitro analysis of the E1A-h omologous sequences of *RIZ1*. *Journal of Virology* 71:6200-6203.

Xie, M. et al., 1997. Transcriptional repression mediatedby the PR domain zinc finger gene *RIZ. Journal of Biological Chemistry* 72:26360-66.

He, L. et al., 1998. *RIZ1*, but not the alternative *RIZ2* product of the same gene, is underexpressed in breast cancer and forced *RIZ1* expression causes G2/M cell cycle arrest and/or apoptosis. *Cancer Research* 58:4238-44.

Huang, S. et al., 1998. The PR domain of the Rb-binding zinc finger gene *RIZ1* is a protein-binding interface and is related to the SET domain functioning in chromatin mediated gene expression. *Journal of Biological Chemistry* 273:15933-40.

Huang, S. et al., 1999. The retinoblastoma-protein interacting zinc finger gene *RIZ* in 1p36-linked cancers. (invited review) *Frontiers of Bioscience* 4:528-32.

Jiang, G.L. et al., 1999. Decreased *RIZ1* expression but not *RIZ2* in hepatoma and suppression of hepatoma tumorigenicity by *RIZ1*. *International Journal of Cancer* 83:541-47.

Jiang, G.L. and S. Huang, 2000. The yin-yang of PR domain family genes in tumorigenesis. (invited review) *Histology and Histopathology* 15:109-17.

Fang, W. et al., in press. Mapping of a minimal deleted region in human hepatocellular carcinoma to 1p36.13-p36.23 and mutational analysis of the *RIZ* gene localized to the region. *Genes, Chromosomes, and Cancer*.

ABSTRACT

Shi Huang was born in Dalian, in the north of China. His mother was a doctor assigned to a military base there, but his father, also a doctor, had been assigned to another base in Beijing. Because this was during the Cultural Revolution, Huang's parents were assigned from time to time to other locations, to "serve the peasants." Huang was sent during those times to his grandparents' house in Wuhan, once when he was about six for a year or so; and his younger brother was sent to relatives in Shanghai. This practice was common at the time in China. When he was seven or eight Huang and his mother moved to Beijing to be with Huang's father. Huang's mother found a job in a hospital nearby, and Huang's father was a microbiologist on the military base. Life in the compound, according to Huang, contained most things people needed, so except for school he seldom ventured outside the walls.

In school he did well, being attracted to painting, mathematics, and ping pong. He remembers school as being a school mostly for peasants, so not difficult; he had to learn a lot of political tracts, how to march, and how to work in the fields. He finished his school in Beijing and then went to Shanghai for college. He would have preferred the art academy, but he failed its entrance exam and decided to study genetic engineering instead. The Chinese recognized that at time the United States was superior in science, and many university students wanted to attend American or European graduate schools. He did well on his exam for the graduate program and was selected to participate in the CUSBEA (China-U.S. Biochemistry Examination and Application) program. This was a joint program between China and U.S. professors. Huang studied English for a year at the Guangzhou English Language Center, where he also learned something of American culture and prepared to apply to U.S. graduate schools.

He joined John W.B. Hershey's laboratory at the University of California at Davis; there he used a gel electrophoresis assay to study RNA protein interactions. He met his wife, Chen Ruo Ping, who had come to the U.S. on the CUSBEA program as well. She works for a start-up pharmaceutical company, and the Huangs have two children. Huang accepted a postdoc in the Wen-Hwa Lee laboratory at University of California at San Diego, where he initiated a project to express the *Rb* protein in bacteria. From there he was invited to join the Burnham Institute in La Jolla, California, where he continues his work on RIZ as a tumor suppressor gene and of course continues the scientist's continual search for funding.

UCLA INTERVIEW HISTORY

INTERVIEWER:

Helene L. Cohen, Interviewer, UCLA Oral History Program. B.S., Nursing, UCLA; P.N.P., University of California, San Diego/UCLA; M.A., Theater, San Diego State University.

TIME AND SETTING OF INTERVIEW:

Place: Huang's office, Burnham Institute, La Jolla, California.

Dates, length of sessions: January 19, 2000 (114 minutes); January 20, 2000 (111); January 21, 2000 (73).

Total number of recorded hours: 5

Persons present during interview: Huang and Cohen.

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's Pew Scholars in the Biomedical Sciences Oral History and Archives Project. The project has been designed to document the backgrounds, education, and research of biomedical scientists awarded four-year Pew scholarships since 1988.

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

For technical background, Cohen consulted J.D. Watson et al., *Molecular Biology of the Gene.* 4th ed. Menlo Park, California: Benjamin/Cummings, 1987; Bruce Alberts et al., *Molecular Biology of the Cell.* 3rd ed. New York: Garland, 1994; Horace F. Judson, *The Eighth Day of Creation.* New York: Simon and Schuster, 1979; and recent issues of *Science* and *Nature.*

The interview is organized chronologically, beginning with Huang's childhood in China and continuing through his undergraduate work at Fudan University, his graduate work at University of California, Davis, his postdoc at University of California, San Diego, and the establishment of his own laboratory at the Burnham Institute. Major topics discussed include his childhood and education during the Chinese Cultural Revolution, his continuing research on *RIZ* and the PR gene group, and his personal philosophy of life.

ORIGINAL EDITING:

Ji Young Kwon, editorial assistant, 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.

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

William Van Benschoten, editor, prepared the table of contents. Kwon assembled the biographical summary, interview history, and index.

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INTERVIEWEE: **Shi Huang**

INTERVIEWER: **Helene L. Cohen**

LOCATION: **The Burnham Institute, La Jolla, California**

DATE: **19 January 2000**

COHEN: I usually like to start with something very simple, like when and where were you born?

HUANG: I was born October 26, 1961, in a coastal city of China called Dalian, in the northern part of China. That was at that time in China right after the Great Leap Forward movement. There was a lot of farming and bad nutrition, so kids born at that time generally didn't have very much food. You can see that most of the kids born at that time were kind of malnutritioned.

COHEN: Were you born in a farming community?

HUANG: No. My mother [Peng Jing Min] was a doctor in a military hospital in that city. Generally speaking, the military personnel fared better than the average people in the factory or in the village. But my father [Huang Ce] was in Beijing, so my mother and father were separated at that time.

COHEN: By their choice, or they were separated by the--?

HUANG: Well, they were separated after graduating from medical school. One was assigned to Dalian, and the other was assigned to Beijing. I guess they were not in love in college. They started their relationship after graduation, and then they tried to work out the family. That was only later. Then my mother moved to Beijing.

COHEN: But that was after you were born?

HUANG: After I was born, yeah. Maybe when I was about six years old the family moved to Beijing.

COHEN: Now, was your mother in the military, or was she a civilian doctor working with the military? Is there such a distinction?

HUANG: Well, now there is. But at that time, no; they wore military uniforms. Both my parents went to this college in Harbin, the north part of China--Manchuria.

COHEN: Manchuria?

HUANG: Yeah, in that region. [They were at] that college--at that time it was the 1950s--from 1951 to '56 or '57. In '49 the communists took over China and then they fought the Korean War with America, so my parents were recruited right after the '49 revolution into the military, together with many high school--about a hundred, two hundred or so--graduates mainly from three provinces in central China: Hubei, Henan, Hunan. They were recruited to get trained so that they could later go to Korea to fight the war, and because they were educated, they were not trained, actually, as soldiers, but they were trained probably as doctors. So they were wearing uniforms when they were in this college. Then the war in Korea was over before they graduated. In '53 I think the war was over, and in '56 they graduated. Then all of their class got assigned to different military units all over the country, either in biomedical institutes or hospitals. So my father was assigned to the Chinese-- Academy of Military Medicine. Then my mother was sent to this hospital in Dalian.

COHEN: Now, were they trained in Western medicine or in traditional Chinese medicine?

HUANG: Western medicine. Yes, that whole college was in Western medicine.

COHEN: So when did they marry?

HUANG: When did they marry? 'Fifty-seven, '58. I'm not sure exactly, but around that time.

COHEN: But they were still in two different places at that point?

HUANG: Right. At that time that was not so uncommon actually and people didn't take it as such a strange thing. So that was common. You saw this kind of family everywhere.

COHEN: Do you have other brothers and sisters?

HUANG: Yeah, I have a younger brother [Huang Wei], who is one and a half years younger.

COHEN: So you were the first?

HUANG: Yes.

COHEN: This was before the time they started limiting families to one child?

HUANG: Right, that was before.

COHEN: That was during the Cultural Revolution?

HUANG: After, I think. In the seventies they started to have that. Yeah, some of my parents' classmates--one of them is very close--had actually three children.

COHEN: So the first few years of your life were in this northern province?

HUANG: Yes.

COHEN: Did you see much of your father during that time?

HUANG: Not much. When I was born, I think he was not there. My father was more like a workaholic. My mother's more the traditional type of woman that takes care of the family. So yeah, not much.

COHEN: Did your mother stop working when you were a baby? Because in many families, the grandparents took care of the children and the women worked.

HUANG: Yes, that happened also in my case. My grandparents [Huang Guo Yu and Xia Xiao Yu] sometimes came over to live with us for a few months or half a year to a year. Also, I was sent to my grandparents' home in the city of Wuhan, and I was with them for one year or so.

COHEN: How old were you when that happened?

HUANG: I think it was first grade. I actually attended school in that city. Yeah, that happens. So the grandparents did take part in raising us. Also, we hired a nanny-type to help when I was in that northern city. My mother continued to work.

COHEN: I see.

HUANG: Yeah, you don't expect to quit work in that kind of a situation.

COHEN: So would these be your mother's parents or your father's parents?

HUANG: My father's parents. My mother's parents were already dead at that time, so I've never seen my mother's parents. But that was partly because my mother was the smallest child of her father. Her father [Peng Shan Tian] had remarried, so my mother's mother [Zhu Hua Xiu] was her father's second wife. During the war with Japan, my mother's mother died of pneumonia, which if it were not for the war, could have been cured easily with antibiotics. At that time it was just not available in this very backward city.

COHEN: Well, actually, penicillin didn't really become available until the mid-forties anyway.

HUANG: Yeah, that's when it happened, in the 1940s. With the war in Japan, I think it was around that time. That's my impression. So she died relatively young. Then my mother's father, of course, was already pretty old when he had my mother, so he had this hypertension problem. He passed away with bleeding in the brain or something.

COHEN: A stroke?

HUANG: Yeah, a stroke or something, in the fifties.

But my grandparents on my father's side were very healthy. They lived well over eighty years old. They only passed away after I came here to the States, maybe three years ago.

COHEN: Okay, so what is your brother like?

HUANG: My brother is a typical secondborn, I guess. Very low-key, relaxed, and not very competitive. He did very well academically in middle school, so from middle school he went to a very good, very prestigious high school in Beijing. But then he started going downhill academically [laughs] because he started playing, so he ended up going to an average university in Beijing. From there he went to an institute related to his major, which is something about mechanical engineering. There's really not much to do in that kind of research institute. Then he got a chance to go into an international trading company. It's called CATIC [China National Aero-Technology Import and Export Corporation]. It's something related to aircraft equipment and all sorts of machinery. They're doing a lot of deals with South America right now, so my brother, right now, is in Peru; he's trying to sell them military trucks. He got into this kind of business. I guess, financially, he is doing very well right now. And this is a state-controlled trading company. In the past, all the trade between local factories and the outside world had to be mediated by intermediary agencies like this trading company. So that's what they're doing--connecting the customers in the West with the producers in China.

COHEN: When you were a kid, did you get along with him?

HUANG: Yes, mostly. As I said, I was more of a typical firstborn. He was a typical secondborn. So most of the time he would just obey me.

COHEN: How lucky for you.

HUANG: Sometimes we fought also. [mutual laughter] Yeah, that's kind of unfortunate. Sometimes your birth order controls your fate and your personality. I see that now from my own two boys. The second one [Samuel Huang] is just-- You worry how he will survive in this competitive society [mutual laughter] with all the firstborns being so dominant.

COHEN: So is that how you would describe yourself growing up--more dominant?

HUANG: Yeah, I would say I 'm more dominant, more conventional, conservative, traditional--that kind of thing. Even now if I talk with my brother about politics and stuff, we have very different views. For example, Taiwan. I'd like to see it reunited with China even if we have to take it by force, but my brother's not so much worried about that. I'm more of a conservative, I think.

COHEN: At what age did you start to go to school?

HUANG: Seven.

COHEN: Oh, not till seven? Wow. That's late compared to here. Kids here start at three.

HUANG: Three?

COHEN: They go to preschool.

HUANG: That's preschool, yeah. In terms of kindergarten, I went to kindergarten.

COHEN: Kindergarten's five usually, here.

HUANG: By seven I meant going to real primary school--first grade.

COHEN: I see.

HUANG: Before that I did go to kindergarten, maybe [when I was] four or five.

COHEN: Is kindergarten academic at all, or is it just mostly play?

HUANG: Mostly play. That's my memory. I don't remember learning anything special.

COHEN: So when did you go to Beijing? How old were you?

HUANG: I'm not sure exactly, because at that time there was-- My memory is that I also went to Wuhan. I attended primary school there.

COHEN: That was with your grandparents?

HUANG: Yes. The reason for that was my mother had to be sent to the countryside to be a doctor for the peasants and to get educated. You know, they're intellectuals, and the government at that time was sending all these intellectuals to factories, to villages, to the countryside, and to work in the field in the meantime to serve the peasants.

COHEN: When you say to work in the field, you mean to do farming in addition to--?

HUANG: Yeah, yeah, right. In addition to taking care of them.

COHEN: Okay.

HUANG: So my mother was sent to [Shanxi province]. Shanxi is a place [where] Mao [Ze-dong] led his troops into the city. After the Long March they went to Shanxi for some time to fight the Japanese. It's still a very poor place. My father was somewhere, working, so both I and my brother then were sent to relatives' homes. I was sent to Wuhan to live with my grandparents, and my brother was sent to Shanghai to live with a relative on my mother's side. So I remember I spent a year or so in Wuhan, and then I came back to Beijing maybe when I was seven or eight.

COHEN: You know, the culture here is such that we would be horrified at splitting up a family like that, but I guess this was sort of normal at that time.

HUANG: Yeah, at that time it was very normal.

COHEN: Do you recall how you felt about it--you know, being sent away from your mother and younger brother?

HUANG: I don't remember anything.

COHEN: You don't remember?

HUANG: Yeah, I don't remember that much. I guess I was used to [being] without a father. I don't remember how I felt when I was separated from my mother. I think I was more close with my mother than my father. That's for sure.

COHEN: So what were the circumstances that brought you all back together in Beijing again?

HUANG: I think somehow my mother managed to find a job in the Beijing military hospital. I don't know how they found it, but that's how she moved to Beijing. She had this job in another military hospital which was not too far from where my father worked. It was about fifteen minutes by bus.

COHEN: At that point did you all live together?

HUANG: Yes. We lived in my father's military compound, where you actually had walls separating [you] from the streets, the outside. The compound was guarded by about thirty soldiers with guns standing at the door. That was a research institute of this military academy.

COHEN: So your father was a researcher--

HUANG: Yes.

COHEN: --rather than a-- Did he practice?

HUANG: No, he didn't practice medicine at all, I think. Right after graduation he was assigned to this institute to do research. At the time it was considered a more prestigious job to do research than to practice medicine.

COHEN: And what did he do? What kind of research?

HUANG: He did microbiology. It was mostly an applied type of microbiology, like how to detect pathogens. In the military during wartime, if there is some bacterial warfare or something, you need to be able to detect the bacteria or the pathogen. So I think he studied how to detect them using antibodies. He was into developing antibodies, monoclonals. He also developed some kind of instrument, a convenient type of microscope that was portable and could be carried by soldiers in the field. Especially this fluorescent microscope-- Normally, it's a big setup. He developed this convenient setup to put immunofluorescent capacity to a regular microscope. He did that kind of work.

I think that work was highly praised in China; he got some prize for that and he wrote a book about it. It was especially difficult to do because he did all this work in this Cultural Revolution period when most people were not working on this type of work. So I think he did pretty well in his career. In his military academy, he was maybe one of the top fifteen professors.

COHEN: So it sounds like you were around seven when you went to Beijing, right?

HUANG: Yeah.

COHEN: Now, let's see, this would have been-- You said you were born in sixty--?

HUANG: One.

COHEN: So this would have been about 1968?

HUANG: Yes.

COHEN: When did the Cultural Revolution start? It was right around there.

HUANG: 'Sixty-six.

COHEN: Okay. So tell me a little bit about your school experiences and then anything you remember about the Cultural Revolution.

HUANG: I think for primary school we basically--because of the Cultural Revolution--could not go to very selective places. We went to school based on geography. This school happened to be nearby, so we went to it not because it was a good school-- If it was a bad school, we had no choice but to go. So the school I went to was not particularly great. It was in the countryside. This military compound was located in the suburbs of Beijing, so it was not in the downtown city area; it was surrounded by farms. So this school was sort of like a farm school, and the quality was not so good.

I think we still went through all the normal classes. I don't remember that we learned. Just played. There were still classes every day, except the text that was taught was related to the

Cultural Revolution. So there were a lot of political articles to learn, like Mao's thoughts, Mao's writing. A lot of his writings were in the textbook. I remember memorizing some of his articles. But I think the classes were not very heavy.

I think I had some interest in physical education and also art, like painting. At that time I was very much into playing Ping-Pong, so I spent a lot of time after schooltime playing Ping-Pong. At that time I think Ping-Pong was also very popular in China. Some people won the championships, so I dreamed of becoming a professional Ping-Pong player. [mutual laughter] So I basically had two hobbies at that time: Ping-Pong and art.

I did well in those schools. I was sort of a class captain. In China, every class--about forty-five, fifty students--selects some leader-type position to head the students or something.

COHEN: Is that based on your academic achievement or your popularity?

HUANG: I think it's the relationship with the teacher and academic achievement.

COHEN: So the teachers selected the leader--

HUANG: Yeah, I think the teachers selected.

COHEN: --not the other students?

HUANG: Not the students voting or something [mutual laughter], but I think my academics were very good. I always remember being at the top of the class in academics.

COHEN: Now, I actually have already interviewed another person who grew up in China during the Cultural Revolution, and I'm interested in what your perspective on it is, because Americans have this perspective that the Cultural Revolution was a very repressive time in China. But the other scholar that I interviewed said exactly the opposite.

HUANG: Oh, repressive? No, I did not feel repressed, because I think my parents were not that repressed by this revolution, since they were-- Well, my father's heritage must have been okay with the Chinese government. My grandparents were peasants, so you can see they were Red. [laughs]

COHEN: That's a good thing to be.

HUANG: That's a good thing. My mother's side was a little bit of a problem. It was more like a capitalist type of heritage. But since they were both in the military-- The military was relatively protected in the Cultural Revolution, so I don't feel they were repressed, even though I sometimes worked with my father to-- How do you say this? Basically, the military had a duty to provide energy to-- During cold weather, you need--

COHEN: Oh, a power plant?

HUANG: A power plant. And this was burning coals in this big stove to produce steam to warm--

COHEN: For heat?

HUANG: --the houses for heat. My father actually was assigned to do that. So I remember--

COHEN: How old were you then?

HUANG: I think it was second or third grade.

COHEN: Okay.

HUANG: But I sort of think that was fun. It was not repression. So especially from my perspective, growing up in the military compound was a lot of fun because you got to play a lot. Mostly, of course, we played with kids in this compound, and at the time there was a lot of activity going on--you know, all these kids playing together and group activity. Sometimes the kids--a group inside the compound--would fight with kids outside, throwing bricks on either side of the wall. It was very typical at that time in Beijing, because there were many military compounds all over the city and there was, all the time, fighting between the military kids and the nonmilitary kids. It was group fighting--hundreds of people involved. There's a good movie describing that period of life. It won some award in some European movie festival.

COHEN: What's the name of it?

HUANG: *In the Heat of the Sun.* It describes this little kid growing up in a military compound, what his life is like during that period. I saw that movie, and I can relate to it so much. Basically that movie tells you these kids had a lot of fun. [mutual laughter]

COHEN: Now, did your family have its own apartment? Because I know there are periods of time in China where families had to share kitchen facilities. You know, they might have sleeping quarters that were their own, but there was a common kitchen.

HUANG: No, I remember they always had their own units. It was more like the condominium type of arrangements here. So it was a stretch of units, and each family got a single unit which was separated from the others, but they shared walls. So all the housing was in this compound.

We always kept moving, with the houses [getting] bigger and bigger.

COHEN: So periodically you improved your--?

HUANG: Yeah, yeah, exactly, because ranking moves up as you get older. They moved to the kind of houses that fit their ranking.

COHEN: So how much of your life was inside this compound? Did you get out to do things, or did you pretty much live there?

HUANG: Well, you go to school. That was outside. After school it was pretty much inside. Then if you went shopping, you had to go outside. Yeah, at that time if I was playing Ping-Pong-- Actually, the compound had better facilities. Yeah, [I spent] a lot of time in this [compound].

COHEN: Well, American military bases have everything. They have shopping and they have movies.

HUANG: We had everything.

COHEN: You could conceivably never leave.

HUANG: That's true. We had a small grocery shop for some food and stuff, but not for clothing of course. [For] that you had to go out. This military compound, this institute, had everything, and they took care of everything.

COHEN: How long did you live there? Did you spend the rest of your childhood there?

HUANG: Yes, I think pretty much after I came to Beijing. I stayed there until I graduated from high school. Then I went to university in Shanghai.

COHEN: Okay, we're going to get to that in a little while. Tell me a little bit about the school system. Here we have elementary school, then middle school, then high school. How is it where you were?

HUANG: At that time we had primary school; it was five years. At that time they were just beginning the transition. Before the Cultural Revolution, primary school was six years. Then [with] the Cultural Revolution, they shortened that into five years. So I ended up with five years of primary school.

COHEN: So until about twelve?

HUANG: Yeah. Then [there's] about five years of middle school and high school, so basically middle school for three years and high school for two years.

COHEN: How did elementary school differ from middle school and high school?

HUANG: How did they differ? Usually they were at different locations, different schools. Here, sometimes they have everything from first grade to tenth grade all in one school sometimes.

COHEN: Usually not.

HUANG: Usually not, okay. There it's somewhat separate. Then of course the curriculum is different.

COHEN: The big difference here is that in elementary school, kids have one teacher the whole

day. Then when they go to middle school, they have different classes. They go from class to class, so they have one teacher for history and one for English and one for--

HUANG: That's sort of like in the university setting already.

COHEN: A little bit, yeah.

HUANG: They don't really have a fixed class.

COHEN: Well, no, it's fixed, but it's different rooms, different teachers. They go every day to the same classes, but--

HUANG: Do you sit in the class with the same classmates every day?

COHEN: Yeah. So what was it like there?

HUANG: There, the classes were always fixed. For primary school you stay with the same class for all five years. It's not like here. Every year they break up the class-- from my kids' experience. So you stay with the same class for the whole year. I think that's also true until high school; all the way through high school you stay with the same class. Then the primary teacher is responsible for the general activities in his class. This teacher can happen to teach different subjects. It doesn't matter. He can teach mathematics or literature or history, but he is also responsible for one of the classes. And then different teachers will teach this class.

COHEN: So the teachers come to you, or do you go to the teachers?

HUANG: Teachers come to this class.

COHEN: I see. You said academically that you did very well when you were little. Did that continue on?

HUANG: Yeah, that continued on basically. That was not that demanding--the school classes.

Then during middle school there was a lot of emphasis on the students to learn something

else in addition to the traditional classes. So we learned from the peasants, we learned from the workers, we learned from the soldiers. Each quarter we were sent to the farms to actually help the peasants to harvest the crops for two weeks maybe. Then [during] some quarter we were trained by soldiers to walk straight.

COHEN: March?

HUANG: March--things like that.

COHEN: Did you like those things?

HUANG: I think I didn't like the farm work that much, but the training by the soldiers was okay. Also, we were sent to hospitals to learn from the doctors how to treat patients. I remember doing acupuncture.

COHEN: Oh, really?

HUANG: Yeah, on patients. I learned that. I even remember I did that on my grandparents.

COHEN: Oh, really? [mutual laughter] That was brave of them to let you do that.

HUANG: But acupuncture is well accepted in China. It's not considered that dangerous.

COHEN: Oh, no, I mean it was brave of them to let a little kid do it.

HUANG: Yeah, even in the hospital they let us do it.

COHEN: Yeah?

HUANG: I also remember I learned to sell stuff in a grocery store.

We did all these extracurricular activities during the middle school years, so you can see the classes were very light. There was no real pressure on performing well for these studies,

since there was no future. At that time nobody thought they were going to end up going to universities, because at that time universities stopped recruiting students the normal way, because universities recruited from the students who had worked in the countryside and then the selection was not based on academics.

COHEN: So at that point in your life, what did you think you were going to end up doing in the future?

HUANG: One is, I worked real hard on my Ping-Pong. The other-- In middle school there was a good art teacher. At that time, besides learning all this other stuff, they also encouraged you to participate in clubs of music, art, and stuff. So I was in one of the art clubs--groups, they called it. I remember doing very well in my painting. At least in my school, I must have been at the top. So that further got me interested in it.

Up to this day I never thought I had a talent in art.

COHEN: Oh, really?

HUANG: I always thought that I did well in art because I trained hard. I was trained that way. But then I realized from my kid--his art-- I have two kids [Matthew and Samuel Huang]. The younger one [Samuel] is excellent in his art. Just natural. That talent was noticed by the teacher in his kindergarten. He just continues to be very good. Recently, one of his pictures was selected for exhibition at the San Diego [Museum of] Art in Balboa Park. One out of eighty students in his class. He said he didn't even pay attention; he just drew it. That's it. And the teacher selected it.

[END OF TAPE 1, SIDE 1]

HUANG: From him, Sam, I realized he must have a talent, because his older brother [Matthew Huang] is obviously not as good as he is. It's very clear. And he certainly was not trained by anybody. It's just natural. So that makes me think that maybe I also have some talent.

COHEN: Since you studied genes, maybe--

HUANG: Yeah, that's how I feel now. But at that time in China, nobody--the teachers or anybody--said this had anything to do with talent. We didn't get that impression from the teachers. So I dreamed about being a Ping-Pong player or a professional artist.

COHEN: Was that actually a possibility? I mean, my understanding is that pretty much people were sent to the country, to farms.

HUANG: Yes, that was a possibility. To be a Ping-Pong player, definitely. To be an artist, you don't have to go to a formal academy to get trained--that's my understanding--so I think that was a possibility.

In fact, that was very popular at that time since there was not much formal academics you needed to spend time on which had no hope. If you do academics, the aim is to go to a university. If university is not the outcome, then you do something else. So I think art is one of the things that kids did at that time. Another is music. A lot of kids studied music. My brother actually studied a little bit of violin, but he was not interested in that at all.

COHEN: So when you graduated from high school-- Let me back up for a minute. Did you have any aptitude yet that you knew of for science or math or any academic pursuits?

HUANG: Oh, yeah. I remember I was very good at math. That was one of my strong points. I even got the impression that people who are good at art are also good at math, because one of my art teachers at the primary school also happened to teach mathematics. So basically, I was interested in math and trying to do a lot of homework and participating in the math olympiad and stuff. [I had] no particular interest in science, because I knew in general that I would be pursuing science-related topics in contrast to literature or that kind of thing.

COHEN: You did know that?

HUANG: I did know that.

COHEN: Did you get a choice?

HUANG: No, I didn't get a choice. But somehow-- You know, we did have these different classes [to] study this and that--math and history and literature. I enjoyed reading novels and stuff, but I think that there is something to do with Chinese traditional values [so that] I thought I would pursue real substance careers. [mutual laughter]

COHEN: Which would be things that are more math and science?

HUANG: Yeah, more material--math and science. But not medicine somehow. I don't like medicine.

COHEN: So when you were a kid, I know you played a lot of Ping-Pong and did artwork, but did you play at science at all? Some of the people said they liked to build things or they liked to take things apart.

HUANG: Yeah, there were students that played [with] radios; some had radio transmitters and stuff. I actually didn't do any of those. Probably Ping-Pong and art kept me, already, busy enough. I was pretty determined at that time. I'd wake up at five or six in the morning--it was still dark--and I started running, to train.

COHEN: For Ping-Pong?

HUANG: Yeah, for Ping-Pong and also just to keep in shape in general.

COHEN: Wow. How many hours a day did you practice?

HUANG: I don't remember. Some days it was very long; some days short. It was not a formal kind of training. It's not like when you go to a club. These days if you want to learn something, there's always a class somewhere. You pay the fee and then you get in.

COHEN: Here or there?

HUANG: Both places now.

COHEN: Both places?

HUANG: Yeah. But at that time there was not that kind of thing. It was all between friends playing together.

COHEN: Did you ever actually compete?

HUANG: Yeah, I competed, representing the school to play other schools. The school team--I was on it. But I guess I never moved up higher than that.

My interest in Ping-Pong sort of stopped sometime after primary school. I got more into art, so I was then spending a crazy amount of time in art. Sometimes I remember staying up the whole night to paint, to draw. It was becoming sort of a routine for me to just stay up nights. And now I can never do it. That's too much of a disruption in your whole life. But at that time it was quite routine. Then our teacher that had us as a group of art students in the summer break from the school would have us go to the countryside, go to the scenery, go to the suburbs of Beijing, even the park to draw.

COHEN: This is a little bit interesting to me--that literature was considered a soft pursuit. But art was not?

HUANG: Yeah, art was not.

COHEN: Because here we think of--

HUANG: In China, there is a saying: You have one skill as your specialty, then you can live. You can fare well in society. So art, at least at that time, was considered very prestigious. I don't know if it's useful, but maybe it was prestigious or something. And it's a skill. Whereas literature-- [laughs] Everything in your mind--you have to write it. It doesn't give people the impression that that's a skill.

COHEN: Interesting.

HUANG: So you can make a living by being an artist--a good living actually. That's because, I think, there are a lot of famous artists. They were perceived as very high in society.

COHEN: Okay. So when you graduated high school you were about seventeen or so at that point?

HUANG: Yeah.

COHEN: You said you went to the university and I'm wondering how that happened, because that wasn't--

HUANG: You're interested in art? Okay, [this is] what happened: In the third year of middle school things started to change, in '76 or '77.

COHEN: In the country, you mean?

HUANG: In the country. Deng Xiaoping started to take a position of leadership, and then he started normal university education. And all of a sudden all these high school students had a chance to go to university.

At that time I was in the third grade in middle school going to high school. I was good at both art and the academics--math and stuff--but my first interest was in art. So after the first year in high school, I took an entrance examination for the Central Academy of Art [Zhong Yang Mei Shu Xue Yuan] along with several of my friends. I just barely failed that test, so I didn't get into it. Then there was one year remaining before my formal graduation, so I said, "Okay, there's this one year left. I'm going to try to study hard to get into a regular university to do a career in science." [laughs]

COHEN: So you decided then to do science?

HUANG: Yeah, because I didn't get into that art academy.

COHEN: And why science as opposed to math? Because you said you were more interested in math.

HUANG: Oh, math was just being good at it. I never thought of pursuing math as a career.

COHEN: Okay.

HUANG: So I went to a science university, and I needed to pick an interesting subject. I think maybe my father helped a little bit in that regard, in picking genetic engineering. I think genetic engineering at that time was just up-and-coming, so it was a hot topic right then. That got me interested. I wasn't going to be interested in medicine, so this was a good alternative.

COHEN: Now, did you have a choice though? The other scholar that I interviewed, who is from China, was working on the farm--he'd been sent to the country--and he was just plucked up and sent to a university and told what he was going to study.

HUANG: Yeah, that was before '77, must be.

COHEN: I think it was just when it first started, when the—

HUANG: If he was just picked and assigned to something, then he must be the class that was before '77.

COHEN: The very first--

HUANG: 'Seventy-six or '75. Those are the students who were sent to the countryside and then picked to go to the university. For us, we needed to take an entrance examination, then we had a choice of our universities and also subjects.

COHEN: Okay. So you went to Shanghai?

HUANG: Right.

COHEN: And why did you choose--?

HUANG: Shanghai? I was always under the impression that-- Because I grew up in Beijing and in this military compound, I saw a lot of educated people--professionals, famous scientists, artists, literates. They mostly spoke Mandarin with an accent, meaning that they were not native Bejing people.

COHEN: Not native to Beijing?

HUANG: Not native to Beijing. They all somehow studied in Beijing and stayed on. So to me, it was always romantic to go to a far place to study, just like I imagined these people did when they studied here and then they became successful. [I thought] maybe that's the way to become

successful--to go to faraway places. So I always thought of leaving my family to go to a different place to study. And then Shanghai, of course, is the best place outside Beijing to go--the best universities.

Then in terms of the subject I chose, genetic engineering, the university I went to is actually the best in that subject, not only in general reputation, but particularly in that subject. There's this professor [C.C. Tan] who was a member of the [National] Academy [of Sciences] here--the U.S. academy--a foreign member, maybe the only one from the biology branch in China. He was a famous professor in China, so I ended up going to that subject.

COHEN: Now, when you describe your high school years, you say it wasn't really very strong academically.

HUANG: Right.

COHEN: So how did you do at the university if you didn't have a very good background?

HUANG: For one thing, most of the high schools were similar at that time, because there was no hierarchy—you know, "This one's better than the other one." Traditionally there are better ones; there are poor ones. But because of the Cultural Revolution, every school was made pretty much average. And the students the schools had were also students who lived nearby, so there was no real selection for good students for certain schools. You know, a lot of the good schools are good because their students' scores are also good, not simply because their teachers are good. So in that sense, most of the high schools at that time were pretty similar--comparable--although some schools were better. They had more students getting into universities.

In my case, my background was really not that great, especially given that I spent a lot of time in art. I was okay, but I wasn't at the top of the entering class of my university, maybe below average in terms of the entering score. But somehow I've always had this idea that if you put me in an environment with a group of students, then I would generally come out on top of this group of people. I got that feeling when I was starting art. My art, when I got into that group, wasn't at the top. But somehow I ended up being at the top by working hard. So I was confident I was going to be okay. It turned out to be soon after, maybe in a year or so, [that] my academics was already at the top of the class in the university. That doesn't have too much to do with what you have learned in high school it seems to me. So if I start fresh entering the university and just study the subject-- I just remember my test scores were pretty good--always at the top.

COHEN: I want to back up for just a second. Were you disappointed when you didn't get into the art school?

HUANG: Maybe a little bit. I don't remember how exactly disappointed, because I know that even when I tried to do the test, I think I knew the chance of getting in was not going to be very good. It's just that there were so many good competitors, especially [because] this was the first recruiting exam after the Cultural Revolution and you had accumulated all these different ages of students that had worked in the countryside and worked in various places. All their spare time they were doing art, and you had to compete with all these [people]. I was among the youngest of the students who competed--most of them were older--so I wasn't expecting to really get in. Besides, my regular school subjects were very good--math and stuff--so I had an alternative way to go.

COHEN: Right, right. And by this time, because of the changes in the government, there really was an alternative.

HUANG: There was an alternative, right. I was pretty good with the other alternative also, so I wasn't that disappointed. It's not like this was the only way to go: "If I don't go into this, I have no choice."

That's different from a close friend of mine [He Fei]. The two of us were from the same school--we were from the same military compound; his parents were classmates of my parents--so we both took the exam. My score was actually better than his, so he didn't get in, and his regular subjects were relatively poor. He also decided to try to go to a regular university the next year, so he actually participated in the exam for the regular university. But he failed. He didn't get in. Then he decided to just do art. He persevered for several years. Eventually he went to an art academy. So now he's a professional in art.

COHEN: Okay. So you were okay and happy with the idea of doing science at this point?

HUANG: Yeah.

COHEN: Now, I'm trying to picture a map in my head to see how far away Shanghai is from Beijing, and I can't quite picture it.

HUANG: I think it's about one thousand kilometers. Is that about right? It's pretty far. So if this is like a China map [draws a picture of a map of China], this is the ocean side--the Pacific Ocean. Beijing is up north; Shanghai is south.

COHEN: Right there? Okay. And how did you get there?

HUANG: By train. That was how long? Twelve hours.

COHEN: I'm asking you this because I talked to the other scholar about the train trip and he told a story about how hard the train trip was. How was it for you?

HUANG: I always enjoyed the train trips actually.

COHEN: You did?

HUANG: When I was young I took train trips from Beijing to Wuhan, Wuhan to Beijing, stuff like that. Once my head was broken by a kid who threw bricks into the train. So I enjoyed that kind of trip actually.

COHEN: It wasn't too crowded?

HUANG: Sometimes it was, and sometimes not.

COHEN: Okay. So when you were in school, did they have dormitories for the students?

HUANG: Yeah, yeah. Eight students in one little room.

COHEN: Eight?

HUANG: Yeah, eight students! [mutual laughter]

COHEN: Not much privacy.

HUANG: No. And then the beds were stacked up.

COHEN: So how many people in a stack?

HUANG: Two. One on top and one on the bottom. I was at the top because I went in late. After I got into the dormitory room there were already six or seven students who already took their positions. [mutual laughter]

COHEN: And you got what was left.

HUANG: I got what was left, which was not very good--near the door, the top. The better ones would be near the window. I think it's still like that.

COHEN: So did you enjoy the university?

HUANG: Yes, I think I enjoyed it a lot. It was a good period of time. Academically, it was not so difficult, it turns out. I was doing very well, especially with my English and math and biology-related subjects.

COHEN: Did you speak English when you went there?

HUANG: Yes. We had to take this English test, so we studied some English in high school. Then in university, of course, we also have English classes all through the four-year period.

COHEN: I always think English would be really hard to learn if you weren't born speaking it, if it weren't your first language.

HUANG: It may be hard. I just don't know how to compare it because I haven't learned any other foreign language, like Japanese or Russian. I've only studied English. Yeah, I was doing very well in that.

COHEN: Okay. So how long did you spend at the university?

HUANG: Four years.

COHEN: And you came out with something like a bachelor's degree?

HUANG: That's right--a bachelor's degree in genetics.

COHEN: I noticed from your résumé that then you went to an English program for a year.

HUANG: Yes. Right, right.

COHEN: Tell me a little about that?

HUANG: That was not an English program. That was basically a prep school for getting into a U.S. university for graduate studies. At that time the normal path was for the graduates, if they want further education, to get into a graduate program either in China or in foreign countries. To go to a foreign country based on a government scholarship was very selective, so the students--most of the graduating class--would take this national entrance exam again, this time for graduate school.

COHEN: To go to a Chinese graduate school?

HUANG: Yeah, to go to a Chinese graduate school. But they also understand that the better ones--the ones that have high scores in those tests--would have a chance to get picked to go to a U.S. university or another country for study. Well, that was my aim at that time--to try to be selected for graduate school in the U.S.

Then there was this program called China-U.S. Biochemistry Examination Application program--for short, CUSBEA. That program was sponsored by the Chinese government and the American university professors, especially this Chinese American professor called Ray Wu. Basically, he started this program by coordinating about fifty, sixty U.S. universities to participate in this program to recruit Chinese students. Each year they would select about fifty to sixty students from the graduating classes of all the universities in China.

So what happened was, I did well on my test for the graduate program, and then I was selected to participate in another test for getting into this CUSBEA program. I did well on that one too, so I ended up getting among the top fifty students who then were going to go to the U.S. Before that happened, all these students were sent to the Guangzhou [English] Language Center to prepare for American culture, to study English a little more, and--in the meantime--to apply for schools in the U.S.

COHEN: Well, what made you want to go to the U.S. in the first place? I mean, what was it that made you want to do that as opposed to going to graduate school in China?

HUANG: Well, for certain, we all understand that China is relatively backward in science, and to be a successful scientist-- Even at that time I think I was thinking to just get trained [and] eventually I would come back to China. For that aim, training abroad is considered a plus. It has been traditionally. If you look at the famous scientists of China at that time, most of them have training in the U.S. or Europe. So that was a no-brainer. Every student would like to go if they want to study science.

COHEN: Well, you had already left home once--

HUANG: Right.

COHEN: --so that was familiar. But it's another story to go to a completely foreign country.

HUANG: Yeah, I wasn't that afraid, actually.

COHEN: No?

HUANG: Not at all. I think I belong to the adventurous type, you know? I remember reading all these novels about students being sent to remote places in China during the Cultural Revolution. And my dream at that time, actually, before university, was to go to some place like that. [laughs] To be far away from Beijing and to go to the northern border of China or something. I was always like that. Then, of course, going to Shanghai, you really have to get used to living independently of family and parents. I wasn't that much attached to my family in the first place. Since I was growing up pretty much, my father was always absent [laughs], so I was always pretty much independent.

COHEN: Okay. Now, we're going to talk some more about coming to the States and stuff, but before we leave China, how was your social life during this period? I mean, what kinds of things did you do for fun when you were in college?

HUANG: When we were in college what kinds of things did we do for fun? I think at that time it was still quite-- It was not as liberal as it is now, so there weren't that [many] fun activities as

they have now. You're not supposed to get involved in a relationship with a female classmate, for example.

COHEN: Oh, you weren't supposed to?

HUANG: No, you were not supposed to. Of course, there were some dancing parties occasionally, so I went to those occasionally. I think my goal was pretty clear in the university period, which was to study hard and then, also, to keep in shape. So study and exercise were my two major activities.

COHEN: Were you running still?

HUANG: Yes. So I studied very late, to eleven or eleven thirty in the evening, and then got up early in the morning to run. That was like six or seven o'clock. Then I went to classes, and then in the afternoon after class, about from four or five or six, I would participate in the exercise again, like volleyball, Ping-Pong, and stuff. Then after dinner was study again. On the weekends I sometimes went and visited my relatives living in Shanghai, or I visited friends in other universities. The rest was just study.

COHEN: Did you meet your wife [Chen Ruo Ping] here?

HUANG: Yes, here.

COHEN: Okay. Well, we'll get to that. So then you went to this sort of prep school for about a year.

HUANG: That was a wonderful-- [laughs]

COHEN: That was wonderful?

HUANG: --period of play and relaxing, because you know you don't have to pass any tests anymore. Basically you are studying some English. Of course, you have to get a certificate, but that was routine; you normally would get it. So that was really fun. You study, and the classes were light. Then you get to play with all these friends in the same class. And then you are in this different city, Guangzhou, a southern city that was in the forefront of opening up, being

liberalized in China, so you could get to visit a lot of places in the city. So that was really a lot of fun.

COHEN: Sounds like it was no pressure.

HUANG: Right, no pressure. You could say that, yes. So after four years of hard study, all of a sudden you are released.

COHEN: Sure.

HUANG: You have a bright future in front of you, right? So it was really-- Everybody was in a happy mood.

COHEN: And it was during this year that you started applying to schools?

HUANG: Yes, during this year you started applying to schools and waited for the response. Then after you knew which school you got into, some students were happy, some were not happy based on whether they got their ideal school or not. One of my friends--we were living in the same dormitory in this language center--was from my same university and he had a top three finish in the test scores. He was expecting to get into Harvard [University] or something. Among his list--among five choices--he was given Harvard. And when it turned out he wasn't going to get into Harvard, he was so shocked that he went crazy. I think he had a schizophrenia type of history before, in college. He was off of school one year to recover from that, and this triggered a second burst of this break. He stayed behind in China.

COHEN: So where did you apply? I know where you ended up.

HUANG: I applied to UC Davis, [University of California] Irvine, Dartmouth [College], [University of] Utah. I forget the other places. I think there were about five. My score at that time was in the top fifteen. It was not in the top ten, so I wasn't going to get into Harvard or something. But the top fifteen is, among fifty, already a privilege, because we get actually government money, whereas the rest don't have any government money from China. They rely totally on U.S. universities to provide the support, whereas for the top fifteen students, we have the first-year support covered by our government; some universities require that first-year students have their own financial support, which is the case with UC's. So among the five I was given, I thought that UC Davis would be the best. So that's where I ended up going.

COHEN: So that was your first choice out of the ones that--?

HUANG: Right, right.

COHEN: This business of getting the money from the government-- I want to ask you about that because you didn't go back.

HUANG: Right.

COHEN: Were there any, we would say, strings attached?

HUANG: At that time, no. The Chinese government then was not led by some experts in anything. They do things by learning gradually. So at that time they didn't realize; it was new for them to start this kind of program, so they didn't attach any strings to this. But now I've learned that they do.

COHEN: So you were kind of lucky. You slipped in during this little window of time.

HUANG: Yeah, maybe. But in truth, we were really not thinking of staying in the U.S. either. Even when I was here the first year, I wasn't thinking about staying. I was still thinking [about] learning and then going back.

COHEN: Sure. So when you arrived at Davis-- I'm familiar with Davis because my daughter went there. It's kind of out in the middle of nowhere.

HUANG: That's right.

COHEN: In fact, some of the dormitories are right next to the cow pastures.

HUANG: Yeah.

COHEN: What was your first impression when you got there?

HUANG: My first impression was kind of, I guess, a cultural type of shock. It was so much different from the city where I used to live. You know, Shanghai, Beijing-- They're all big cities. All of a sudden, you're in a countryside where you can't go anywhere without a car. Biking is popular there, so I ended up with a bicycle the first few days of arriving. Basically, it's so different. On the streets, you don't see people walking. It's really a deserted place. So the first month was a little bit miserable. Yeah, I felt a little bit homesick.

This was in contrast to my friend who later came to the States. He directly came to New York. I visited him three or four days after he landed in New York, and I said, "What's your impression?" He said, "Just like Shanghai." [mutual laughter] So apparently if you first arrive in New York, you can feel that way; you don't see too much difference. But Davis is quite different.

COHEN: How were your language skills at this point? I mean, could you get along okay with your English?

HUANG: Yeah, I think so. Yeah, I don't feel that language was a big problem.

COHEN: Okay. I'm trying to remember what it was that you studied there. Oh, you were with Dr. [John W.B.] Hershey, right? And you went into biochemistry.

HUANG: Right.

COHEN: So what made you decide on biochemistry from genetic engineering?

HUANG: Well, there was not much of a choice, actually. The program that accepted me was the biochemistry program. The genetics program was not participating--

COHEN: Oh, I see.

HUANG: --in the CUSBEA program. So from UC Davis, biochemistry was the program, and Hershey was actually the coordinator for the Davis program in regards to Ray Wu. So Ray Wu actually contacted Hershey. Hershey was coordinating this Chinese student program, actually.

COHEN: I see.

HUANG: But I picked Hershey not because of that reason. I chose that subject based on my feeling of what was the best science available on this campus. I was selecting research topics mostly based not on my interest in a particular subject, since I didn't really have a preference for any of those. I just [wanted] to get trained with a scientist who was at the top of his subject. At Davis, there are not too many professors like that. I thought Hershey was at the top of his field, so I thought that he would be a good choice.

COHEN: Well, I have learned a couple of other languages over the years, and I know that even though I'm pretty fluent, the idea of having to sit and write an exam, for example, is a pretty daunting idea. But you said you felt like you were pretty well able to do that?

HUANG: Yeah. At least I don't feel that my language was a limiting factor in my performance in the classes--in the tests and stuff. [With] most of those, you may have some difficulty in understanding the teaching [in a] class, but you can always study the books.

COHEN: But how about your dissertation, for example?

HUANG: The dissertation? Writing papers?

COHEN: Yeah.

HUANG: That was already four years later. You are already adjusted very well at that time. I wrote my papers, and then the professors corrected them and put them together. That was it. So it wasn't such a big deal to write this dissertation. It's just two papers that you have to write for publication purposes. In this case, we just made it simple; we just combined the two papers. That was the dissertation.

COHEN: I see. So what was that lab like?

[END OF TAPE 1, SIDE 2]

HUANG: I got a good impression of the lab. It was a friendly lab with about a dozen people. Very American. Nice. We had birthday parties almost every month since you had close to

fifteen people. Everybody's birthday party was celebrated. [mutual laughter] You buy a cake--wine--and then just have the party in the lab. And we had postdoc students from America, from Europe. We got two from Britain, one from France, one from Switzerland. My first direct supervisor was a postdoc from Scotland. So I got to learn different cultures.

I worked pretty hard in the lab. The professor [John W.B. Hershey] did not push at all. I had to push the professor to get him interested in what I was doing and to get papers published. He pretty much operated that you get your own ideas and you pursue them. [He] let you do your things freely.

COHEN: Was that good or bad?

HUANG: I think it was good.

COHEN: Some people need more direction and some people prefer not.

HUANG: Yeah, but if you want to be an independent-thinking scientist, it's better to be trained that way--that you're left alone. But when you needed guidance, he was available. It was also nice that you could pursue your own idea right from the beginning. That was my case. I did a rotation in the lab, and then I started working on the project in the lab. He laid out about a dozen different things in the lab that were going on and asked me which one I would be interested in doing. I selected one, so I worked with that postdoc that was working on that project.

During the few months of working on that project I got an idea of studying this by sitting in on a seminar. The speaker had talked about a method of studying DNA protein binding interactions using a gel electrophoresis assay. Our lab was interested in studying RNA protein interactions, so I thought, "I'll just use the same technique to apply it to RNA instead of DNA." I thought that was a great idea since even for the DNA protein interactions field, that was just beginning to be used, and it had never been used for RNA. So I mentioned this idea, and the professor liked it a lot. Indeed, I spent two years on this idea, using this assay to study all these factors--RNA binding translation factors--that Hershey was involved with to figure [out] what their function is in RNA binding stuff. So you can say I pretty much pursued a project that was based on my idea.

It was kind of tough because you don't get too [much] help, since this is new and everything you have to solve yourself. And then initially it looked pretty exciting, but gradually we couldn't really make an interesting story out of this. So that work lasted for two years, and still I didn't get a paper out of it.

COHEN: Oh, that's hard.

HUANG: That's hard, but I learned how to pursue things and do things your way and get things done. And even though nothing in terms of a paper came out of this study, I think the way I pursued it and the way I got this idea impressed my supervisor a lot.

But anyway, after that we talked about doing a project that could quickly lead to something publishable and get my degree. So then he suggested an idea. I worked for one year, and then--

COHEN: Is that the initiation factors?

HUANG: Yeah, that's the *MCB* [*Molecular and Cellular Biology]* paper [S. Huang and J.W.B. Hershey, 1989. Translational initiation factor expression and ribosomal protein gene expression are repressed coordinately but by different mechanisms in murine lymphosarcoma cells treated with glucocorticoids. *Molecular and Cell Biology* 9:3679-84]. So that was finished in the fourth year in the lab.

COHEN: Okay. Now, you hear all these stories--I've heard many of them by now--about how many hours people work when they're in graduate school, and some people work like eighteen hours a day, it seems like. What was your schedule?

HUANG: I came to the lab maybe at nine or ten. I usually worked at night, so that meant after dinner I would go back to the lab. I don't remember how late [I worked], but not too late, I don't think. Maybe ten, eleven. Then, also, weekends I would work. To me it was fine. I liked to do it, it seems like. It didn't feel like because the boss asked me to do it or something-- Most of the time I felt I was most productive when the boss was on sabbatical. [laughs]

COHEN: Somewhere else?

HUANG: Yeah, for the last half a year or year he was in Japan on sabbatical. That was when I was finishing my degree. So I finished it up without him being present.

COHEN: Oh, wow. And were you still running and doing your physical--?

HUANG: Absolutely. I dropped the Ping-Pong.

COHEN: Yeah?

HUANG: Yeah, because I got interested in tennis and I got interested in badminton. I think tennis I picked a little bit, but I was playing, heavily, badminton. Yeah, very heavy, like, maybe four o'clock to six o'clock. Most of the afternoons I'd go play badminton sometime in the evening.

COHEN: It sounds like sports were pretty important to you.

HUANG: That's right, I was always keeping up with sports. I don't know why. I think maybe also I have a natural talent again.

COHEN: It was a natural talent?

HUANG: Again, from my second son [Samuel Huang] 's experience. My older son [Matthew Huang] was not very athletic at all, not interested in any kind of sports, whereas my younger son was good at tennis and picked up golf easily. Just naturally more athletic. You can tell.

COHEN: Okay. So what year did you finish? I have it on your record, but I don't remember.

HUANG: The end of '89.

COHEN: And at that point you had to find a postdoc.

HUANG: Right.

COHEN: So you went to UCSD [University of California, San Diego].

HUANG: Right.

COHEN: How did that come about?

HUANG: How did that come about? Well, this had a little to do with my wife [Chen Ruo Ping].

COHEN: Oh, had you already met her?

HUANG: Right.

COHEN: Okay, let's back up then. Tell me about meeting her?

HUANG: My wife was the next class of CUSBEA [China-U.S. Biochemistry Examination and Application program]. I came in '84, and she came in '85.

COHEN: To [University of California] Davis?

HUANG: To Davis, under the same CUSBEA program. So I met her at the airport because she had already contacted me; from this program they knew who was there before, so she contacted me and asked me to pick her up. I went and then we met each other and it seems like we liked each other. So we started a real serious relationship maybe a couple of months later after we met.

She went to a lab in the genetics department for about two years. Then the boss was on sabbatical, and she started not liking the subject that much. Then she was interested in switching to a lab, or better, switching to a different university. At that time I was also very encouraging since I knew I wasn't going to stay at Davis for the postdoc. So it was a good arrangement--it turned out to be--that she ended up at UCSD to continue the graduate program. In the UC [University of California], you're allowed to do this: you will still get a Davis degree, but you do your thesis work on a different campus. So she selected a very good lab here--Jeff [rey] Rosenfeld, who was later to become a member of the [National] Academy [of Sciences]. She came here in '87 sometime--summer of '87--and during all these things we still kept the relationship. I'd often drive to San Diego. She also went back to Davis often.

Then I graduated and I started looking for postdocs. Even though San Diego was in my mind, I really did not limit my selection to only San Diego. Mostly [I was looking at] Boston and San Diego, I believe. Then it turned out that this lab at UCSD--I realized it was an emerging field--was considered to be at least in the forefront of that field. That was always my selection criteria: that whether it's interesting or not, the lab doing it has to be in the forefront. So even though this lab wasn't that famous, because it was an assistant professor [who] just discovered something big--had a paper in *Nature* and *Science;* that's how I found out about this--I thought, "He is working on an interesting subject, and I can at least do something in this field that may

later lead to a career."

COHEN: This was the--?

HUANG: Tumor suppressor, *Rb.* Yeah, at that time it was just being cloned as a gene.

COHEN: And this is Dr. [Wen-Hwa] Lee?

HUANG: Yes. He happened to be in San Diego, so that's how I came there.

COHEN: And when did you marry?

HUANG: In 19--

COHEN: Don't hesitate too long.

HUANG: [mutual laughter] It's tough because we really didn't have a formal ceremony. Both of our parents are not here, and I am not into that formality and she is not either. So 19--

COHEN: Well, in China you just have to register, don't you?

HUANG: Yeah, we just have to register. So we registered at the China consulate in L.A. I think it was in '89 or something. I think marriage was in '89--the spring of '89, sometime around April.

COHEN: Let's just talk briefly about your postdoc, and then we'll wrap it up for today. Were you particularly interested in tumor suppressor genes before you came here? Did you know that was what you wanted to do, or were you just looking for an interesting topic?

HUANG: I was just-- Yeah. You see, I studied translation. Nothing related to cancer. So I wasn't particularly interested in tumor suppressor. I was more interested in finding a good lab with a good research subject. So in my selection of postdoc labs, the specialty of the labs varied a lot. It just happened that this tumor suppressor worked out. Then once I got into this, of course

I got myself interested.

COHEN: Sure. And how did this lab differ from Dr. Hershey's lab?

HUANG: Of course, the lab head was not American. He was educated in Taiwan. So there were probably no birthday parties [mutual laughter], and there were more Chinese than Europeans and Caucasians.

COHEN: You said he was young?

HUANG: He was relatively young, right. Also, it operated as a husband and wife team. So it was quite different in terms of culture. It was much less relaxed. More pressure, I guess. With Hershey we sometimes went on wine-tasting trips in the Napa Valley. Here, we didn't really have lab trips.

COHEN: It sounds like the lab was a place to work and there wasn't a social life.

HUANG: Right, it wasn't social at all. Just work.

But in terms of my own-- I didn't feel too much of a difference since I'm mostly self-driven. And again, the projects I've become successful [at were] all initiated by my own thought. [When] I first came, I was given a subject to do, which was to clone the *Drosophila* homologue of the *Rb* suppressor gene. That was the topic I was given, so I did that. But I knew from the beginning this was going to be a shaky project--could work, may not work--so I could end up doing a lot of work for nothing. Cloning something is always-- Until you get it, all your hard work is nothing.

Based on my graduate training experience, I knew I had to have something going on the side--to keep productive in case this one didn't work out. So I also did another thing, which was my idea--to try to study *Rb* binding to viral protein, to just study the interaction a little more in detail. I mapped which regions of *Rb* are involved in binding to this viral protein. That turned out to be successful. The *Drosophila* project really didn't pan out after half a year, but in the meantime, this one worked out. That ended up being in *EMBO* [*European Molecular Biology Organization]* journal [S. Huang et al., 1990. Two distinct and frequently mutated regions of retinoblastoma protein are required for binding to SV40 T antigen. *European Molecular Biology Organization* 9:1815-22].

Then soon after that I initiated this project to express the *Rb* protein in bacteria. At that time the professor was always saying, "That cannot be done," because it's big and stuff. But I

did it anyway, and got it expressed as a truncated form. Immediately with these reagents, I did the next thing, which was to see if there was a cellular protein that can bind to *Rb.* That also worked out, and that was the basis for the *Nature* paper [S. Huang et al., 1991. A cellular protein that competes with SV40 T antigen for binding to the retinoblastoma gene product. *Nature* 350:160-62] establishing the concept [that] there is such a protein [that] exists in the cell that normally binds to *Rb.* Before that, people just knew there was this viral protein that could bind to *Rb.* They always suspected that there should be a viral homologue in the cell that binds to *Rb,* so that paper addressed that issue.

This basically opened up the field for the binding protein business. From then on you've got many, many binding proteins being characterized now.

COHEN: So how long were you in the postdoc then?

HUANG: I was there two years and a half. Then the lab moved to San Antonio. I knew I wasn't going to go, so I started looking for faculty positions.

COHEN: Had your wife graduated by this time?

HUANG: By this time? Not yet.

COHEN: So you kind of needed to stay somewhere on the West Coast?

HUANG: Yes, somewhere here, preferably. Just for the sake of it, I searched other places. But in the end, I did prefer here.

COHEN: And you ended up here.

HUANG: Right.

COHEN: Now, it's not entirely clear to me what the relationship is between the Burnham Institute and the university.

HUANG: Oh, the Burnham Institute was a private, nonprofit institute that was independent from the university--nothing at all related. But recently they've tried to have some kind of

interaction--more. So we have some sort of joint graduate program, so some graduate students from UCSD can somehow work in our labs to get their degrees from the school.

COHEN: But do you have the title of professor even though you're not at a university? You do, don't you?

HUANG: We do have professors. That was only recently [that] they switched this title. They had been always debating what title we'd call ourselves. When I first started, we called ourselves staff scientists. But then two years ago, after we established this joint program, some faculty here actually taught classes there. Then we said, "Okay, we should call ourselves professors just to make it easier for other people, colleagues, to understand what's going on." You know, if we go out and call ourselves staff scientists, they don't know how this is relative to the professorship.

COHEN: They think you're in industry, probably.

HUANG: Right.

[END OF TAPE 2, SIDE 1]

[END OF INTERVIEW]

INTERVIEWEE: **Shi Huang**

INTERVIEWER: **Helene L. Cohen**

LOCATION: **The Burnham Institute, La Jolla, California**

DATE: **20 January 2000**

COHEN: As always, I have a few follow-up questions after reviewing yesterday's tapes. One of the things I was wondering was whether, when you were growing up in China, you had any kind of formal religious training?

HUANG: Not at all. [laughs]

COHEN: Any religious training at all? None?

HUANG: No, not at all, even though my mother [Peng Jing Min] went to a religious school in the city of Wuhan.

COHEN: Was that like a missionary school?

HUANG: Yeah. That was before the '49 revolution. But since the communists took over, basically no religion was allowed.

COHEN: Right. Is that anything that you wish you had--or not?

HUANG: Not really.

COHEN: Not really?

HUANG: Yeah. After we came here we were invited a few times to some religious practices or gatherings, and we really didn't like what was going on there.

COHEN: Okay. Do you think religion and science can coexist?

HUANG: I think so, yeah. Religion, I think-- Even though I'm not into religion, I'm very much interested in philosophy and how people view life and stuff--what do they consider to be happy and stuff like that. So I think I consider myself to have some sort of faith. You can call that religion or you can call that philosophy in terms of how I view life. I came to that view by my own experience without reading so much about religion or philosophy. I came to some conclusions which I found sort of interesting and very true to me, and I thought, "This is such a simple idea, it must have been written down somewhere in the history books or the philosophy books." And indeed, it was written down more than two thousand years ago by the Chinese philosopher.

COHEN: Confucius?

HUANG: Mencius, isn't it? [Confucius] and [Mencius] are always stated together as two names. Maybe Confucius is more famous in the West.

So things like that I sort of figured out by myself. And then I have my own way of thinking. Therefore, I do not really need any religion, even though many religions probably have some common ideas as I have. I think religion is helpful to people who don't really have their own thoughts in terms of viewing the world and life. They need some guidance, and religion can come in to really help them out in that fashion.

COHEN: So what was the enlightenment that you had?

HUANG: Well, that is based on my experience. Things have come to me the hard way, basically. I had to pay the dues before I got something good in return. It never comes as total luck. Even if something came, maybe I expected that good things would happen. But then it was soon followed by something bad. It always goes like this. Luckily, the trend has always been moving up; it's like this [indicates upward line of trajectory]. So I concluded that you have to pay your dues. You have to work hard in order to get what you want.

But I think there is one thing that is still missing among things that have been written by philosophers. I view this as sort of random chances. It's almost like a probability issue. Once you have something bad happen, your chance of having another bad thing is going to be low, whereas your chance of having a good thing happen is going to be high. So then, naturally, we have something nice happen later on. It's sort of like fate. It's sort of like God is coming in. If you have suffered a lot, then God may come in to make sure you will have something good. Some people will usually think this is cause and result--you know, you work hard, therefore you naturally get that. But that's not necessarily true. I think it's something to do with the chance

happening of things.

So this idea of working hard and then getting things in return, getting rewards, was in the writing of Mencius two thousand years ago. Literally, he says you have to starve to death before God, Heaven, or something is going to put some real responsibility to you or let you accomplish something really important. He's going to let you work really hard and starve yourself to death and suffer. And I've found my experience has been like that.

That is actually very good in terms of having a positive outlook, so that when you're down, you don't really suffer that much. You always think something nice is going to happen. But then when you're very successful, you need to be careful not to get excited too much. Then the next day somethingbad is going to happen.

COHEN: Disaster is just around the corner.

HUANG: Yeah, right. There is this Chinese philosopher-- Taoism considers everything should be natural, and if you are at the peak, you are to fall down deeper than the average person.

COHEN: I was also thinking a little bit back to when you were a child. We talked a little bit about your education and whatnot, but I was wondering what expectations your parents [Huang Ce and Peng Jing Min] had for you and your brother [Huang Wei] in terms of what you would do, what you would achieve. Did they have expectations?

HUANG: I'll first refer to myself and then my brother. For me, I always was sort of a very determined person from very young. So like I said, when I was at primary school, I started playing Ping-Pong, and I think my family was basically very supportive of whatever I chose to do. I didn't really get the impression they specifically wanted me to become a Ping-Pong player, for example, but if I worked really hard on that, they also did not stop me. Then I changed to painting, and again they were very supportive of that. Of course, the regular academics--because I was generally, most of the time, very good-- I also didn't get that impression that the parents were trying to push me in that direction.

But I can tell that if I did poorly in academics, probably my parents would not be happy. The first example of that was when I came from Wuhan to study in the Beijing school. I was a little bit backward in terms of my academic status compared to my classmates in the new school. I wasn't able to memorize the numbers times numbers--you know, the basic three times three equals what--and the parents really just forced me to improve on that. I think from that incident you can tell they expected me to be good at school. So even though I had all these extracurricular activities, my school academics were always good.

For my brother-- He was expected to learn something besides school; maybe the school

academics were not so heavy and he had much, much more free time. So he went to study violin for a while; I think that must have been my parents' idea. It turned out he didn't like it that much-- he didn't practice very hard--so my parents also didn't push very hard in that direction. And that was that. Then I think my parents were, again, very forceful in terms of, "This kid has to be good with academics."

COHEN: With your brother, you mean?

HUANG: Yeah, with my brother. My brother was doing well before high school, as I told you. That high school entrance test he did very well, so he moved up from this local middle school where my home is close to the high school in downtown Beijing, one of the best high schools in Beijing.

COHEN: So he did better than you did, because you stayed at the local school.

HUANG: Yeah. But that was because in his time there was this, again--

COHEN: The chance of going to college now.

HUANG: --chance of going to college and also going to the key schools, they call it. They started this program again, so he was able to go to a good school, a key school. He actually lived on campus and just came home during the weekends. It was just like he went to university in that sense.

Then he started to play soccer--just played with a lot of friends--and his academics really dropped, maybe below average in his class. Sometimes his test scores were so poor. So my parents were so concerned. Every time they would talk to my brother. They even went to the high school to meet with the teachers to discuss what was going on. They were really concerned over that.

So I think yeah, indeed, they did have some kind of expectation that "You need to perform well in school." But they were not like some parents like I see here that really spend so much time with their kids in terms of helping them learning some skill, like figure skating or tennis or soccer. The parents actually go with the kids and spend all the time-- I didn't see my parents spending a lot of time, you know, trying to help me with painting or something. They pretty much left us alone. Once we had an interest in something they thought was useful or good, they left us alone. They didn't try to spend extra effort to cultivate that interest.

COHEN: You know, here, there's a lot of pressure on kids, because you have to get into college and you have to get into grad school. There are all these things. Whereas when you were growing up, there wasn't even the likelihood that you would get into college. Do you think that your parents maybe were more relaxed with you than your brother because the situation was different or because you were more of a self-starter?

HUANG: Yeah, I think I'm more self-driven--they could see that--and my brother was not like me.

COHEN: I see.

HUANG: He's much more relaxed, and they could see that his doing poorly in school was simply because he was playing too much. He was not paying attention. It was not because he was dumb or something. So they just had to change his attitude. [mutual laughter] For me, there was no attitude problem. So I didn't need an extra push in that regard. I push myself, already, pretty crazy.

COHEN: Okay. You also mentioned that your dad was a workaholic. That was your word.

HUANG: Yeah, he was traveling a lot. Even when we were living in Beijing again, he was always working in some other provinces and cities and Shanghai. He was always traveling.

COHEN: I wonder whether that was a trait that you inherited or not. Do you think you do the same thing?

HUANG: I think a little bit. Yeah, I think I consider myself--not these days, anymore, but when I was a student in high school or university or graduate school-- Basically, once I set my goal, I will just do everything I can to achieve it. And I always feel panicked or uneasy if I find I have nothing to do. I like to be busy.

COHEN: Has having children changed that for you?

HUANG: A little bit, yeah. Yeah, I'm definitely not my father in terms of the relationship with the kids [Matthew Huang and Samuel Huang]. I think I spend a lot more time with my kids now than he used to with me.

Also, slowly, I realized once I worked on something-- For example, I set up my lab and worked on a project that I picked. "This lab would be the only lab in the world to work on this subject." Then it seemed that working like crazy didn't really get things done as expected. Sometimes it's a matter of time. Sometimes it's being patient. The result will come. When the situation is not mature yet, no matter how hard you work, it's not going to get done.

In a way, I'm working on stuff that is, you could say, not as competitive, so I don't have to really work twenty-four hours a day so that if I don't work that way, then somebody else is going to find something. We are not working on those kinds of projects. At this point it's either I'm going to make it this way or it's going to be too late for me to work on something else. So I've been relaxing a little bit more than before.

COHEN: Okay. You mentioned that your wife [Chen Ruo Ping] is also a scientist. What does she do?

HUANG: She was, as I said, in the same CUSBEA [China-U.S. Biochemistry Examination and Application] student exchange program with the U.S., so she had a very similar background as I had. She spent a year in that Guangzhou [English Language] Center, and then she came to the U.S. to do graduate school in biochemistry also--same program. She spent a longer time doing her Ph.D., maybe seven years, but she had two kids during that period. Then she did a postdoc at the Salk Institute [for Biological Studies], and then she went to a local company called Vical [Incorporated] for two or three years. Then she felt that the work there wasn't that challenging intellectually, so she called up a friend, a colleague who used to be at Salk at the same lab. That colleague had just started a company called Arena [Pharmaceuticals], also in San Diego. She felt that a start-up company was more exciting and more challenging and [would have] more financial payoff in the end, so she joined that company. That's where she is now, and she's doing pretty well there.

She is pretty good in what she does. She is a very good scientist. But we have felt that there's no way she is going to pursue an academic job.

COHEN: Because?

HUANG: Just because it's going to be too demanding on the family. So even though she's very smart and very good, she is more into the family.

COHEN: Well, this actually brings up one of the questions that I ask everyone, which is, there's a big difference in graduate school and in postdocs--about half of the people are women. But when you look at the academic centers, the universities, it's about 5 percent.

HUANG: Is that right? Five percent?

COHEN: Yeah, it's very low.

HUANG: Actually, in our institute, there are a lot more.

COHEN: Well, it's interesting because--

HUANG: Especially in science, right? I don't think in history or in literature.

COHEN: In science, yeah. It varies from institution to institution, but it's pretty low. So one of my questions is, what happens to the women? In your family, it sounds like the two of you kind of made a decision that she shouldn't go that route.

HUANG: Yeah. She probably doesn't want to go [that route] herself. She wasn't that motivated to go in the beginning. I have met other women scientists who were much more determined to want to be an academic, sometimes even more determined than their husbands.

But that, usually, is a personality issue. You probably noticed this also, that when you have a strong husband, generally the wife is less dominant and more family oriented rather than career oriented. That's how you can have a family between the two. There's somehow natural selection to find each other attractive. This is complementary. Whereas two career-motivated persons-- To have a family is going to be very tough. That's why you either find this family has a strong, dominant husband or a very strong, dominant wife. So what I've noticed is there are families where the wife is a professor--sometimes even the husband also is a professor--but even in that case when the wife is a professor, the wife is usually dominant in that relationship. And I think this has a lot to do with personality.

COHEN: So in your family, I take it you're the dominant one?

HUANG: Right.

COHEN: So how does the work of the family divide up?

HUANG: The work is divided. I think I'm more into mechanical things, like cars. Then my wife would take care of bills and money issues--financial things, investments--which I'm not so much interested in, and also general housecleaning and cooking. When she does the cooking, then I usually do the dishwashing.

COHEN: How about with the kids--the taking to school and taking to lessons?

HUANG: Taking to school I usually do in the morning. That's now what's going on. Before I took them to school in the morning, and then she [brought] them home in the afternoon, because I usually work later. Now it's going to be still this case, except now her parents [Chen Xing Qiu and Ye Ying Geng] are here, so the kids can go home right after school--about three o'clock in the afternoon--by bus.

COHEN: Are they here permanently?

HUANG: No, just for one year or so, half a year.

COHEN: Okay.

HUANG: So that's how we divide it. I would say she does a lot more housework than I do.

COHEN: Okay. Some of the things that you said you liked to do when you were a kid, like painting and different sports things, do you do those things still? Do you paint, for example?

HUANG: No, I don't paint anymore. I do sports a lot. I play tennis at least once or twice a week. I play in the San Diego local tennis league. I 'm a level 4 .5 or 5 player. Two months ago I hurt my ankle during a league match, so I haven't played for the last two months. About a year ago I started playing golf. I enjoy that a lot, and I think I'm picking up golf very fast. It's because I do well [that] I enjoy doing it. So golf and tennis are the two things I'm doing.

Painting, basically, is going to take a lot of time, and I don't see where it's going to lead--what's the purpose of doing it. If it's just for relaxing, then I'd rather go do some sports. Otherwise, I like to do things that are going to be enjoyable and also do some good for my body or whatever. When I was painting, my goal was to become a professional or something. Once that dream is done, then no more.

COHEN: Away it went.

HUANG: No more. So unless in the future, after I retire and have got more time-- Then I may paint. But I'm not going to just paint for the sake of painting. Probably I'm going to paint and then this painting's going to be for something, either for sale or for exhibition. Yeah, I'm just not going to paint for myself to enjoy.

COHEN: Well, you had mentioned earlier that you thought there was a relationship between art and math. One of the things that I think about is that in order to really be a good scientist, you have to be creative.

HUANG: Right, I think that's very true. I think that people with artistic talent are generally thinking in a more creative way and also doing things in a more creative fashion. They do not like to do very detailed, routine kinds of tasks.

Even in painting, there are two different kinds of painting, especially in Chinese painting: There is this kind of more artistic but less detailed type of painting. Then there is this very craftsmanlike type of painting where every hair is being drawn; if you have ten thousand hairs, it's going to take ten thousand brushes to do it. Whereas the other type-- Just one brush. That's your hair. It's done. I like this more wild type of painting. I don't like the other type, which is craftsman type.

In my way of doing science, I also do not like to do the work that's going to fill in the details for some existing topic; somebody has opened up the field and I go in and just do some minor things to make the picture more complete. I'd rather do something that I initiated, so I [can] take credit for it--something new, something that has not been done before. That gets me motivated to do it.

In fact, that's what I have been doing since graduate school. The first project was like that. I felt very excited about the idea and pursued it for two years. Even though it didn't pan out, I still kept that kind of work habit or something.

COHEN: That was the RNA?

HUANG: That was the RNA. Of course, for finishing the degree's sake, I did something just for the sake of doing it to get a paper out. So I did that. Then during the postdoc period-- First, on entering the lab, I took a project that was given to me, so that had not too much to do with my interest or not. Just the lab wanted to do it, so I did it. But I thought, "This has a good chance of not working," so I thought of something that I could do, and then I did it. So two ideas, and they both worked. That led to two papers from the postdoc.

Then after I started my lab here, the general direction I still followed, which is to clone and study the proteins which can bind to the *Rb* tumor suppressor-- At the time that I started, none of them had been isolated, although they had been proven to be present. But one needs to clone them, so that's what I started doing. And I, indeed, cloned several genes. One of them was particularly interesting for the structure and I thought that one was really the [one the] protein people were looking for. Then it turned out there were other people who cloned something which is [the thing] people were looking for--that turned out to be the correct thing--the *E2F*. So my thing didn't turn out to be that protein which I was expecting. But it has, itself, some interesting characteristics which I think are going to be interesting or important. So I went ahead and just focused my lab working on this gene.

COHEN: Which gene is that?

HUANG: This is the *RIZ*, the zinc finger gene. And pretty much, I do not have much interaction with the rest of the field who works on *E2F*, so I am pretty much in my own little world of this gene, which I cloned, patented, and tried to make a name [for myself] by working with this. So that is [what] we have been doing for the last eight years--all around this gene and the family members of this gene. When we discovered this gene, we also discovered a new family, a new protein motif. So a number of things are exciting about this.

In the beginning we didn't know what this gene was in terms of its role in tumorigenesis. We were still pursuing its interaction with the *Rb* protein, although at the time the *Rb* function was pretty much thought to be mediated by this *E2F* protein that other labs have cloned. So they were the dominant ideas: the *Rb* and *E2F*. And for *RIZ* to somehow play a role in *Rb* function-- We're still saying there is a role for *RIZ*. However, it has been very difficult to establish that role. I think it may have something to do with our protein being present in very, very low amounts in the cell. It's very difficult to work with: it's a very large protein, and we're really lacking a lot of reagents that can get something done easily. So the role in *Rb* is still not clear at this point.

But slowly, gradually, we realized another aspect of this gene could be even more interesting. That is, we want to establish *RIZ* as, itself, an important tumor suppressor gene. And that turned out to be the case, slowly. We now really have some solid evidence to say, "This is an important tumor suppressor." The papers are being published at this moment for the final evidence to come out. Before this we had published papers in *Cancer Research, JBC* [*Journal of Biological Chemistry]*, to suggest such a role in tumor suppression. But those papers did not have the solid, convincing evidence that the field was going to accept this concept.

COHEN: Now, one of the things you gave me to read--I think the title of it was "The Yin and the Yang"-- Is that the article that you're talking about that's going to come out?

HUANG: No, that was a review paper just summarizing what we had published before.

COHEN: Oh, okay.

HUANG: So that one doesn't really have-- You know, all the existing literature right now on *RIZ*--and what we have published-- None of those have the missing genetic data that people are looking for to say whether this is a tumor suppressor or not. What we have now is the data, which we are submitting right now. One of them, I think, is in press in collaboration with another scientist, where we found indeed that *RIZ* is mutated in human colon cancer and gastric cancer. We also have found this mutation in human non-Hodgkin's lymphoma. Furthermore, we have done the knockout mice; we inactivated *RIZ1*, and these mice developed tumors.

That should convince other people, and that should make our life a little bit easier--to go out and say why we are studying this gene. Before I had some difficulty justifying-- You know, "Why are you studying this? You haven't shown it's important or anything."

COHEN: Well, you had said just a few minutes ago that you are doing something that no one else is doing in the world, and that kind of brings up the whole question of competition in the sciences. It sounds like you're not really competing with anybody at the moment, but in a lot of areas there's tremendous competition to get work done, to publish, to be first. Did you just fall into something that isn't competitive, or is it your nature not to want to be in a competitive situation?

HUANG: Actually, my nature is I like to compete. That is how I ended up in this postdoc lab doing the *Rb* stuff. At that time the *Rb* field was very competitive. The lab I was in was one of the three labs that cloned this gene, so you can imagine all these labs were competing with one another to do this work. I wasn't afraid of that, and I did it pretty much in a timely fashion.

It's kind of interesting you mentioned competition. Both of my papers [were competing with] similar papers published from other groups publishing about the same time. The *EMBO* [*European Molecular Biology Organization]* paper came out when another lab from Cold Spring Harbor [Laboratory] had a similar paper in *EMBO.* And then my paper in *Nature* [S. Huang et al., 1991. A cellular protein that competes with SV40 T antigen for binding to the retinoblastoma gene product. *Nature* 350:160-62.] was also either followed or [came out] about the same time as another paper from Harvard Medical School that was published in *Cell.* So you can see my postdoc work was competitive work.

Then once I started the lab, the work I started doing was also competitive, which was to clone the proteins that *Rb* can bind to. Our *Nature* paper demonstrated such proteins exist in the cell, and now it's a question of studying what they are. So that was basically what everybody in

this *Rb* field was doing--to clone those proteins. And now there must be like forty proteins that have been identified to bind to *Rb.* So you can say that field was also quite competitive.

The reason that I ended up not competing is because the gene that I cloned has turned out to be something that nobody else is working on. I feel that it's an interesting gene and has some potential to be important, so I think it's worth it to devote my effort to work on this gene. Compared to working on *E2F,* for example, which would be a hot topic, competitive, because a lot of people are going to work on that--it's obviously important--I do not feel that the potential reward for me would be greater than if I stay with my own gene. Why? Because this, again, goes to the question of doing work just to fill in the details. Basically, the guy has cloned *E2F1.* So if I didn't clone it and I started working on it, there's no way that--there could be a small chance that I could do something great--I will overtake the original discoverer of *E2F.* Most likely, that is not going to happen. So no matter how many good papers I can get from this, in terms of your accomplishments in the history point of view, fewer people are going to remember, you know, one of the hundred people who worked on *E2F* to add something to this story.

[END OF TAPE 3, SIDE 1]

HUANG: So, always, the guy who cloned *E2F* is going to take all the credit.

For example, the *p53* work: The guys who discovered *p53,* Arnold Levine and David Lane, are going to claim all the credit for *p53.* Eventually, if there's going to be a Nobel Prize awarded for *p53,* they are the people who are going to get it. However, how many people work on *p53?* Every week there are like seventy papers published on *p53.* There are all these great scientists who actually made their name working on *p53* by discovering various aspects of *p53* function, but still, they are not at the same level as the guys who initially discovered it, even though these people may not have contributed as [much] as some of the later people in terms of studying how *p53* works. But still, you view them differently. So they are not on the same level.

COHEN: So how important is it for you to get that recognition? Is that what it's about, or is it about doing something different? Or both?

HUANG: Yeah, I think it's doing something important [so] that you can be recognized as somebody special and to try to be in an important position--as important as possible. When you are young, you shouldn't go for the safe way of pursuing things. The less risk you take, the less reward you are going to get. It's very similar to the stock market. And I'm the adventurous type, the artistic type, the creative type. I want to do something that is going to have the potential to be something important. You know, that's a matter of luck. A lot of these things you don't know when you're starting to do it. You know, this gene could turn out to be something really not interesting. I could spend all my life [laughs] chasing something not interesting. But at least

while you are working on it, you think there's a good chance there's going to be something important. And if it's important Imagine if it's like *p53,* then my position would be--

You have to put yourself in that kind of pursuit to at least have a chance to be at the top of your profession. You need to work on something that could potentially lead you there. So you don't want to limit yourself this early to work on something safe but you know there's no chance to get to the best, highest possible place you can be. So that's my motivation--just to be original, to have a chance to be the best.

And I can see this is a risky approach. A lot of times you feel isolated because you've got no colleagues to talk to. Nobody's working on this. You have to do it yourself, isolated and ignored. That happens. I sometimes worry about all these things, but somehow I've stuck it out. So far I think it's going to pay off in the end. My experience during the past eight years, again, affirms my belief in this: You pay your dues, you get your rewards.

I thought that I had paid my dues two years ago when my first RO1 was not renewed and I had a lag period where I only had one grant left. I had to let everybody in the lab go. Basically, I was alone for a few months.

COHEN: Oh, wow. All the technicians and the--

HUANG: Yeah, they were all gone. Then I started from zero again--recruiting and getting to this point. Even then I told my postdocs that I had to let them go. At that time I didn't know my grant was going to be turned down. I said I was still pretty confidant they were going to give us-- I even told them, "If they turn me down, that means this *RIZ* gene is going to be really important," [mutual laughter] based on my belief in this: You suffer first. You're almost bankrupt. You are at the edge of losing everything. Somehow if you can survive that period, then things are going to turn around.

COHEN: Now, does this institution--? If something like that happens to you, some places will tide you over for a little while. They'll give you some money to keep it going.

HUANG: Right, right, they will do that. I really have not been in such a sad situation that I have had no money at all left. If that happens, I don't know what's going to happen. Maybe they can give me some money or maybe they won't. It depends on if they think my project is going to have some future or not.

What happened in my case was I lost one grant, [but] I still had a medium-sized grant so that I could pay myself and maybe [pay for] some of my supplies. Then immediately I got another grant.

COHEN: A new RO1?

HUANG: A new RO1. So the old RO1 was not renewed, but in the meantime I had applied for a new RO1.

COHEN: Oh, okay. So it was a short time that--

HUANG: Yeah, it was a relatively short time.

COHEN: Okay. Well, there are so many things that PIs [principal investigators] have to do nowadays--grant writing being one of them--and I actually wanted to talk about that just a little bit. How much time does that take for you? Is that something that eats a lot of your time or not much?

HUANG: Yeah, it's a significant portion of time, I would say. Maybe three months out of a year.

COHEN: Out of each year? That is a lot of time.

HUANG: Right.

COHEN: In terms of the writing-- I know that you said writing has not been a big problem for you. Actually, I was reading over your Pew [Scholars in the Biomedical Sciences] materials. I think it was Dr. [John W.B.] Hershey who actually-- He wrote you a letter of recommendation for the Pew. You probably haven't seen it--

HUANG: No.

COHEN: --but I have. [mutual laughter]

HUANG: Yeah, you've seen all the recommendation letters.

COHEN: He said that your writing skills were competitive with the American students, which I find incredibly impressive, because writing in another language-- And especially the difference between-- You know, when you have languages of two different alphabets, it's pretty difficult.

HUANG: Right. I don't know. I have seen, now, many Chinese postdoc students who study here, and I've thought their writing was very poor even compared to my own writing. I can see that for most Chinese students, the postdocs, it is a big problem in terms of writing. Few of them can write a grant proposal or fellowship by themselves.

COHEN: Can you do it yourself?

HUANG: I did it. Of course, I did my fellowship writing as a postdoc myself. I even wrote a review for the professor, even though we coauthored it. But I wrote it. So I can say, I think, that after graduate school, my writing was already competitive. Then it's a matter of when did I achieve that level of competitiveness. In graduate school, maybe? I don't know. I did write my own paper for my graduate work, and John Hershey helped in editing it. I find his writing very helpful, and it's much better than [laughs] mine. I learned a great deal from that.

COHEN: Do you need any editorial help at this point?

HUANG: At this point?

COHEN: Yeah.

HUANG: Rarely. The [Burnham] Institute actually gives us $1,000 each year to seek professional editing service for our papers and stuff. I did it once with one of the review papers, and I didn't particularly find them to be very helpful. It's mostly grammar type of changes. Whereas in our writing, I think [what's] more important is how to make the idea flow more clearly, make the text more easily understood, or make the sentence read more smoothly or something. Some kind of grammar type of correction is not going to really drastically improve the paper that much. So I wasn't that enthusiastic sending the paper out, even though I had this money which I'd better use. Otherwise--

COHEN: They take it back.

HUANG: They take it back, right. So I don't find that too useful. Whereas it could be very

useful for an experienced, very good scientist with a good writing style to actually help to correct or edit.

COHEN: Well, the last thing about the grants that I kind of wanted to explore with you is, there's an uncertainty which all scientists live with and which you actually had to face once, which is not having any money or enough money.

HUANG: Right.

COHEN: How do you handle the uncertainty?

HUANG: That is an issue my wife always argues with me about. [mutual laughter] "Your job is so insecure. You'd better move to a safer place." Again, as I have mentioned, I want to put myself into a situation where I can do the best. My goal is not just to get the grant money. My goal is to do good science, top science. Then the money will come. Whereas if I chase money, then I really need to worry about it all the time and then my science actually will suffer.

There are really two ways of doing science, biomedical work, these days. Most people are doing it by chasing money, regardless of the topic. So a lab may have three grants. The three grants are on different subjects. They were written because they think it's going to get them money. The three things are not that related--maybe somehow indirectly related--and none of them may be that unique or creative. And maybe they're all competitive, because to work on something that other people have done, especially if some dominant figure in the field has done something-- You come in to work on some aspect of it, generally, you will be favored, at least by the dominant guy. He sees all these people working on his subject and building his own story. That's something I'd like to see for my own subject [mutual laughter], so I can feel that. That's something I don't want to do--to do something just for the sake of getting money.

So my dream is to establish my own topic. Once I establish it to be so important, then I don't have to worry about grant money anymore. Think about if you're in a position like some of the very big scientists. They don't worry about money. Money will flow to them.

COHEN: It is harder, though, to sell the NIH [National Institutes of Health] on a new area, because they like a lot of supporting data--

HUANG: That's right.

COHEN: --in order to fund-- In fact, they pretty much want the study done before they fund it.

HUANG: Right, right, right. That's why in the past seven or eight years we have been kind of struggling with grants, since we haven't really opened up this area to say, "Oh, this is clearly important. There is no question you should fund this." But I think now it's going to turn around.

COHEN: Well, how important are the alternate sources, like, for instance, the Pew [Scholars in the Biomedical Sciences] money, which you didn't have to wait for the NIH for?

HUANG: Yeah, the Pew is important. Actually, we started this knockout project with the Pew money. Without the Pew money, it was probably going to be a little bit more stretching, but we would probably have done it anyway, regardless of whether we had the money or not. But having the money certainly helps. I think in terms of money, the Pew money wasn't really such a big plus for the lab. You know, it's not that much money.

COHEN: It's not a lot?

HUANG: Yeah. I think what it does to somebody like me who is working on some new area that is kind of isolated-- This Pew award gives you the additional confidence that you know you're onto something important. You have been partially recognized. Not fully recognized, but you know that somebody is recognizing this as being important. They think you can do it. So that helps you to stick with the plan, just go for it, and ignore all the criticisms. Without the Pew, you probably will start to doubt yourself, even though you consider yourself self-confident. But confidence also needs cultivating. It needs feedback. So we occasionally should get some positive feedback. I think in that regard, it helps you raise your perspectives. Once you view yourself as [being] among the best scientists, then you should ask, "Are you doing work that justifies you being in that group? What kind of work are you doing?"

COHEN: So there's some prestige associated with the award.

HUANG: Right, right, right.

COHEN: Well, most of the scholars that I have interviewed before talked about how nice the meetings were; of course, I hadn't experienced one until just last week. The meetings are very good from a-- Well, they're very pleasant for one thing.

HUANG: Yeah.

COHEN: But it's also not very often that you get to go to a multidisciplinary conference.

HUANG: That's right. You don't usually go-- In a way, you learn, maybe, all kinds of different things that get different perspectives. It's helpful in that regard, especially when you are starting out. You haven't really a fixed idea on what you want to do, and your attitude is still trying to learn something new. That's going to be very helpful.

But once you are at the point that you're pretty much satisfied with what you are doing and you have enough things to worry about, you don't want to get distracted. [mutual laughter] I see people going to these meetings, and generally they are just pretty absorbed with their own interest. So they still just like to listen to the talks that they have some interest in. Whereas some other talks that they have no idea what's there, they even don't bother to go to listen. You can tell from this meeting that a lot of people were not in the meeting room during some of the talks, right? Maybe half of us go to play somewhere.

COHEN: Parasailing?

HUANG: Yeah, right. So I've gradually found the meetings to be this way. Even though some meetings are broad topics, people still go just for their own little field. Students may be more broadly interested. For a scientist, to be good at what he is doing, to know more doesn't really help. Knowledge is not necessarily a good thing. [mutual laughter]

COHEN: Okay.

HUANG: It kills creativity.

COHEN: Okay. Well, we touched on the grant issue, but there are many things that PIs have to do. Besides grant writing, many have to teach. Now, you mentioned that up until recently there was no formal affiliation with the University [of California, San Diego]. But now some people from here are actually teaching classes over there.

HUANG: Right.

COHEN: Do you have any teaching responsibilities?

HUANG: No, I don't have [any] at the moment. Maybe in the future. I don't know.

COHEN: Is that something you would want to do or--? You know, some people wish it would go away, and other people like it.

HUANG: Yeah, I hope that I don't have to teach. I don't really have the motivation to teach. I'd rather get my work done. Yeah, I'm pretty much one directional, focused, once I set a goal. If this is the work I do, I'll pretty much do this. It's very hard for me to enjoy other things if that thing is not really related to this. Teaching is, from the students' perspective, of course, very important. But for the teachers, they are basically just donating their time. They may learn something also, but mostly they are contributing something. And I don't know what's the motivation for people who want to teach. I think educating youth, they enjoy doing it. I'm naturally not a good teacher, I think.

COHEN: Because?

HUANG: I'm kind of impatient. Also, I think I'm not very good at explaining complicated things in simple ways that other people can understand easily. You know, you can see I interact with my postdocs all the time, and I'm not teaching in a class type of way, but you can call that, also, teaching.

COHEN: Informal.

HUANG: Informal, yeah. And I think sometimes I don't do it very well.

COHEN: Do you have graduate students or just postdocs in your lab?

HUANG: Just postdocs in the lab.

COHEN: Well, I want to come back in a little while to your lab and how you run it, but let's move along with these PI responsibilities for the moment. What about paper writing? How much of your time does that take up?

HUANG: Nowadays my focus is to get all these papers published. It's been my full-time job

almost. Every day I will do some writing on papers and also, of course, some lab work, which is mostly designing type of work. I have to worry about what the technician will do. Besides that, I'll mostly write papers.

COHEN: If you could just describe, maybe a little bit, the process that you go through in writing papers--

HUANG: Well, we first have data--generate it--and then we make the figures. Then we'll write the results and the procedures, the introduction, discussion. Once you get used to it, it seems not so difficult. You can even copy from your old papers some of the same paragraphs. For example, the procedures: the same procedure was used before and you use it here and just copy them, paste them, and stuff. You can generate a paper pretty quickly that way.

COHEN: Who writes? Do the postdocs write, or do you write?

HUANG: It depends. For some postdocs, if they can write, they do. If they cannot, I will do it. And even when they do, they will usually just give me a draft to work on it substantially. Mostly they will get the results written down and they will make the figures. Sometimes I do it myself. And it depends on how involved was the postdoc in terms of carrying on this project. Sometimes many, many persons are involved in the project. Like these knockout mice took five years. The postdoc who did the initial work had long left, and then, of course, I had to be the person to write the thing. [For] some other project, the postdoc had the idea to work on it and basically carried it by himself all along. Then it's a good idea to let him do everything.

COHEN: Do you like writing for publication or is it a chore?

HUANG: I think I like it if I have something to write about. [mutual laughter] It's exciting.

COHEN: It always helps if you have something to say.

HUANG: Yeah, if you don't have something, it's not good. Now, comparing benchwork or writing, at least at this moment, I don't miss benchwork. In the beginning of my lab I was working a lot. Of course, that's natural; I didn't have much data to write about. But now I have more data than I can write, and to get all this published is more important to me at this point than generating more data, because the data we already have is so important that it's going to be very essential to have them published in the best possible way. So I realize that, and I'm willing to spend whatever is necessary to do it.

COHEN: Do you have any administrative responsibilities?

HUANG: Not really. That's what's pretty nice here: the bureaucracy--they try to limit that. PIs generally do not have real responsibility other than running their labs. Some PIs may run a facility, like a sequencing facility or a mouse facility, which not every PI will do. At least for me, I haven't gotten involved with any of these activities. Once I ran a seminar series when I hosted speakers and invited speakers. Other than that, right now I'm basically just [running] my lab.

COHEN: It's interesting because you are at a private institute, which is, I imagine, in some ways like Cold Spring Harbor—

HUANG: Right, exactly.

COHEN: --like Wistar [Institute].

HUANG: Same outfit.

COHEN: It's a different life than people who are at academic institutions, because most of the time they have a lot of teaching to do and they're drowning in administrative committees and things other than that. It sounds as if you're a little more able to devote yourself to the science, being that you're not at an academic institution. Is that a fair assessment?

HUANG: Yes, I would say it's true. Yeah, I would say we spend more time on our science than professors in a university. Well, I think it depends on individual professors. Some professors spend a lot more time teaching; some spend very little. It varies, especially in some medical schools. All they teach is one or a few classes of medical students. So yeah, it's true, generally speaking. We definitely have more time devoted to science.

COHEN: Is there any disadvantage to this kind of a situation as opposed to a university?

HUANG: In what respect a disadvantage?

COHEN: Well, I don't know. Prestige, maybe? Is it more prestigious to be a professor at Harvard [University] or not? I don't know that it is. I'm just throwing that out as a possibility.

HUANG: You know, that is really not the issue here--to be in a prestigious position. The bottom line is how is your work there. You can be a professor at Harvard, and your work is so-so. And what's your prestige? Your prestige-- There's always "Who are you talking to?" If you are talking to somebody who has no real education--people outside of the field—if you tell them you're a professor at Harvard, you may get more respect. But once you are in the group of people that really count--you know, who value your work--then it doesn't matter anymore.

COHEN: Now, what about-- For example, in academic institutions--many of them, although not all of them--eventually, you can get tenure, which won't do you much good if you don't have grant money in terms of doing your research. But at least you won't starve. Is there any kind of situation like that here--that after a certain amount of time or a certain number of publications, you have more security?

HUANG: Not really. Here, everybody is dependent on their grants. They don't really have tenure--that they'll keep you even if you don't have money. That doesn't exist. If that is a concern--that is, if you're not doing well--I think, then you'd better think of some safer way. For example, if someone's project is going downhill and they realize it's not going to get them somewhere and then they're also too old to start something new, then I think it's better to go to a place and get a position that's more secure.

Whereas for young people who start out, this should not be their number one concern. They should consider what kind of institution will help them to do their work the best, to help them be successful. They should go to that place regardless of whether they're at universities or institutes or [there's] tenure or no tenure. Once they are in there, if they're successful, then it doesn't matter anymore. Once you are number one, then tenure and money will come to you, even if you don't want them. [mutual laughter] So that's your goal. Whereas if you start out with your goal being tenure, then probably your science is not going to-- [laughs] Because your goal is pretty minimal, right? If that's your goal, you're going to end up in a state university, maybe, instead of here. And then you could be killed that way.

COHEN: Literally or scientifically?

HUANG: Scientifically, not literally. For example, I had the opportunity to go to the University of Florida, but I decided to stay here. Then a friend of mine went to Gainesville--the University of Florida--a couple of years later. He went there as an assistant professor, and after two or three years he had to quit because he was never able to get a grant to fund his work. So he quit.

COHEN: Was that because of his work or because of being in Gainesville, Florida?

HUANG: I don't know. That's something that's hard to tell. Maybe it was his work. He's also the type of person who would rather do something important and unique even if he has to lose everything than to work on something safer. Indeed, he is working on something very new and not that accepted, so the reviewers were very critical of his stuff. So he just couldn't get his funding.

But this, again, maybe has something to do with the wish of God. If he would have come here, maybe he would have run into a different reviewer or something, because here, they know you're under big pressure to get funded, whereas in Gainesville, they expect you to have some state money or something. Here, I either have this grant or I die. There you may be expected to at least survive by some way. So you're at less risk there than here, but then things also don't come your way. Whereas here, when you're faced with no choice, somehow it will work out.

For example, if I had decided to go to Florida, I probably would not have gotten into the Pew Scholars [in the Biomedical Sciences] program, because I don't think that Florida was invited to nominate somebody there. I was lucky also, [because] my nomination was the first time this institute was asked to nominate a candidate to this program.

COHEN: So you kind of blazed the trail for everybody? Has there been another one here since then?

HUANG: Yes, there's another one that's currently-- They're going to meet in March. So there are two right now, but we got another one nominated this year, also, who for sure will get in.

COHEN: Okay. You talked a little about how you tend to work a little bit later in the day. How do you juggle all these things that you have to do at the same time? You know, you're writing grants, you're trying to get papers published, you're trying to run your lab, you have to supervise the technicians, you have to design the experiments for the technicians.

HUANG: How? Well, there are at least eight or ten hours a day, and definitely you can do a couple of hours. First thing in the morning I go supervise the technicians, check with them what they have for today. I have two technicians right now. I used to not have technicians, but then I realized that it's beneficial to have some technicians, especially when I'm not doing a lot of experiments. I can count on the technicians to do my ideas. Whereas to tell postdocs to do things all the time-- So I check with them and see what they have and tell them what they should do today. Sometimes they have enough to do from previous experiments, and they just continue.

Then there's not much.

I don't deal with postdocs a lot on a daily basis.

COHEN: They're on their own?

HUANG: They're on their own. Then I come back to the office--write papers or do some computer work or research. A lot of my work right now involves database analysis. Since we have this family of genes, I can discover new genes just by database searching. So I do that and then paper writing. Then it's about time to go home. [mutual laughter]

COHEN: So what time do you leave here most days?

HUANG: Now I'm pretty on time--about six o'clock--because my parents-in-law are here. If I want to have a family dinner, I'd better go home by six. Otherwise, I will just eat leftovers. [mutual laughter] That sometimes happens if I have something really late. Then I don't usually work any more.

COHEN: That's it?

HUANG: Yeah. After dinner I find myself not comparable to when I was young. When I was young I could work until eleven thirty and still have a nice, sound sleep. Nowadays it seems like if I write or read too heavily, then I lose sleep.

COHEN: Well, what kinds of things do you do in the evening?

HUANG: Mostly reading papers. The magazines I will carry home--

COHEN: You mean journal papers?

HUANG: Journals, yeah.

COHEN: Not the newspaper?

HUANG: Not the newspaper. The newspaper-- I have some in the morning.

COHEN: That'll disturb your sleep--reading the newspaper.

HUANG: Oh, really? [mutual laughter]

COHEN: Well, there's all the awful things going on in the world.

HUANG: Well, yeah. But the *San Diego Union t-Tribune]* paper we have doesn't have too much international stuff. So pretty much it's reading some light stuff.

COHEN: Well, there are two other things that eat up people's time a lot. One is the Internet; a lot of people spend a huge amount of time on the Internet. The other is television. Do you spend time on--?

HUANG: No, we spend very little time on television, even though I enjoy it. My wife hates it. Purely, I enjoy sports, so I sometimes watch a lot of sports on television, but that is mostly on weekends. On weekdays we pretty much do not have television on for the children's sake. We don't want them to watch TV, and that's why we're not having too much TV at night. The kids will do homework. On the weekends I sometimes watch a little bit of tennis when there's a tournament.

[END OF TAPE 3, SIDE 2]

COHEN: I think we were talking about tennis on the weekends.

HUANG: Yeah. So for me, I spend a lot of time on sports. On weekends I usually play two hours each day and sometimes I watch some television, but not a lot. Generally, we try not to watch television at home. We still don't have a very fancy television set.

COHEN: What about the Internet?

HUANG: The Internet we do quite a lot. The kids [Matthew and Samuel Huang], my wife

[Chen Ruo Ping] all do it. My wife usually works on the stock market--analyzing the companies and stuff. For me, I usually don't work on the Internet because I think it's pretty slow at home, whereas here, it's much faster. Sometimes I read a little bit of the news magazines on the Internet, and the kids just play games. So generally there's not too much. I sometimes take my kids to golf practice or tennis. And my older son was taking piano lessons once a week.

COHEN: Do you work on their schoolwork with them?

HUANG: Not myself. Mostly my wife. They have a Wednesday folder that parents are supposed to look at and check. That's what my wife does.

COHEN: How old are your children?

HUANG: Ten and nine. They're about one year and a half apart.

COHEN: Oh, wow. That's hard when they're really little, but now it's not so hard.

HUANG: Right, they can play with each other.

COHEN: Okay. Well, going back just a little bit to your lab- - You know, most people learn how to run their lab from having been in someone else's lab, and you had two very different experiences. So how do you--? I mean, do you have birthday parties in your lab?

HUANG: No, no.

COHEN: How does your lab work?

HUANG: I think things changed from the beginning to now. Right now I think the lab is-- I hope the postdocs are self-motivated and work hard, of course. I give some ideas, some little guidance, but hopefully the postdocs will just be able to carry on something by themselves. And I wish that they will work on something that is their idea. At least, they should feel that it is their idea. I didn't used to do it this way. I used to just give the postdocs what I thought was important and just let them do it. Now I realize that's not the best approach. People are much more motivated when they are working on something they take credit for. I learned that, and I try to do it this way now. That really released myself from a lot of work too; I can spend more time on

my own work instead of talking to them all the time. We just meet once a week to discuss what they have done and what their plan is, so there's not too much daily stuff unless they want to show me something. For technicians that's different.

COHEN: What kind of a boss are you?

HUANG: What kind of boss? I think I'm pretty fair and businesslike. I don't get too much involved with personal relationships. Just be professional, I think. I just try to be like that.

COHEN: Because some people have said--of course, if you don't get involved in it, it's not a problem--that one of the hardest things about becoming a PI [principal investigator] was having to sort of learn how to manage people, because you're not trained for that in your own training and then suddenly, you have all these people.

HUANG: Right. How to manage people-- Yeah, I think that's a learning process. I'm probably better than I was before. I used to easily get impatient and talk in a nasty way, not nice, and make the postdocs feel unhappy. I guess I felt pressure from my mood. I think that was probably not a good idea. So I have learned to help them more. When they have problems-- Don't try to blame them. Try to be helpful in terms of solving it. Just be more calm. Of course, I also learned that you need to manage different people differently. Some people may handle your temper a little more. Then you can be more [mutual laughter] liberal with that. Some people are more sensitive. Then you have to be careful.

COHEN: Well, life is a learning process.

HUANG: Right, I think it's a learning process. And you learn from your mistakes. I think that's the best way to learn, actually. If somebody tells you how to do it, you're probably still going to make some mistakes anyway.

COHEN: Well, the irony of being a scientist is that you don't get trained for any of the things that you have to do after you become a scientist. I mean, most people don't write a grant until they become a PI. Depending on where you did your work, there are some labs where the PI does all the writing, which means you didn't write until you become the PI. You don't have to manage people or teach or do any of these other things.

HUANG: That's right. So different labs can really train different people, and some postdocs, some students, are better qualified for being a scientist than some others. Even though they

probably have the same number of *Cell* papers, that could be very different. In some labs the postdoc is treated like a technician and is doing all the work following the boss's idea. Then I don't imagine this postdoc will become successful as an independent scientist. Whereas a postdoc from another lab that was totally independent--from writing papers to designing experiments-- He was already trained this way. He was experiencing being a professor already, even when he was a student.

COHEN: Well, some of it he didn't experience--you know, grant writing.

HUANG: Well, he might because he might write a fellowship, which is pretty much similar to a grant.

COHEN: Sure. So how prepared did you feel when you--?

HUANG: I was very prepared in terms of pursuing my independent project, in terms of having independent thinking, in terms of feeling confident that you can do a lot of the things that the first-class scientists are doing based on the experience I have. I started my real lab work by working on something that was my idea, so I never experienced working for somebody and just doing what they told me to do. I never had any technician type of experience. The only thing was, in order to finish my degree, I did something that was just for the paper. Then for the postdoc work I was very proud of the fact that my work there was cutting edge and the ideas were mine. So I felt like I could compete with anybody, even the best lab in the world. A lot of people may also have the same thinking. You don't have to be afraid of competition when you start out your new lab, because you're basically competing with a postdoc in that big professor's lab, and you can compete with any of those postdocs. So I was feeling pretty okay to start a position.

In terms of writing grants, I think I was also prepared very well since I wrote my papers. All the papers for my postdoc I wrote--the first-authored ones. Even my Ph.D. work, the paper, I wrote. John [W.B. Hershey] basically did a lot of work for the introduction. He changed, substantially, the introduction for that paper and the way the results were written. But he left the discussion totally to me, so I pretty much wrote the discussion. I was trained quite heavily in that regard. In a way, I feel I was better prepared than most people. I can see how the postdocs were used as technicians in some labs, or the students were used as technicians. So you can have some students with very impressive publication records that still don't have a clue about how things are done.

COHEN: Yeah, it's actually kind of a disservice to a postdoc to use them as a technician.

HUANG: Yeah, it is. But sometimes you get lousy postdocs that don't have ideas, and you are left with either this guy who is going to sit there doing nothing or you tell him to do something. [laughs] You make the best out of the situation, you know? So if the guy has a very good idea and is very driven and very enthusiastic about projects, then you should definitely try to avoid telling him what to do.

COHEN: Okay, there's one other thing I'd like to touch on today, and then I think we'll wrap it up until tomorrow. We talked a little bit earlier about the gender thing--you know, what happens to women in science. But I wonder if you've ever encountered any ethnic or racial discrimination or problems in the sciences?

HUANG: Well, a Chinese background is not really a minority in the sciences. You certainly don't benefit like blacks in terms of getting academic positions. Same thing for the Chinese American students. They have a tough time getting into the universities. It's reverse--

Otherwise, I think it's mostly natural. I don't feel there is a special force--that these people have a secret, mutual agreement to discriminate against some group. If there is some discrimination, it's just being the unavoidable type of things. Being human. Being natural. That's part of the reason that I want to do something that's either going to be good or-- Maybe I'll get nothing. I don't want to be mediocre, you know? I feel that being not Caucasian, to achieve something here, one has to be especially good.

COHEN: If you're not Caucasian?

HUANG: Yeah. Well, if you are a Caucasian, you may be okay with being mediocre in what you're doing, and still, by playing some politics, you can get along well with your career or whatever you're doing.

For me, at least, I think doing the best science is the only way I can realize my ambition. In science, basically, it doesn't really matter what your background is. Your work should speak for itself. But sometimes good work also needs people to help [by] say[ing], "Okay, this work is good." Sometimes you can do good work and people ignore you.

COHEN: Yeah. That's true.

HUANG: I don't know if that's the case--whether your ethnicity may influence how your work is being perceived. I don't think that's too important. I think your work still is the number one thing that's in view. It doesn't matter whether you're black or whatever--who did the work. If this work is important, it's going to be realized sooner or later.

COHEN: Well, at a place like this, when you look at the scientists here-- You said there were a lot of women here, I know, but what percent would you say--? I'm not asking for a scientific statement, but just approximately.

HUANG: I don't really have a-- Maybe 40 percent.

COHEN: Are women?

HUANG: Yeah.

COHEN: What about by ethnicity? There are lots of Chinese scientists in the United States, I know that. But—

HUANG: Here we have mostly foreigners.

COHEN: Oh, really?

HUANG: Europeans from Finland, from Sweden, from Germany, from Russia more recently, and from Spain. From China we have three faculty here. Several from Japan.

COHEN: Are there any black or hispanic--?

HUANG: No, I don't think so. There's one from Italy. There's a good mix. There are some Americans too.

COHEN: Sounds like they're in the minority.

HUANG: Yeah, in terms of number.

COHEN: It's interesting.

HUANG: Foreign and American-- The Americans are the minority, I think.

[END OF TAPE 4, SIDE 1]

[END OF INTERVIEW]

INTERVIEWEE: **Shi Huang**

INTERVIEWER: **Helene L. Cohen**

LOCATION: **The Burnham Institute, La Jolla, California**

DATE: **21 January 2000**

COHEN: There were a few things that I wanted to kind of go back and touch on from yesterday. We talked just a little bit about competition and the fact that your field-- You're pretty much the only one doing it. But on a more philosophical level, how do you think competition affects the sciences?

HUANG: It's a good thing in terms of moving a field fast. Once a field is started by some pioneers, the work can get done really fast. For example, the *Rb* field started out with the cloning of a gene by three or four independent groups, so already in the beginning there was big competition. But then the competition got even more severe once the genes were in hand and many people started requesting the genes. They [wanted] to get involved. They [wanted] to work on those. And indeed, the field has moved really fast. There were many papers published. Many times two or three papers were published on the same topic with the same kind of conclusions and a similar set of data. I already mentioned in my case that both of my papers on *Rb* during the postdoc period were accompanied by similar papers by other groups. So in a way it's good for this field that lots of activity is going on. People immediately, quickly, learn a lot of things about this field.

But on the other hand, the really creative work does not result from competition. The person who's pioneering a field usually does not have any competition when he is working alone. For example, even for the case of *Rb*--the cloning--there was competition. But then figuring out the mechanisms really had something to do with Professor Ed [ward L.] Harlow's work early on, before *Rb* was even cloned. He was working on proteins that would bind to the *E1A* viral oncogene. Three or four years before the cloning of *Rb* he had identified a group of cellular proteins that would bind to *E1A.* Of course, he had no idea what the identities of those proteins were. Then all of a sudden, he realized once the gene for *Rb* was cloned--the protein product was identified--that one of his proteins had a very similar size with *Rb.* So he just tested whether that turned out to be *Rb,* and indeed, it was *Rb.* This opened up the idea that *Rb* somehow works by binding to proteins. Also, this led to the idea that a viral oncogene transforms by binding to cellular tumor suppressor genes like *Rb* and somehow inactivates the tumor suppressors. That's how maybe they transform.

So this idea really was started out by him working with the *E1A* binding protein. At the time he was working on that, really there wasn't much competition and his work was pretty much ignored. People thought, "Just a whole bunch of proteins sticking to a viral protein--

What's the significance of that?" Really, he had no idea. It wasn't until he found one of them as *Rb* that all of a sudden, every one of these guys became important and people started cloning more and more of those binding proteins. Indeed, several have turned out to be very important later on. So you have to give Harlow credit for sticking with his work while there was no competition. No other people were interested in his stuff. He was having a tough time, I understand, at the time to continue that line of work. If it wasn't for *Rb* coming out at that particular time, he might have had trouble continuing that line of work. There are many examples like that from history--creative works that were not generated by competition. Mostly, the real creative work is done by somebody working alone and finding something very unique that later on turns out to be of some general interest or general importance.

Really, I think competition is not the ideal way of doing science if doing science is to really be creative. Competition maybe is for the other way of doing science, which is just to generate data and to get grants. [mutual laughter] That's a nice way of doing it, because if you go into a competitive field, the only way that that field can become competitive is because that topic is hot at the moment. So you may have a lot more competition, but because it's hot, everything you touch should be fundable and should be publishable. So if you want to get involved in this topic, you can always do something that's going to be different. Or if they are similar to what other people are doing, it doesn't matter. You still get your results published, you still get funded. In a way, it's a more sure way of pursuing things; you know you're going to get something. Whereas if you work on something nobody's doing, you have no idea in the end if you're going to get anything out of this. So it's less risky, I would say, even though you may think it's more risky--you're working in the competitive field; you may get scooped or something.

COHEN: Has that ever happened to you? Because you said your paper came out at the same time as another paper. Did that scoop you or--?

HUANG: In those two cases that I managed to publish, I didn't get scooped. But I did get scooped for my third paper out of my postdoc, which was that the *E2F* is the *Rb* binding protein. My paper in *Nature* had identified a protein that's 46-kilo dalton size in molecular weight that binds for *Rb;* that was a band in a gel. We didn't have any idea what this protein was in terms of sequence and stuff, but that was enough to be published in *Nature* because it established the concept that cellular proteins exist that bind to *Rb.*

Now the next question for us was to figure out, what is this protein? At the time *E2F* was known, but it wasn't known that it binds to *Rb.* There were certain papers published around that time by Joseph R. Nevens's lab in *Cell* saying that *E2F* was released by *E1A* somehow, that the *E2F* activity could be regulated by *E1A. E2F* has a certain molecular size; they figure it's about 50-kilo dalton. So I had at the time made a very reasonable guess that *E2F* looks very much like an *Rb* binding protein. "Probably it's the 46 K," I thought. So based on that idea, I made some collaboration with *E2F* people and, indeed, confirmed that *E2F* is the *Rb* binding protein.

Then we tried to publish that, and we sent it to *Nature*--the paper. They said they already had similar papers in press, so they could not take ours anymore. In the end, we did manage to have our paper published later in the journal *DNA and Cell Biology.* So in a way, I was scooped in that instance.

COHEN: Well, one of the questions about competition is it does spur people on to work and to get things done and to try to get the information out in a timely manner, but it can sometimes, I think, lead to sloppy science in the rush to get something out. Have you experienced that at all?

HUANG: That really is not the case, I don't think, because sloppy or not, the conclusion cannot be wrong. If they want to publish something, they must be very sure about what they are trying to say. Maybe some of the data is not as solid, but in the end, the conclusion should stand. You probably would wish you had more data to support it, but because of competition, you have to publish now. But you are still pretty confident that this is going to turn out to be correct.

Indeed, I think in some other instances it has generated some artifacts, like the *BRCA1* field. It was very controversial in terms of where it is located, what's the size of it, and which band on this gel is the *BRCA1* protein. At the time the gene was cloned, all these tumor suppressor guys switched from *Rb* to *BRCA* and started making antibodies, and everyone was trying to publish as quickly as they could. Then, indeed, there were very different stories. The papers were published about the same time, but they got very different conclusions. And somebody must be wrong. [laughs] If they had more time, they could solve it. But in some ways, they could not wait. And in many cases, to identify such a protein by antibodies is very difficult. We can speak from our own experience in terms of identifying the *RIZ* protein. We had misidentified a couple before we ran into the real result. So if we are under time pressure and we have to publish, then we may publish something wrong.

COHEN: With regard to the *RIZ,* which is the work that you've been doing now, for eight years, you mentioned yesterday that you had very important data that you're writing up now and getting to publish. I don't know if you want to go on the record yet, since it's not published, but it will be awhile before this hits the library shelf. In terms of this work, how is this going to contribute to our understanding of cancer?

HUANG: Well, right now the field is basically characterizing the cancer genes. We think cancer is caused by mutations in cancer genes. We, indeed, in the past have identified many of them.

COHEN: In cancer genes or cancer suppressor genes?

HUANG: Cancer genes can be classified into two groups: tumor suppressor genes and

oncogenes. They operate in a yin-yang fashion. For a lab like mine to have a place in this research, we need to have our own cancer genes instead of other ways [where] we work on somebody else's cancer genes--*BRCA*, *Rb*. I think it's much more important to come up with our own genes. There still are many, many cancer genes remaining to be discovered, and there are probably novel mechanisms of tumorigenesis that are going to be discovered because of new genes that are being discovered. That's our goal: to identify new cancer genes. If we're lucky, we also can identify new mechanisms of tumorigenesis.

So after six years we have, indeed, solid evidence now that *RIZ* is a new cancer gene, and probably it has some novel mechanisms of tumorigenesis we have still not yet figured out. In the meantime, we think we've also identified a family of cancer genes that's related to *RIZ*. This family probably has a dozen or so members. So far only three are characterized, and all three turned out to be cancer genes.

So in a way, we contributed to the cancer research field by adding new members of cancer genes, but our work really hasn't changed the whole paradigm. The paradigm is that cancer results from mutations in cancer genes. I think for the next five or ten years this paradigm will still hold and new discoveries are mainly going to be more discovery of cancer genes. More genes will be discovered, so eventually we hope we will be able to identify all the genes that are mutated in cancer. Then we can somehow generate a picture of exactly what's going on in the cancer cell. Then we may have a handle on the mechanisms as well as on how to treat them.

COHEN: So these genes that you've identified, are these oncogenes or suppressor genes?

HUANG: These are kind of a unique class of genes. They could be viewed as tumor suppressor genes. On the other hand, they also encode alternative products that act sort of like oncogenes. So in this family of genes, one gene gives you at least two products due to two different promoters. The products are basically identical in their C-terminal part. They differ a little bit at the N terminus because of this domain that's defining this family--about a hundred amino acid motif called the PR domain. So you will have a gene that will give you a PR-plus protein and a PR-minus protein; the only difference is the PR between these two. But interestingly, the PR-plus form appears to be tumor suppressive, whereas the PR-minus form is oncogenic. Normally, both products are expressed, so normally there will be a normal balance of the two. But in tumors, this balance was disrupted by one of the two ways. In the case of *RIZ*, the PR-plus form was always lost or mutated and the PR-minus form was always present in tumors.

COHEN: I'm sorry-- If the PR-minus is the tumor suppressive--?

HUANG: No, the PR-plus is the tumor suppressive.

COHEN: Okay.

HUANG: Another gene of the family, called *MDS1-EVI 1*-- Then the PR-minus form was overexpressed in tumors, whereas the PR-plus form was disrupted. So at least we have two genes like that. In fact, the *MDS1-EVI 1* gene was first identified as an oncogene. It was an oncogene. They didn't know it even existed in this PR-plus form; they thought this gene just had the PR-minus form. And it was through our work that we predicted there should be a PR-plus form. And indeed, there is.

COHEN: That's interesting. It's the yin-yang thing again.

HUANG: Yeah, it's a yin-yang thing within one gene. Of course, we can consider the oncogene and tumor suppressor genes-- There's a yin-yang balance there too. Here, it's kind of unique: within the same gene, you've got the yin-yang there.

COHEN: It's interesting. Well, can you think of potential applications for this?

HUANG: Potential applications-- If gene therapy will work out in the end, if they can overcome some of the technical difficulties of delivering genes specifically to the tumors, we might be able to use the PR family genes, *RIZ1*, in a gene therapy type of protocol to treat human cancers. We can use *RIZ1* this way--same as we use *p53*--to do gene therapy of cancer. That's one possibility. The other one could be that we could screen drugs--small compounds--that would somehow affect the *RIZ* function or affect the yin-yang balance of *RIZ* to treat the cancer using small compounds. We could also maybe develop some compounds that would activate *RIZ1* expression in tumors, because in tumors we see loss of *RIZ1* expression, but the gene in most cases seemed to be intact. Maybe the promoter for *RIZ1* is somehow inactivated by something. So maybe it's possible, if a compound can be identified that can somehow reactivate *RIZ1* expression in tumors. So *RIZ1* maybe can be used in that fashion for cancer treatment.

COHEN: Is there any place for screening people for these genes? With the *BRCA1* and *2*, there are screening tests now. I don't know what you do with the information once you get it; that's another whole ethical issue. But is that a possibility with these? Are you not sure?

HUANG: Yeah, this *RIZ* is maybe a little different from *BRCA*, at least, [because] they screen normal people for *BRCA* mutations, because *BRCA* mutations are present in the germ line; it's actually passed on. And we don't know if such germ line types of mutations exist for *RIZ*, whether there is a cancer type that's familial cancer and that is caused by *RIZ*. We don't know that yet. It's possible. We just don't know at this point. So I don't foresee the screening of

normal people for *RIZ* mutations.

However, there might be *RIZ* polymorphisms [such] that one form of *RIZ* versus the other--people who carry that one particular form--may be more susceptible to tumor formation. If we can identify what kind of *RIZ* form they have, then this may give them some idea of how susceptible they are to certain cancers. We have some work submitted in that direction. We have actually identified a *RIZ* polymorphic allele. We have found that this allele is more popular in Asians—Koreans and Chinese--versus Caucasians. And we have some evidence that this allele is a better tumor suppressor allele; it's more popular than the other ones. So if this one is more popular in Asian populations, we are trying to suggest that maybe that has something to do with the lower tumor incidence in Asian populations versus Caucasians, which is well known. Most people think that is due to diet or something. But that may not be the case. Diet may not be the only thing, is what I think, because they have noticed this difference in tumor incidence even among Asians living in the U.S.

COHEN: Americanized and eating the junk food that Americans eat?

HUANG: Right, right.

COHEN: That's interesting. Lots of things to think about. Of course, there are all kinds of social issues that revolve around testing people for predisposition for cancer.

HUANG: Right. Yeah, it's going to need a lot of discussion on the government level to see what they want to do with all this genomic information.

COHEN: Well, one of the things that I like to talk about is--especially because yesterday you mentioned fate--sometimes people stumble onto a great discovery by accident.

HUANG: Most of the time that's what happens. [mutual laughter] Discovery is made by accident.

COHEN: By serendipity.

HUANG: Yeah, usually the great ones are like that.

COHEN: What about in your life?

HUANG: In my life, serendipity-- Well, for the work I did before I became a professor, I don't think there was any accident involved. It was pretty well thought out, logical. The first work, the postdoc work, they had identified that *Rb* can bind to *E1A.* I wanted to know what domains of *Rb* were involved in binding, so it was just straightforward work--to map the domains. Then the next thing is-- You know *Rb* binds to *E1A* and you think there must be an *E1A*-like molecule in the cell that binds *Rb.* So you go ahead and identify that. No big deal.

Now, I think in terms of the *RIZ* work, there was probably some luck involved. We gained something, we lost something in this case. We had thought that we were going to contribute to the *Rb* work by isolating this *RIZ* gene, but that has failed so far. We haven't really contributed much in that regard. However, a good thing happened: *RIZ* has turned out to be important in its own right without having a relation with *Rb.* In a way, I set out to do the work without even dreaming about [how] I would be able to clone or identify a novel cancer gene. I was only hoping to get an *Rb* binding protein and do something in relation to *Rb* under the big *Rb* umbrella. And now I can see that *RIZ* can, itself, become an important topic of study and has its own importance and interest and has become a tumor suppressor.

And the way that I cloned *RIZ* and found it as a tumor suppressor really is kind of luck, because normally to clone a tumor suppressor takes more work. It usually involves a large group and is a very labor-intensive type of cloning. You go from positional cloning. You first identify where you think the tumor suppressor is on the chromosome and then walk from the site you know into the region. So typically it has been by positional cloning. That's how *Rb* was cloned. That's how *BRCA* was cloned. It involved so much competition and a lot of work. That's why when I started my lab, I didn't really dream of cloning such a gene, because it was just beyond my power to do it. But in the end, it came out this way. It was better than I hoped.

COHEN: How did it happen? You said it didn't happen in the usual way with this positional cloning. So how did you stumble onto this gene?

HUANG: Oh, well, you clone it because it binds to *Rb.*

COHEN: So you knew about it?

HUANG: Now, it binds to *Rb,* but that doesn't mean it's going to be a cancer gene.

COHEN: Okay.

HUANG: Just because something binds to *Rb* doesn't mean-- Now, gradually, piece by piece, we have realized it may be a cancer gene. How did it come about? The first thing was, there's a hint because this gene shares a piece of homology with another gene. That was initially why we called this domain a PR domain. P stands for the other gene, R stands for *RIZ.* We found this domain, and this didn't tell us, really, right away whether this was going to be a tumor suppressor cancer gene, because the other gene was not known to be involved in cancer. But then we realized this PR motif was present in this cancer gene that I just told you about--the *MDS1-EVI 1* oncogene. That tells you that this *RIZ* gene is related to a known cancer gene. So it has the potential to become one itself, too. Then we started having evidence that in cancer cells, the expression of *RIZ* was altered, like I told you. The *RIZ1* was always lost and the *RIZ2* was always there. Under normal circumstances for a gene that has only one product, if you find that the product is lost in cancer cells, you would not be as impressed because it could happen randomly, because cancer cells are known to be unstable. And if you find your gene product is present in this cell line but absent in the other cell line, you probably wouldn't pay too much attention to that. But in our case, the yin-yang phenomenon was quite striking. The *RIZ2* is always present. There was almost like a selection for it to be expressed. Yet *RIZ1* was commonly found [to be] lost. We thought that had some real meaning to it, and that triggered us to suggest that *RIZ1* is a tumor suppressor in that case.

Another piece of serendipity, luck, has to do with the knockouts. In the beginning when we first cloned *RIZ*, we did not realize there was a *RIZ2* product. We always knew there was this PR-plus form--*RIZ1*. The short form we hadn't realized in the beginning, so we had tried to do the knockout the moment we cloned the gene. We knew the PR motif in this N terminus was important, so we set out to knock out this motif in particular. Hopefully, this would inactivate the whole gene. And we designed this targeted strategy without realizing there's a *RIZ2*.

Now it turns out to be that this strategy has turned out to be perfect for our idea to prove whether *RIZ1* loss, but not *RIZ2*, is going to cause cancer or not, because this targeting strategy turned out to just inactivate *RIZ1* without affecting *RIZ2*. So we have created a mouse line that mimics the human tumor situation; these mice do not express *RIZ1* but express *RIZ2*. And what happened to these mice-- We initially had no idea, because when we made these mice, we had no idea that *RIZ* was going to be a tumor suppressor yet. On the other hand, these mice were viable. They were normal--we could not detect any abnormalities--so we thought, "Ah, this is failure. We didn't succeed in achieving what we wanted to in terms of studying the function of *RIZ."* And we just sort of gave up on these mice. Therefore, we pretty much killed most of the mouse colony, most of the animals, but fortunately we had left about a dozen alive. We kept them alive for their whole life. Then [after] about two years, about twenty months of age, we noted that these mice developed tumors.

COHEN: Totally unexpected. You were just warehousing them?

HUANG: Yes, yes, unexpected. And that was very exciting. But the number was too small to publish, so we immediately expanded our animal colonies and waited for another two years.

This time it repeated the results basically. Indeed, these mice are tumor prone and support our hypothesis.

COHEN: Now, by the time the second group was two years old, had you figured about *RIZ2* yet?

HUANG: Yes, at that time we had--[at] about the same time, I believe.

COHEN: Well, one of the things that interests me about this serendipity is, it not only has to happen, but your mind has to be open to it happening. You know, if Alexander Fleming had just thrown away those plates with the mold on them, we wouldn't have penicillin.

HUANG: Right. Yes, it's absolutely true that luck is only for the prepared mind, as they say. You know, definitely, we are prepared for anything that's going to happen. And I think this is bound to happen no matter what. If you're good enough, you work on something and you may fail on your initial goals, but in the process of doing this, you should be able to find something else. In a way, fate comes in. Fate lets you fail something, but also lets you gain something. That's certainly true in our case.

COHEN: Okay. Well, in terms of a discovery like this one, another sort of ethical issue comes up, which is can or should scientific ideas be owned by anybody? I know you hold several patents and you have a couple more pending, and people are patenting genes like crazy and whatnot. What do you think about that?

HUANG: Well, if there's no commercial thing attached to a scientific discovery, then definitely, we don't need to patent anything. Patents, in my view, are still good at this point because our work may have some application that's going to be good for human society. So to patent our work would actually benefit society, because that would really give people incentive to actually develop their ideas into some products that can be useful. If we don't have the patent to protect [our work], then it is going to be difficult to attract people to work on these things, because they don't see their effort, their investments, being protected. So this is good from developing a product point of view. On the other hand, it's good also-- It doesn't really interfere with scientific discovery, because in the academic world, you can still do whatever you want to do regardless of whether you have a patent or not.

Sometimes, maybe in terms of exchanging materials, it gets slow because some institutes require people to sign an MTA, material transfer agreement. Sometimes the terms in that agreement are not very good to the other party, and then they don't want to accept this agreement. Then they may be denied those reagents. In that sense, you can say, "Okay, this

hurts scientific discovery." But from the other side's point of view, if they have no interest in commercial things, then they really shouldn't care about the MTA agreement. If all they're doing is pure scientific discoveries, then they should be okay with any kind of agreement, because these agreements basically limit their use of those materials for commercial purposes, not for scientific discovery. So in a way, you can see it's the commercial things that get in the way of scientific discovery. It's not the patent.

COHEN: Now, I know some people are reluctant to share their data because they don't want to be scooped on something. Do you think that helps or hurts the process? Or maybe it doesn't affect it at all?

HUANG: Well, that's just the way it is. [When] people do science, the only reward they get is recognition for what they've done.

[END OF TAPE 5, SIDE 1]

HUANG: So I don't think that in any way-- Even if it hurts scientific discovery in the short term, it should still be that way. I don't think it hurts scientific discovery that much anyway.

COHEN: In the long run?

HUANG: In the long run. Maybe it hurts your data for two years. What's the big deal for two years in terms of the big picture? Definitely, when you're not ready to release your data, you just don't release it. Of course, that will hurt somebody who's working on something related. But so be it. That's the way it is.

COHEN: It sounds like you are sort of a capitalist now.

HUANG: What do you mean by that?

COHEN: I mean, the capitalist economy versus the communist economy, where things are profit motivated and you look for a commercial reason to do things. Would you say that--? I mean, I'm kind of teasing you a little bit, but it sounds like you've sort of adopted that philosophy, which was not the one you were raised with, I guess.

HUANG: Oh, definitely I don't have that communist view--not that much. I think there are pluses and minuses for both views. I like the communist view that people do things based on certain ideals--you know, more romantic type. Whereas this capitalist is more material driven. So there are pluses and minuses. I think there needs to be a balance.

COHEN: Kind of on that same line, are you naturalized? Are you a U.S.--?

HUANG: No. I'm a PR.

COHEN: Permanent resident?

HUANG: Yeah.

COHEN: Do you ever think you might go back to China to live?

HUANG: Yeah, I don't mind actually. Yeah, I might. I might, once I realize my dreams here. Yeah, I always enjoy going back to China. I always enjoy the trips. I wish I could do it once a year, at least.

COHEN: Would the possibility exist for you to work there in a similar way that you work here?

HUANG: Not really. I don't think you can do competitive work there. Conditions are not right yet.

COHEN: Well, in terms of your career--we'll do that first--how do you think you're doing? Are you about where you thought you would be at this stage of your life? Or have you done more or less?

HUANG: You know, we always have high hopes. Definitely, I probably haven't reached the ideal situation I wish I had. But then you will never be able to achieve what you hope you will. People, just by nature, are not going to be satisfied with whatever they have. There are always some people that are going to do better than you and then some people worse than you. So you need to find some balance there. And if you want to be happy, then you need to be a little bit content with what you already have.

I think I'm doing fine. I told you that initially when I started this lab I wasn't expecting to clone a cancer gene. So in that regard, I think I have fared better than I had thought. Of course, the work that I've described has not gotten publicly recognized because our paper's still in press. So I haven't reached that level that once your work is recognized, what is life going to be like? I haven't gotten there yet. I'm still not a big professor or a famous one. [laughs] You know, most people are trying to get there. So I don't think I have realized my dreams yet. We will still need a few more years of work to get there, but I think we are on the right track right now.

COHEN: How about on a more personal level? When you look at your life in general, is this--?

HUANG: In general, I think my life has been pretty positive. I'm pretty much optimistic about what's happened. Yeah, I think my career has always been going up instead of going down. I haven't reached the point [where] I think I have reached the highest and then [will] start to come down yet, so I still think my career is moving up. I realized during this process that there were going to be dark periods, difficult times. But somehow I've survived all of them and things have come out better than it was before. So I'm pretty positive in this regard. I think I have, generally, good fate. [laughs] Some people I have talked to say, "I always have bad luck. Never good luck." I tell them, "That's not true. You probably need to change your perspective."

COHEN: Have you heard the expression, the glass half full or half empty?

HUANG: Right, I've definitely heard of that. Depending on how you view this thing, it can be bad, it can be good.

COHEN: What do you see yourself doing, say, five years from now?

HUANG: Well, pretty much working the same direction--get more work done, expand this PR family to discover a few more cancer genes. We have identified several new ones, and we're testing if they are also cancer genes. There's a good chance they will be. In five years we probably should know how many of these genes will be cancer genes. In the meantime we should try to do something even bigger than just adding new genes to the cancer gene list. We should try to figure out the real mechanisms of tumorigenesis, although it's going to be really tough. It seems like the paradigm is, in general, correct, and that may be unlucky for our generation. [laughs] There's only one DNA structure to be discovered. Once it's done, it's done. So I don't know if we can ever achieve something greater than what we are doing now.

COHEN: How about in ten years? Can you think that far in advance?

HUANG: In ten years? In ten years--

COHEN: What do you see yourself doing? I mean, obviously you can't know what the experiments are.

HUANG: Exactly. I'm a more spontaneous type of person, so I don't really have a lot of plans. I believe things will come either by accident or something's going to happen, so that can lead you somewhere. I'm just taking the attitude of, "Go and see," so it's really hard to imagine anything ten years down the road. My wife [Chen Ruo Ping] always keeps asking me, "You have to plan for ten years to know what's going to happen." But I really don't have any plans. I think anything's possible. I may quit what I'm doing here and start something totally different--go to a company or start a company or retire. Or maybe I will have made enough money and then do something else. Science is moving so fast nowadays, it's hard to imagine that what you're doing now you will still keep doing in ten years.

COHEN: Well, a lot changes in life in ten years. You know, in ten years your kids [Matthew and Samuel Huang] will be grown up. Lots of things will be different.

HUANG: Right.

COHEN: Okay. Well, what is the thing that you like the most about being a scientist, if you had to narrow it down?

HUANG: The freedom that you control your own destiny and you work for yourself in the process. I agree very much with some professors who say that you're having fun and, in the meantime, you're getting paid. You're doing science that is a purely self-satisfying endeavor. You know, you're being creative. If you are indeed creative, you get recognized for doing that. And in the meantime you can have pretty much all the benefits that other professions have--getting a decent salary to have a life, to have a family. I think in a way science is like art. You get lots of satisfaction from creating something. This is basically your hobby, if you think of it. You're doing it to satisfy yourself, not to satisfy other people, not to work for a company or something. So I think it's a very good profession. I wouldn't mind doing it again. Especially if money is not an issue, I would think that most people would prefer science than medicine or something else.

COHEN: Prefer science than medicine?

HUANG: Yeah, because if grants are not a major issue, if money's there--

COHEN: And why is that? I mean, I have my own ideas, but I want to hear yours.

HUANG: For example, being a doctor, your job is kind of boring--you know, seeing patients. Of course, some difficult diseases require some creative thinking and treatment, but in general, most doctors just do quite routine type of work. Whereas a scientist can be creative every day and is enriching himself with creating new things. His time is spent creating. Whereas a teacher or doctor is not really generating anything new. So I think just like if the economy was not a concern, there would be more people doing artwork, maybe, instead of having to have a profession to make a living. So it is quite a good profession for a human being.

Unfortunately, because of the grant pressure and the limited money, if you do science, you have to be able to handle the pressure of getting grants and stuff.

COHEN: So then the flip side of that question is, what's the thing you like the least? Is it the money stuff or something else?

HUANG: In science?

COHEN: Being a scientist, the thing you like the least.

HUANG: Being a scientist, the thing you like the least--I don't really know. Certainly I'd like to see that the grant is not such a big thing. However, if you are doing great science which is recognized, then the grant is really not an issue anymore. It's only an issue when you're starting out, when you're in a difficult situation and your work is not going well.

Well, I dislike people who do science as a way of just making a living on a salary. I think they should not be in the field of science. I like people to be enthusiastic about what they're doing and to think about science all the time--think about what they're working on--and just be very driven about it. More and more, you see postdocs-- I don't know what they're doing, what they're thinking. [laughs] Definitely not a lot of them are thinking in terms of making some great discoveries. I think that was my idea in graduate school. I always dreamed about discovering something important and was always very enthusiastic about what I did. I [would] like to see that more in all these postdocs and students.

COHEN: Do you think postdocs have changed over the years, or are they just different from the

way you were?

HUANG: No, I don't think it's changed. I think somehow, in this population of scientists, there are always going to be the creative ones, the enthusiastic ones, and then there are those who just treat it as work. Unavoidable. Just like not every Ph.D. student will end up being a PI [principal investigator] of a lab.

COHEN: Well, if tomorrow someone said to you, "Sorry, you can't be a scientist anymore," what would you do with yourself? What would you do if you couldn't be a scientist?

HUANG: I'd still have to have work, right?

COHEN: Well, I don't know. Maybe you could go be a beach bum. What is your sort of fantasy that you would do if you were not a scientist?

HUANG: You mean if I retired, like, tomorrow?

COHEN: Okay.

HUANG: [laughs] How would I live retired life, right? We have already planned some fantasy about what I will do after retirement, which is playing golf in the morning and tennis in the afternoon. [mutual laughter]

COHEN: Okay.

HUANG: I don't know. At this point I don't think I would start something new and try to make a career again. Probably I'd just enjoy myself and be happy. In the end you accomplish things and you realize, historywise, it doesn't really matter unless it's something really great. [laughs] That's more related to fate rather than working for it. Happiness doesn't depend on success, as you probably know, and doesn't depend on how much money you earn. It's more related to your perspective about yourself. Gradually, I've learned that point, and I've tried to be less competitive in that regard, tried to not compare myself to other people.

In the Chinese tradition, that has been a very different idea. In China, we start comparing ourselves to our contemporaries--classmates--right from the beginning, from school.

COHEN: Oh, really?

HUANG: Your grades and stuff are always known, and you're always classified relatively--where you stand in this order of status. That has something to do with Confucius's idea. So you see a lot of Chinese paying more attention to these outside success symbols. Then we come to America, you see people pay less attention to these symbols of success, and you see many happy people even though they're just taxi drivers. That's something I have gradually learned. And I think that's important. I'm always very much interested in books on these topics. What is the philosophy of happiness? What is it?

COHEN: So this is what you read?

HUANG: I read a little bit of this, yeah.

COHEN: Well, actually I've asked you all the questions that I have to ask. Usually when I come to the end of my questions, I like to just give you an opportunity to add anything you would like to the record before we finish up. So is there anything you'd like to say?

HUANG: Well, I don't really have too much. I hope this serves as something that has recorded some of my philosophical views. I find that may be useful and valuable later on. [laughs] I'm always very much interested in philosophy.

So again, one point I think I have realized, and which I'm not sure how many others realize, is this fate thing--this pay your dues business, perseverance. You work first and then get rewarded. You suffer first and then achievement is rewarded later. Most people, I think, think of it purely as cause and result. Certainly, you have to work in order to get something. But I tend to view that there is a certain amount of probability or mathematics involved. My general view is [that] God, whatever it is, is fair, just like probability. It's fair. [If] you have great fortune in getting something, your fortune of getting the next big thing is going to be very small; your chance of doing that again is going to be small. On the other hand, if you've suffered a great deal, then the chance for you to have another great suffering is going to be minimal. On the other hand, your chance of success is going to be higher because you already have suffered. In that way, I think it comes out all right.

Anyway, I think there is an element of fate in this whole philosophy idea about work and success, and I don't know if that element has previously been recognized. As I told you, I was thinking I should write something about this idea for a book. Then I realized two thousand years ago a Chinese philosopher had written it. But still, I don't know if, in his writing, this element of fate is actually there or not.

COHEN: The probability part of it?

HUANG: Yeah, the probability part of it.

COHEN: I know I told you I had run out of questions, but I just thought of another one. If you were to write such a book, would you write it for an English-speaking audience or in Chinese?

HUANG: Well, probably English, since I'm more comfortable now with English writing than Chinese writing. I haven't written in Chinese for fifteen years. I don't usually write letters, you know. It doesn't really matter actually. Presently I'm reading a novel by a famous Chinese author. This novel was written by him in English, and it's about things about China. This book is now translated in Chinese and I'm reading the Chinese version of it.

COHEN: Oh, that's interesting.

HUANG: Yeah, it's very interesting. Even though that author was trained in China, he can certainly write in English.

COHEN: Sure. Okay, anything else? No, that's it? Okay. Well, thank you very much for participating.

HUANG: It was my pleasure.

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[END OF INTERVIEW]

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