JANET DAVISON ROWLEY

Session I - June 6, 2005

Interviewer: Andrea Maestrejuan (AM)

I. Early Life: Parochial Early Education and Laboratory High School at University of Chicago

AM: It is June 6th, 2005. I'm Andrea Maestrejuan here with Dr. Janet Rowley at her office at the University Of Chicago School Of Medicine to conduct her interview for the UCLA Human Genetics Oral History Project. We'll start at the very beginning, and I'll ask you when and where you were born.

JR: I was born in New York City on April 5th, 1925.

AM: There's quite a bit written about you and some interviews done, and you end up in Chicago. How long were you and your family in New York City?

JR: We came to Chicago when I was about two years old. My father [Hurford Davison] was in retail store management and was recruited by a department store in Chicago to come here, so my family moved. My mother [Ethel Ballantyne Davison] had been born in Chicago and her family was all here, so for her it was like a homecoming.

AM: So you don't have any memories of -- you didn't spend much time in New York City?

JR: In New York City, no.

AM: I also know that both your parents went to the University of Chicago, but could you tell me a little bit about both their family backgrounds? Did they come from educated families? Had they come from parents who had gotten college degrees?

JR: My father came from families that -- I know his mother went to college, and I believe his father did as well. He was a businessman and insurance salesman, so he had that kind of background and work. My father then went to college at Drake [University] first for a year and then came to the University of Chicago, and then went on to Harvard Business School to get a master's degree, an M.B.A.

My mother's family was not educated beyond high school. My grandfather was a worker in the steel mills here. He came from Scotland. And my grandmother had been born in England but her father was a miller, milling wheat

in Kansas, and she came to Chicago at age 19 and worked as a bookkeeper for Albert Pick who built the Pick Hotel. My mother was almost the first person to go to college in her family, though her brothers later also went to law school, so she wasn't the only one in the family who went to college. She was the only girl, though, who went to college, in the family.

AM: And did she have sisters then?

JR: She had three sisters and three brothers. She was one of seven children.

AM: Was your father's family then originally from Chicago? Where were they from?

JR: They were in Iowa. My grandmother's family especially [was] in Iowa following the Civil War, so they were established, and my great-grandfather was the founder of the Lincoln Drug Company in Lincoln, Nebraska.

AM: So early science background somewhat.

JR: Well -- more business, I think is fair to say.

AM: And what brought your parents to New York City?

JR: My father, when he graduated from the Harvard Business School, got a job in New York City at Lord and Taylors[1]. He and my mother were married, so they lived there, and I was born in New York City.

AM: Did they meet at the University of Chicago?

JR: Yes, through a mutual friend at the university.

AM: And you don't have any siblings?

JR: No, I'm an only child.

AM: What kind of expectations did your parents have for you in terms of professional life and educational attainment?

JR: They both thought I was smart, and they expected me to do something. The implication was [that] I [would] do something special, but what it was I was going to do was left open. So when I showed an interest in science, particularly [in] the biological sciences, early in high school, they encouraged me. But in fact, at the end of seventh and through eighth grade, I really loved Latin and I was going to be a Latin teacher, because it was such a logical language. I just thought it was marvelous.

[1] Lord and Taylors, based in New York, was the oldest luxury department store chain in the nation.

AM: What was it about science that they saw you were interested [in]?

JR: Particularly much of the biological sciences. The sophomore class that I had at a Catholic girl's school[2] that I went to was very focused on the phylogenetic tree[3] and all of the different phyla and what the characteristics were, and then all of the classes and the families. Again, it was the logical nature of that that really appealed to me. I don't think I would have said in my freshman or sophomore year that I was going to go into science, but it certainly was an area that I was interested in.

AM: How about earlier, in elementary school? Did you go to parochial school [then] as well?

JR: No, I went to public schools here all over the South Side of Chicago, so I've probably been in four or five public schools in the South Side of Chicago, because my family moved a great deal. It was during the depression and things were difficult. I only went to a Catholic girl's school because my mother was a high school teacher on the South Side, and she didn't want me to be being taught by any of her friends and colleagues. She thought it wouldn't necessarily be good for me to be a special person in that context, so that's why I went to the Catholic girl's school for two years.

AM: And this was here in Chicago?

JR: Yes.

AM: What subjects did your mother teach in high school?

JR: English. My mother was an outstanding teacher of English and composition. I met many of her students' even years afterwards who would comment on how important she was, because she really graded papers, she commented on style, made suggestions to improve style.

AM: Maybe this is asking the obvious, but what kind of religious traditions did you grow up with?

JR: My mother and her family were Episcopalians, so I went to the Episcopal Church. I was a pretty good church-goer until probably about my junior year in high school. Then I would go but not as frequently.

AM: And your father's side of the family?

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[2] Mercy High School at 81st and Vernon

[3] A phylogenetic tree is a visual representation of the evolutionary relationship between different groups of organisms. For an image visit this website at: http://tolweb.org/tree/learn/concepts/whatisphylogeny.html

JR: I'm not sure. Probably Presbyterian, but I don't [know] -- he never went to church, so it wasn't something that he contributed toward my education or my background.

AM: Was it important for your mother to raise her child within the Episcopalian tradition? How important were religious values?

JR: I don't think religious values were terribly important to my mother, and my father both. They were very moral individuals, with high moral standards of what was proper behavior and what were ethical ways to behave to other people [and] how they expected me to behave. But that was in the sense of proper morality, not in the sense of specific religions.

AM: So how important then was the religious aspect of parochial schooling in this all-girl's Catholic high school?

JR: I didn't have to go to the religion classes because I was Protestant. I suppose the other religious influence that happened to me, in eighth grade, [was] my paternal grandmother came to take care of me for about three months because my family was moving back to Chicago and it was important that I complete eighth grade where I was. She's a Christian Scientist, so for her Christian Science was very important. We used to go to the Wednesday evening sessions almost weekly for those three months. I was very taken with Christian Science from the standpoint of how important your mind is in influencing how you feel. That's a component of Christian Science religion/philosophy that I've kept with me always.

AM: Okay. I know you have four children[4] of your own, and what kind of religious traditions did you raise them with?

JR: Well, for the first two -- they're all boys and they've all been baptized in the Episcopal Church-- the first two we actually took to Sunday school. I had a next door neighbor who was also Episcopalian, and she had two girls the same ages as our boys. So we would spell one another off on Sunday mornings of getting our children to Sunday school. That probably lasted a year or so. Then the boys rebelled and the girls didn't want to go either, so our children have had no religious training at all, basically.

AM: Okay. This may be an overgeneralization, but there seems to be a real dichotomy between religious beliefs and scientific beliefs (I guess would be the way to put it) in the United States, especially now, [the idea] that there's some kind of incompatibility between the two. How much were your own religious traditions or beliefs changed by your growing interest in science, [especially] in the biological sciences?

[4] Oldest son Donald Rowley; second son David Rowley; third son Robert Rowley; youngest son Roger Rowley.

JR: I don't think they were changed a whole lot. Though some Episcopalians believe in the Virgin birth and in the Apostles' Creed[5] -- there were a number of things in the Apostles' Creed that I didn't believe. I think that many of the aspects of strict religious teaching I never did believe, so as I became more familiar with science, there weren't really conflicts.

Coming back to my children, they have no religious upbringing, but they are four of the most moral, ethical people. They are good men. They're very honorable in all their dealings, and I'm very proud of their behavior. That's always been, for me and for my husband, what is most important.

AM: Some denominations of Christianity, for instance -- to get back to this interest you had in Christian Science -- are some religions more compatible with scientific doctrine than others, would you say?

JR: Oh, I think they are. I think Unitarians and some others are probably more compatible [with scientific doctrine]. It is ironic in a way that though it's called Christian Science, they carry the notion of mind over matter to such an extreme -- or many of the practitioners do -- that they won't take antibiotics for severe infections and won't get blood transfusions or have an appendectomy, which is *fatal* for a number of them. So I've never espoused that aspect of Christian Science. But the thought that a lot of your own mental attitude has a major influence on how you feel, and how you deal with feeling not-well, *that* I think is very helpful and important.

AM: I also went to an all girls Catholic high school and I can recall, at least in my high school, that the education of physical and biological sciences was not encompassing, by any means. In retrospect, how would you describe the education that you received at your high school?

JR: I went there only two years, so I had general science and I had this class in the biological sciences, which was strictly on phyla, and there were excellent teachers. Both of the nuns were very good at that level. My mother knew about the University of Chicago and the fact that they had developed a program that included the junior and senior years of high school and the first two years of college in what [Robert M.] Hutchins[6] called the four-year college, and they offered scholarships to that, so I took a scholarship exam and passed it and won a scholarship. My last two years of high school were here, at the [University of Chicago] Laboratory School at the university.

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[5] The Apostles Creed is an ancient, succinct statement of the central tenets of the Christian faith, including the virgin birth of Jesus and his resurrection from the dead. For the complete creed in the original language and in translation visit the website at: http://www.creeds.net/ancient/apostles.htm

[6] Robert M. Hutchins (1899-1997) was dedicated to educational reform, and as president of University of Chicago, founded the four year college of the Laboratory School program at University of Chicago in order to implement some of his educational theories.

AM: Before you got to the university, what were some of your other interests outside of the classroom?

JR: My father started me on stamp collecting. I'm going to guess that I was maybe eight or nine years old -- tt's hard to know chicken and egg. I've always thought that my skill in cytogenetics[7] [i.e.] looking at chromosomes and looking at very subtle differences, particularly when banding[8] was developed, [that] probably I was good at it because I had spent years and years looking at stamps with very fine detail, watermarks[9] of paper and a Scott [Standard Postage] Stamp Catalogue and whether there was a period, or whether there wasn't a period, or a little blip here and there. Then there were different stamps in the Scotts catalogue [that I compared]. So I had training through stamp collecting in terms of pattern recognition, and very precise pattern recognition.

I loved stamp collecting. I did that through till twelve years of marriage. Then we went to England for a year, and I just didn't continue on in England. Then when I came back things were different, and I didn't pursue that. That was a major thing.

My family had a small farm in southern Wisconsin. They bought a farm, no livestock on it, but -- this was just before the Second World War in the spring of 1940-41 -- we bought it before the war. We could grow a lot of vegetables, not only for us but for my grandmother, and my aunts; we did canning and things. I had a raspberry patch, which was there on the farm. I took care of it, and then raspberries I could sell to people living in the area and that was how I made my money in the summer.

AM: Were your parents living up in southern Wisconsin as well?

JR: This was weekends, and my mother (being a schoolteacher) had the whole summer off, so we went up there in the summer. My father was in the army after about 1943, so he was away then.

AM: You mentioned you moved around a lot growing up. Was that within the Chicago area, or were you outside of the--?

JR: It was always in the South Side of Chicago. Why we moved, I'm not really sure. Part of it was to find adequate housing with a good school that the family could afford.

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[7] Cytogenetics is the study of the structure of chromosomes. For more information, visit the website at: http://www.pathology.washington.edu/galleries/Cytogallery/main.php of the University of Washington School of Medicine Department of Pathology.

[8] Chromosomal banding is a technique used to distinguish and identify one normal or abnormal chromosome from all other chromosomes. Certain dyes are introduced to the chromosome which stains the length of the chromosome with alternating light and dark bands. For more information visit the website at: http://www.pathology.washington.edu/Galleries/Cytogallery/main.php?file=banding%20patterns

[9] A watermark is the impression of an image made on still-wet paper. Such watermarks help to identify sources and to date different paper products, including stamps. For more information, visit the website at: http://www.hobbizine.com/page0023.html

AM: What did that mean for your after-school friendships?

JR: I was pretty much a loner, because I would no sooner get some friends than we'd move. There was a time when I did have several very close girlfriends in third and fourth and fifth grade, and we'd play together in the afternoons. But for much of the time I didn't have that.

AM: Just describe briefly what it was like to grow up in the South Side of Chicago in the early thirties and forties.

JR: Well, it was very much different racially, because all through the 1930s virtually all the South Side of Chicago was white, and many of the people living on the South Side were like my grandfather, Scottish or Polish or Italian immigrants, or Irish, who worked at the steel mills. So, all the schools that I went to were always white. I didn't have any interracial experience as a child.

Actually, Chicago (in my growing up) was fabulous. It was fabulous because I could get on a bus or the streetcar for three cents, and in 1933 and '34, there was the Century of Progress [Exposition] down where the Field Museum [of Natural History] and the [Adler] Planetarium are, and they had 'Nickel Days'. So for eleven cents, I could go by myself -- I was eight years and nine years old -- and get on the bus and go to the World's Fair and spend the day and have a wonderful time. *Now* parents can't even think of letting children do that.

I'd been to the World's Fair with my parents, so I sort of knew what was available. I went through a black area down what was called South Park Avenue, it's now Martin Luther King Jr. Drive, but I never felt unsafe on the bus. I think that children just really miss so much by [not] being able to get around and do things independently and determine how they want to spend their time. I may have only gone by myself three or four or five times, but I remember the freedom that I had.

AM: Were your children also able to do this, or had Chicago and the South Side changed by the time they were growing up?

JR: They didn't go far away on their own, but they started riding their bicycles to the lab, again not quite a mile, here in Hyde Park. They started riding their bicycles to school when they were in third grade. Before that, they took the school bus. Once they went off on their bicycles, I suppose it's bad of me to say that I didn't have a clue, but they were free to bike to a friend's house, to bike to the lake, to bike to places where they played soccer, played baseball.

AM: But they didn't get to see the World's Fair.

JR: [No, they] didn't get to see the World's Fair.

AM: I was trying to look up a little bit about this Laboratory [school] —- [it was] kind of [an] experimental high school here at the University of Chicago. Could you tell me a little bit about the history? Had it been going on for a while when you were accepted into it, and what meanings were attached [to it]? If you got accepted into this special program, what you were supposed to do and [what were] the expectations for your work?

JR: I probably don't have as precise a knowledge as I ought to. Hutchins' view was that American education was badly organized in terms of the basic structure. [The American system] was based on the German system and that originally, as I recall what he was saying, schools were six years long in Germany -- for grammar school. Then they added two more years to sort of give people a smattering of more history and more math and things of that sort. Then afterwards high school was added on to that. Hutchins thought the German system (as I describe it) was an anachronism. He thought that seventh and eighth grade didn't make any sense, and [that] grammar school should be six years, and high school should be seventh and eighth grade and the first two years of high school. So he did away with 7th and 8th grade. Then students were ready for college. So the last two years of high school and the first two years of college were put together as the four-year college. [The Hutchins system] was developed or strongly influenced by John Dewey[10] who had very liberal ideas about education.

This was separate from the traditional university program here. There were sixty-five people in my class that were [either] juniors in high school or freshmen in the four-year college. Probably about half of them were students who had already been in the Lab School, and for them it was the third year of high school.

About half of us, thirty or so, were here at the university on scholarship. Some of our classes were in a separate building that was really a house, with wallpaper and fireplaces and a kitchen and all the rest of it. Then you had chairs with the armrests on [which] you took notes, et cetera, and outstanding teachers. It was organized chronologically, both history and art, and literature and music, so that history, of course, was ancient history first, so all the literature and the art and the music were all ancient history. They were two separate classes, but the subject matter was correlated.

The sciences were more typically taught in that you could either take two years of physical sciences or you could take two years of biological sciences. I took two years of physical sciences in high school, and then my biological sciences [class] was the standard university class, which I took along with others who were then conventional freshmen, and it was my third year in the program.

It's impossible to say too many good things about that program. You were dealt with as a responsible individual who was interested in learning. They were there to teach you. It was just really a fabulous experience.

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[10] John Dewey (1859-1952) was an American philosopher and psychologist who was very much a part of the Progressive Movement during the 20th C. He was also known for his educational ideas, and greatly promoted educational reform.

AM: Of the students who went there, half of them had been in the program and the other half -- were they selected like you were from across Chicago, or were they selected from even further outside the Chicago area?

JR: They all came from the Chicago area because otherwise it would have meant that they would have come as boarding students. I think Hutchins had assumed that this would be like an eastern boarding school for some students, but I don't know how much influence the [Great] Depression had on it. I don't know that they ever went and really tried to market the program for that, so that it was very small. A number of the students [in the program] had what was a conventional senior high school graduation -- a proper graduation in the Rockefeller Chapel from high school. Particularly the girls, some of them, went on to eastern colleges -- Smith, Vassar. Then when we graduated, it was '42, so some (though very few) of the male classmates went in the army right away.

AM: Was it expected, though, that you would more than likely go on to college, you and your classmates would go on to some sort of college?

JR: Yes. We were already in college – so it was just a continuation. I don't know about the typical U High [University High School] person, but virtually everybody did go to college, so it was just assumed that the whole class would go.

AM: This may be difficult to recall, but [how] was the kind of teaching being done at this high school different from the kind of teaching that was being done where you did your freshman and sophomore years of high school?

JR: The subject matter was more intense and you had to do more homework. I think it was just assumed that you'd read more primary papers. We certainly had textbooks, but [it was assumed] that you also would read primary papers and be thinking about these things and about what they meant. So it was a much more intellectually challenging sort of experience. Thirty of the students were scholarship winners just like you, and the others came from a very affluent, educated background, already at the Lab School.

AM: Were they mostly children of faculty here at the University of Chicago?

JR: More of them at that time, I think, were families living in Hyde Park. There certainly were faculty children, probably much more than 50%. The tuition was not cheap! But the rest of those who'd been in the Lab School were just from families, some of whose parents had already gone to the Lab School[11] and lived here in the area and wanted their children to have the same experience they did.

[11] The four year college at the University of Chicago was a program which integrated high school students into university-level courses at the University of Chicago.

AM: And was this program still in existence when you were sending your children to school?

JR: No. The four-year college stopped, and I ought to know [when] and I don't know. I graduated in '44 and probably two, three, four years later it didn't exist anymore. There were lots of reasons. I'm sure that it was an expensive program to run. After '46 and '47 you had returning veterans, and they weren't coming back into high school, they were coming to the conventional college. And Hutchins' term at the university was winding down. I think there were multiple, complicated reasons why it stopped.

[There was] the notion of survey courses in the conventional college, which focused on a general education for every student. All students take a series of courses and then have comprehensive exams, which were six hours [long], and that was your grade for the whole year -- the comprehensive [exam]. Everybody took several years of humanities, everybody took social science, everybody took science classes, everybody took English unless you passed out of it. This was true regardless of what you were going to do later on. You had to have a broad general education. That was Hutchins' legacy, which is still, with modifications, a basis for education here at the University of Chicago.

II. Undergraduate and Medical school at University of Chicago

AM: So you entered the University of Chicago as an undergraduate at the same age as everybody else -- or did you enter earlier?

JR: No.

AM: Basically, the same age as any other freshman?

JR: That's right. I didn't skip any grades or anything.

AM: How did your experience at this high school help you prepare for your first year of college?

JR: Well, you see, because the history [and] the social studies were three-year integrated courses, when I was a freshman, I was really taking the third year of a sequence that I had already started. I took college biology with everybody else, all the entering freshmen. I took that because I'd taken physical sciences in high school. I had already taken second-year French in the college as a senior in high school because I'd had all the French that high school taught, so I went off to college to do that. It was very easy to take college classes in high school if you could get the timing right. It was no transition at all to go to college. I lived at home, a few new courses, but nothing strange.

AM: Did you ever consider not going to college or going to some other college besides the University of Chicago?

JR: I never thought of *not* going to college. That just was the only way you were going to get an education. My father was away in the army, and I'm an only child, so going away to school and leaving my mother alone was just not an option. Again, I had a full scholarship to the University of Chicago, so my college expenses [were paid]. Tuition was a hundred dollars a quarter, and you went three quarters, so my scholarship was three hundred dollars a year from the university. But with no living expenses and very little in the way of meals and transportation, books was the major expense that we had. Given all of that, there was really no question [where to go to college].

AM: How soon did you have to declare a subject specialty when you entered the university officially?

JR: Well, practically, for myself, [I declared] when I began the last year of the four-year college, [which] is the equivalent of a sophomore year in college. It was clear that I was interested in the biological sciences, so I started taking all the classes to get a bachelor's degree in the biological sciences. Many of my lab partners were mainly males but also declared premed. I thought for a while of being more in physiology because I liked the function of various organ systems. Then as I talked with [premed students], and [about] their focus on human diseases, it seemed like a much more interesting area to go into than physiology. So I changed and became pre-med.

AM: What made the implications of work in physiology different from say premedical health and disease?

JR: You could do, in fact, everything that I liked about physiology in humans (rather than in animals), and I liked the contacts with my fellow man. I thought that I would have the kind of personality that was caring and would enjoy doing that. I have to say that I was a very immature young person. I had lived a very sheltered life at home. I really didn't know a whole lot about many areas. Sex was not something that was discussed at home, and I was pretty ignorant. Though I took some of the classes, I still was a pretty naive young person. I actually had hoped to enter medical school in a class that began in September of 1944, so that would have been just as I was finishing the four-year college. I did some summer work at home to get all of the requirements to enter medical school.

AM: Without a bachelor's?

JR: I got the bachelor's at the end of the four-year college. That was a bachelor of philosophy, a unique degree to the University of Chicago, a Ph.B., which everybody thinks is a typo.

AM: I didn't think it was a typo, but I was wondering what that meant.

JR: That was the degree that you got at the end of the four-year college. As I say, I could really have finished all of my requirements for medical school, such that I could have entered in September of '44. I would have been nineteen. [But] the quota for women was filled. There were three women in the class of sixty-five, so I couldn't get in. The university gave me another year scholarship, and I took a number of classes not related to medicine -- geology and philosophy and things of that sort -- and then entered medical school in June of 1945, so I was just twenty.

AM: And what happened to your interest in Latin?

JR: Well, I didn't have a terribly good Latin teacher at Mercy High School as a freshman.

AM: At a Catholic school you didn't have a good Latin teacher?

JR: It was more rote and not really much more advanced than the one I'd had in seventh and eighth grade at the school in New Jersey. I think also that the interest in science probably made me realize that Latin was not going to be a good thing for a long-term career. My parents were never enthusiastic about it, because what in the world was I going to do for a living getting a degree in Latin or teaching Latin?

AM: So they saw the future of Latin as a high school subject as going to be disappearing. Okay. Just to make it clear in my mind, by the time you're a senior, what we would call a senior in high school, you were already involved with people that were oriented toward premedical studies?

JR: No, that was really after my sophomore year in college, maybe toward the end of the freshman year. The freshman year in college I was taking basic biology, and then the next year, as a sophomore, I was taking all of the biological science classes.

AM: And that's when you became interested [in premed]--?

JR: Yeah.

AM: So within a short period of time you could finish up and apply to medical school?

JR: That's right.

AM: In the four-year college, was there any particular emphasis in the curriculum on life sciences, physical sciences, social sciences, humanities? Or could you describe it as a liberal arts-type curriculum?

JR: I think it was liberal arts, but the focus was probably on the humanities and the social sciences, and one certainly had good training in the sciences. It was more feeling that you were learning to be an educated human being. This isn't to say that educated human beings shouldn't know science, they certainly should, but I think the major emphasis was on the other areas.

AM: What kind of opportunities did you have as an undergraduate to do laboratory research, hands-on kind of work in a lab?

JR: We had that as part of our classes. Not so much in the survey course. We had a lot of very good discussion groups. I don't really recall a hands-on lab in that survey course. But as soon as we got into a three-quarter sequence called "BZP," Botany, Zoology, and Physiology, then there was a great deal of lab work: dissections, microscopy, botany [in which] obviously you don't do a lot of dissection, but you certainly get used to working with a microscope, things of that sort.

In zoology, we were doing all the various anatomic dissections. In fact, I took the zoology part in the previous summer, home study, because that was how I was going to be able to get into medical school in September. Because [back] then, zoology was a prerequisite for comparative anatomy, and having done that, then I could take the comparative anatomy and get that done. [That] summer, at the farm, I got all this stuff in the mail, pickled this and that and the other thing. Then I'd be writing the person who was my professor, you know, “I don't understand this”, and “This is what I see”, and “What's that?” It was a challenge, but I did it. Every week [I] got stuff and sent it back.

AM: Did you have a microscope at home?

JR: Yeah. We could rent a microscope, so that wasn't a problem.

AM: Did you have these chemistry kits that you could buy from Sears?

JR: Well, no. I was never much into chemistry. All of this -- I think the Carolina Biologic Supply House [Carolina Biological Supply Company][12], or something like that, was constantly sending me whatever it was that was part of the course of study.

AM: What sense did you have in college that you could have a career in the biological sciences that [didn’t] specifically end up with a degree in medicine, that you could have a research career as opposed to where most students who were studying biological sciences were headed to medical school?

[12] Carolina Biological Supply Company is an independent supplier of biological and science teaching products. For more information visit, their website at: http://www.carolina.com/category/customer+service/about+us.do

JR: Many of the professors [were botanists]. And certainly my advisor when I started out (because he was my advisor in the biological sciences, and then when I became pre-med he could still be my advisor) was a botanist, Merle Coulter. He was excellent. I wasn't all that interested in plants, but there were other people in the zoology department that were outstanding, and it was pretty clear that if that's what you chose to do [i.e. zoology], or physiology, there were very prominent people. Anton J. Carlson - "Ajax" Carlson[13] - co-wrote the textbook [in physiology] along with Victor Johnson; they were both my professors as a freshman in college (my 3rd year).

AM: So for you, premedical studies really had this more applied, greater-good, doing-something-for-the-betterment-of-[the-world-connotation], as opposed to just doing research. Would that be a correct?

JR: I think you're putting too adult connotations on it. I wasn't thinking in those kinds of terms. The fact that if I went into medicine, I would have contact with patients and I maybe could do something to help patients who are sick -- that was something. It wasn't certainly very well thought out. I come back to [my earlier point about] being very naive. I'd been pushed to believe that I was smart and that I could do something, but what it was was rather open. When I declared pre-med, my parents were delighted and very supportive.

AM: And because that was better understood as a profession than say, becoming a teacher in Latin?

JR: [My parents said], "There's going to be no opportunity [as a Latin instructor], so Janet, how are you going to support yourself?" I think by the time I was a freshman in high school, Latin had disappeared. This was just an outstanding Latin teacher in grammar school that turned me on, and that was what I wanted to do [at that time].

AM: Okay. How aware were you, at the time that you were going to school, of the role the University of Chicago would play in the development of nuclear physics, and the physics program here, and the Manhattan Project, and that this would become one of the major centers of the physical sciences?

JR: That was a very well-kept secret. There were places on campus you couldn't go, but that was just part of wartime. We had *tons* of soldiers and sailors and Air Corps all over campus being trained. We had a big meteorology program for the army. We had Signal Corps[14]. I actually graded papers for the Navy Signal Corps and others [graded as well] -- they took tests all the time -- I can't

[13] Anton J. Carlson, aka "Ajax" Carlson (1875-1956) was a physiologist and one of the most prominent men in his field during his lifetime. He was a professor at the University of Chicago, and appointed chair of the Physiology Department in 1916. Carlson was also the President of the American Physiology Society (APS) from 1925-25 and studied the role of the hunger mechanism in human health, among other things. For more information and a brief biography, visit the APS website at: http://the-aps.org/about/pres/introajc.htm

[14] Signal Corp is a branch of the US military which specializes in communication and information technology.

remember now if my pay was twenty-five or fifty cents an hour. The Thurstons, who were prominent in developing tests, were developing tests for the navy to see how well these people had learned what was required of a Signal Corps man, for example. Their exams had to be graded, and I was one of a bunch of students who just graded papers.

The army was all over, they took over our high school gym – no, the navy did that. The army took over International House [of Chicago][15], and the university trained thousands and thousands of men during the war. The Manhattan Project[16] was something you knew nothing about. It was the "Metallurgy Project", and they were just trying to develop better metals for airplanes or guns or whatever. You didn't, or *I* didn't inquire a whole lot. It all came out as a big surprise afterwards.

AM: What kind of genetics was being taught? How was it being taught as an undergraduate here at the University of Chicago?

JR: I never had a class in genetics, never, ever in my life.

AM: Ever? At least it was a part of maybe zoology or botany?

JR: Well, botany, [Gregor Johann] Mendel[17], and green and colors of peas, and things of that sort. But I was going through and taking some of those classes, after all, in '43 and '44, and that was just when [Oswald T.] Avery[18] discovered genes were made of DNA. Before that, that wasn't known. So genetics --

AM: You didn't have Sinnott and Dunn [E. W. Sinnott and L. C. Dunn, *Principles of Genetics*[19]] or any of those genetics textbooks from the early twenties?

JR: No. There certainly were genetics and Drosophila [genetics][20] people around, but as a premed I didn't take any of those classes, so I never had a

[15] International House of Chicago is a housing complex associated with the University of Chicago built to promote interaction and understanding between its student residents. For more information see the website at: http://ihouse.uchicago.edu/

[16] The Manhattan Project is the code name for the secret American program during WWII which developed atomic energy for use as a weapon, i.e. the atomic bomb. For more information visit the website at: http://www.atomicarchive.com/History/mp/index.shtml

[17] Gregor Johann Mendel was a priest and scientist who was the first person to begin to unravel the principles of genetics through his experimentation and observation of pea plants. For more information, visit the website at: http://www.mnsu.edu/emuseum/information/biography/klmno/mendel_gregor.html

[18] Oswald T. Avery was a molecular biologist who, along with his colleagues Colin Macleod and Maclyn McCarty, discovered that genes and chromosomes are made of DNA. For more information visit the website at: http://profiles.nlm.nih.gov/CC/Views/Exhibit/narrative/dna.html

[19] E. W. Sinnott and L. C. Dunn were the authors of an early textbook on genetics titled Principles of Genetics which focused on plant genetics. For more information on Dunn and his work in genetics, visit the website at: http://www.amphilsoc.org/guides/glass/dunn.htm

[20] Drosophila genetics is the study of genetic traits, etc. accomplished through laboratory breeding and observation of a certain fruit fly called Drosophila. The Drosophila is a genus of fly which is often used in genetics research because of its widespread availability, fecundity, and rapid life cycle. For more information

genetics class. Ironically, top population geneticists such as Sewell Wright were at U of C; I just had no contact [with them].

AM: And that's true for medical school as well?

JR: Yeah. There was medical genetics and teaching medical students [genetics]. I was involved with Bernard [S.] Strauss[21], who was chairman of -- maybe his title wasn't chairman, but the senior person in the basic science department here, who said that we should have a medical genetics course. I think that was '64, '65, something like that. At that point, I'd come back and I had learned cytogenetics, so I gave six lectures to medical students on cytogenetics and meiosis and mitosis before banding. You knew Klinefelter's [Syndrome][22] and Turner's [Syndrome][23] and Down's [Syndrome][24], but you couldn't tell the chromosomes apart.

AM: Just to get back to the chronology a little bit -- you enter medical school in the fall of '45?

JR: June of '45.

AM: Then you get a B.S. degree in '46. How did that work? Is that just because you only had this Ph.B.?

JR: For the university to give you a bachelor of science, you had to have a certain number of credit hours in a particular field, and the freshman year in medical school with histology[25] and the equivalent of four and a half quarters of human anatomy -- that gave you enough credits in anatomy to qualify for a B.S.

AM: And why was it necessary if you were already in medical school to get a bachelor's, to finish a bachelor's degree?

JR: That was just -- everybody did it. Because a lot of people -- well, we had sort of a motley class because June of '45, it was clear the war was ending. The

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on the use of Drosophila in genetics studies, visit the website at: http://biology.arizona.edu/sciconn/lessons2/geiger/intro.htm

[21] Bernard S. Strauss is a professor emeritus at the University of Chicago in the Department of Molecular Genetics and Cell Biology.

[22] Klinefelter's syndrome is a chromosomal disorder which causes males to be born with an extra X chromosome. The most common effect of Klinefelter's is infertility. To learn more, visit the website at: http://www.nlm.nih.gov/medlineplus/klinefelterssyndrome.html

[23] Turner's Syndrome is a chromosomal disorder which causes the partial or complete absence of an X chromosome in females. The most common effect of Turner's is infertility. To learn more, visit the website at: http://www.turnersyndrome.org/

[24] Down's Syndrome is a chromosomal disorder caused by the partial or complete presence of an extra 21st chromosome. The most common effect of Down's is developmental disability. To learn more visit the website at: http://www.medicinenet.com/down_syndrome/article.htm

[25] Histology is the study of the anatomy of tissues and cells at the microscopic level in both plants and animals.

army and the navy, who had preempted most of the spaces in medical school, cut back substantially on the spaces that they required. The medical school then had to fill up their class with 4F's[26] and women. So going from three women in the previous class, there were seven women in my class, and [also] many people who couldn't qualify for the army and navy. So we still had a lot of people in the army wearing uniforms and in the navy wearing uniforms. There were certainly fifteen or so people in the class that were, as I say, women and 4F's.

AM: Again this probably is a silly question, but did you have any thoughts of going anywhere to medical school besides the University of Chicago?

JR: I applied to all the medical schools in the Chicago area because I didn't know that I would necessarily get in, and UOC [University of Chicago] is competitive. So I applied to the University of Illinois and Northwestern [University]. I think I was accepted at all three, but I have to say that when I was accepted to the University [of Chicago] there wasn't any question that that's where I'd go.

AM: At that point, it probably was still considered the top of the Chicago medical schools? Was it, at that point, the same in terms of reputation?

JR: Well, yes. I think much more so -- you're going to get people at Northwestern saying that they've caught up to the University of Chicago. And certainly in some areas they have. I don't know a whole lot about their medical education.

AM: Just -- we're at a good place to stop -- just describe your experience in medical school.

JR: I had a great time in medical school. I didn't do well in terms of becoming AOA [Alpha Omega Alpha], which is the Medical Honor Society, but --

AM: Was that a goal?

JR: No. But I certainly enjoyed [medical school] a great deal. I particularly enjoyed the clinical years with patients and being able to develop good relationships with some of my patients. I invited them to my wedding. The students were all very helpful. Some of them became good friends. The faculty, by and large, were supportive. And I enjoyed it.

AM: When did you start thinking about a medical specialty?

JR: Well, I didn't think about a medical specialty, and nobody ever really sat down and talked to me about that. I'm not going to say I have any regrets, but -- I

[26] 4-F is the term for a draftee determined to be unfit for duty (usually but not exclusively physically) and therefore exempted from military service.

graduated from medical school, [and] I got married the day after. My husband was a year and a half behind me. And nobody ever said, "Well Janet, you should go off and get your internship and then you can start a residency, and he can be catching up to you." I just graduated from medical school and stopped and took a laboratory job for a year and a half until he caught up to me. I never had a medical specialty, I never had a residency.

AM: Although, at that time that still was typical, to do an internship and then do a residency. Or no?

JR: Well, it would be typical. Not quite to the extent probably that it is today, but most certainly a large portion of my class was going on for residency. I never even gave [going on to a residency] a thought.

AM: I know in the last several months of medical school -- you had said this in your other interview -- that you were really focused on finishing medical school so your parents [would] know you had finished, and preparing for your wedding. But what did you think then you would do with this medical degree?

JR: It wasn't very clear, because being married and having a family was important. If I had chosen, I probably would have gone into pediatrics, and I didn't think, well -- nobody ever sort of said, "Well Janet, you should be thinking about this, and what *are* you going to do, and what do you think about yourself once you get the M.D.?" Nobody asked and I didn't think about it on my own. I was more focused on my husband, or my husband-to-be. It was very clear he was going to go into medical research. The Department of Pathology here was outstanding in experimental pathology, and that's what *he* was going to do, and that was fine. I didn't think very much about what *I* was going to do.

III. Marriage, starting a family, and early clinic work

AM: There is a history about the forties and fifties in the United States -- particularly with opportunities for women -- that World War II opened up a lot of work opportunities and career opportunities for women that didn't exist [previously]. Then with demobilization after World War II, the expectations put on many women were that they would have to go back to their homes (to put it poorly) and open those jobs back up to returning soldiers. What were the thoughts running in your mind in terms of expected roles, and could you be married and have a family and pursue a career full time, or was that something that you knew you were going to have to put on hold once you got married until you had your family raised? What options were you thinking that you had?

JR: I didn't think about it very much, except that I never considered a full-time career. That just wasn't the way I was going to operate.

AM: And you're 'not full-time career' would be something in medicine?

JR: Yeah, that's what I assumed. We finished interning toward the end of June of 1951, because my husband graduated in 1950, so we took a rotating internship here in 1950. We lucked into an internship in the U.S. Public Health Service, which meant that we got a ton of money and it was just wonderful. Then there was the Korean War, and he wanted to go into research. We were both in the Public Health Service, and the Public Health Service allowed him to do his service at NIH [National Institutes of Health] in research. So, we moved to Bethesda, Maryland and we were there from '51 to '54. He was doing research.

I got pregnant right away. Then after the baby was born, I did take – [no], before the baby was born -- I took the exam. I'd taken the Illinois medical licensing exam before I finished interning in 1951, and then in Maryland I could take the Maryland board exams mainly on the basis of reciprocity in 1951 or early 1952. I don't think I took actual exams. I think I went and talked to people and showed them my credentials, and they issued me a license to practice in Maryland based on the Illinois license.

Then I explored the possibility of working in well-baby clinics in Montgomery County [Maryland]. I could work in as many well-baby and prenatal clinics as I wanted to.

AM: So at this point, when you were thinking you'd always have at least a part-time career in medicine, was it always conceived of as clinical?

JR: Yes. Oh, absolutely. Research was what Donald [A. Rowley] was doing. I wasn't doing that.

AM: Okay, great. I think we're at a good point to stop.

JR: Okay.

AM: Thank you.

End Session I

AM: It is June 7th, 2005, and I'm Andrea Maestrejuan with Janet Rowley at her home in Chicago, very near the University of Chicago, and we have a spectacular view of her beautiful garden. I think yesterday we left off basically with you finishing medical school and getting married, and that your career decisions at that point were not well formulated and you were waiting for your husband to finish medical school. Why don't we talk a little bit about your husband, how you met, where he was in medical school, and what his career decisions were and how they related to yours?

JR: Okay. We were both medical students, though actually at the time we met he had been in medical school and then got kicked out, had gone to the Philippines during the Second World War, come back, and then [had] come back

to the Department of Pathology at the University of Chicago working first as a technician with Paul Connor, chairman of the department, and then enrolling as a graduate student. So he was doing research projects in collaboration with Professor Earl [P.] Benditt[27] at the time that we met.

He shared a laboratory research space with a person who was one of my partners in medical school. Groups of three would go around on different services, three students, and the person who was one of my partners was actually on the faculty in the Department of Pathology. He had an office, something none of the rest of us had, so I could use his office at night writing up case histories and doing reading, and Donald used that office for part of his research projects, doing experiments. So he'd be in and out of the office and so I knew him. Then one evening I went to the ice skating rink and was--

AM: --Can we just pause for a second?

[PAUSE]

AM: Okay.

JR: I like to ice skate, and I had some free time one evening because I was in the senior year in med school, so I went over to the ice skating rink and was skating around. Donald was there because he was born and grew up in Minnesota and was an expert hockey player. He saw me tentatively skating on the ice, so he came over to help me skate around better. Then we continued and went out for coffee. That was the beginning of a wonderful friendship and then engagement and marriage at the end of December of 1948.

AM: So was he a medical student at that time, or was he finishing his master's? I think he has a master's.

JR: Well, He got his masters after we were married in March (I think) of 1950. Then he actually then went back into medical school. He got readmitted into medical school after we were married and finished up, because he had about a year and a half still to go. It was clear that he was really fascinated by the areas of experimental pathology, how tissues react when you introduce certain chemicals and drugs, particularly interested in mast cells and in histamine and serotonin and all of the reactions of cells and blood vessels to those substances.

He was going to be in academic medicine. That was clear. As already indicated, and you can ask why, I didn't give a whole lot of thought to what I was going to do after medical school. It's inexplicable to me why I didn't think about it, why my mother and none of the people in the medical school said, “Well Janet, now that you're getting your degree, this is the normal process of going on for

[27] Earl Benditt (1916-1996) was a distinguished experimental pathologist. During his life he received numerous awards in recognition of his scientific achievements, and held a professorship at the University of Chicago. For more information about his life, visit the website at: http://www.nap.edu/readingroom.php?book=biomems&page=ebenditt.html

internship and residency." That never happened. So it was getting the M.D. and that was just sort of the end.

AM: You had mentioned that you were one of six or seven females in your medical school class.

JR: Right.

AM: What were they doing as they were finishing up medical, or did you keep in touch with them?

JR: Well, I don't remember having lots of discussions with them as to what they were going to do. Nor did I have a lot of discussions with male colleagues, either, about who was going to go on and do what. There probably were people who were talking about that, and somehow that didn't include people with whom I mainly associated.

AM: So you don't know if you had a similar situation in which you got the M.D. degree and then you were getting married and were making career decisions along with family decisions? You don't know if your path was different or the same as other female medical students?

JR: Well, I don't. Now, Nancy [E.] Warner[28] was a classmate of mine, and she became chairman of pathology at USC [University of Southern California], so she went into pathology and things. I certainly knew Nancy, but we didn't talk about her career goals. If I talked about it with people, I just have totally forgotten that.

AM: And how much of your career plans and your husband's career plans did you both discuss together? Was there any kind of discussion of, "Okay, this is what I'll do and then this is what you'll do"? Or was it that well thought out?

JR: I don't think it was that well thought out, except for the fact that I did make a decision very early on, but I don't remember giving more than ten seconds of thought to the decision, that I would wait until he graduated and then we would intern together. In retrospect, you can say, well, why didn't somebody say rather than spending eighteen months as the equivalent of a research technician in the laboratory, sort of marking time, why not take that time and be going on your own training? That never occurred to me. It was clear before he graduated that he would not practice, but would go into research.

AM: So for one year you were a research assistant, or technician, at the University of Chicago?

JR: Yes, [a] research assistant.

[28] Nancy E. Warner, Professor Emeritus, Chairman of Pathology Department at University of Southern California Keck School of Medicine.

AM: What did you do in this particular lab?

JR: There was a laboratory on campus called the toxicology laboratory that was funded by the Atomic Energy Commission. It was trying to look at various aspects of radiation and various components of the atomic bomb and problems [with it]. The person with whom I worked, Julius [M.] Coon[29] -- he wasn't the director but he was one of the senior people who was a pharmacologist -- was interested in the effects of beryllium. He was particularly interested in the effects on blood pressure. I worked on what really is a very artificial system of giving rats or rabbits beryllium intravenously and then watching a major fall in blood pressure at the time. I did that for a year and a half. Now, we certainly modified some things over the course of time, but I don't remember doing many other things than the beryllium experiments.

It's interesting, at that time it wasn't recognized how very dangerous beryllium was, because with other people in the laboratory, we would put beryllium in water, [that is] the [beryllium] powder, into water and it foamed up and we'd just stand around and watch it foam and store it and then go and use it. I have to say there was a period of time when it became clear how serious berylliosis was in terms of the toxins to the lung and causing pulmonary fibrosis. I really expected to be dead in five or so years from this unwitting exposure to beryllium. Fortunately, that didn't happen.

AM: One common theme that emerges from many of the interviews is the affiliation with the Atomic Energy Commission or with the Biological Effects of Atomic Radiation, a lot of government support or reliance on geneticists. What do you think the impact was on the field of genetics, with all the attention on the effects of atomic radiation, to give geneticists a kind of a spotlight that before this they really didn't have? Or even funding that they wouldn't have otherwise had before this period of NIH funding?

JR: At the U of C it took a special pathway, and that [was] in part because of the interest of Leon [O.] Jacobson[30], who turned out to be very important for me and my future career. As a hematologist, there was great concern about one of the immediate effects of radiation, which was destroying the hematopoietic cells in individuals [when] exposed to radiation. After all, Marie Curie died of hematopoietic blood cell failure and (I think) leukemia, almost certainly due to radiation. [Exposed individuals] got anemia and low platelets counts and also low

[29] Julius M. Coon was a pharmacologist at the University of Chicago, a charter member of the Society of Toxicology, and later the Head and Professor of Department of Pharmacology at Jefferson Medical College in Philadephia, Pennsylvania.

[30] Leon O. Jacobson (1911-1992) was an eminent hematologist who spent his career at the University of Chicago, where he became Chairman of the Department of Medicine in 1961. His special field of research was red blood cell production and he helped pioneer chemotherapy. He was nationally recognized for his work and won many awards for his achievements. For a review written by Janet Rowley on Goldwasser's biography of Jacobson, visit the website at:
http://muse.jhu.edu/journals/perspectives_in_biology_and_medicine/v050/50.4rowley.html

white counts. He was looking at the effects of radiation on bone marrow in experimental animals.

I didn't have anything to do with that, but that actually was while I was at the tox[icology] lab and afterwards, because the AEC [Atomic Energy Commission]also funded a lab at the University of Chicago in an old horse stable on 62nd [Street] and Ingleside [Avenue] or Drexel [Avenue], something of that sort, just south of the Midway. Austin [M.] Brues[31] was the director of that. This was the beginning or the forerunner of the Argonne National Lab[oratory].

That doesn't answer your question, but the question about the impact of the AEC and this kind of funding on genetics wasn't really apparent here at the University of Chicago. I realize it would be [for] Liane [B.] Russell[32] at Oak Ridge [National Laboratory]. It was certainly a major focus there.

AM: So you were finishing this year and a half of doing this research, then your husband finished his medical [degree]. At that point did you then discuss -- you were going to do your internships together -- but where and what, and what kind of planning at that point were you thinking about?

JR: The major thing was to get an internship where the two of us could be together. Back in 1949 when we were applying, and in '50 when we actually began, that was not a time when most hospitals or medical centers were interested in married interns, so our choices were in fact very limited. One of the things that happened was that we had applied to the Public Health Service, because actually someone who graduated with me and who went on and interned in July of '49 when I *might* have interned, he interned at the Public Health hospital on the North Side of Chicago. So we applied for a Public Health internship.

The way the system works is, there's a particular day in mid-March when you're informed as to whether you have been accepted by various hospitals or not. We had heard from several hospitals that the two of us *were* accepted, but we hadn't heard from the Public Health Service. Finally, the afternoon of that day, or maybe the next day, I called the Public Health Service and said that we hadn't heard. The man seemed quite surprised. He said – and I'm going to be vague on this -- but the implication was, 'Wait a day or so'. It turned out that they did not fill the internship on the North Side of Chicago, and they accepted Donald and me as interns.

That was great, first, because we didn't have to move. We could stay in the small apartment that we had. Secondly, he got pay as a second lieutenant -- in the Public Health Service they use the navy system, [and] he was a lieutenant

[31] Austin M. Brues (1906-1991) was a graduate of Harvard Medical School, became a professor at University of Chicago in 1945, and was a pioneer in radiation biology. He was president of the American Association for Cancer Research and director of the Argonne National Laboratory among other prestigious awards and positions. For more about him, visit the website at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2376513/

[32] Liane B. Russell is a mouse geneticist, head of Mammalian Genetics at Oak Ridge National Laboratory from 1975-1995. She earned her PhD. at the University of Chicago and has received numerous awards and is credited with the hypothesis (later confirmed) of the inactive X chromosome. An interview with Dr. Russell is available in this collection.

in the navy. He got paid; he got subsistence for himself and me. Then I got paid and I got subsistence for myself. So we were as rich as could be. I don't remember what we got totally. He may have gotten eight thousand and I may have gotten six thousand dollars, which for interns, when you got fifty dollars a month and were lucky, we just felt as though we were rich beyond compare.

AM: And your internship lasted a year?

JR: Yes. It was a rotating internship. The Marine Hospital in Chicago took care of the Coast Guard, also took care of Great Lakes fishermen and then other people who were government employees, could, under certain circumstances with injuries related to government work, were also patients there at the hospital. They had no obstetrics and no pediatrics, so we went to Children's Memorial Hospital for a month for a pediatric rotation, and then the [Chicago] Maternity Center, which is on Maxwell Street in the South Side of Chicago. That was all home delivery, so we went all over the South Side of Chicago delivering babies, mainly [of] poor black women who could call and say they were about to have a baby and they needed a doctor there, and we would go.

It's kind of surprising again, to my knowledge, nobody ever got hurt going out from the Maternity Center. We were always told that our black bags somehow protected us. We went into some terrible, terrible homes and saw the poverty of those people and [we were] trying to help with the deliveries.

AM: And the Public Health Service, besides the Coast Guard and the fishermen, served the poor of Chicago?

JR: No. It was just because we were then at the [Chicago] Maternity Center [which was] run by obstetricians who were involved. That was their clientele.

AM: Did the internship do what it was supposed to and focus you into some kind of clinical specialty? Were you thinking about a clinical specialty at that point?

JR: I wasn't. It became clear that I was probably not going to be a good physician in major emergency situations.

AM: Why was that?

JR: I just felt too insecure in my ability to really take care of really sick people. Somebody would come in with a heart attack and you have to figure out exactly what to do. You're the only person available to take care of that individual. I found those situations really very stressful. I didn't feel, “Well, this is very exciting and I'm going to go on and learn how to do this and do this better.” That certainly was not my reaction to an internship. Now, you can say maybe [it was] because of the Marine Hospital, there were only I think six or eight of us as interns, and I don't recall whether they had residents or not. There certainly were people

between us and the senior attending, but it was pretty thin, so I probably didn't have as much hand holding as would have been good for somebody in my state of ignorance, if you will. I just didn't find it very attractive.

Donald [Rowley] was going to go to NIH [National Institutes of Health] because he wanted to continue working in research and he didn't expect to be a practicing physician. He might have been a practicing pathologist, but that was unlikely. He was going to go to NIH, which is a Public Health Service facility as well. Many of the people there were in the Commissioned Corps. I did want to have a family, so I just figured that there ought to be some way that I could use my medical training, but I didn't feel as though I needed additional medical training.

AM: Your husband's decision to go to NIH, was that to get more bench training? Was it as a staffer? Or was it more like what we'd call a postdoc position? What were his plans and motivations to go into the NIH?

JR: Well, looked at [it] in one practical fashion, there was the Korean War. He certainly wanted to get more training and to have more exposure to research, but it was also -- the Korean War was an impetus-- to see if there were openings at NIH, then he would go. And he ended up going to a unit in what was then [National Institute of] Allergy and Infectious Diseases working on a particular fungal infection with a very eminent mycologist, Chester [W.] Emmons[33]. So we went there right after our internship. He went and I went along. This is really the story of my life. I just sort of go along and then see what happens.

AM: Let's talk a little bit about when you started having children. When did you have your first child?

JR: The baby was born nine months after we finished interning.

AM: So you were in Maryland, at the NIH, at this point.

JR: Yes.

AM: I know you have four kids, so why don't you put them in a chronology with where you were.

JR: We had the first son, Donald, in '52, and two years later we had a second child, David, also [born] in Maryland. Donald had decided that he didn't want to stay on in the Public Health Service at NIH, and he wanted to go back into academic pathology, academic medicine. When David was born in March, we

[33] Chester W. Emmons (1900-1985) was a medical mycologist and made significant discoveries about fungal pathogens. In 1939 he became the first medical mycologist hired by the NIH, and worked there for the next 30 years. He was given the Distinguished Mycologist Award by the MSA, in 1982. For more information about him see Medical mycology in the United States: a historical analysis (1894-1996), by Ana Espinel-Ingroff

had made the decision to come back to the University of Chicago. Then the other two sons were born in Chicago.

AM: Did you have any children in your first trip to Oxford [University]?

JR: Oh, yes. We had three.

AM: And then your second trip you had four?

JR: [Yes], four.

AM: Okay. Just to talk about them a little bit. I imagine their childhoods were kind of filled with science, between Mom reading her karyotypes[34] at the kitchen table -- that's a story that I read -- and their dad also involved in academic medicine. Were your kids infused with science and medicine from their very beginning?

JR: I think the answer is no. In fact, I know the answer is no. Because Donald and I bent over backwards not to influence our sons to feel as though they had to do what we were doing. Our conversations around the table, particularly as the children got older, were very much child-centered. We'd talk about what happened during the day or schoolmates or things of that sort. We didn't either one of us talk very much about what our own research was. He and I would talk, but not necessarily when the children were around. Certainly they heard it. But there was a certain feeling on parenting back then that you should be non-directive, and we were that in the extreme.

AM: And it seems like *your* parents were very vigilant about your education in elementary and high school. Were you as vigilant with your children's education, where they went [to school], the kind of instruction they had, the opportunities, any special programs, and did they also go to the University of Chicago?

JR: They all went to the Lab School, and it was good for two of them and not good for two of them. We certainly tried to see that they had a rich life. We lived in a house, 5401 Greenwood, about two hundred yards from here where we live now when they were all children and then moved into this present house in 1965 when the youngest was two. We were surrounded by other children, children of university faculty, all of whom went to the Lab School. That was the neighborhood school here. So the school took care of the educational things. We certainly went to parent-teacher [meetings] and things of that sort. We felt that the school took care of those needs.

I took them to museums a great deal. The boys all learned how to play hockey very early. We're sailors. They all started going sailing early on. We bought property and built a cottage at the dunes on the shore of Lake Michigan.

[34] A karyotype is an image displaying the characteristics of a set of chromosomes, detailing their shape, size, type, etc.

We spent all of our summers there, so they were swimming and sailing. So, that was it.

AM: Did any of them become physicians?

JR: The second child became a geologist, and he actually now is chairman of [the Department of] Geophysical Sciences here at the University of Chicago and that's a great pleasure to us. He's an outstanding geophysicist- geologist really- interested in plate tectonics and many things, just super.

AM: It sounds like Davison-Rowley is really entrenched here at the University of Chicago! And your other sons, what did they do?

JR: Our oldest son died, unfortunately, when he was about thirty in a windsurfing accident while at our cottage. He went out windsurfing on a very, very stormy day, and he died. The third child is an avid skier and surfer. Surprisingly enough, one can surf on Lake Michigan. I bought surfboards in San Diego at one hematology meeting in December of 1975 thinking they would be good Christmas presents, and the kids have been surfing -- particularly Robert [Rowley] -- ever since. He lives on a property that my parents bought on retirement in Virginia, and he takes care of that. It's an old house and needs a lot of attention. The youngest son is interested in photography. He got a master's in fine arts and is curator of the Pritchard Art Gallery for the University of Idaho in Moscow, Idaho.

AM: So their interests went all over the place.

JR: That's right.

AM: Then to get back to what you were doing and the decisions about your career if you were having children. I know you go and work at an infant and prenatal clinic in Maryland. I mean, it seems like you had the opportunity to just stay home with your children. Why did you decide to take, I assume, part-time work at the clinic?

JR: Well, I did enjoy medicine though I didn't enjoy the stressful parts. It was very easy for me to work in the Montgomery County prenatal and child care clinics. They met at defined times. I had many stay-at-home mothers in the community that we lived in near NIH, so babysitting was readily available. They had children the same ages as mine, really very young children. So two afternoons a week I would go off to clinics. I enjoyed getting out of the house and being with the patients and felt that by being somebody who was interested in their children and their problems could contribute something.

AM: And that ended when you both decided to move back to the University of Chicago?

JR: That's right.

AM: To an academic position, and leave the NIH. And why did your husband not -- what was it about working at the NIH that he wasn't satisfied [with]?

JR: I think he realized that he could stay at NIH and do what he was doing for the rest of his life, and that was a scary proposition. Here's his life all set out for him, and he felt that he was being supported by the government, and that wasn't right, either. We looked at several positions, including one at UCLA. We went out there one December, and I should say it was the first time I'd seen flocked Christmas trees. This was 1953 in December, and I was pretty horrified. But we had a lovely time. Brentwood is obviously a beautiful area. It was pretty clear that wasn't where we were going to live. [The position] was in the Department of Microbiology, and he actually initially accepted the position. But the more we talked about it, the more we decided we were probably too Midwestern for UCLA.

Professors that Don had worked with, including Earl Benditt, were still here at the University of Chicago, so he called them up and they said, “Sure, come back and we'll give you a position as an instructor or an assistant professor”, or some such. And he came back. I didn't want to come to Chicago.

AM: Oh really?

JR: I had grown up here. It was a dirty city. When I was a child, coal furnaces [were] fired with southern Illinois coal, which is amongst the most pollutant coal around, and [in] winter the snow turned black within twenty-four hours, and I did not want to come back to Chicago. But that was his decision and I followed along.

IV. Direction: Early training and research in cytogenetics at the University of Chicago and at Oxford

AM: And what did you think you'd be doing then here [in Chicago]? What were the opportunities for you to either not work in a similar situation like you were doing in Maryland, or to do something else, or even not do anything related to medicine at all?

JR: It never occurred to me not to do something related to medicine, and sort of following my previous pathway, the path of least resistance, was to do what I had done in Maryland. It did work out well being part time. I think I felt so strongly about not working full time because my mother as a schoolteacher worked full time. There were times as a child when I really wanted her to come to something at school or be more available for me -- maybe because I *was* an only child -- and she couldn't be. I don't remember having real conversations with my mother about what I thought was this lack, but it certainly influenced me in how I wanted to be with [my] children.

Again, coming back here, the city has clinics, the Child Care Society had clinics, so I began working. I didn't work in any prenatal clinics here in the city. They were all well-baby clinics, giving immunizations and checking on children and things of that sort. I worked three afternoons a week.

That actually caused a lot of problems in the city which I'd never had in Maryland, because rather than asking my neighbors to babysit, I had [hired] women -- because of the available pool, always black women -- but I only wanted them to work a half a day, because I only needed them a half a day. For a woman, that meant that instead of getting a full day's pay, she only got a half day pay. So time after time, it would be time for me to leave to go to the clinic, and the housekeeper wouldn't show up. I think within a four or five month period, I went through three or four different babysitters, if you will, and that was very stressful. Finally, there was someone who was working for a neighbor who was leaving [and] going to the University of Washington, and that person came to work [for us]. She stayed [and] worked all day, and she was with us for fifteen or so years. So my child care situation changed dramatically and that stabilized things.

At the same time, one of the physicians who was also working in the clinic -- usually they were residents who would come over so there were several physicians in every baby clinic -- one of the residents said there was a clinic at Cook County Hospital that was looking for a physician to work a couple of days a week doing physicals, and it was a clinic devoted to mentally retarded children run by Abraham Levinson in memory of his son, [Dr.] Julian [D.] Levinson [Dr. Julian D. Levinson Research Foundation]. So I went for an interview to Dr. Levinson. I knew almost nothing about mental retardation. We had it in medical school, but it was a very minor component of pediatric neurology. But he was willing to give me the position, so I went there. Then I started working full days two days a week, and that was fine.

AM: How unusual was it to find part-time positions for physicians during this period, where you could just be at the clinic two days a week?

JR: I don't know. I never talked to other physicians. But I had almost no contact with other physicians. I did in the well-baby clinics, but then all the other people, as I say, were generally residents at Cook County, University of Illinois, Rush [University Medical Center], mid-town, downtown hospitals. We didn't have much chance to socialize because we were there to see the patients.

AM: Working at the Dr. Levinson Foundation, was this when you got your appointment in clinical neurology at the University of Illinois?

JR: No, it was separate. I was probably at the Levinson Foundation for at least a year. Many of our children were going over to the University of Illinois for electroencephalography [EEG][35] because many of them had seizures. That was

[35] An EEG, or an electroencephalogram, is a test which measures the electrical activity in a human brain. It is primarily used to determine if and what kind of seizures someone is experiencing.

just about two blocks away from the Levinson Foundation clinic. I was interested in how you did EEGs and [I was] trying to learn more about what they meant clinically and some of the basis for them. If I had free time during the day at the Levinson Foundation, I'd go over to the EEG clinic and just get to meet people. There was Dr. Frederic [A.] Gibbs, who was the director of the whole program, and his wife, Erna [L.] Gibbs[36], who did [the] reading [of] all the EEGs, and Dr. Fred Stamp. They were very nice and interested that I was interested.

Dr. Stamp approached me with the fact that they also had a clinic at the University of Illinois for epilepsy and they needed physicians to do the history and the physical, which he was doing. He approached me about would I be willing to come work there? So I worked there three days a week in the late fifties. But my two boys were both in day school by then, or in kindergarten and first grade, so I took on the extra day. In that position, I became clinical instructor of neurology at the University of Illinois.

AM: What was driving your interest in learning more about EEGs? Was it the fact that you had no specific clinical training and what you were being presented with clinically? Or was there kind of a more intellectual interest in the phenomenology of brainwaves?

JR: It was actually a realization that I could do more than just go to the clinic and do physicals, and [I was] trying to search for a way to have more intellectual challenge. I actually did think about taking a residency in neurology. I went and spoke to a former professor of mine at the university about the possibility of being a neurology resident -- because it was clear that we had all of these different children coming to the clinic that I didn't know anything about, and being as ignorant as I was was unsatisfactory, at least from my standpoint.

So he said he'd be quite happy to have me come as a neurology resident. I think the salary was eight thousand dollars a year, and I'd be on call three nights a week and one weekend out of every two or three, or something like that. I just looked at him in amazement, because a full-time housekeeper was going to be [costing] far more than that. And could you stretch out the residency so you did a part-time residency but for a longer period of time? [No] that was just out of the question.

Then there was a person at the university in the neurology department, Ward [C.] Halstead[37], who was very interested in both trying to test but also [trying] to understand the function of different areas of the brain and cognition and different aspects of not only cognition but other motor functions and things of that sort. So I went to Ward Halstead. Well, [he said] he would be happy to have me come in some kind of a program that they would develop to teach me more

[36] Frederic A. Gibbs (1903-1992) and Erna L. Gibbs (?-1987), a husband-and-wife team of neurologists, pioneered of the use of EEG's with epilepsy patients. They married in 1930 and they jointly published papers for the rest of their careers. Frederic was made professor at the epilepsy clinic at the University of Illinois School of Medicine in 1944.

[37] Ward C. Halstead (1908-1969), along with colleague Ralph Reitan,developed the Halstead-Reitan neuropsychological test battery which is used to evaluate the brain and nervous system functioning in children and adults.

about these areas of the brain and what we knew about cognition at the time. It wasn't clear that he was going to have any money to do this.

I spent a lot of time with records of all the children that I'd seen, trying to see if I could make something out of what the prenatal history was, or the genetics in the family, with what kind of disorder the child had. I spent hours and hours at home at night working on those records. I have no idea where they are. I assume they're tossed out somewhere.

None of that was leading anywhere. Then Donald decided to apply to go and work with [Sir] Howard Florey[38], who was then in Australia. So we were going to go to Australia, I think, maybe in 1960, or something of that sort. Well, then Florey moved to Oxford. Ultimately, in 1961 Donald got a year's sabbatical to go to Oxford and work with Florey. In the meantime, [Jerome] Lejeune[39] had discovered that Down Syndrome was trisomy 21[40] and the largest group of patients in the clinic [that I worked in] with a definable phenotype were Down Syndrome. I thought, "Well, that's great! I can go to Oxford and learn how to do chromosomes, and then I can come back to the clinic and do karyotypes on all the patients. Isn't that great? Now I finally have something that I can do, or learn to do."

I applied for an NIH Fellowship to get training in cytogenetics, and I got the Fellowship and I got the Fellowship to work in England. Fortunately, Oxford was one of the few places where people were doing cytogenetics. I applied to work with Charles [E.] Ford[41], who was at [Medical Research Council] at Harwell. He was just moving laboratories, so he wrote back and said he wasn't able to take me as a trainee.

Then, [I was] looking at the literature, [and] there was another paper that Charles Ford was on, but one of the other authors was Laszlo [G.] Lajtha[42]. He was a hematologist in Oxford. Dr. [Leon O.] Jacobson, who was an important person in medical school for me, knew Dr. Lajtha, so he could write to him, and Dr. Lajtha accepted me as a Fellow in his laboratory. Now, he didn't know chromosomes himself, but he had actually provided the bone marrow cells to

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[38] Sir Howard Florey (1898-1968) an Australian pathologist and winner of the Nobel Prize in Physiology or Medicine. He, along with his colleagues Ernst Boris Chain and Sir Alexander Fleming, developed penicillin. For more information, visit the Nobel Prize website at: http://nobelprize.org/nobel_prizes/medicine/laureates/1945/florey-bio.html

[39] Jerome Lejeune (1926-1994) was a cytogeneticist specializing in chromosomal abnormalities of genetic diseases. He identified the first chromosomal abnormality in humans, trisomy 21, which causes Down Syndrome, a genetic disease characterized by a range of cognitive and physical deficits. For more about Lejeune's work, see: Knudson AG Jr. (1970) Jérôme Lejeune: The William Allan Memorial Award presented at the annual meeting of the American Society of Human Genetics, San Francisco, California, October 3, 1969. American Journal of Human Genetics 22(2):119-20

[40] Trisomy 21 is the term used for the triplication of the extra 21st chromosome found in those with Down's Syndrome. For more information see note 22.

[41] Charles E. Ford was a cytogeneticist who worked at the British Atomic Energy Research Establishment at Harwell and, along with his colleague John Hammerton, confirmed Tijo and Levan's discovery of 46 human chromosomes.

[42] Laszlo G. Lajtha (1920-1995) hematologist and professor at Oxford University. He was appointed the first full-time director of the Paterson Institute for Cancer Research in 1962.

Charles Ford and Pat [Patricia A.] Jacobs[43], who actually did the work for the paper for Lajtha. He provided bone marrow cells that they used to study chromosomes. So I went to Laszlo's lab in July of 1961.

AM: Okay. Well, to take it back a bit. When you were working in the clinic where you had a bunch of mentally retarded children [at Cook County Hospital which was separate from] the University of Illinois where you had your clinical neurology appointment, how many people were involved in looking at the hereditary components of the genetic diseases that might be contributing to these clinical observations, or these clinical children?

JR: No one. At the clinic for retarded children, it was Dr. Levinson while he was alive, and then when he died, the director was another neurologist, Sherman Kaplan. He was trained in neurology but not in genetics. There was myself, and then there was a psychologist who did all of the clinical testing of the children, and there was a speech therapist who also was head of a school for retarded children in Skokie. That was the clinic staff there. At the U of I [University of Illinois], it was Dr. Stamp and Dr. and Mrs. Gibson and myself were the only people I ever interacted with.

AM: Was this neurology just general neurology or pediatric neurology?

JR: No, this was all epilepsy. This was the epilepsy clinic at the University of Illinois, and I did the clinical exams.

AM: Where was the idea coming from to look at these children, in you? What was driving this idea that maybe we could look at this genetically, or use some of these new techniques to look at this problem in a different way?

JR: Well, it was the discovery that Down's Syndrome was a specific chromosome abnormality (and these were all patients at the Levinson Foundation). That, really, at least from my point of view, was a totally new idea. My husband was going to Oxford. I was going to Oxford. What was I going to do at Oxford? Voilá! Luck again! Just by chance a year before somebody found this, and I could write what clearly was a plausible application to go and learn cytogenetics.

AM: With the expectation that you would return? [That] you would both return to Chicago, you would go back to your practice or your position?

JR: That's right. My expectation was that I would go back and be at the University of Illinois and Cook County Hospital, and I would karyotype all of the

[43] Patricia A. Jacobs is a distinguished British geneticist and the first scientist to identify and describe the chromosomal abnormality known as Klinefelters' syndrome in 1959. She a professor of Human Genetics at the University of Southampton and a Fellow of the Royal Society.

children -- not all, but starting out with Down Syndrome and probably some others.

AM: I know in the interview you did with the GSA [Genetics Society of America] you described your scientific work that kind of was launched in this period of your first trip to Oxford. I'm not going to ask any specific questions, but describe your experience there in a way that -- I guess the question I have then is how was the environment in human genetics different in Oxford and England than, say, what was going on in Chicago at the time, particularly in the new genetic technologies of looking at chromosomes?

JR: This was never a focus of mine. Laszlo Lajtha and the lab I worked in was interested in the timing of DNA replication and the pattern of DNA replication in cells, hematopoietic cells in the bone marrow, and they used tritiated thymidine[44]. They added it to bone marrow cultures and watched cells grow.

I specifically wanted to look at chromosomes and learn cytogenetics, so Laszlo Lajtha said, "Why don't we look at the pattern of DNA replication of individual chromosomes?" In 1960, of course, you couldn't tell chromosomes one from another except by gross morphology of the chromosomes. And also at the same time, Peter Nowell[45] had discovered phytohemaglutinin[46] and stimulated lymphocytes[47] to grow and divide, so you could take peripheral blood from anybody, often myself, and grow them for seventy-two hours and the last two, three, four hours you could add tritiated thymidine and harvest the cells. Then doing autoradiography[48], you could look at the pattern, what chromosomes were labeled, what regions, and things of that sort. That was my research project in Laszlo's lab. It became clear fairly early on that one of the chromosomes that could potentially be an X chromosome was late labeling in females. I don't know that I looked at male cells. I must have, but I don't recall that.

At the same time, about three or four miles down the road was the MRC Unit for Population Genetics with Alan [C.] Stevenson[49]. One of the members of that unit was Marco Fraccaro[50], who was originally from Pavia, then went to

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[44] Tritiated thymidine (HTdR) is the result of tritium, a radioactive isotope from hydrogen, being attached to the chemical compound thymidine. Thymidine is one of the building blocks of DNA and attaching the isotope to it makes DNA synthesis visible. For more information, visit the website at: http://www.bnl.gov/bnlweb/history/bio_history.asp

[45] Peter Nowell, and his colleague David Hungerford were the first to identify the Philadelphia chromosome, aka the Philadelphia translocation in chronic myelogenous leukemia [CML] in 1960. For more information see note 86. An interview with Dr. Nowell is available in this collection.

[46] Phytohemaglutinin is a lectin found in plants, especially in kidney beans, which effects cell metabolism and is used in research to induce cellular mitosis.

[47] Lymphocytes are a type of white blood cell essential to the body's immune system.

[48] Autoradiography is a technique used to identify molecules using an X-ray sensitive film by radioactively tagging certain molecules, including DNA.

[49] Alan C. Stevenson was a geneticist and the director of the Medical Research Council for Population Genetics Unit at Oxford.

[50] Marco Fraccaro (1926-2008) was a pioneer in the field of human cytogenetics and especially interested in sex chromosomes. Among other positions, he was the head of the Euratom Group of researchers in human cytogenetics and set up his laboratories in his native Pavia, Italy. He also became a professor at the University of Pavia, and chaired the Department of General Biology and Medical Genetics in 1968. For a

Sweden and worked with Jan Lindsten[51] and moved to the MRC Unit. So Marco taught me cytogentics. The first time I got chromosomes -- my own and presumably I got some photographs of cells from them -- Marco was the one who taught me how to identify the individual chromosomes, putting them into the groups that was the standard nomenclature back then in the sixties.

When I discovered that one of the chromosomes in females was late labeling and therefore was likely to be an X chromosome, Marco, because of his previous contacts with Jan Lindsten, said, "You can go to Sweden and get patients that Jan had been studying the sex chromosome abnormalities of, [i.e.] males with four X's and a Y, females with iso-X chromosomes or deleted X's, all sorts of different abnormalities. You can go, and take the tritiated thymidine with you, you'll add it to the cultures, and then you could come back with that material and study it further."

So I went to Sweden. I remember being there with Marco and traveling to Uppsala with him (because in fact he was in Sweden at the same time, but it was not planned that way) but I don't remember his involvement anymore. Jan Lindsten did have all of the patients come in and had blood cultures from the patients so that I could add the tritiated thymidine, which I just carried on the airplane with me, and made the cultures, harvested them through fixative, and then [I] could carry the cultures back and make the slides in England. Working with material from the male patient with four X's and a Y, but then doing autoradiography could show that the X chromosome -- there were three late-labeling chromosomes in that patient indicating that except for one X (because he had four X's), the other X's were inactive, just like the X chromosome in a female. That was a paper that was published in *Nature* probably in August or September, sometime in '62, right at that point.

In the meantime, Laszlo had moved to Manchester to the Christie Hospital and Paterson Research Laboratory [The Paterson Institute], which he was named director of. He moved in January, more or less, of '62. The last part of my research time, he wasn't there as I was doing the experiments. It was probably early March or April of '62 that I went to Sweden and did those experiments and then started to work on them when I got back.

AM: Did you have a sense then that the direction of clinical medicine with regard to a genetic understanding of human disease was different in England and Europe and Sweden than it was in the United States?

JR: Certainly [it was different] than [what] I had been exposed to, that was true. But the MRC Unit was population genetics, and I didn't really -- I went to the MRC Unit to see Marco and to learn chromosomes. I don't remember going for seminars there at that time. Again, at the Karolinska Institute, Jan was very interested in sex chromosome abnormalities and certainly there were also a

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portrait and to read his full obituary, visit the website at:
http://www.online.karger.com/ProdukteDB/produkte.asp?Doi=188967

[51] Jan Lindsten, a Swedish geneticist, is a professor emeritus of Medical Genetics at Karolinska Institutet in Stockholm. Between 1979 and 1990 he also was secretary general of the Nobel Assembly and the Medical Nobel Committee as well as member of the board of the Nobel Foundation.

number of other people interested in various endocrine abnormalities, some of which were genetic. But that wasn't anything I was interested in, so I didn't pay a whole lot of attention.

AM: Was there a sense that there was a lot of cross-fertilization going around in Europe, particularly in northern Europe, between different groups that may be working in human cell culture, and were there publications coming out of the United States that you were reading in your area? Or was it really this group in Europe, and what was going on in this kind of small field in the United States? So were you picking up US-based publications to read for the latest work?

JR: It was early days. As I say, Lejeune's paper[52] was [published in] '60 – [no] probably '59. You have to go back and remember that [Joe Hin] Tijo and [Albert] Levan's "The Correct Chromosome Number of Man" was [published in] 1956[53]. Before that, we thought that there were forty-eight chromosomes, and you couldn't look at human chromosomes anyhow. It was often some sort of peripheral field, and whether it was going to have much to do with anything that was important I don't think was very clear. Clearly, Ted [Theodore T.] Puck[54], then at the University of Colorado Medical Center, Denver (formerly at U of C) was instrumental in the early sixties in gathering together all the people who had published karyotypes, because different people organized the karyotypes differently.

So certainly Puck…I should know when the Denver Conference met and it was published…it's my guess that it was around '61 or '62 or '63. I used to know that, but I've forgotten. Anybody who had published a human karyotype came to Denver. They all agreed on how it (the karyotype) would be arranged and that most of the chromosomes, you couldn't tell one from another. You could identify chromosome numbers one, two, and three, and that was the A group, and the B group, et cetera. But beyond that, you were lucky if you could figure out what group a chromosome fell into, and an extra chromosome particularly. But tying that into genetics right away, or at least, for me, not having any genetics background, I didn't make those associations.

AM: Okay. I wanted to ask what was your sense that a lot of work that was done in what we call classical genetics today and organisms like Drosophila or corn, and transposable elements, all that had gone on in the twenties, thirties,

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[52] Lejeune's (and M. Gautier's and M. Turpin's) paper: Lejeune J, Gautier M, Turpin R (1959). "Etude des chromosomes somatiques de neuf enfants mongoliens". Comptes Rendus Hebd Seances Acad Sci 248 (11): 1721–1722. http://gallica.bnf.fr/ark:/12148/bpt6k32002/f1759.chemindefer.

[53] Joe Hin Tijo and Albert Levan's seminal paper: Tijo JH & Levan A (1956) "The chromosome number in man." Hereditas 42: 1-6. For more about this discovery see the article at this website: http://www.springerlink.com/content/f7q425r58882nk33.

[54] Theodore T. Puck (1916-2005) was an accomplished cytogeneticist and an important confirmer of the correct number of chromosomes in man as 46. He was a professor at the University of Chicago. Puck's brief autobiography was published in American Journal of Medical Genetics in the section "Living History Biography" (Puck 1994). For a succinct biography also visit the website at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1380277/

and forties was going to have relevance to what you were doing in Oxford at this moment?

JR: I wasn't even aware of those studies, so it had no impact at all.

V. Development: "Dabbling" in ctyogenetics, first publication and space in a lab

AM: Okay. You threw off this, "Oh, yeah, and I got my paper published in *Nature* in 1962." Now, I've interviewed quite a few young biomedical researchers who were just within their first five years of their tenure track position, and to them, getting a paper published in *Nature* would be like finding the Holy Grail! This is one of your first publications, and it hits the jackpot in *Nature.* What was your sense that what you had done could be career-making or had reached an audience of significant proportions, that this was some validation of your work?

JR: In one sense, I was too naive to really appreciate that. It was certainly Laszlo Lajtha, who was the senior author on that paper, who submitted the paper to *Nature* and then shepherded it through. I did the work, and then we left Oxford and went for a vacation on the Continent for six weeks, and Laszlo was shepherding it through. So I don't take any credit at all for getting that in *Nature*. That was strictly his doing.

AM: But did you have a sense that this was -- for your own identification as a scientist, as well as a physician, was this a point of departure?

JR: Well, I wasn't really a scientist then. I was a dabbler. It was clear that it was important when I came back to the university because I had decided -- and I don't know when it was that I decided -- that I didn't want to go back to the clinic, that I was finally on to something that I found intellectually challenging and that I wanted to do. The question was, how was I going to be able to do it, and where? The where, if I was lucky, was straightforward, it would be at the University of Chicago. And with whom I could do this, because it was my research, not that of anybody [else] at the university, and who was going to be generous enough to take a chance on me, totally untested, with no credentials except this one paper, to go off and do my own thing?

Leon Jacobson was my knight in shining armor. I remember going and talking with him when we came back, so it would have been probably middle September of '62 when the kids were back in school. I talked with Dr. Jacobson about the fact that I'd had this experience in Oxford, that I had all these other samples from Jan Lindsten's patients with extra X chromosomes and abnormal X chromosomes and a ring X chromosome, and that I wanted to continue studying these. Everything was all done, and I believe I had done the autoradiography in Oxford, so I'd already got them all cover slipped -- not cover slipped, but the film, the radio sensitive film that you use for autoradiography, they were all done. All I

needed was a microscope and some ability to photograph some of the cells, and then I was in.

One person whom I'd had early on in histology was interested in having me come and work in his lab because he was particularly interested in lymphocytes, and that was William Bloom[55]. But it was clear that if I worked with him, it would be mainly on his projects, and I could maybe do some of my own. With Dr. Jacobson, it was clear that I could do what I wanted. He was director of the Argonne Cancer Research Hospital, which was a newly built structure where we met yesterday, six floors, funded by the Atomic Energy Commission. The whole building was funded by a block grant every year from the Atomic Energy Commission, and he was director of that.

So he had space and the microscope, because he was head of hematology. They all used microscopes to look at the bone marrows of the patients, and they had extras around. I told him I wanted to work three days a week, and I'd like to get paid. And he said yes. I got five thousand a year for working three days a week and came back to the University of Chicago.

AM: And your husband was planning to come back to the University of Chicago after his sabbatical in Oxford, England?

JR: Oh, absolutely. There was no question.

AM: Were you still considering yourself at this point, when you returned to the University of Chicago, a dabbler?

JR: Yes.

AM: Or were you defining yourself a little bit differently?

JR: Well, to the extent that my family and my life was still the major focus of my life, [that is] my children, my garden, I was weaving, I went to museums, I read books, I had a wonderful life. Why would anybody be so stupid as to work full time? I had it made. I never intended to work full time. My life was a full, rich life. My job was a part-time job, and it was certainly off as (really) a minor component of my life. And it was like that till 1972.

AM: Before we jump ahead there, what did you learn about your hands in the lab? You went from really very clinical observational skills in the clinic in Chicago to very much working at the bench and learning to use your hands to generate data. How were you in the lab?

JR: Oh, I'm a klutz. I am absolutely no good. That's putting it too bluntly. I was able to do autoradiography, and I could subsequently do other things in the laboratory, but what I was really good at was microscopy. I sat there and

[55] William Bloom, noted histologist and molecular biologist at the University of Chicago. He co-authored, with Carl H. Krekeler, a text book titled General Biology, a unified text manual.

counted grains on the chromosomes, and that's a mindless task, of course. [I] did that for the statistics that were thought to be needed at that point to look at the pattern of DNA replication. But my husband is fabulous, just technically adept, does i.v. tail-vein injections in mice. He's marvelous. I'm not any good at that.

AM: So since you're very good at counting and doing that -- I just came from Jim Crow's[56] where we talked about this -- it sounds like you would have been a good Drosophilist[57], counting mutants.

JR: I probably would have, and looking to see what the mutation was. Pattern recognition -- it became clear that that was something I *was* good at. But it took a long time to find that [out].

AM: What was it about the environment at the University of Chicago and/or Jacobson and/or the time in which you returned that allowed for this convergence of events that would allow you to be a dabbler in this field and have all your other interests, and still get paid and have a space, even have a microscope, even have a seat in a lab?

JR: I think it just is the fortunate congruence of a lot of small things. Firstly, Dr. Jacobson did have a block of several million dollars. Now, I had to write a progress report each year as to what I was doing, which then went to the Atomic Energy Commission. They did have external reviewers who came in and reviewed the program, of which I was a miniscule part. As long as I didn't do something terrible, or not do anything at all, I got carried along by people like Gene [Eugene] Goldwasser[58], who was working with Dr. Jacobson on erythropoietin[59], and many people who were all involved in radio isotopes[60], the development of new radio isotopes, the development of gallium[61], which ultimately became used for identifying lymphomas and things. Short-lived radio isotopes -- that was the focus. I was this unseen bit over here, and five thousand, six thousand, eight thousand dollars, that didn't matter.

AM: It's hard to imagine anybody functioning on a budget that small.

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[56] James F. Crow, professor emeritus at University of Wisconsin-Madison, is an important geneticist. He is a member of both national and international scientific societies, including the National Academy of Sciences. His most important achievements are in the field of population genetics and in Drosophila studies. An interview with Dr. Crow is available in this collection.

[57] A drosophilist is a scientist who studies genetics using the Drosophila fly.

[58] Eugene Goldwasser is professor emeritus of biochemistry at the University of Chicago. Perhaps his most important achievement is in his research resulting in the isolation and characterization of the hormone erythropoietin. He is also the 2005 recipient of the Prince Mahidol Award.

[59] Erythropoietin (EPO) is a hormone produced in the kidneys and in the liver. It is important for bone marrow health, where it regulates red blood cell production.

[60] Radioisotopes are atoms which, as they decay, can be used as tracers in the body to diagnose illness in different organs. For more information about the use of radioisotopes in medicine, visit the website at: http://www.world-nuclear.org/info/inf55.html

[61] Gallium isotopes from the element gallium (Ga) are one type of isotope used in radiography. See note 64 for more information.

JR: Well, I had no help. Finally, when I needed someone to help with the photography, there was a college student who was working for someone else who was there who had a functioning laboratory. He was very generous and said she could work part time for me doing what I needed, so I had it. I was doing something that nobody else was doing, so nobody paid a whole lot of attention to me, and that didn't matter.

I did start going [to meetings]. The first meeting that I went to in the States (probably in October and it may even have been November of 1962) was a cytogenetics meeting. I think it was called Chromosomes Today or something of that sort. If not the first meeting, it was a very early meeting of a group of cytogeneticists at Oak Ridge [National Laboratory]. I had the paper on the four X and Y's, so I went down to Oak Ridge and presented that paper. Everybody who was anybody in cytogenetics in the United States was there. T.C. [Tao-Chiuh] Hsu[62] was obviously one of the important people. [H.] Bentley Glass[63] was there. I was a true novice and a true outsider because I didn't know any of these people.

So I presented the four X and Y, and then somebody else pointed out that other people had also reported -- if not at the same time, slightly thereafter -- research that I was ignorant of because I didn't pay a whole lot of attention to the literature at that point. That was the beginning of my participation in the larger scientific community. But again, it was strictly all chromosomes. Kurt Benirschke[64] was there, and he and T.C. Hsu were looking at all the karyotypes of all the strange critters that were around. Kurt was still at Dartmouth [Medical School] at that point. That was an eye-opening experience.

VI. Dabbler No More: Learning banding techniques in Oxford and full-time research in Chicago

AM: This may be asking the obvious. You mentioned that you considered yourself a dabbler until '72. Why don't you talk about your work that kind of forces you into defining yourself as a full-fledged professional geneticist?

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[62] Tao-Chiuh Hsu (1917-2003), a Chinese-American cell biologist, was a professor at University of Texas for most of his career. He made important advances in the study of cancer biology, techniques for studying chromosomes, and the accurate identification of 23 pairs of chromosomes in each human somatic cell. His autobiography was published in the American Journal of Medical Genetics 59:304-325 (1995). For a portrait and obituary, visit the website at: http://www.karger.com/CGR

[63] Hiram Bentley Glass (1906-2005) was an outstanding geneticist. He was a professor at Johns Hopkins University and later at the State University of New York at Stony Brook. Among his contributions to the field of genetics, Bentley was an important (and controversial) theorist, promoting the concept of using the science of genetics to prevent genetically malformed offspring. An interview with Dr. Hiram Bentley Glass is available in this collection.

[64] Kurt Benirschke, a German-American mammalian geneticist, is known for his work in placental and reproductive pathology. He and T.C. Hsu worked together to karyotype over 400 different mammals. He was chairman of the department of pathology at Dartmouth Medical School, in Hanover, NH and is now a professor emeritus at the University of California, San Diego. For more about him, visit this website: http://placentation.ucsd.edu/authorfs.html

JR: Okay. The period of coming back to the university in 1962 to 1970 was one of continuing -- at least for most of that time -- continuing to use autoradiography as a tool to study chromosomal abnormalities. Probably around 1965, I met Gene [Eugene] Pergament[65], who was a geneticist but a medical student at the University of Chicago. Gene, as a cytogeneticist, had identified several patients with unusual chromosome abnormalities, and the question was whether we could use autoradiography to identify which chromosome, and it involved members of what was called the D group at that point, thirteen, fourteen, and fifteen. So I used autoradiography on material from his patients.

Then I was in the section of Hematology/Oncology because that's where Dr. Jacobson had his primary appointment in the Department of Medicine. He saw patients. Over the years, once, twice, three times a year, Dr. Jacobson would ask if I would look at the chromosomes of patients. [Peter] Nowell and [David] Hungerford had identified the Philadelphia chromosome in chronic myelogenous leukemia [CML] in 1960, and I didn't look at all the CML patients, but I looked at occasional patients. He also had patients who were developing leukemia and wondered if I could see anything abnormal about those.

AM: Was this a directed program, or was this more like a fishing expedition – "Since we do have these samples, let's see what they look like"?

JR: He had to give me the sample, and I had to process them especially for chromosomes, because he was just doing straight morphology or iron metabolism, or things of that sort on them. So if I would do a study, then he would get me a sample specifically for me to prepare for chromosome analysis.

AM: Because you were there and you were cheap?

JR: Because I was there and cheap-- I didn't charge him anything! I think it was intellectual interest on his part as to what was the chromosome pattern in these patients. He and several other people at the university -- Matthew Block and Bill [William F.] Bethard -- were very interested in a condition that Dr. Jacobson called "preleukemia", the patients with unexplained anemia or low platelet counts or low white counts, who in three to six to twelve months went on and developed leukemia. And was there any clue as to the nature of the development of leukemia from looking at the chromosomes of these patients? Beginning, I would say [in] 1968, I became more closely involved in doing cytogenetic studies on this group of preleukemic patients. I didn't get cells from *every* patient, but I'd get samples from most patients who were being studied for preleukemia to do chromosome studies on.

It was very interesting that many of the patients were missing a C group chromosome. That's the largest group of medium-sized chromosomes. But you couldn't tell which one was missing, or if there was an extra chromosome, you couldn't tell which one was extra. So in different patients, with gains or losses of

[65] Eugene Pergament is an active professor at the department of obstetrics and gynecology at Northwestern University. He is a specialist in cytogenetics.

the chromosome, was it random? They were clonal because although the patient may have some normal cells, they had fifty, seventy-five, even a hundred percent of cells that had forty-five chromosomes or forty-seven chromosomes, but we couldn't tell them apart. I actually published a paper on C group chromosome abnormalities (I think in *Blood*) in preluekemia, probably in 1966. But beyond that, we couldn't tell.

Then my husband went back to Oxford on the second sabbatical, this time working with Jim [Sir James L.] Gowans[66], and Walter [F.] Bodmer[67] was just coming to Oxford as a professor of genetics. I was in correspondence with Walter about [if] could I come to Oxford and do a sabbatical with him. He was very gracious and said yes, I could. It also was clear that he was arriving -- his whole physical space was being gutted and redone, and I wouldn't have much laboratory space to work in when I first arrived. But again, Donald was going so I was going.

That turned out to be very fortunate from my point of view, that is, the disruption in Walter's lab, because the MRC Unit again, in population genetics, had Peter [L.] Pearson[68]. Quinacrine mustard banding[69] had just been discovered by Lore Zech[70]. It was obviously used by [Torbjorn] Caspersson[71] in maize, in plant chromosomes, but Lore made the link to human chromosomes, which Caspersson didn't want her to do. The only paper that Lore is on as a single author is an abstract in the Icelandic Genetics Society, showing that the male Y chromosome is brightly fluorescent. She then transformed the field and went on to study human karyotypes, and of course Caspersson is on all of those other papers. Banding really transformed the field because suddenly all these C group chromosome abnormalities that I had been studying, you finally could figure out what they really were.

AM: Were you aware of this when you planned to go back to work with Bodmer at Oxford, or was this something that you were made aware of when you got to Oxford?

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[66] Sir James L. Gowans is a pathologist known for his important work on lymphohcytes. He was a student of Sir Howard Florey's (see note 35). He is a professor at the Sir William Dunn School of Pathology, Oxford.

[67] Sir Walter F. Bodmer is a geneticist of German-Jewish background. Educated at Cambridge, Bodmer taught at the Genetics Department at Stanford and became chair of Genetics at Oxford, and is now Director of Research of the Imperial Cancer Research Fund of London. He is perhaps best known for his research of HLA (Human leukocyte antigen) genes. For more about him, visit the website at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1685126/

[68] Peter L. Pearson, a geneticist who worked at the MRC unit in Oxford, and later at the Department of Medical Genetics, University Medical Center, in Utrecht, the Netherlands. He specializes in sex chromosomes and fertility.

[69] Quinacrine mustard banding is a technique for identifying and differentiating chromosomes using quinacrine mustard dye. For more information about chromosomal banding, see note 5.

[70] Lore Zech is a geneticist at the Karolinska Institute in Stockholm who developed quinacrine mustard banding technique (see note 66), which helped identify XYY syndrome in 1969, among other things.

[71] Torbjorn Caspersson (1910-1977) was an influential Swedish cytogeneticist, who along with Lore Zech, developed quinacrine mustard banding in 1969 at the Karolinska Institute in Stockholm. He made many other important discoveries in the field of genetics, including the fact that DNA was a polymer, contrary to previous theories. For more information about him, visit the website at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1715562/?log%24=activity

JR: My recollection is that I was made aware of it when I went to Oxford. The Y chromosome abstract of Lore is [from] either '69 or '70, and we went in '70, so the arrangements to go to Oxford were totally independent of this. But it was pretty clear once I got there… I don't recall the sequence of events. I did meet Peter Pearson -- because I had not known Peter before -- fairly soon after we arrived in Oxford. I made arrangements that I could use his microscope at night, because he and Penny [Penelope W.] Allderdice[72] [were there]. [Penny was] there also on more than a sabbatical, she was there for more than a year, she and her husband, Bill [Allderdice] were there. So I could use their fluorescence microscope at night.

AM: So you didn't go there specifically to learn banding techniques.

JR: No. That was luck.

AM: To go back a little bit and ask a couple of clean-up questions. While Jacobson had given you this space and this microscope, what was expected of you in terms of productivity measurement? Were you expected, even on a small part of this grant, to publish your results? What was expected?

JR: There was *nothing* expected of me.

AM: Okay. So, when you went to Bodmer, you had the paper in *Nature*, and you certainly had some publications in *Blood*. Could one say you had a reputation within a particular field that Bodmer would say, "Oh yes, I read the paper in *Blood*"?

JR: No.

AM: Then I'll commit the biggest sin an historian can make and ask you a counterfactual question, and that is, what do you think would have happened if Bodmer hadn't been reorganizing his lab and you were shunted over to Pearson?

JR: Well, that's in fact what happened.

AM: Right. So what if that hadn't happened and you *had* worked more closely with Bodmer?

JR: I set up Walter's cytogenetics laboratory. He wasn't really ready to do that physically for some months after I got there. One aspect of Walter's work was somatic cell hybrids[73] with Markus Nabholz[74]. Here they had these mouse-

[72] Penelope W. Allderdice, a geneticist then at Oxford, is now at the Department of Human Genetics and Development, College of Physicians and Surgeons, Columbia University.
[73] Somatic cell hybrids are cells which are the result of a fusion of two somatic cells from different species. Somatic cells are cells which will not become gametes, and thus will not pass any genes on to future generations.

human hybrids, and [which] were the human chromosomes? Now, you could sort of figure that out, but sometimes it was very difficult to know which ones were mouse. These were 3T3 cells[75], they were wildly rearranged, a lot of big metacentric chromosomes[76], and trying to karyotype them and karyotype the hybrids was not hopeless but very, very difficult. And to prove that it had this human chromosome in it also was extremely difficult.

So Walter was interested in having cytogenetics come to his laboratory program. He had decided…[or rather] he and Markus had agreed on that. So with banding available, it was clear that my learning chromosome banding and bringing those techniques back to Walter's laboratory to set them up so that they would be an ongoing part of his research facility, that there was no question [about]. Even if Walter had an ongoing laboratory, it would certainly have included banding, and somebody else would have been doing it. The way it evolved was [that] *I* was the one who was doing it in Walter's laboratory.

Then Sally Craig[77] -- Ian Craig[78] was there and Sally was his wife, and she was pregnant and then had children -- I think twins. She wasn't around very much, but Sally was going to be the person who would take over when I finished sabbatical, at least for part of it.

I learned from Peter what the equipment was that was needed. We ordered the equipment for Walter's lab. So probably by January or February, somewhere along in there – [maybe] March, I had the equipment in Walter's lab and did all my work there in the genetics laboratory.

AM: Just a brief pause here. We're at an hour and a half of interviewing, and I certainly could go on, but I don't know what your schedule is.

JR: I said I'd be at the hospital at 11:15 so they changed the meeting from 11:00 to 11:15, so I've got another ten minutes or something like that, because I'll get on my bike and go.

AM: If it's okay to do another ten minutes, why don't we, because we really haven't gotten as far as I thought we'd get. Okay.

JR: You have a very verbose respondent {laughter}.

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[74] Markus Nabholz is a geneticist specializing in human-mice cell hybrids (among other things) who taught at Stanford, and later at the Department of Biochemistry, in Oxford, and most recently does research at the Swiss Institute for Experimental Cancer Research, Epalinges.

[75] 3T3 cells are animal cells (originally from Swiss mouse embryos) cultured in a lab which encourage the growth of keratinocytes (skin cells).

[76] Metacentric chromosomes are chromosomes which have their centromeres roughly in the middle of the chromosomes, the two arms of the chromosome being of approximately equal length. For more information visit the website at: http://ghr.nlm.nih.gov/handbook/basics/chromosome

[77] Sally P. Craig is a geneticist who worked at the Genetics Laboratory, Department of Biochemistry, University of Oxford.

[78] Ian Craig is a geneticist who specializes in sex differences, previously researched at the Genetics Unit at Oxford, where he worked on isolating genes for kidney failure and blindness. He currently teaches at St. Catherine's College, Oxford. See his faculty page at: http://www.stcatz.ox.ac.uk/academic_staff_pages/craig_ian.htm

AM: No, this is great! You have a great way of setting this up. I'm waiting for this build-up to the big events. Okay, so it sounds like [during] your time at Oxford you were being as helpful as you were learning, learning and producing at the same time, or at least setting up the cytogenetics lab in Bodmer's --

JR: Yes.

AM: When you started working with Jacobson [with] the samples of blood, how much cancer biology did you know? What did you know about the major issues of oncogenesis[79] and cancer biology?

JR: I didn't know anything. Just like I didn't know any genetics, I didn't know any cancer biology either.

AM: So after learning these banding techniques, were you using the cells that Jacobson gave you, the chromosomes that you were getting from Jacobson's samples in Oxford to learn the banding techniques? [Are those] the cells that you were using? Or did that happen after you returned to --

JR: I used two sets of cells. One [set] was the cells from Walter's somatic cell hybrids. Actually, the first paper out of Walter's lab is again a paper in *Nature* that Walter was responsible for. It was published in six weeks, and I had this (again) totally ignorant naive view that you sent things to *Nature* and they just got published right away.

We did two techniques with the chromosomes. One was the quinacrine fluorescence. And then [we] did the technique that Mary-Lou Pardue[80] and Joe [Joseph G.] Gall[81] developed of G banding, [no, rather] of centromere banding[82], which was modified to *lead* to G banding[83] by the Millers [Orlando J. Miller and Dorothy A. Miller][84]. But it showed that in these abnormal mouse chromosomes and 3T3 cells -- these metacentric chromosomes -- [that] there were very large pale regions on quinacrine banding, and these were the dark heterochromatic regions, centromeric regions, when you did C banding and could have really

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[79] Oncogenesis is the process which results in a malignant tumor. See http://medical-dictionary.thefreedictionary.com/oncogenesis

[80] Mary-Lou Pardue is a prominent geneticist and cell biologist who, among her other areas of research, collaborated with Joseph G. Gall (see note 79) to develop the in-situ hybridization method which resulted in the localization of DNA and RNA.on chromosomes. She currently teaches at MIT.

[81] Joseph G. Gall is a distinguished geneticist and microscopist who, in addition to his discovery with Mary-Lou Pardue of in-situ hybridization, has done important research in chromosome structure. He currently is on staff at the Carnegie Institution of Washington. He has also been noted as an especially encouraging mentor for female scientists, and many of his female students have gone on to have distinguished careers themselves. For more information, visit the website at: http://jcs.biologists.org/cgi/content/full/116/19/3849

[82] Centromere banding (C-banding) is a technique for locating the centromeres of a chromosome, thus differentiating between chromosomes. Certain dyes are used to stain the centromere of a chromosome which, when read under a microscope, indicates which one of 5 possible centromere locations a particular chromosome possesses.

[83] Giemsa banding (G banding) is a chromosomal staining technique which uses the dye Giemsa.

[84] The Millers: Orlando J. and Dorothy A. Miller were both geneticists who together developed the technique known as G-banding, using the stain Giemsa to identify different chromosomes. They both did research at the College of Physicians and Surgeons, Columbia University, New York.

beautiful karyotypes and metaphase cells with Q banding. Then [later when] exactly the same cell [was] G stained for centromeric DNA you could see the correspondence between these.

This correlation of Q band negative and G staining heterochromatine positive regions was written up in a paper, and I was first author and Walter was -- maybe it was just Walter and myself, I don't remember now who the authors are. But [we] sent that off to *Nature* and there it was, lo and behold, published.

I did work [that] could show in the hybrid cells which chromosomes were human chromosomes. I brought back a number of slides from Walter's lab and was continuing on in early '72 with looking at the hybrids. At the same time, because I had these questions about the abnormalities we saw in the preleukemia patients, I knew that banding was going to be the answer. Unfortunately, there was a mail strike in Britain, and I wasn't smart enough, and nobody suggested to me, that we just use some kind of courier mail. I got *some* slides from the United States, and these were mainly older male patients who had forty-five chromosomes that we assumed were missing a Y chromosome, but we couldn't prove it.

So I did fluorescence on those patients -- I think there were three patients -- and sent that [paper] off to the *British Journal of Hematology* while I was in Oxford. But the work on doing banding on C group abnormalities I couldn't complete because I couldn't get the material from the United States. [So instead] I started working on that then when I came back after sabbatical in September or October of '70.

AM: Again was it just assumed that you'd go back in the same relationship to the University of Chicago in your own little part of that large laboratory grant [from the AEC]?

JR: Right -- I may have misspoken. We went to Oxford in 1970 and came back in '71. I think I got the dates a year off. Before we came back, as we were going through Europe, I went to the Paris Nomenclature Conference. Actually, I had been previously at the Chicago conference that was held in '66 in conjunction with the International Congress of Human Genetics, which was held in Chicago, the cytogenetics conference there. Because I had started working with banding, and John Hammerton[85] was involved in organizing this Paris conference, I went to that and participated. That was an excellent experience of getting to know Lore Zech better, and other people.

So then [I] came back in '71, mainly working on the somatic cell hybrids but doing some work on the leukemia samples that I had [as well]. I started doing more and more patients with leukemia, [but] not on an absolutely regular basis, because I had to get the samples from the hematologist. There were all sorts of faculty members, each doing bone marrows, and to get everyone to agree to send me samples was [difficult because it was] an extra sample that they had to obtain from the patients, and it was a hassle and wasn't clear this

[85] John Hammerton, a distinguished human cytogeneticist, who along with Charles F. Ford, confirmed Tijo and Levan's correct numbering of human chromosomes at 46. For more, see note 38.

was anything except for trying to jolly me along. So it was spotty in late '71 and early '72.

I began to focus more and more on the samples that I got, and I was very fortunate early in '72 that we had two patients with the same abnormal pattern of chromosomes. Again using the old nomenclature, they had an extra D group chromosome and an extra E group chromosome, and they were missing a C and missing a G group chromosome, using the Denver nomenclature. Using banding, I could show that that was a (8;21) translocation in two patients, and they were both missing an X chromosome. That was very exciting to me, and I sent it off to the *New England Journal of Medicine* and they wrote me a polite -- I think a polite -- letter back saying it wasn't of any interest. I keep everything, but I don't have a copy of that correspondence.

I had known Jean de Grouchy[86] and particularly met him again in Paris at the Paris conference. Jean was editor of *Annales de Génétique*, so I sent all this -- the second place I sent it was to Jean de Grouchy -- and he published it and it's now the most cited paper in the *Annales de Génétique*. Why didn't I send it to some other paper? Why didn't I send it to *Blood, Lancet*? Who knows? That's it.

Then the question still was, in patients with CML[87] with blast crisis[88], they often get extra C group chromosomes. We hadn't resolved the question whether it was the same one or different ones. The next thing I began to look at was patients in blast crisis with CML and with these extra C group chromosomes, trying to figure out what [the identity of the extra C group chromosome] was. It's that table in there that I would cut them out [on]. I was still working three days a week, so [the] days when I was off, if I had time or wanted to [I would work on them]. It became more and more interesting, and I would have the chromosomes cut out, and it was pretty clear that the C group chromosome was always the same, and [there were] some other abnormalities I could identify which were all the same in different patients.

But it was also of interest that when you really looked carefully at all the chromosomes, one chromosome nine was abnormal. There was the Philadelphia chromosome[89], but here was nine with a longer piece. I had chronic phase[90] cells from these same patients that I had never looked at, so I could go back and do quinacrine fluorescence on the patient's samples obtained when they were in the chronic phase and see that they too had the extra piece on

[86] Jean de Grouchy is a French cytogeneticist. He knew and was influenced by Lejeune in his study of genetics. De Grouchy, besides doing pioneering research in the field, was the editor of important publication Annales de Génétique.

[87] CML-- chronic myelogenous leukemia, a cancer of the blood.

[88] Blast crisis is the last phase of CML in which large numbers of blast cells (immature blood cells) are present in the bone marrow.

[89] Philadelphia chromosome, aka the Philadelphia translocation, is the chromosomal abnormality which causes CML. It is named for the city of Philadelphia in which it was discovered by Peter Nowell and David Hungerford in 1960 .

[90] Chronic phase is the term for the early phase of CML and other leukemias during which abnormally high amounts of white blood cells are produced and mature in the bone marrow.

chromosome nine. So it wasn't a result of blast crisis, and it was logical to think that this too could be a translocation[91].

I had three patients by that time that I was looking at. They all had the (9;22) translocations, both chronic phase and blast crisis. So I sent off a letter to *Nature* and got it rejected, saying that it wasn't clear, that this was just a polymorphism, things of that sort.

In the meantime, I had gotten peripheral blood from these patients, at least [from] some of them [who] were [still] alive. Their peripheral blood was forty-six, perfectly normal, so this wasn't an inherited abnormality. I had gone from three patients to seven patients, so I rewrote it. Donald helped me a great deal in the writing and trying to make it more precise. Then *Nature* accepted that paper probably in February.

In the meantime, I'd gone to the chromosome meeting in December and told them about my findings. Then I went to a major meeting of Clinical Investigation, a major meeting of physicians, and [I] was in the plenary session and presented that [paper]. Not a single question was asked of me in the plenary session. I expected this paper to be out in *Nature* in six weeks, and I went through a period of maybe at least two months thinking that somebody else –- *anybody* -- could go and look at the cells that they had and send [the discovery] off and I was going to get scooped. I have to say I was pretty frantic. It seemed to me it was published in June or July in *Nature*. It took a long, long time for that paper to get published.

Then all of a sudden here was this fascinating question of what were all these chromosome abnormalities? What implications did they have clinically? How many were there? How did they happen? So all of a sudden my career moved from being *very* much on the sidelines to being very central. And finally -- this was '73 –- [by] 1975 I decided that as long as I was working full time, I might just as well get paid full time, so against all my better judgment, I began working full time.

AM: I think we're at a good point to stop, and you need to go to a meeting. Thank you.

VII. Expansion: Important discoveries, publication, and a faculty position

AM: It is June 8th, 2005, and I'm Andrea Maestrejuan with Janet Rowley at her house to finish her interview for the UCLA Human Genetics Oral History Project. There were a couple of questions from yesterday that I wanted to follow up on. You had mentioned yesterday that you hadn't really followed the literature at your first presentation at one of the Hematological Society [American Society of Hematology] meetings, but in your '73 *Nature* paper [Rowley, Janet D. (1973). "A New Consistent Chromosomal Abnormality in Chronic Myelogenous Leukaemia

[91] Translocation is the transfer of part of a chromosome to another chromosome. Such translocations can cause cancer. One such transfer is called the Philadelphia translocation, see note 94. For more information visit the website at: http://en.wikipedia.org/wiki/Chromosomal_translocation

Identified by Quinacrine Fluorescence and Giemsa Staining." Nature 243(5405):290-3.] where you identify a translocation in CML, were you aware of the [Peter] Nowell and [David] Hungerford paper?[92]

JR: Oh, yes. I knew that, and I was friends with Peter and [had] met him before, so that was something I was very aware of, and [I was aware of] work that had been done at NIH, Jacqueline Whang-Peng[93] being the first author of that paper, showing that patients who appear to have something called chronic myelogenous leukemia [CML], some of them with the Philadelphia chromosome did better than those who lacked the Philadelphia chromosome. So there was this question [about] the Ph1 positive CML as compared with Ph1 negative CML. That was a prominent discussion in the late sixties.

AM: Okay. I wanted to ask a little bit more about how you were interpreting your rejection from *Nature*. Because your first two *Nature* papers went in with relative ease, but they were coming out in collaboration with large, well-established labs, [for example] Bodmer [though] his lab [in Oxford] wasn't well established, certainly he had a reputation. How were you interpreting this rejection in terms of your own ability, being kind of isolated at the University of Chicago, working *very* independently, to get your work out to a wider audience?

JR: Well, it's a mixture, because the first paper that went in had about three patients, and I didn't have peripheral blood studies on those patients. That was one of the concerns of the reviewer. Again, I don't know that I saved that review, but it was written on an old typewriter that had funny characters to it, and it looked to me as though the reviewer wasn't terribly knowledgeable.

In the meantime, while I was waiting for the response [from] *Nature*, I'd done many more patients and had normal samples from some of the individuals. So when the rejection came back, within a week I rewrote the paper, again with substantial help from my husband, and could show that in fact in seven patients these were consistent findings. It was that [revised] paper then that went back to *Nature*. As I recall, it was accepted fairly rapidly, but the thing that concerned me was the delay in getting it published, actually in print.

AM: I wanted to get back to that very point, because at the beginning [of our interview] yesterday, you [said that you] were doing this part time and you described yourself as a dabbler, or maybe that was the word I used, and it still seemed that way [at that time]. Part time you were looking at the pictures at home of the chromosomes on your kitchen table. But what happened that you were nervous that you weren't going to get this published at *Nature* in a timely manner and you'd be scooped? -- That is what I believe you said yesterday.

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[92] The landmark Nowell and Hungerford paper was titled “A minute chromosome in human chronic granulocytic leukemia”. Science 1960, 132:1497-1501

[93] Jacqueline Whang-Peng, an eminent cytogeneticist from Taiwan, is now the Distinguished Investigator and acting director of National Institute of Cancer Research at NHRI (National Health Research Institutes) in Taiwan.

JR: That's right, because I did realize that it was extremely important, and it was accepted as a plenary paper for the American Society of Clinical Investigation, which is the top medical scientific society and that was in April. So here I was presenting this before several thousand people with no protection at all, except for the fact that it was out there. But that doesn't give you much in the world. Of course, it was the second translocation because t(21) was the first. Because it was the first and who knew whether it meant anything in the larger sense, I sent that off to *Annales de Génétique*. Between the two, and the fact that the Philadelphia chromosome had assumed such importance in hematology, as well as in cancer cytogenetics, this was different.

AM: Okay. You've mentioned this in some of your other articles, and I think in your other interview, that you would get the Sunday morning sessions at the Hematological Society meetings and do this preaching about the relationship of chromosomal abnormalities and cancer, and you did this for several years. What was it about either the field of cancer -- or if we could call it cancer genetics at that point -- or our understanding of chromosomes and chromosomal abnormalities that you kind of needed to proselytize this idea?

JR: Cytogeneticists get their material from hematologists, so the first people you have to persuade that they should share a sample of the patient's bone marrow with you are the hematologists. You had to show that it was in their interest, and in their interest in how they would treat a patient, to have this information. Back in the late seventies, which is when I was giving these talks in the education sessions for the Hematology Society, we still didn't have good data showing that it was really important for the patient clinically, but at least we could say -- and I had discovered several more translocations by that time, each one uniquely associated with a particular kind of leukemia and then with lymphoma -- we could say that these are important chromosomal changes which represent unknown genetic events, but whatever they are, they are associated with a particular type of leukemia or lymphoma, and when we understand better, we're going to see what they involve. But at least, in the meantime, you should be getting samples on your patients so that we as cytogeneticists have the samples and can look at them.

AM: This is a bit of a tangent, but I'm going to bring it up because I was reading through the transcripts of the President's Council on Bioethics[94] and it came up. From my perspective, even you getting the cells from Jacobson and kind of saying, “Okay, let's just take a look at this”, and [the] environment *now*, in which we have HIPAA [Health Insurance Portability and Accountability Act][95]

[94] President's Council on Bioethics, commissioned in 2001 by President George W. Bush, was created primarily to advise the president on issues relating to bioethics raised by medical science and technology, such as cloning, sex selection, stem cell research, etc. President Barak Obama has since disbanded the council. For more information, visit the website at: http://www.bioethics.gov/

[95] HIPAA, Health Insurance Portability and Accountability Act protects individuals health insurance when they change or lose their jobs. It also includes guidelines protecting patient privacy and provision for the

regulations, could you have done the same kinds of work with the cells that you received from Jacobson in that time period? Is the kind of research that you did in the sixties and seventies possible in this post-HIPAA age?

JR: It's extremely difficult now to do that kind of correlative work. That is, here's a chromosome pattern, what happened to the patient? Were these chromosomes associated with good outcome, bad outcome? That is difficult, though if you have all the proper protocols, then you can proceed. What was true in hematology then and is now, and particularly now, is it's established that chromosome changes are so important as prognostic factors. This is a perfectly reasonable, legitimate diagnostic test to give the physician the information he or she needs to treat the patient adequately.

So getting the sample wouldn't have been a problem. To then go back and say, “Okay, what are the clinical correlates of this particular pattern?” -- that's difficult. Now, at least with older samples, to use them for molecular studies when the patient didn't necessarily consent to have their sample studied molecularly can pose problems as well.

AM: So what's your assessment of HIPAA and the privacy act?

JR: I think that it's being interpreted far too narrowly. That's particularly true in academic hospitals because several of them have been cited by HHS [United States Department of Health and Human Services] and all of their grants withdrawn or stopped [such as John] Hopkins, for example, Northwestern [University], University of Illinois. And it's very time consuming and really disruptive to have to go back and either change the procedures you're using or justify why what you did was not really illegal. I think that it's just gone to the extreme.

AM: And in terms of clinical research, what is the impact on progress and clinical research because of HIPAA? Is research inevitable, do these regulations just add barriers that can be overcome? What is it?

JR: I think there's a good example from Lou [Louis M.] Kunkel[96]. Lou got a hundred samples of breast cancer, actually got a hundred samples presumably of normal DNA from individuals who had breast cancer, and found that five of them had BRCA1 mutations. Because the samples were unlinked to clinical information, he doesn't know which five of the hundred have BRCA1 mutation. So you have to go back and do the DNA analysis on a hundred women, all over again, to do that. Now, that was the way he could get the samples because they were unlinked to any patient identifier.

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maintenance of that privacy in the midst of the growing digitalization of health care records. For more information, visit the website at: http://www.hhs.gov/ocr/privacy/hipaa/understanding/index.html

[96] Louis M. Kunkel specializes in neuromuscular diseases and currently works at HHMI (Howard Hughes Medical Institute) as an investigator and professor of pediatrics and of genetics at Boston Children’s Hospital and Harvard Medical School.

AM: Let's go back. You have this pretty much path-breaking paper that comes out in *Nature*. What's happening at the University of Chicago? Are you still in your little area with your microscope, with the title of Research Associate?

JR: I was given larger space in the late sixties, so as laboratory space opened up, I got probably a two hundred square foot lab and a full-time technician that was supported by Argonne [Cancer Research Hospital]. Then after discovering the translocations, and certainly by '74 or '75, I was applying for NIH grants on my own. So I began to get NIH grants to support the work, as well as getting funding from the Atomic Energy Commission.

AM: Did you have any institutional support, salary support, other than space from the University of Chicago?

JR: Not really. I pretty much was supposed to be responsible for providing my own support, except that because I did have the support still from the Atomic Energy Commission, they were picking up what the NIH grants didn't do. If I wanted to expand the lab and have more technicians, I had to find the money to do that.

AM: So how did this work change the way you approached your research program? You now were a serious player, and you were worried about being scooped. This wasn't just a hobby anymore. What changed?

JR: Many things changed. I really worked full time, and finally in 1975 I actually officially asked the university to put me on the full-time payroll rather than three days a week. Previously, because I was involved in teaching the medical genetics class and some other things, other faculty members proposed that I become an associate professor. [I had become an associate professor] I guess in 1969 or so. I'm vague on the dates.

AM: Was that a faculty position, or were you more research, or a full faculty position?

JR: That was a faculty position but not tenured.

AM: Okay. You mentioned before that when you were at the University of Chicago there wasn't any genetics being taught in medical school. When did you start teaching medical genetics? And (I take it) to medical students?

JR: That's right [I taught medical students]. It was a class for sophomore medical students. It was a half credit course, so I think they had lectures three times a week for the quarter, and different members of the faculty taught different areas. The instigator of that was really Bernard [S.] Strauss, who was probably a professor, and maybe at that point chair of microbiology. He realized that the students needed to have exposure to genetics, so I gave six lectures to the

medical students on cytogenetics. Probably it was the late sixties, early seventies. I'm not sure. I was involved maybe for six or seven years in that capacity.

AM: What about graduate students in the basic sciences? What kind of genetics were they being taught then?

JR: I don't have a clue.

AM: Did you have any basic science students taking your classes through the medical school, the medical genetics class?

JR: We certainly could have had some, but it wouldn't have been very many. It would have been primarily medical students.

AM: What was the response of medical students to your course?

JR: Oh, they thought it was awful. I got reasonably good comments, and students were reasonably polite. You also have to realize that students in the late sixties and seventies were very, very difficult, at least U of C medical students. The Vietnam War was on. [There was] a real sense that they wanted to be taught things that were strictly clearly going to help them as doctors, and much as you might try to help them to see, they didn't see that medical genetics was anything they needed to do and it was an extra class that was just thrown at them as a requirement. They were pretty disenchanted, by and large.

Some of them did appreciate it. Actually, at Alumni Week this past Friday, one of them, coming back for a fortieth reunion, said that he really remembered cutting out his own karyotype, because Bernie [Strauss] in the microbiology lab had them do PHA-stimulated peripheral [phytohemagglutinin] blood cultures on themselves, and I offered to help them karyotype themselves. So for some people it had an impact.

AM: Up till the point where you were still teaching the class, or still involved with the teaching of medical genetics at Chicago, how did these attitudes change over time, or have they?

JR: Well, I think they're much different now, but I think the class is taught by individuals who were directly responsible for the clinical care of patients with genetic disorders. During the time I was involved in it, the students maybe became a little bit more mellow, but I don't know that they thought it was a particularly valuable use of their time.

AM: And at that point, this was just a course. Medical genetics at the medical school didn't have any higher organization than that?

JR: That's right.

AM: What about your colleagues? Were you able to convince them that cytogenetics and cancer genetics may be an important research program that they should invest resources in and attract faculty to?

JR: Well, that question has several parts. One is, my colleagues in hematology were supportive of what I was doing and by and large we were successful. This was especially helped because Harvey [M.] Golomb[97], who was a Fellow with [Victor A.] McKusick[98] in medical genetics at Hopkins, decided he wanted to go into oncology, Hem/Onc [Section of Hematology/Oncology]. He moved to the University of Chicago as a Fellow, and he and I together decided -- this was in '73 -- that we would do a consecutive series of patients with acute myelogenous leukemia and try to see what the chromosome pattern was in every single patient, and then subsequently try to relate it to the patient's response to treatment. So Harvey also had a vested interest in seeing that I got every sample. And as a hematologist, even though he was the most junior one in the section, he got his colleagues to be sure that they sent samples to the lab. I then was assured of a source of material. As to what impact it had on other faculty on campus, I'm really not sure.

AM: Okay. When I was looking at the website, there seems to be two departments, the Department of Biochemistry and Molecular Genetics and then the Department of Human Genetics within the medical school. Maybe you can talk about how genetics or human genetics was raised to the departmental level, whether at the medical school or within the Graduate School of Biological Sciences.

JR: You really have to look at the Biological Sciences as a division with a single dean. The basic science [departments] underwent several different reorganizations. There was a Department of Microbiology and there was a Department of Biophysics and a Department of Biochemistry, then Zoology and Botany, et cetera. A number of those departments were reorganized, and I'm going to guess it was in the middle eighties, to [Department of] Biochemistry and Molecular Biology, and [the Department of] Molecular Genetics and Cell Biology. So those are the two large departments that sort of incorporated all the other smaller departments, and Botany and Zoology became part of [the Department of] Molecular Genetics and Cell Biology. Then the Drosophila [studies] (we've always had a strong role in evolutionary biology) and there was a separate Department of Ecology and Evolution and an Anatomy Department.

But human genetics didn't really exist, and I thought that this was really a great misfortune. I should add that we had also a Committee on Genetics. We

[97] Harvey M. Golomb specializes in hematology and oncology and is currently a professor at the University of Chicago Medical Center.

[98] Victor A. McKusick (1921-2008), a pioneer medical geneticist, is widely considered the founding father of the field. He was University Professor of Medical Genetics at Johns Hopkins Hospital. He founded the first medical genetics clinic at Hopkins in 1957 and he was the creator and editor of Mendelian Inheritance in Man. An interview with Dr. McKusick is available in this collection.

had a training grant that supported pre-Ph.D., predoctoral, as well as postdoctoral Fellows, and that was administered by the Committee on Genetics. People from all the different departments could be members of the committee, so there were some people in the medical school who were particularly interested in genetics who could be members of the Committee on Genetics.

I was a member of the Committee on Genetics. I also had a secondary appointment in [the Department of] Molecular Genetics and Cell Biology. Once I became a member of the National Academy of Sciences, I was considered appropriate for being a member of that department.

But we were really very, very weak in human genetics. There were a few people in pediatrics who were interested, there were people in obstetrics who were interested, as well as, [who were] obviously physicians taking care of patients with genetic disorders. But it was very fragmented, and as I went around to other institutions, I could see how the lack of a focus on human genetics and medical genetics was really a detriment to any of these areas of science at the university.

So, I proposed to the dean that we begin to look at the question of setting up a department. Departments, of course, cost money and deans aren't anxious to spend more money, necessarily, unless you can show that there's a good reason for it. Then you have to get support not only within the division, but you have to take it to the university faculty and finally to the board of trustees, and all of them have to approve before you can develop a department. You also have to show that if the department's going to grant degrees, that there's an adequate academic training/teaching program, as well as opportunities for students to do research to qualify for a Ph.D. So it's not a simple matter. I was chairman of the committee that reviewed both human genetics [and] medical genetics departments elsewhere and could show that we desperately needed it.

My own preference, really, was to reorganize [the Department of] Molecular Genetics and Cell Biology, take the genetics out and make a Department of Genetics. It seemed to me -- and I'm going to be vague on the dates -- by the early 1990s maybe, David [H.] Ledbetter[99] was the first chair of the department, so it was l988, '89 [that we established the Department].

The faculty committee that looked at the question of human genetics was broadly based, including people in statistics who had been working with faculty in the biological sciences on genetic problems. We managed to pass all of the hurdles, both within the faculty of the division, the university, and finally the board of trustees, so then a Department of Human Genetics was developed.

The question was should it be human genetics or medical genetics? I thought that medical genetics was too narrow a term and that it should at least be human genetics. As I say, I would have preferred to reorganize the division and make a Department of Genetics, but the status quo was too hard to overcome.

[99] David H. Ledbetter, who specializes in genetic causes of developmental disabilities, made important discoveries in chromosomal abnormalities in graduate school. Later he became chair of department of Human Genetics at University of Chicago, and is now a professor in the Department of Human Genetics at Emory University School of Medicine.

AM: Just to get at this a little bit more, why did you see creating a more broadly defined genetics department that would include molecular genetics and human genetics be better than the way that it was being divided between molecular genetics and cell biology and human genetics?

JR: Well, because there was no human genetics, and we were just missing out on a very important part of science. In the biomedical sciences broadly interpreted, we were missing out. This was long before the sequencing of the human genome, but we were being left behind.

AM: And what was the justification to keep molecular genetics separate from human genetics -- just to get a fragment of genetics?

JR: It would have taken a lot of effort, and probably spending some political capital, to take a department that had been functioning (more or less) and take genetics out. People in yeast genetics didn't fancy themselves being with a lot of people doing human work. I don't know about other places, but certainly here at the university, there is this distinction between those who work on, quote, “basic problems” using yeast or C. elegans [Caenorhabditis elegans[100]] or Drosophila, and those [who] applied genetics, working on the same genes in patients. We're sort of second class citizens, which is an untenable position but it's held by a number of my colleagues.

AM: Where did other mammalian geneticists, say mouse genetics, fall?

JR: We had no mouse genetics, so it wasn't an issue. We had lots of people in pathology working with mice, and immunology, et cetera, but we basically had no mouse genetics.

AM: And what has been the impact of creating, at the departmental level, a Department of Human Genetics, and what, if any, have been the consequences of keeping the human genetics separate from molecular genetics?

JR: I think the Department of Human Genetics has become an important intellectual force in the division. It's small and it still is new, but it has excellent faculty, focusing in large part on population genetics or the genetics of complex traits. As I say, David Ledbetter was the first chair of the department, and then when he left it went to -- we just recruited [T.] Conrad Gilliam[101] from Columbia, who's interested in trying to identify genes that are important in complex genetic human diseases. I think that with his arrival, the department is going to be even stronger, with a greater emphasis on and more resources to use bioinformatics,

[100] C. elegans: Caenorhabditis elegans is a small nematode (round worm) found in the soil of temperate regions. Sydney Brenner began using the worm in genetics research in the 1960’s. For more information, visit the website at: http://elegans.swmed.edu/

[101] T. Conrad Gilliam, currently the Chair of the Department of Human Genetics at the University of Chicago, specializes in genetic disorders of the nervous system. Previously he was Director of the Columbia Genome Center.

because this is an area that we're not strong in -- in the division -- as we ought to be. With the present dean, there is very great support for improving bioinformatics.

AM: Have there been any disadvantages to dividing genetics narrowly into human genetics and molecular genetics?

JR: I think there certainly is some intellectual disadvantage of treating the genes that function in yeast and Drosophila as different from the genes that function in humans, but where individual faculty chooses to collaborate or see the unity, there isn't any impediment. Particularly all of the individuals can be members of the Committee on Genetics. The Committee on Genetics still has students applying to it and [it] supports students. It also supports students in departments – Ecology, Evolution, or in Human Genetics. So there is a meeting ground. I think the Department of Human Genetics has been very attractive for students. They get a number of graduate student applicants and students matriculating within the department for degree programs, and that's due to the strength of the faculty.

AM: I'm going to be throwing out some very broad questions. I find it fascinating that you could be considered also a molecular geneticist at this point, and your work and interest in these consistent chromosomal translocations has shown that there are homologs in other organisms, like Drosophila, so that you can fit into many different boxes if you choose to divide genetics into these different [categories]; molecular genetics or human genetics versus medical genetics.

We really haven't gotten to your move from cytogenetics, where your work in the seventies seems to be like the top hit list of identifying important translocations, to then moving into the molecular age and cloning genes. I guess what I'm trying to do is move this into how your own work has kind of defined you as what kind of geneticist, and what kind of intellectual grounds do you get stimulated by? Where do you look to? What kind of genetics do you look to to help your own research program develop?

AM: Firstly, I would say that, though I am a cytogeneticist, I've never thought of myself as a geneticist. I'm a physician, and I happen to be in a Section of Hematology/Oncology, though I have absolutely no training in that area. But my intellectual interest has really been in cancer biology, and particularly that area of cancer biology that chromosomes can provide some insights as to the genes involved in the processes.

It was pretty clear to me as we were discovering all of these different translocations, not only in my lab but in others, and they were specifically associated with different kinds of leukemia, that it had to be something about the genes at those translocations that were critical. They were different, of course, in each one because different chromosomes were involved. But what was going on? That was really a major question.

How having said I'm not a geneticist, I had a wonderful trip probably late 1970s visiting Barbara McClintock[102] at Cold Spring Harbor [Laboratory]. I was going to a meeting in New York City and I wrote and asked her if I could come sometime before that meeting, if it were convenient with her, and just meet with her and talk with her about chromosome translocations. She was very gracious. [She said] I could come, we set the time, she met me at the train from Long Island Railroad and took me to Cold Spring Harbor. I spent the afternoon, then she took me to the train and I went back to New York City.

She not only showed me her lab and all her stocks and talked to me about her personal life, but also this question about translocations, because why did specific translocations occur? Were there any precedents in biology that would help to explain this? She talked to me in terms of genome instability, and once some event happens, then that rearrangement then destroys the order in mitosis[103] and all sorts of things happen. Of course, she was famous for lots of things, but particularly [for] transposable elements, which jump around. That was sort of her view of translocations.

But I went to a number of people trying to say, "What would explain these consistent translocations?" There wasn't any explanation, and there wasn't an explanation until they actually were cloned and we could find the genes. That was something I was searching for for a long time, and I was therefore really excited in 1982 when Carlo [M.] Croce and Bob [Robert C.] Gallo[104] collaborating, as well as Phil [Philip] Leder[105] independently, cloned the breakpoint[106] in the (8;14) translocation and showed that it was *MYC* on chromosome eight and the immunoglobulin heavy chain gene on fourteen that were right at the breakpoints that were rearranged, and that this led to an altered expression of the *MYC* gene[107], which by then was known to be a proto-oncogene[108] because it had first been identified in a retrovirus.

AM: So how does one become a very excellent cytogeneticist into a cytogeneticist who used molecular techniques, which seems to me is very

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[102] Barbara McClintock (1902-1992) was a Nobel Laureate in 1985 in Physiology or Medicine and one of the most exceptional cytogeneticists in history. Her work in maize genetics led to her discovery of genetic transposition, perhaps her greatest scientific achievement. For more about her, visit the website at: http://profiles.nlm.nih.gov/LL/Views/Exhibit/narrative/biographical.html

[103] Mitosis is a process occurring in eukaryotic cells during which a cell divides its chromosomes, creating two identical sets of chromosomes. Normally, mitosis is followed by the division of the parent cell into two, each of the daughter cells carrying genetic material identical to the parent cell. For more information, including animation of mitosis, visit the website at: http://www.biology.arizona.edu/cell_bio/tutorials/cell_cycle/cells3.html

[104] The ground-breaking paper: Riccardo Dalla-Favera, Marco Bregni, Jan Erikson, David Patterson, Robert C. Gallo, and Carlo M. Croce, “Human c-myc onc gene is located on the region of chromosome 8 that is translocated in Burkitt lymphoma cells,” Proc. Natl. Acad. Sci. USA, 1982, 79 , 7824–27.

[105] Leder’s paper on same topic: R. Taub, I. Kirsch, C. Morton, G. Lenoir, D. Swan, S. Tronick, S. Aaronson, and P. Leder, “Translocation of the c-myc gene into the immunoglobulin heavy chain locus in human Burkitt lymphoma and murine plasmacytoma cells,” Proc. Natl. Acad. Sci. USA, 1982, 79 , 7837–41.

[106] Breakpoint [cluster region] BCR, is a gene found at the translocation breakpoint on chromosome 22 in the Philadelphia chromosome and associated with CML.

[107] MYC is a gene which codes for a protein which binds to the DNA of other genes. If the Myc gene is malformed, it often causes cancer.

[108] A proto-oncogene is the healthy version of a cancer-causing gene.

technologically driven and very technologically intensive? You yourself admitted that you have a keen eye but not really good hands.

JR: I've never isolated DNA from anything. I recognized that if we were going to make progress, we had to have people who could actually work with the DNA and isolate genes at breakpoints. Harvey Golumb, who I mentioned earlier as a Fellow who worked with me in the seventies and saw that we got the patient material, he and I continued to collaborate very closely. He became head of the section. And in 1981 when he became head of the section, he was given additional resources by the chairman of the Department of Medicine, and some additional space, and he gave that space and those resources to me. So together we could recruit somebody who knew how to manipulate DNA, who could begin to do the molecular analysis of chromosome abnormalities.

The person we recruited was Manuel [O.] Diaz[109], who had been working with Joe [G.] Gall at Yale [University]. Manuel came and set up the laboratory, had a technician who worked with him, and we began. Very fortunately, at the same time, I also recruited a new young Fellow, Michelle [M.] Le Beau[110], who had gotten her degree with Joe Leigh Simpson[111] in, I believe, sex chromosome abnormalities in patients. Parenthetically, Joe thought she was foolish to change from human genetics to cancer cytogenetics, that [cytogenetics] was a dead-end field if ever there was one.[Laughter]

But Michelle came, and she and I worked together. Of course, now she's extremely well known, and she's director of our cancer center. She moved to using modern techniques, labeling of DNA, so she and Manuel could work together. In terms of isolating DNA probes, she labeled them and did autoradiography, initially looking at the location of different genes on chromosomes. Later she used fluorescently labeled probes and did FISH [fluorescence in situ hybridization] and helping to map genes.

With the two of them, we were able to approach the question of cloning translocation breakpoints that we'd identified. I'm very much a saver, so we had saved extra bone marrow cells on patients that we had done karyotype analysis on so for many of the patients, we could just go back to our stocks and isolate the DNA and look at the breakpoints.

AM: Before Le Beau and Diaz, how well and what kind of backgrounds of students -- graduates or postdocs -- were you attracting?

JR: I had students of various backgrounds, Ph.D.'s mainly, who were interested in cytogenetics and who then wanted to come and study the

[109] Manuel O. Diaz, educated in Uruguay, is currently a professor at Loyola Marymount Medical Center, Department of Hematology/Oncology and Director of the Program in Molecular Biology. For more, visit his faculty profile at: http://www.stritch.luc.edu/node/562

[110] Michelle M. Le Beau, a cytogeneticist, is a professor of hematology and oncology and Director of the University of Chicago Cancer Research Center as well as Director of the Cancer Cytogenetics Laboratory there.

[111] Joe Leigh Simpson was both Chair of the Department of Obstetrics and Gynecology and a professor in the Department of Molecular and Human Genetics at Baylor College of Medicine. Currently he is Executive Associate Dean of Academic Affairs of the College of Medicine at Florida International University.

cytogenetics of various leukemias. One of the very first postdocs I had was Joe [Joseph R.] Testa[112], and he's now at Fox Chase [Cancer Center] working on solid tumors. Joe was there when we first were beginning to identify the (15;17) translocation in acute promyelocytic leukemia. I'd identified the translocation and the paper was published in 1977, but Joe came a couple of years after that and we had many more patients to look at. So he looked at the additional chromosome abnormalities that were present in some leukemic cells, as well as the translocation, and worked with Harvey Golumb, as well as clinical Fellows, to see what the correlations were in terms of response to treatment and outcome.

I was also very fortunate to have Dr. [Shirou] Fukuhara[113] come from Japan, from Kyoto [School of Medicine]. He was interested in lymphomas. I'd never studied lymphomas, but that's what he wanted to do. My view is you let people do what they want to and try to direct it. He had these awful chromosomes from these lymphomas that he obtained, but together it was a fair amount of guesswork. It seemed to me that all of the ones of a particular type as defined by our pathologic colleagues had the (14;18) translocation, so we discovered the (14;18) translocation as a recurring translocation in a particular subtype of lymphoma. I think that was published in '79. The focus was entirely on chromosomes and what you could learn by studying the chromosome pattern in various subsets of tumors.

AM: Yesterday you mentioned that when you got these cells from Jacobson you knew nothing about cancer biology, and now you're certainly seen as an international leader in cancer biology, cancer genetics. You've won all the prestigious awards, including the National Medal of Honor. How does one go from knowing nothing about this in the sixties to becoming a leading expert within twenty, twenty-five years?

JR: Firstly, you give me too much credit. I've never shied away from asking what appear to be dumb questions. We don't have [lab meetings] anymore because I don't have a large enough group, but we used to have regular lab meetings. This included several different senior investigators, so our students and postdocs and technicians would all get together. As people presented things -- how you went about isolating DNA, what the pitfalls were -- I kept pushing them to explain things to me. How did you know that, or why did you do this, and why didn't you do that? They were very, very good about explaining to me on a very elementary level the various aspects of working with DNA and the pitfalls of incomplete digestion and all sorts of other things. On a technical level, I tried to understand what was involved and what the problems were, even though I didn't do it myself.

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[112] Joseph R. Testa, who earned his BS at Southern Connecticut State College, is currently Chair in Human Genetics and Co-Director of the Cancer Biology Program at the Fox Chase Cancer Center. For more about Testa's life and career, visit the website at:
http://www.southernct.edu/alumni/southernmag/07winter/features/p10.html

[113] Shirou Fukuhara was Assistant Professor of the First Division Department of Internal Medicine Faculty of Medicine, Kyoto University. Later Fukuhara did research at the First Department of Internal Medicine, Kansai Medical University, in Osaka.

Similarly, in cancer biology -- and you have to remember that in the eighties and nineties, cancer biology was very, very much simpler. You could count the number of cancer genes on two hands. All the interacting pathways that you see now that are mind-boggling in complexity, that wasn't apparent. It was a simpler view of cancer in the nineties than we have today, and I wouldn't begin to pretend that I understand all of the complexities of the RAS pathway or MAPs [mitogen-activated proteins] and MEKs [mitogen-activated or extracellular signal-regulated protein kinases] and ERKs [extracellular-signal regulated kinases], and whatever. I understand the general melody but not the specific notes.

VIII. The Politics of Genetics: Nixon and the War on Cancer and fragmentation among geneticists

AM: It seems that as you were deciding to move your scientific career into a full-time mode, [Richard M.] Nixon was declaring war on cancer and created the National Cancer Act[114] in 1971. What was the impact of making cancer research a national agenda, [or] an item at least in the national agenda, on your own career, whether you want to look at it in terms of funding or attracting attention to your work?

JR: It had an impact in all those areas. Firstly, by 1986 I had five NIH grants, four RO1s and one PO1, so funding was relatively easy to get. I was fortunate that I had made important contributions, so I could have a grant for myeloblastic leukemia, acute lymphoblastic leukemia, for lymphoma. I also had shown that patients who received various kinds of chemotherapy, some portion of these patients subsequently developed acute leukemia which was *likely* induced by the treatment they had for their prior cancer. So I had a grant for that. So funding was easy.

Many people were very interested in chromosome abnormalities, and especially in the eighties and early nineties, as we became better known as a laboratory for cloning translocation breakpoints, people were interested in identifying those genes and coming to work in the laboratory. I had many inquiries, both from Europe and Japan, as well as students that were matriculating at the U of C, come and work in the lab. So it was an exciting place, and I had a lot of money.

AM: Did you think that the stakes or the expectations were raised for *you* in terms of what your research needed to accomplish?

JR: Well, the stakes were raised in the sense that there was more competition. Back in the sixties, who went into cytogenetics? That was a backwater, and nobody who was interested in being famous was going to do that. You were a virologist or you were an immunologist. One could lead a relatively calm

[114] National Cancer Act, enacted in 1971 by President Nixon, was legislation intended to promote cancer research with the goal of eradicating cancer as a major cause of death in the US.

intellectual life in studying cytogenetics, and weren't they interesting? and wasn't it fun to find something new? And all of a sudden, there were a *lot* of people.

Once you get into the molecular era in '82, then there was a great deal of competition amongst various people for cloning breakpoints. And there was serious competition in one of the last breakpoints that we mapped and cloned in our own lab. We published the mapping of a translocation that involved 11q23 in a number of different acute leukemias, both lymphoblastic as well as myeloblastic leukemia. I published a paper in PNAS [*Proceedings of the National Academy of Sciences of the United States of* America; Rowley JD, Diaz MO, Espinosa R 3rd, Patel YD, van Melle E, Ziemin S, Taillon-Miller P, Lichter P, Evans GA, Kersey JH, et al. (1990). Mapping chromosome band 11q23 in human acute leukemia with biotinylated probes: identification of 11q23 translocation breakpoints with a yeast artificial chromosome. PNAS 87(23):9359-62.], I think in 1990, showing exactly where that breakpoint was and which YAC [yeast artificial chromosome] contained the breakpoint.

Then a number of other laboratories went on from those studies, and four people cloned the breakpoint, including our own lab, within a year. Each one called it something different. I am fortunate that the name I chose is the name that is now generally accepted. But it became very competitive.

AM: Again looking through the transcripts of the President's Council on Bioethics, one of the papers discussed research imperatives. In part of the debate, which included text from you, you had mentioned in this particular context that there can't be any research imperatives. I would like to move that (taken out of context) and talk about the War on Cancer and Nixon's agenda and ask if that wasn't a type of research imperative, directed by the state.

JR: The War on Cancer could be interpreted as a research imperative in that sense, but then how [that research] was carried out was left to the creativity of the individual investigator. It was assumed at that time that viruses were going to play an important role in cancer, so people spent a lot of time looking at viruses. It turns out that certainly viruses are now shown to be involved in *some* cancers, but based on animal work, it was assumed that the RNA tumor viruses held the key. And it turns out, in human cancer, that it's probably the *DNA* tumor viruses that are important. Nonetheless, they discovered that the RNA viruses had picked up unique human genes and altered not only the protein produced by the gene but the level of expression in ways that led to cancer. Those are the so-called oncogenes for which [J. Michael] Bishop and [Harold E.] Varmus[115] got the Nobel Prize. Now, they did that work in Peter [K.] Vogt's[116] laboratory, and Peter Vogt started it, so one of the deficiencies of the Nobel Prize selection committee is that the major player in that didn't get recognized. But that's an aside.

[115] J. Michael Bishop and Harold E. Varmus received the 1989 Nobel Prize in Physiology or Medicine for their discovery of the cellular origin of retroviral oncogenes. For both their brief autobiographies, see their page on the Nobel Prize website at: http://nobelprize.org/nobel_prizes/medicine/laureates/1989/

[116] Peter K. Vogt currently does research at the Scripps Institute.

All of a sudden we had all of these human genes taken over by viruses, and once you found the human gene or the mammalian gene in the virus, you then had DNA probes to go and say, “What are these genes doing in tumors? How do they differ from normal genes?” And that opened up the field. That's not what they expected to find, but it is [what they found]. I think that [the War on Cancer] gave money to focusing on RNA and DNA and the techniques that went along with being able to work with these, which were applicable to all of biology. I think that [the War on Cancer] benefited many, many areas, as well as cancer.

AM: How do you assess the creation of the National Cancer Act and the War on Cancer so far? And the second question, is this a model that we should use to go about funding research?

JR: Your first question --

AM: How successful has the War on Cancer been?

JR: The War on Cancer was very successful in showing us the complexity of human biology, which we still don't fully understand. When people say, “Here we've had this war and some forms of cancer are increasing in incidence”, at certain periods of time that's partly because of human lifestyle so that the failures there are, in a sense, of our own making. But I think that by really opening up the complexity of cellular biology, it's been important.

I think that in regard to your second question, you can say the human genome project was, in a sense, another major federally-funded attempt to do big biology. Now, we're going to understand so much about not only human biology but the nature of genomes in multiple organisms based on the human genome. And of course now the NHGRI [National Human Genome Research Institute] is funding the sequencing of many other species, not only mammalian but multiple Drosophila species and yeast, so we're getting an enormous database. We don't have the bioinformatic tools to figure it out yet, but those will come because scientists need them, so people will work on how to do it better.

My concern is that we focus on doing this kind of big science and don't always look at the other things of which we're ignorant. One of the things that came out of the human genome project in 2010 was that there appear to be about twenty-two thousand protein coding genes. People had numbers up to over a hundred thousand genes, so that there are so few is a shock to everybody. You could say, “Well, you can develop a functional human being with those few genes because the cell uses alternative splicing, so all the different splice forms can have different functions, and that's it.”

Our own work of using SAGE [Serial Analysis of Gene Expression] to study cells -- that's a technique developed at [John] Hopkins [University] by Ken [Kenneth W.] Kinzler[117] in Bert Vogelstein's[118] group -- you look at all the transcripts in a cell, and we found that many of those transcripts were not in any

[117] Kenneth W. Kinzler is a professor at the Department of Oncology at Johns Hopkins in
[118] Bert Vogelstein is a noted oncologist and pathologist at Johns Hopkins Medical Center.

database, so they're novel transcripts. I kept asking, "What are these novel transcripts?" Well, now there's a paper from [Thomas R.] Gingeras[119] in *Science* also showing that if you use Affymetrix [Inc.] microarrays [and] genomic microarrays, there are many, many transcripts that we don't understand and don't know about.

What we have to do now as a community is to say, "What's non-coding RNA doing and how is it regulating other genes, how does it influence cell biology?" This is not a question people have been asking because they haven't known it was a question to ask. So I think that we have to keep paying attention to the fact that as we look and see a certain organization and a certain set of questions, that we don't ignore all the other things on the fringes that aren't neat and tidy but that probably are very important.

AM: Some critics would say, on the War on Cancer, [that] we really haven't won, and with the human genome project, that was a *lot* of money to find out some information, but still the public has no better means of dealing with [the] disease. From their standpoint, support was promoted with the hype of the human genome project and the hype of the War on Cancer, which was a presidential election agenda item, but the human genome also got a lot of press, and this was going to be a major breakthrough.

But for the average patient who comes in with a form of leukemia, it's still not generally sensed it's a good thing, that this is something that we can always necessarily treat across the board. Certainly your work and your involvement in drug therapies have changed that, but still, cancer is a bad word. It's not quite clear, (since we don't know what all the genes do, [but] we know what these genes are) to the average lay person.

You're speaking to a member of the choir, but to stand on the other side -- how do you justify all this money and yet there is no cure for cancer? We know what the genes are, but we have no idea what they do, and we certainly don't know [how to cure cancer]. Systems biology is just getting underway, and gene interactions we don't understand, and gene interactions with the environment we still don't understand. So exactly what has been accomplished by either the War on Cancer or the human genome project?

JR: If we go back to the War on Cancer, we used to think of cancer as sort of a single process, and work in the leukemias showed, at least based on chromosome patterns, that it wasn't one disease but each leukemia, or each subset of leukemia, had its own unique genetic changes. I think it's very clear that that's what's happening in the solid tumors as well, that breast cancer and lung cancer are multiple different types of tumors and that each one has to be both diagnosed in terms of the specific genetic changes and then treated in individual ways.

We certainly know this in the leukemias. Gleevec® is great for CML [chronic myelogenous leukemia] if you have the Philadelphia chromosome. It

[119] Thomas R. Gingeras was a professor and Head of Functional Genomics at New York University. He is Vice President Biological Sciences at Affymetrix, Inc.

doesn't [necessarily] work on other kinds of leukemias. Herceptin® now is clearly wonderful for patients with breast cancers that express high levels of the *HER2/neu* gene but not for other patients. I think that we're learning that we're probably dealing with a thousand different cancers, each one of which will need its own special treatment or modifications on several basic patterns of treatment tailored to fit the genetic changes. In the long run this is going to benefit patients because they'll have more effective therapy and it will be less toxic. But we're still years and years away from getting there.

But as we have success in the War on Cancer, we're equally going to be understanding much more basic biology, because it's understanding of the basic biology in fact that comes back and helps you treat cancer. I think the same thing is going to be true for the genome project, except it's much bigger because it's all the genes, not just those that go awry in cancer. We will, in the future, be able to look at the DNA of a patient and say you have a high risk for this or that, and the prudent thing for you to do in your lifestyle is this or that. We're already doing that for patients with familial polyposis[120], for example. They have frequent colonoscopies to catch any early tumors involving the GI tract[121].

AM: In your own work, how much do clinical genetics aspects play in your research program, your basic science program?

JR: It's all focused on chromosomes, so we continue to clone chromosome translocation breakpoints, depending on whether it involves genes that we're interested in or not. Many of the translocations in the leukemias involve basically two chromosomes, but then you'll see variant translocations where one chromosome is still involved but with a different chromosomal partner -- What's that gene? -- How is it different from the most common translocation? We continue to clone translocation breakpoints.

The gene that I mentioned on chromosome band (11q23), what we call the myeloid-lymphoid leukemia gene[122] or *MLL*, has at least sixty different partners. Now why is that? You have one gene on chromosome eleven involved in sixty different translocations in leukemias. We don't understand that. What's the basis? What is MLL doing to change these genes, or what are the other genes doing to change *MLL*? These are still unanswered questions. Some of them, we're pursuing. I have to say that other laboratories are far more active in this area than we are. We clone the breakpoints and say “Isn't it interesting? These are the genes”, and then that information is available for others to pursue.

AM: You mentioned early on in the interview that you knew that you would never be a clinician, that in some situations that wasn't where your skills lay. How much patient involvement do you have at this point?

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[120] Familial [adenomatous] polyposis is a disorder which causes cancer of the large intestine and rectum. It is genetically inheritable. For more information, visit the website at: http://ghr.nlm.nih.gov/condition=familialadenomatouspolyposis

[121] GI tract: gastro-intestinal tract.

[122] Myeloid-lymphoid leukemia gene; MLL also known as the mixed-lineage gene, is a gene which is associated with leukemia.

JR: I don't have any patient involvement and haven't in Hem/Onc because this is not an area that I'm at all trained in. It's interesting that at least several of the patients who have particular chromosome abnormalities know that I have studied their abnormalities. One of them was a teacher at the Laboratory School, so I knew her and her husband, and we had different a relationship. But by and large, I don't have any contact with patients.

AM: What significance did your medical training have on the kind of very basic research that you ended up doing?

JR: I always relate what I'm doing in the lab to how it's going to influence patients, either to improve more precise diagnosis of patients, particularly in the leukemias and lymphomas, or how can we use this information to improve treatment for the patients. I haven't been involved in any kind of drug development, but it certainly has been at least the focus of how I interpret some of our results for physicians is to say, “This does have an impact on how you treat the patients, and therefore this is information that you should have for [the] medical benefit [of] the patient”.

AM: I'm going to be jumping around here as we try to wrap things up. You joined the ASHG [American Society of Human Genetics] in 1963 I think -- it’s in one of the articles that you were writing about -- and you became president in 1993, was it?

JR: I guess.

AM: In your presidential address, you mentioned that there was a lot of fragmentation going on in the seventies among human geneticists. What did you think was the cause of this fragmentation? And [you mentioned that] that you had hoped that this organization would be able to maintain some kind of unity. What's the advantage of having an organization like the ASHG to bring human geneticists together and keep them there, so to speak?

JR: There are several different tensions. One is between the geneticists that really are focusing on patients and patient diseases and trying to understand those and also to figure out both what the basis is and (therefore) how one treats those diseases. You have other individuals in genetics worrying about chromatin structure or methylation[123], which does have an impact in some diseases, but they are, if you will, far more basic in their application.

Then there was another whole category of population geneticists, who were really looking in epidemiology[124] census in large groups of individuals to try

[123] Methylation is the adding of a methyl group to a compound. It is catalyzed by enzymes and the process effects genetic expression.
[124] Epidemiology is the study of diseases, especially where and how they occur.

to understand what the impact of the prevalence of alleles[125] of a certain gene were in a population. It was during this period that it was thought that sickle cell anemia[126] actually protected you against malaria, so the reason it was so high in blacks was because of the interaction of malaria and the sickle cell gene in that vulnerable population.

Trying to show all those individuals interested in genetics that they really had a basic commonality of at least some aspect of their intellectual endeavors and that they were far better off being together rather than separating, it seemed to me, was important. Which isn't to say that the separate groups shouldn't also meet as separate groups, but it shouldn't be at the expense of ASHG.

I think the recognition of medical genetics as a medical specialty (Charles [J.] Epstein[127] and David [L.] Rimoin[128] were certainly instrumental in having medical genetics accepted by the American Board of Medical Specialties) was important for legitimizing medical genetics as a proper medical specialty, and of course had financial implications as well. But that did fragment ASHG in one sense.

The same thing has happened in the cancer research community. AACR, the American Association for Cancer Research, was the umbrella organization. ASCO, the American Society of Clinical Oncology, was an offshoot of AACR and now is as big an organization as AACR. Some people belong to both, some go to one or the other. I think to the extent that the practitioners and the users, if you will, of basic knowledge (whether it's genetic knowledge or cancer biology), the users have to still have some close ties to the generators of that knowledge if the strength of the discipline is going to remain.

AM: Okay. Again a really broad question about your own development as a scientist. You came into your research area without any formal training in genetics or human genetics, certainly at a time when there was no real institutional support for these disciplines, and you worked in relative isolation on your project, at least initially. And you flourished and you became successful, and [you have] the accolades and accolades. Why is it important to have these kinds of organizations, whether a board for medical genetics in terms of the medical specialty, or a society in which you can identify yourself as a human geneticist and participate with other human geneticists, when it seems to me that

[125] An allele is one half of a pair of an alternative version of a gene found in a specific chromosome at a specific site on that chromosome.

[126] Sickle cell anemia is an autosomal recessive genetic disorder characterized by the formation of an abnormal hemoglobin protein in the red blood cells, often forming them into the recognizable sickle (or crescent) shape. Patients suffer from anemia, jaundice, severe pain, and organ damage, due to abnormal blood flow and vascular blockage. Sickle cell disease is most commonly found in West and Central Africa and in African-Americans, but is also seen in the Mediterranean area, in the Near and Middle East, and in south Asia. More information can be found at this website: http://www.sicklecelldisease.org/index.phtml.

[127] Charles J. Epstein is a noted geneticist who specializes in Down's Syndrome. He is a professor in the Department of Pediatrics at the University of San Francisco.

[128] David L. Rimoin, currently Steven Spielberg Chair and Director of the Medical Genetics Institute at Cedars-Sinai Medical Center in Los Angeles, is best known for his work on the genetics of skeletal dysplasia, and for his pioneering recognition in 1967 that common diseases like diabetes mellitus were not single-gene phenotypes, but could result from any one of a group of genetic variations. An interview with Dr. Rimoin is available in this collection.

you actually really flourished under a system that allowed you to tap in to so many different areas and pursue what you wanted to do in relative independence, and, I think, your ignorance of the literature, so to speak?

JR: I think that there are multiple answers. The one I would give is that I was very isolated intellectually at the University of Chicago, particularly in the sixties and early seventies. So the societies were extremely important to me. Most important were the chromosome meetings that were held every year, where I could go and talk with other cytogeneticists and see what they were doing and discuss their questions and issues and *my* questions, and [get] a sense that I really wasn't alone in the universe, but [instead that] there were other people who were interested in that.

Because initially I was ignorant of the literature, I certainly, once I got back to the states in '62, was reading journals and keeping up with the literature, at least related to chromosomes in both patterns of replication and then also, as I moved more into hematology, chromosome abnormalities in leukemias and related fields.

I think the societies provided me with a framework and contacts, so if I really had some kind of question, you just could call somebody up on the telephone and talk with them, or write them letters if they were in Europe. For me at least, that was sufficient.

I have to say that all of my colleagues at the university have always been supportive of me. Nobody ever told me what to do, including Dr. [Leon] Jacobson, who was giving me the money, but he never told me what I should do. I felt that people were interested, and whatever I thought I wanted to do was fine with them. And that was okay.

Again I have to come back, I have a husband who was and *is* an outstanding experimental scientist, so I would talk over my problems or my questions or things with him. He didn't know anything about chromosomes or hematology necessarily, but just discussing some of the broader issues with him was always very helpful, *is* helpful.

AM: Again, another broader, more philosophical question; it seems to me that at key periods in your life you were able to go into a very intellectually exciting environment. In Oxford, both times you went to speak with Barbara McClintock, and you learned new technologies, new techniques and learned new ideas. Then you would come back and work rather individually at the University of Chicago. What do you think is more important to scientific progress? Is progress made at the level of the individual, or is it in these kind of critical masses of intellectual ferment or maybe gardens where ideas can be tossed around?

JR: I think it's a mixture. After [our interview] last night my husband and I were talking. He doesn't think I'm as undirected as I make myself sound, but I think I wasn't driven by a single idea. I didn't have a notion, “I'm going to do this and by the time I'm thirty-five this is where I'm going to be”. So I was open to whatever was around. I could just as well have gone into something besides

chromosomes. It just happened to be what seemed logical at the point (being interested in mental retardation and going to Oxford) so that was the path that seemed sensible. I think that I've tried to see what I was interested in or what I was doing, how it could relate to some other question that would be challenging to answer and then go do it. It's certainly been anything but a straight line in terms of my own career. I've spoken about luck or happy chance or things of that sort.

IX. Controversy and commercialism: stem-cell research and medical patents

AM: Okay. Well, to get back to a couple of more tangible questions. In the early eighties, you were a member of the [National] Cancer Advisory Board. I picked this up through some editorials you had written in collaboration with some of the other members about a period on this board in which basic science seemed to be being shunted aside in terms of the composition of this board. I wanted to pursue this a little bit, and to ask what was going on on the advisory board, which served a larger role in terms of its influence on the National Cancer Institute [NCI], that seemed to be raising concerns about developments and that maybe it was becoming too clinical at the expense of basic scientists [and] basic research.

JR: I was on the board I think from '79 to '84. Initially, there were a number of basic scientists on the board, and then after I'd been on the board for a year or two, there were individuals who were clinically oriented, but they were appointed to the board because they'd been major contributors to President [Ronald W.] Reagan's financial campaign. They came often with very narrow views of where the resources of NCI should be focused. I thought that we were not going to solve and improve cancer treatment by focusing on these narrow issues because we still were so ignorant of the basic biology of cancer cells, or of normal cells for that matter.

Rather than put a lot of money in clinical trials, there was the development at that point by Dr. [Vincent T.] DiVita[, Jr.][129] of the [Community] Clinical Oncology Program, the CCOP program, which was bringing in smaller hospitals, trying to have them work with larger cancer centers to improve the collection of untreated patients. I didn't disapprove of that necessarily, but I thought that, to the extent that we reduced the proportion of funding for RO1s (that is - individual investigator initiative research), that that was really the wrong way to go. And because the board was being stacked by people who didn't necessarily have any interest in RO1s, what *I* held near and dear was at risk. The same thing is happening under the present administration.

[129] Vincent T. DeVita, Jr., a pioneer oncologist, was appointed Director of the National Cancer Institute by the President in 1980. He is perhaps best known for the collaborative development of MOPP, a chemotherapy treatment which combines 4 different drugs. MOPP greatly increases the cure rate of patients with Hodgkin's disease. Currently, he serves as Chairman of the Yale Cancer Center Advisory Board and is a Professor of Internal Medicine and Epidemiology and Public Health.

AM: I think that's a great segue to ask you about your role on the President's Council on Bioethics. Initially, I think, it was thought about by [William J.] Clinton and mandated by [George W.] Bush to discuss some of the new technologies that are available in biomedical research. I guess my first question is what was your interest in serving on this national governmental committee, especially since you seemed to have some experience with the Cancer Advisory Board that wasn't particularly -- [since] you saw some things that you didn't like there?

JR: It probably is partly my personality, partly the U of C [University of Chicago], which is you always fight for lost causes. I have to say, when I said I would be willing to be appointed to the President's Council, I had no idea who the other members were. How it was going to be composed was unknown to me at the time that I had my first conversations with Leon [R.] Kass[130]. I did think that it was important for individuals who were concerned about the application of science to public policy that we be at the table to at least express our views. That's still my opinion. I think that we're far better off being there and being in a minority than not being there at all. I can see in a number of the reports, particularly some of the more recent reports that my being involved in editing and reediting and re-reediting the editions makes them more generally thoughtful and somewhat less biased than they would be otherwise.

AM: Leon Kass was at the University of Chicago. I don't know if he still is.

JR: He still is. He still has a faculty appointment.

AM: Did you know him before you went on this council?

JR: I knew who he was, and we had passed pleasantries on several occasions, but I'd never had a substantial conversation with him before he came and asked me would I consider having my name proposed to the White House.

AM: I didn't get through all the transcripts during all the council meetings that you attended, but I'll focus now a little bit on an editorial you wrote with three other council members, and then an article you wrote with [Elizabeth H.] Blackburn[131] in the *Public Library of Science*. It seems to me that this tension between different opinions on this council with regard to stem cell research policy -- what's a neutral way of saying this? -- caused enough tensions that council

[130] Leon R. Kass was appointed in 2001by then-President Bush as Head of his Council on Bioethics. Kass, a well known educator as well as a bioethicist, is known for his strongly conservative views on stem-cell research and on other bioethical issues. He is a professor at the University of Chicago.

[131] Elizabeth H. Blackburn, a renowned Australian molecular and cellular biologist, is currently a professor in the Department of Biochemistry and Biophysics at the University of San Francisco. Perhaps her most important scientific achievement was the co-discovery of the molecular nature of telomeres and the ribonucleoprotein enzyme, telomerase, for which she and her colleagues Carol W. Greider and Jack W. Szostak received the Nobel Prize in 2009. She was also served on the President's Council on Bioethics until Feb. 2004, when her term expired and was (controversially) not renewed. For an interview with Dr. Blackburn about her scientific achievements, see or listen to her interview on the Nobel Prize website at: http://nobelprize.org/nobel_prizes/medicine/laureates/2009/blackburn-telephone.html

members, including yourself and Blackburn, sought outside audiences to discuss what was going on in the council, like your editorial. Can you describe what happened in the course of your experience on the council with regard to stem cell research and where you see the future for stem cell research in this country, at least under the current administration?

JR: I think that we're not alone in writing separate editorials or commentaries. Leon Kass has done that, other members of the council have, so we've all had our individual opinions, or group opinions, published in various fora. We were concerned that the initial vote -- and there's only been one issue on which we took a vote, and that was on stem cells -- that the initial vote was seven people in favor of proceeding with federal funding for embryonic stem cell research with appropriate guidelines in place. Seven people said that we hadn't had enough discussion and they didn't think that the guidelines were sufficient, so they voted for a four-year moratorium. Three members voted against stem cell research because they equated it with murder.

The way the report came out was, the three people joined with the seven who wanted a moratorium, so the final vote was ten to seven, ten people supporting a moratorium and seven of us saying that [the research] should go ahead. We, in our editorial or perspective in *Science* said, given the history and the many presidential commissions that had already discussed this (including the one under Clinton headed by Shirley [M.] Tilghman[132] that came out with guidelines and actually had a board at NIH equivalent to the RAC [NIH Recombinant DNA Advisory Committee])[and were] all ready to step in and supervise stem cell research, then in fact we should go ahead.

We thought that it was really important to try to bring that point of view to the science community, that we as scientists accepted external guidelines and restrictions on what we did and careful review both locally and nationally of any research, but that the research itself had such promise that it should move ahead. And [we wanted] to try and have scientists help to educate their legislators because this was going on in the background, if you will, simultaneous with congressional committees. The House had passed a bill that made it a criminal offense to do any research with human embryonic stem cells, [punishable by] a jail term and a huge fine. The Senate never passed that, so it didn't get anywhere. It wasn't clear what was going to happen, and it was important for scientists to make their views known, not only to Congress but also to various patient groups, who were the ones, really, who had the strongest vested interest in this.

AM: Did Blackburn resign from the council?

JR: No--

[132] Shirley M. Tilghman, a Canadian-born molecular biologist, is currently the President of Princeton University. Tilghman is known for her groundbreaking research in mammalian genetics. For more information about her, visit Princeton's President's biography page at: http://www.princeton.edu/president/biography/

AM: Or did her term come to an end?

JR: Well, you're appointed for two years. We were appointed in November 2001 and in November 2003, Liz's term was not [renewed], she wasn't reappointed, and Bill [William F.] May[133] wasn't reappointed as well. Both of them had actually supported the notion that we'd already had enough discussion [about stem cell research] and [said] “Let's get on with it.”

AM: And yours was renewed?

JR: Yes. Mine and all the other members were renewed, so it was just two people, Liz Blackburn and May, who were not renewed.

AM: What do you think the impact is going to be on American biomedical research if this moratorium continues on embryonic stem cells?

JR: I think it's going to have a very serious impact, particularly because other countries are moving ahead, some of them very aggressively, especially the countries in Asia. South Korea just had another paper in *Science* on how they've improved the efficiency of doing somatic cell nuclear transfer[134]. Chinese, Japanese, Singapore, Hong Kong are all putting major, major amounts of money into this because they see this as an important *commercial* venture in the future.

The only way we're making progress on this in the United States is [in] individual states, California being notable for this. But even in California now there is, as you know better than I do, concern -- and I think it's a legislator whose name is [Senator Deborah] Ortiz[135] who's in favor of stem cell research but feels that the conflict of interest rules guiding who gets the money are sufficiently inadequate, for her at least, [to say] that things have to be modified still further.

The sad thing is that we really don't know whether embryonic stem cells are going to do what we hope they're going to do, but we won't know that without actually proceeding with the research. To the extent that we can do it with as little cost, if you will, in using human embryos or in using oocytes[136] from donors, I think that we're better off. But at the same time, I think that many of these embryos are going to be discarded anyhow. They're already being discarded, and rather than discarding them, I think that they should be available for use for

[133] William F. May, a scholar of medical ethics, was a member of the President’s Council on Bioethics from 2002-2004. May is now Professor Emeritus, and taught at Smith College and at Indiana, Southern Methodist and Georgetown universities.
[134] Somatic cell nuclear transfer is a technique which removes the cell nucleus from an ovum and replaces it with the nucleus from a somatic cell. This technique has the potential to produce cells which are genetically identical to the donor. For more information, including a video of nuclear transfer, visit the website at: http://learn.genetics.utah.edu/content/tech/cloning/whatiscloning/
[135] Deborah Ortiz was originally elected in 1998 to the California State Senate and has drafted important legislation, such as the Cal Grant scholarship program.
[136] Oocytes are egg cells.

thoughtful experiments that will help us to see what the potential for the research is.

Problems in the past have been that the stem cells have been grown on mouse fibroblasts[137]. The Korean research team used human fibroblasts. At [University of] Wisconsin, one understands that Jamie [James A.] Thomson's[138] group has developed synthetic media, so there are no other cells at all. This is the way to go because if you're going to implant these cells into a patient, you want to minimize the possibility of any extraneous either infections or foreign antigens being associated with the cells that could interfere with their usefulness in therapy.

What becomes clear is that we really don't know how you make a human embryonic stem cell turn into a beta cell[139] in the pancreas. It's not going to be easy to figure that out. What is the proper cocktail? There's a great deal more biology that we need to understand. It's interesting, in a recent [article],I think it's in *Nature,* talking about niches and that stem cells of all tissues have preferred locations within whatever organ it is that's involved. They're adjacent to other cells that are both maintaining their stemness but also then instructing them [the cells] to divide. One cell of the two cells that occur after division is on the path to maturation. The other remains as a stem cell. And it's all due, apparently, to their geographic location and their adjacency to critical cells that are nurturing them.

All of this is important for us to understand and will be needed as we try to figure out how to use these cells most effectively to treat patients. It's an area that we should move into, but again, I think that it has to be done thoughtfully.

AM: At one point in one of the transcripts on medicalization, it mentioned that you saw the role of the council as to separate society and politics from these issues and be very cautious about how the council dealt with these issues. That struck me, because it seems to me that, given the current administration's stance *against* stem cell research (which was clear at the time this council was formed), would you agree that it would be possible for a council appointed by the president to remain apolitical?

JR: I don't think that any advisory body appointed by this administration would be constituted such that you could get thoughtful independent advice. In the National Academy of Sciences workshop and the guidelines that were published the 29th of April this year, which were fairly detailed, it was recommended that there be a national advisory review body, but how that review body should be constituted and where it should be located was not specified. That's in part because of concern that this administration is so biased that the review body

[137] Fibroblasts are a connective tissue cell which produces fibers essential to tissues, such as collagen.
[138] James A. Thomson is a developmental biologist. Perhaps his most important contribution is the development of the use of human skin cells in place of human embryonic stem cells, making the controversial use of human embryos in research potentially obsolete. He is currently a professor at the University of Wisconsin School of Medicine and Public Health and was named one of the world's 100 most influential people by Time magazine in 2008.
[139] Beta cells are found in the pancreas and manufacture insulin.

would be biased. If the review body's responsibility is to review the validity and the ethical manner of carrying out science regarding the human embryonic stem cells, for the body to be constituted such that it thinks that that's an oxymoron and that *no* research is ethical, then you're going to have a body that says no to everything. That's not very useful.

AM: How optimistic are you? Can scientists hold their breaths until this administration is over? What will have to change?

JR: I think that we're going to have to say that it's up to the states to take the lead in this. If you happen to be a scientist working in a state that's supportive of human embryonic stem cell research, that's fine, and you can carry it out. You may not carry it out with any federal money, but you can carry it out with state money. The concern, given the fact that the Supreme Court just said that federal law regarding marijuana trumps state laws, is very worrisome. Congress can ban this [stem cell research] and make it a criminal offense. Presumably that law would be challenged, and it would be years before it would be implemented, but it certainly has a very chilling effect, I think especially for young scientists.

Why go into an area where what you're doing in your research lab is a criminal offense, when there are so many questions and problems to ask in biology? You just don't do that one, you do something else that's going to be equally challenging. So I worry about the impact on young individuals. I think that's worrisome.

AM: One last area and then we'll move away from this council. It seemed to me that some of the concerns against embryonic stem cell research and all the issues that are involved in that kept coming back to this idea of the fear that people would use genetic technologies for human enhancement and that they would want to have babies that were taller or more beautiful, or whatever. You and your colleagues, some of your council members, kept coming back to the fact that this is not even possible, so it's not really an issue. This is so far off in the future this can't be part of this discussion.

It struck me as curious because, in the early twentieth century, genetics in the United States was really tied to the eugenics movement[140]. Not all geneticists were eugenicists, but there were certainly some geneticists that were and promoted it. Within this council, it sounds like now it's the non-scientists who are worried about this enhancement effect, and it's the geneticists and the biomedical researchers who are saying, “No, this isn't even possible.” I was wondering -- because that was such a stark contrast but the tables have been turned a little bit -- how much do the ghosts of early genetics in the United States (that was so much tied to the eugenics movement) haunt the work that you do and the implications of the work and how you promote and publicize and write about your results?

[140] The eugenics movement applied selective breeding techniques to human beings in order to “improve” the species. To learn more, visit the website at: http://www.eugenicsarchive.org/eugenics/

JR: I haven't really thought of it in that particular framework. I suspect that for some individuals it may have an influence. My own feelings have been that it's pretty clear that most of the kinds of features that they were concerned about -- intelligence, strength, athletic ability, musicality -- are multigenic, and it's going to be a long, long, long time before we understand how all of the different genes interact to give you a high IQ or a low IQ. To think that you could manipulate ten or fifteen or twenty genes such that you would influence and enhance the IQ of somebody is just *very* remote, and for us to worry about that now is both ludicrous, [and] also just a red herring that you throw out there to scare people when it isn't a realistic possibility.

One of the important things that came out of this current issue of *Science* from the South Koreans -- and probably the work actually of Gerald [P.] Schatten[141] -- is that they have obtained cloned stem cells from oocytes with nuclear transfer and implanted embryos derived from those cloned stem cells into macaque monkeys. A hundred and thirty-five embryos have been implanted in eighteen different females, and none of them have really implanted or survived. So the notion that we're going to have a cloned baby is again extraordinarily remote. I think this is just another thing that is used by some individuals to becloud the issue and to raise red flags that don't exist.

AM: I have about three more questions, but it's five minutes to eleven.

JR: I'm okay.

AM: Okay. The next area I wanted to talk about is I notice on your CV that you have a patent, and I went to the patent office records and looked it up, and it actually lists two patents that you have with [Manuel O.] Diaz. I was curious to know a little bit more about why you took out a patent, the specifics of it, especially when you discuss in the council transcripts that MTAs, (Material Transfer Agreements) have really added a bureaucratic layer to a researcher's plate. What was the motivation to take out a patent on these nucleic acid probes?

JR: I don't really remember the motivation. This [patent] was on the *MLL* probe at (11q23) where we cloned it and we had a cDNA probe that could detect all of the rearrangements and translocations and could be used diagnostically. Also [we had a patent on] a larger probe that could be used cytogenetically to determine and detect translocations.

I suppose it's the awareness that -- for instance, erythropoietin was identified at the University of Chicago. It was never patented, so Amgen gets a billion dollars a year on erythropoietin. None of that money comes to the university.

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[141] Gerald P. Schatten is Professor & Vice Chair of Obstetrics, Gynecology and Reproductive Sciences, and Cell Biology and Physiology, University of Pittsburgh and the Director of the Division of Developmental and Regenerative Medicine, University of Pittsburgh School of Medicine. His main research interest is in understanding different aspects of human reproduction through stem cell research. He also testified to the President's Council on Bioethics.

It wasn't clear at the time [whether the probe should be patented] and we went to the university tech transfer office and they agreed that this was something we could and should patent, and they helped us with that. It was sort of the notion that you didn't want this to be something which in the future would turn out to be important and you hadn't done anything to protect, really, the *university's* interest in this.

As it turned out, we licensed the probe to a particular company that became defunct, and they were bought by another company that does sell the probes, so we get modest royalties. The university gets some and we get a small portion of what the university gets. But it was more the thought that the university has been extraordinarily lax in trying to develop intellectual property and that if this were going to be important in the future that at least the university should have some protection.

AM: In the sixties and early seventies as you were beginning your research program, where was this idea that your ideas may have some commercial value, or your results would have some commercial value?

JR: That never occurred to me. When I look at some of the patents now, I could have patented chromosome translocations as an important cause of leukemia, but of course when you find the first one, even the second one, it's not at all clear that they are going to be as important as they turned out to be. So I never thought that any of that would – [I] never thought of patenting any of those ideas.

AM: If the lab wants to use one of your probes to do some other experiments in the same area, how willing are you to let them use those probes?

JR: Individual laboratories that write to us, we just send them the probe. We ask for a letter from them stating that they won't use them commercially and they won't give them to anybody else without our knowledge. Initially, when we cloned the *MLL* gene and the probes, we got a lot of requests. Now we really don't get very many, so it's not an issue. The one company that we licensed them to has the probes, but the larger company, Vysis, which has been bought by Abbott Laboratories, is really the major producer of these probes. And we don't get anything from them, and they're pretty expensive.

AM: We talked about individuals and critical masses of areas, say, in the laboratory, in which ideas are generated, both from the individual and from the collective (I'll put it that way). What do you think the impact is on this idea that it's kind of individual but it's also collective, that this new era has dawned in which scientists who never thought about it before can actually get property rights over particular ideas that they may have? I'm looking at it in terms of how do you assign rights to one particular person, when in the patent application the works of several other people have to be referenced in order to get the patent? And I guess more generally the question is, what is the impact of this patent movement

within biomedical research, particularly university biomedical research and the whole commercialization –- [such as] university faculty members being on the board of directors of drug development companies -- and this kind of whole area?

JR: By and large, that passed the University of Chicago by. Certainly individual faculty members have some involvement in particular drugs and have patented some of them, but that's *very* rare. I'm sure that members of our university are on the boards of directors of some of the larger companies, but I don't think there's quite that kind of closeness that there are on either east coast or west coast schools.

I know that there's a great deal of concern -- I was just reading in either *Nature* or *Science* about some of the patents that people have taken out on RNAi [interference RNA], and anything you do using RNAi, they feel that they've patented. That's going to be an enormous area and tool for people to use in the future. It depends on how that patent is written and interpreted and whether it holds up as to what the impact is. You think of PCR [polymerase chain reaction] and the fact that that patent was then purchased by Roche [Diagnostics], and for a while it was very restrictive and very expensive. I think that's really bad. How one gets around that, or how one fights against some of those patents I think is a real problem.

X. Life roles and role models: Reflections and advice on being a female scientist

AM: Again to switch directions. You've been the subject of a couple of different chapters in books about role models and women role models in science. I certainly want to talk about that, but I'd like to talk about it in a way that it hasn't been done before, and I think you led me into this by mentioning when you went to see Barbara McClintock [that] she spoke about her personal life to you. One of her biographies is called *The Dark Lady of DNA*. We do have a certain persona of [her] -- she represents one role model for women in science, and it seems to me you represent a different role model in science, where she really lived kind of a -- at least from her biographers [accounts] -- this kind of very solitary life, and you seem to have it all. You have kids, you have this great research career, you had the ability to stay home with your kids when they were small, and now [you] are a phenomenal scientist as well. When it came to talking about her personal life, were you comparing notes or talking about what it was like to have a career in science and being a woman and having a family life?

JR: No, we didn't talk about that, in part probably because I was sufficiently ignorant of her own past that I didn't know it. It was more that she said that she stopped publishing (I think in about 1940) because nobody wrote for reprints of her papers. Of course, in the olden days you got reprints because people then would write and ask you for a copy. Nobody asked for any copies of her reprints, so she decided nobody was reading them, so she didn't publish anymore.

AM: Okay. Well then, another way to talk about this is, with my interviews that I've done with younger women in their early thirties who are having to make these decisions, I think they would be struck by the fact that you could work part time for a while, get your kids raised, and then go on and have an established career in an era [in] molecular biology where there's a huge pressure to generate data and to publish.

In terms of being described as a role model, how generalized can *your* history be? Are you an exception? Is there something exceptional about how your career developed and how your family life developed? Or what are the secrets to your success I guess is the [question].

JR: Well, I think the secret of my success is just good luck. When I'm asked to talk to young people, which I am in various different groups, graduate students, postdocs, et cetera, I do indicate that I think that my own path is not necessarily applicable to them. It goes back to the fact that I didn't have a strong drive to do something specific in terms of my career, so my career was going to fit in with the rest of my life. And it has. Instead of being very concerned about trying to get ahead in my career and looking on my family as an impediment to getting ahead, or feeling guilty that I had to neglect my family to advance my career, my career was, as I've said, a hobby.

I think that isn't true of many young women today. They are very dedicated to their career. They have a notion of what they want to be, and they're going to pursue that. They do then have to pursue it in the context of having a family and how you manage your family and your husband and other aspects of your life, as well as advancing your career. That wasn't an issue for me.

I do tell people that you have to hope that you're fortunate. After all, I just celebrated my eightieth birthday. I had family and family life for a period of time, then I had a career. I didn't discover translocations until I was forty-eight years old. So I'm just ten or fifteen years behind everybody else. But I've been able, because I've had reasonably good health, to combine them both.

AM: Is the life cycle of a female scientist different from the life cycle -- things happen differently -- than a male scientist? If so, is there a way to accommodate these differences? You could look at it biologically, but you could also look at it productively. I know that there's a general assumption among postdocs that if they don't do their great work during their postdoc period or within the first couple of years of their independent faculty position, that their career is then set and nothing else exciting [will happen], [that] their big hit has gone, has passed them by.

JR: I think for at least some people that's a fallacy. I can think of at least one other young woman who actually came and did a postdoc in my lab after getting her second Ph.D., which she got after her two sons were teenagers. So she did, in a sense, what I did. She had a career early on, had her family, dropped out, went back, got another Ph.D., and then went on with her career, which has been

very productive in her fifties and probably now sixties. I think that society and the granting organizations and academic institutions should be willing to accommodate a relatively flexible approach to these issues.

I know NIH has a grant program for returning women scientists. I don't know the details of it, but I know that at least in the past it's been available for women who have some sort of advanced degree to then get support to go back in the laboratory and get caught up and then begin what could be a productive career. I think that universities just have to be more willing to accommodate these kind[s] of unusual patterns. But women have to partly also just *insist* that they do this.

AM: So if you were brought in to mediate at Harvard, where the president of the university [Lawrence H. Summers] made some inopportune comment about innate differences between men and women in the sciences, and the faculty who have opposed him -- just on this issue, I know it's a much more complicated issue -- how would you respond?

JR: Firstly, I think there probably [are] in some very narrow sense differences in male and female -- special competencies, that more men have certain features of -- and I don't know exactly how to describe it -- analytical, precise, mechanistic use of physics or mathematics that make those areas just -- they're better able, I believe, to understand some of the nuances, or to put things together in new ways that lead to new knowledge. I don't believe male and female brains are the same. Male brains are exposed to testosterone that has a tremendous effect on all sorts of areas, and I believe it has an effect on certain intellectual areas as well.

That said, there is a great deal of overlap – at least this is the way I look at the world -- so that there are many females who overlap the top males in these kinds of talents. But I think as well that there are many females who are especially good in some of the kinds of correlative science related to biology, and they see certain correlations based on (again) some of the structures in intelligence in them that make certain correlations more obvious or easier to come by. Or just free-floating associations, to think “What if?” and then you look at it and it turns out to be so.

That said, I do think that there are a lot of subtle and not so subtle impediments to women and to young girls, especially in terms of trying to really explore and achieve the potential that they have intellectually. It's interesting, the U of C just had an afternoon session on gender, and they pointed out that in fact there was a higher proportion of young girls in high school who were in physics classes and who did well in physics classes, who then when they got to college, they didn't *take* college physics. So the question is, [women are] not even on faculty tracks, things happen and I think we need to pay much more attention to that.

I guess from the standpoint of Harvard, I would try to look at the culture and the way departments are structured to see [if there] are there some systematic factors in the organization that put women at a disadvantage. And to

the extent that you can change those so that talented women can function within that altered framework and function more successfully -- I think that would be of benefit.

I happen to think (and this goes back to my working part time, and I intended always to work part time), I thought anybody who worked full time -- well, not everybody -- was stupid, but the world was organized by men for their way of living, and that wasn't my way of living. Now, I've been co-opted, and my husband would say that I work eighty hours a week and I'm as driven as anybody else, but that came very much later. I think that to the extent that we make all of academic life more humane, men will benefit as much, if not more, than women will.

AM: And why were you co-opted?

JR: Because suddenly the challenge of finding translocations and trying to figure out what they did was the most exciting thing about my life. It was all consuming. Fortunately, my youngest son was ten years old, and I could be all consumed and it didn't damage -- it damaged my husband more than anybody.

AM: Well, was he able to adjust? Obviously you've been married sixty-some years.

JR: Fifty-seven.

AM: How well did he adjust to having you working full time and then having a very prominent scientific career?

JR: Working full time wasn't the problem, the travel was the problem, because all of a sudden instead of going to maybe two scientific meetings a year and never being asked, or rarely being asked to go give seminars, I was gone once or twice a month. I thought it was very exciting that people wanted to hear me talk, particularly in the late seventies and eighties in line with being a missionary, the more people that I could tell what I thought, the happier I was. But it was very difficult for him. He certainly *now* is my biggest supporter, but there was a time when he was very lonely. I was excited and all these other things, so I wasn't lonely. And I didn't appreciate how important that was and how difficult it was for him.

AM: And how about the mundane task of taking care of a family? Did he learn to cook and do the laundry and clean house?

JR: Yeah--he didn't learn how to do the laundry, and we have a housekeeper, so that's taken care of -- he *did* learn to cook, because in the beginning, when I went away, I left all the meals cooked or in the freezer or something like that. He decided after some months that really wasn't what he wanted to do, and he's a very, very good cook, very creative.

AM: How about your sons?

JR: The youngest was ten, and two of the other sons -- the older two were gone, and after a period the third son was in boarding school. So it was the youngest. When somebody else asked him about this, he said, "Well, whenever I needed her she was there." He still lived in the same house surrounded by friends. So he had good friends in the house here to the west and other good friends all up and down the block.

AM: Did he learn how to cook, too?

JR: Not in that time, but all of the boys are good cooks. But that they just learned. I think they're very good sharing husbands, so they can do lots of things.

AM: One last question I wanted to ask, and then I'll turn it over to you, is that at the very beginning you said you got interested in science because you liked the order of it –- that it intrigued you when the nun was going through the phyla in high school. You've written an article about order, I think titled "Order out of Chaos." It struck me, though, that both aspects of your life, personal as well as your research program, has shown that your life has gone in not such an orderly fashion, not in a way that you had planned it out and followed it through, that opportunity presented itself and you took advantage of it. As well, the kind of science that you started out with turned out to be much more complicated and rich in terms of all the different directions you could take it. Where is this order now and this fascination with science because it's so orderly?

JR: Well, things aren't very orderly in my life right now because I have a lot of things that I'm trying to do. I do still maintain a research laboratory, trying to figure out what all these transcripts in leukemia cells are really doing, and transcripts in normal cells as well. How to use the different RNA transcripts that we find uniquely in one kind of leukemia and not in another, what they really mean biologically for the different leukemias, in part because some of them may turn out to be good therapeutic targets, and we won't know until we explore those. That's probably the major focus in the lab at the present time.

But then I am involved in the President's Council. That got me involved in the National Academy Workshop [on Guidelines for Human Embryonic Stem Cells]. I'm now on the California Institute of Regenerative Medicine [Scientific and Medical Accountability Standards Working Group], one of their subcommittees on science. And other things where I'm asked to go and participate in groups and panels.

Looked at in many ways, my life is particularly disorderly at a time when I'm probably less able to deal with disorder than I might once have been. But it does sort of follow, from chromosomes, to chromosomes in leukemia, to finding the genes that were involved in the chromosome abnormalities, now to go from

genes to RNA transcripts does have a certain logic to it. I think at each stage in my life I was able to look [and ask] what did I need to do to get from here to there. And I could see what was required and do that. Sometimes it took longer, and very often it took other people helping me to get there.

Again, I've been extraordinarily fortunate in having marvelous colleagues, particularly here at the university but elsewhere [as well]. Felix Mitelman[142] and I developed a journal, *Genes, Chromosomes, and Cancer*, which is an important journal in that particular area, the intersection of chromosomes and cancer research. So I'm blessed with friends, and that makes a great deal of difference.

AM: Okay. Well, I'm finished with my questions and I'd like to turn it over to you and ask you what would you like to talk about that we haven't discussed?

JR: I think you've covered everything that I can think of and a great many more [questions]. Coming back to emphasize some of the areas we have talked about, I think that it is extremely important to, firstly, try to get a good education, and then to try to find yourself in a place where you have good colleagues [who], regardless of what they may or may not know about what you do, they support you. I've certainly had that in spades at the University of Chicago, and I've been fortunate in having a wonderful family.

The other think I think is that -- and particularly for women, something we talked about earlier -- that you have to have patience. You count on luck and you can't count on luck, but you have to count that it's going to come and be there for you, that things will turn out all right. That's a Pollyanna statement, but I've been blessed with luck.

I also do think this whole notion that if you haven't done something important by the time you're thirty or thirty-five, you're washed up -- that *isn't* so. I know a number of examples, particularly with *women*, where they have been in their late forties, as I was, or fifties and have made important observations. That again requires support, which is difficult to come by now. It requires good health, which is something that I have been basically blessed with by and large. With those provisos, just take it easy and things will happen. If you're intelligent and perseverant and see where the opportunities are, you can have a productive career.

AM: Were you ever tempted to leave Chicago?

JR: Yes, we were, on two occasions. Well, three occasions really. My husband was offered a name professorship by a former colleague of his here at the University of Chicago, who then was Chair of Pathology at University of Washington, Seattle. I don't know why we didn't respond to that. I think that Donald is sufficiently independent so that he didn't want to appear to be there as

[142] Felix Mitelman, an eminent Swedish cytogeneticist, is Professor of Clinical Genetics in Lund, Sweden. Mitelman is Editor-in-chief and Rowley Executive Editor of the journal Genes, Chromosomes, and Cancer which was first published in 1989 and is currently still in circulation.

a protégé of his former mentor. We were in the process of looking at another position when our oldest son died, and that just stopped. We didn't even go out for an interview, though we were in the process of arranging for that. The third time, we looked but we didn't go. We just talked about going. It was a time when Donald thought that it wasn't going to be suitable for him, so we didn't pursue that.

AM: At Seattle would you have ended up at the Hutchinson?

JR: I have no idea what I would have done. This was probably in the middle sixties, early seventies, so I was into cytogenetics, but exactly how far along I was in looking at leukemias, I don't recall.

AM: Okay. Well, I thank you very much for taking the time, and it's been my pleasure to interview you. Thank you.