Gary Felsenfeld, Ph.D.

This is the first interview in a series on the career of Dr. Gary Felsenfeld. It was conducted on 20 December 1999, in his office on the second floor of Building 5, National Institutes of Health, Bethesda, Maryland. The interviewer is Dr. Buhm Soon Park.

Park: Thanks for your interview. And could you start with your education, why you became interested in science, and who influenced you in what programs, teachers in your college years or high school years?

Felsenfeld: I started to be interested in science probably when I was about six years old, but people didn't know what to call it, not in my family and not in my environment, which was, I mean, we were middle-class people, but I think was simply, scientists were so remote.

Park: Where did you live?

Felsenfeld: I grew up in New York City. I was born in New York City. When I was quite young, I remember going to the doctor--I went to the doctor a lot--and becoming very interested in things like x-rays and how did they see things. And I remember one doctor who actually let me--they used fluoroscopes a lot in those days, and he let me play, put my hand behind and stand in front of the screen and see the bones of my fingers. It was all very exciting, if dangerous, but we didn't know that then. And then, as time went on, by the time I was 10 or 11, I wanted chemistry sets and

things like that, became very interested in chemistry, and I began to have friends. I found a few friends in junior high school who were--we used to even make explosives and things like that, small amounts. We weren't trying to blow anything up. We just wanted to see if they worked.

Park: Where did you make it? In your basement?

Felsenfeld: We had no basement. I was in an apartment. We all lived in apartments in Manhattan. We used to go into the bathroom, and that was difficult, for usually those apartments had one bathroom, and then we were experimenting and nobody could use the bathroom, which presented some problems. I got interested in photography, probably at the beginning, and still am interested in photography, but at the beginning probably also because it was a kind of chemistry that fascinated me. So, then, the first big change was that I went to Stuyvesant High School in New York, and there, suddenly, instead of feeling sort of strange and unlike anybody else, I began to have lots of friends who were interested in science. It was a special school. It has an admissions test. It's one of the few schools, three in New York, for science. Bronx High School of Science, Stuyvesant High School, and Brooklyn Technical High School were the three high schools. And Stuyvesant was known for its math and engineering. And my junior high school math teacher took me aside. I would have gone to Bronx High School of Science, which was more for biology, but she said I was very strong in mathematics and she thought I would do much better at

Stuyvesant. And to this day, Stuyvesant is the place where the great math teams are, and the winners of the various international math contests come from there. So it's still very much that way. So I went to Stuyvesant, and it was wonderful for me. That was the best thing. And there in particular, I remember one biology teacher named Jerry Scher [sp.], who was absolutely marvelous. He taught us about the development of the embryo, and I was so excited by that. And, actually, over the years--he only died about two or three years ago and must have been about 90--and all these years, any time my name appeared in *Science* or any other journal he read--he read *Science* magazine--he would write me a letter saying that he'd read this and that he was happy to see I was doing well, and then I'd write to him. So we had, over the years, still contact. That's a marvelous thing for a teacher and for the students. Just in there, a couple of things occurred. One, among the friends I made was--I don't have him as a friend anymore, although I sometimes run into him--by the name of Hans Mark, and Hans Mark was the son of Herman Mark, who was one of the world's great early structural biologists. He was the first person to actually make an x-ray diffraction photograph of a living, it was of probably cellulose or something like that, but it was the earliest attempt made of fiber diffraction. And Mark had established the Brooklyn Polytechnic Institute--that's what it was then called. It's called New York Polytechnic now--a big center for the study of polymers. And it was really

unusual in the United States and a very important place. And because Hans, his son, was a student at Stuyvesant, Herman and all the other faculty at Brooklyn Polytech came to give our chemistry club lectures. So we learned all about early things in polymer chemistry. But most important, when I entered the Westinghouse Science Talent Search, they gave me a small laboratory at Brooklyn Polytech where I could work. And my project, which was not a success--well, in those days, it isn't the way it is now with the Westinghouse because the projects now are very sophisticated. In our days, no projects were sophisticated. Actually, science wasn't very sophisticated. But I tried to make an emulsion. I was interested in photography. I tried to make an emulsion that would be sensitive to x-rays but not to ordinary light, so that you would have an x-ray film that could be used in daylight. It's not a bad idea. I decided that maybe silver fluoride would be the thing, so I made silver fluoride, and I made silver fluoride emulsions, and then I exposed them to an x-ray beam which they provided to me at Brooklyn Polytech from their x-ray crystallographic study, and sometimes I got black spots. So I wrote this all up and I sent it in to Westinghouse, and I actually was one of the finalists. That was a second really important thing for me because it, when I came to Washington, I met young people who were on the staff of the Science Service, which runs it still, and other people who talked to the contestants, and they persuaded me that I should be a scientist because,

I should say that all this time, I thought being a scientist meant going to medical school. I missed saying that. All the time in my early days, when I was waving my fingers in front of the x-ray machine and so on, all the doctors I talked to said, "You're so interested. You should go to medical school." And my family physician, whom I loved, was one of those classical physicians, told me, he said, "I'm a scientist, you can be a scientist." He was a professor at one of the medical schools in New York, as well as having a practice, and I saw the kind of science he did. By the time I was in high school, he was showing me papers he had written. And the papers actually were about sickle cell anemia. And what they were, were descriptions of patients. It said, "This patient had this blood count, and that patient had that blood count, and isn't that interesting." And I thought to myself, that's very nice, but this is not what I mean, so there's something wrong. There must be something--I'm getting the wrong information. But when I went to the Westinghouse Science Talent Search, they made it clear that there were other ways to be a scientist.

Park: Doing experiments?

Felsenfeld: Yes, and that you didn't go to medical school, you went to graduate school. So, then, so I was one of the second-prize winners, actually, at the Westinghouse Science Talent Search, and then I went to Harvard. And at Harvard, toward the end of my first year, a couple of things happened.

Park: What year is that?

Felsenfeld: Nineteen forty-seven. I went to Harvard, and in my first year I thought I would do something biological, very biological, but the teachers who taught biology at Harvard were not as good as my high school biology teacher. He was a wonderful teacher. And that sort of turned me off to things like comparative anatomy. That's what biology was in those days anyway. There was nothing very intellectual about biology, except maybe Drosophila genetics, which of course I didn't know much about, although at Stuyvesant, they actually taught you to breed flies and look at simple inherited characteristics, so I knew something. But, on the other hand, there was a marvelous teacher of chemistry by the name of Leonard Nash, who was just starting. He's one of the few young Harvard faculty who has really made his name as a teacher rather than as a scientist. And he was allowed--finally, he was given tenure in the general education program. And he's just about retiring now. My son had him for freshman chemistry also when he went to Harvard. But when I heard him, he was inspiring. It sort of pushed me back in the direction of chemistry. But I knew I wanted also the biology.

Park: What textbooks did he use? Do you remember?

Felsenfeld: I really can't remember.

Park: Pauling's book or *General Chemistry*?

Felsenfeld: No, no. It would have been a... *General Chemistry* hadn't been written yet, I don't think. It was just being written, probably, in the '40s. I just

can't remember. Oh, yes, I do, I do. Latimer and Hildebrand, Wendell Latimer and Joel Hildebrand from Berkeley. They wrote this book, and that's what we used. It was about the properties. It was not--there was very little about quantum mechanics. In those days, you didn't study quantum. You studied about orbitals, not the SPD orbitals. You studied about the periodic table and how there were shelves to be filled and then, you know, the S, the P, the D, and you knew what the order of filling in of those was, but you didn't know anything about why. That was just considered too complicated.

Park: Theory.

Felsenfeld: Yeah. And that's an important thing, is to understand that the mathematical sophistication of young people has gone up, of those who are being scientists. And you can actually see that over the whole century, because if you work at Einstein's small book on Brownian motion, published about the early part of, probably the first decade of this century, so 100 years ago, it's addressed "to physical chemists." Well, it's written in kindergarten language. That is, the mathematics are, maybe a high school student could understand, and that reflects, I think, the average state of knowledge of professional physical chemists at the turn of the century. And it's only been gradually, gradually getting more sophisticated with time. But the mathematical requirements….students in the mid-century were really not expected to know anything about quantum

mechanics. So chemistry was first taught, sort of verbal explanations at the college level, and then, later, if you were really serious, you might take some introductory quantum mechanics, but probably not until graduate school. Anyway, toward the end of my first year, I had to choose a major or field of concentration, as it's called at Harvard, and I knew I wanted biochemical sciences, which was also for pre-meds mostly, and I still wasn't sure I was not going to medical school. But I knew also that there was one person who was actually the chairman of that department, who was known to be a marvelous teacher and a very distinguished physical biochemist, and that was John Edsall, and he's beloved by hundreds. He's trained so many people, who are very distinguished people, members of the National Academy. He is a marvelous person and still, still working, thinking, writing. Someone told me Edsall recently fell and had to go to a nursing home for a short period. And they went to visit him, and there he was at 97, in a nursing home, reading *Nature*. I'll bet he's the only occupant of that nursing home who ever read *Nature* either when they were young, or certainly not at that age. Anyway, I went to him and I said I wanted him to be my tutor, and he agreed. And then, for three years, I had the most marvelous personal relationship. So in the sophomore year, I met with him and one other student once a week, and he assigned reading that was aside from the [required] reading. And I'll tell you what that was in a little bit. And then, in the third and fourth years, I met with him once

a week alone, and he continued to assign reading, and it was done just like an English university tutorial. I would read and then I would come and present what I understood as questions. But mostly I had to tell him what I had learned.

Park: Yes. That's very similar to what I was taught from Dr. Davies [?] education.

Felsenfeld: Yes. But it's very unusual in the United States. It's not even usual at Harvard because some fields have tutors, but mostly they don't do that. They don't devote that much time. So, that was tremendously important, reading with him. I loved it. I just--it was a most marvelous thing to have him to myself for an hour at a time. And we read... The things I remember best were *The Nature of the Chemical Bond*, most important. We read our way through a lot of his book. And there was a book by Hammett called something about organic chemistry.

Park: *Physical Organic Chemistry.*

Felsenfeld: *Physical Organic Chemistry*. That's right. We read through that, right through, chapter after chapter, right through. And I looked forward to that so much more than my formal coursework.

Park: So, how did the tutoring go? You read...

Felsenfeld: I read a chapter.

Park: And just discussed that?

Felsenfeld: That's right. And then I came in, a chapter a week, and then he said, "Did

you have any problems with it?" And then he said, "Well, what do you think is the most important thing?" and then I would tell him. And then he would say, "Yes, that's right," or "No, I don't think so," and then we would discuss what he thought. And there were also other things. I mean, he would talk about his interest in... He would tell me about art exhibits he had just been to, and I would think, "Well, here's somebody who's very busy and a very important scientist and devoted scientist, Meyer Hammett, he has time to do these things, so it's good to do these things, and I should have time to do these things." And I do.

Park: Very good.

Felsenfeld: It's one of his gifts. Although I think I'd probably do it even if he hadn't. And we read... Finally, we started to read *The Nature*... He started to read Pauling's *Quantum Mechanics*. And then I also read a book, a more advanced book, by Eyering, Walter and Kimball called *Quantum Chemistry*. I have it here somewhere. It's one of my most treasured possessions. I don't know... Anyway, there's no sense looking for it now, but it's filled with my annotations, and I learned a lot from doing that.

Park: It's just published. It's published in 1945. Right?

Felsenfeld: It was brand new, full of mistakes, which actually was quite interesting. But then, in my senior year, as was the usual thing in that department, I did a thesis, and I did my thesis with Edsall. And at that time, Edsall's laboratory was in the medical school. Afterwards, he moved to the

Biology Department in Cambridge, but then he was in Boston at the medical school. And every day right after lunch, I would take the public transportation--that took about half an hour or more--I would go to the medical school, and I would work on my thesis. And I worked till quite late at night, and then I fit my regular course studies in. That was of much less interest by then. But by then I was taking mathematical physics and I was taking--I had taken advanced physical chemistry, I took advanced organic chemistry. I took a course at the medical school with Edsall, and with him were Edwin J. Cohen, and particularly a man named George Scatchard who was one of the great founders of the thermodynamics of, the thermodynamic analysis of biopolymers, all sorts of important things having to do with ion binding to proteins. And to this day, the Scatchard box, so-called, is used for studying binding, for analyzing binding equilibrium. So that was a course for graduate students that I took. It was easy because I was spending all my time at the medical school anyway. My thesis was on spectra of imidazole and histidine, and, also, I studied the binding of ions, metal ions, heavy metal ions to imidazole and histidine. And ultimately, we published a paper about this in the *Journal of the American Chemical Society*, I think. All through that year, I was trying to decide what to do. Well, during the period before that--and, of course, I was always discussing this with my friends in college, and somebody who had a big influence on me then was named Martin

Karplus. He's professor of theoretical chemistry at Harvard. And he was the first-prize winner in the Westinghouse Science Talent Search the year I won one of the second prizes, and I've known him since then. And he really urged me to go to graduate school and not to go to medical school, and I was moving in that direction. I applied to two schools only, to Harvard Medical School and to Cal Tech, and I was accepted to Harvard Medical School, and I went to see the professor of medicine, that very famous man named George Thorn. And I told him my dilemma, and he said, "You know, I wanted to be a scientist, and I thought I could be a scientist by becoming a physician, but I was wrong, and I never became a scientist. And I think if you want to be a scientist, you shouldn't come to medical school." He said, "If you change your mind later on, we'll accept you." So I said, "Okay," and I accepted Cal Tech.

Park: You particularly had in mind Linus Pauling's...

Felsenfeld: No.

Park: No?

Felsenfeld: I was going to work, I thought, with John Kirkwood. Do you know who that is?

Park: Yes.

Felsenfeld: Yes. He moved to Yale. Well, that is what happened. The summer I moved to Cal Tech, he moved to become the chairman of the department at Yale, and I wasn't going to change my plans. First of all, all the

fellowships had been given out and I had my heart set. Everything was ready. I had a fellowship at Cal Tech. So, I couldn't reapply to Yale, or at least I didn't want to. Maybe they could have changed things. If I had insisted that I wanted to work with Kirkwood, they could have arranged it, but it didn't seem like the right thing to do. I was guided by Edsall in my choice, who said, "The future of biology is in quantitative things, and so you should study, prepare yourself by studying physics and chemistry and forget the biology, because afterward, you'll do the biology. The biology is going to be different."

Park: He's like a prophet.

Felsenfeld: Yes. Well, he was already doing that. He was a physical chemist. He studied the orientation of myosin in the size and shape of myosin molecules by using flow birefringence. That's the sort of thing he did, so he understood what was coming. But in my last year of college, when I was taking this advanced graduate course in protein chemistry, they were still teaching that the structure of [unintelligible] protein was not. And then somewhere right in the middle of that year, Linus Pauling came around the country giving his talk about the new structure of the alpha helix. We heard that. I went with Edsall and everybody else to MIT, where Pauling was giving that talk. I remember it very well. It's the first time I saw Pauling, and he was very impressive. Well, by summer, I knew that I was going to Cal Tech, and also I knew that probably I wasn't going

to be working with Kirkwood, so I was thinking more in terms of Pauling. He was my second, he was my consolation prize. He was my second choice. And I remember going to hear him talk at a meeting of the American Chemical Society, the 75th anniversary meeting, where he talked about sickle cell hemoglobin. No, he talked about hemoglobin oxygenation curves and his model for how that worked. And you got the sigmoid cooperative oxygenation curves. He had a model for that. He had an unusual style. I remember that talk well because in it, he gave his results, and then he said, "And then Dr."--mentioning the name of the postdoc who was doing the experiments--"Dr. So-and-So did something. I don't know why he did it. I certainly never told him to. He did a control." Pauling said, "And the control showed that everything I've been telling you up to now is not right." That was the end of his talk. And I thought, who in the world... I mean, from Edsall, I would never learn such a thing. Edsall was very careful, very proper. So, it was a different style. I went to Cal Tech, and at Cal Tech, you started to work with somebody immediately, no waiting, even in those days.

Park: Did you go to Cal Tech in 1951?

Felsenfeld: Nineteen fifty-one. So, I arrived, by that time, actually, my friend, Martin Karplus had gone through Harvard in three years, so he was there ahead of me. He was already at student of Pauling's. So he was there. And then I shared rooms with him all the time I was at Cal Tech. And he said to me,

"Don't be shocked because they're going to tell you, give you a problem that you're not even going to understand what they're talking about." So, indeed, the first day I was there, I was told by Pauling, who was chairman, who met every student and assigned them to someone--you didn't have a choice--he assigned me to a scientist named Verne Schumaker who was a structural chemist, and who's still alive, and Verne was doing the electron diffraction of gases at that time, and I was assigned to work on that. And I went into Schumaker's office, and he said, "We're so pleased to see you because we've had a failure of the *Born approximation*, and we're sure you can help us." So, fortunately, I was prepared for that. Of course, I'd never heard of the *Born approximation*. The *Born approximation* that when you have interacting particles, there's only a single interaction and not multiple. The problem turns out to be that with very large nuclei, when you set electrons going, and there are lots of electrons around, you set an electron going, it scatters twice, often, and that has to be taken into account. The Born approximation, it only scatters once, as I recall, and has to do with separating the various nuclear functions.

Park: Fixing them to...

Felsenfeld: Yeah. I don't think this is quite the same. But, in any case, what happened was the radium hexafluoride was already, people had a pretty good idea that it was a symmetric molecule with all the six fluorine distances to uranium were the same. Electron diffraction was giving two

sets of distances as though it was an asymmetric. The ends of the octamer were longer, was what they thought. In fact, that's what happened, and the solution was to use higher voltages for the electrons, so they essentially didn't stay around as they went through the electron cloud and came back out. So, I had to learn pretty quickly what this was all about, and I worked for three quarters of a year, about, on this problem, and actually, it ended. Then I was given, assigned a different problem to study the structure of diazomethane. Diazomethane is a really violently explosive compound. I had to study it. I had to purify it, synthesize it, purify it, and then freeze it. So I had solid diazomethane and then let the vapor evaporate into a stream and then fire it into a chamber with an 80,000-volt electron gun firing electrons at it. And in the last experiments I did, the apparatus blew up in my hands. I was wearing a mask, fortunately. And I got stitched up. And I went the next day... Pauling had told me if I was okay for a year, he'd take me on, but he said, "I don't take students on first thing," so I had a different advisor. He was different. Everyone else took the students on right away, but since he was chairman and the most prominent person in the department... This was not hard. There were only about 15 new students a year in the entire department.

Park: Fifteen?

Felsenfeld: Fifteen, 1-5. There weren't that many people interested in science. And so what happened was it blew up and I was all bandaged up, and I went to

see Pauling and I said, “Professor Pauling, I want to stop doing research and start working for you,” and he smiled and he said, “Well, I do research. What I do is also called research.” But he agreed that I could start work with him. And that was just great. And I got, again, advice from somebody, one of the senior postdoctoral fellows, in Ken Hedberg, who became professor at Oregon State, a structural chemist, and he’s retired now. He’s probably about 80 years old. But Ken said to me, “What’s going to happen to you now”--and this is the difference from... Everyone was there looking after everyone else. It was a very small place. Pauling had four or five people working for him, probably directly, six, and that was considered very big. Everyone else had three, four people. It was very small scale. And that meant that you knew everyone and everyone knew you. And as a graduate student...

Park: In the chemistry department?

Felsenfeld: In the chemistry department. And since I lived in the East, for example, I couldn’t go home for Thanksgiving. There was never a thought. Thanksgiving, some faculty member would always invite me. And particularly I remember being invited by Jerry Vinograd, who is now dead, but who was, with Meselson and Stahl, developed the density radiant methods that we use to demonstrate, shortly after I left, we used to show semi-conservative replication of DNA, a very important experiment; and Norman Davidson, who’s still alive and retired but still quite active at

Cal Tech, and I was always in one home or another, as well as in Pauling's, who once a month or more, Pauling invited his students up for Sunday brunch, a swim in the pool, and just talked science. You talked science, and that's all you talked, no small talk, no vitamin C, no politics. Later, he became interested in politics and he wouldn't talk about science. But at that time, only about science. You couldn't change the subject. If you did, it immediately came back to the problem he was interested in.

Park: Did he, did Pauling advise a student on clinical chemistry or mostly structure?

Felsenfeld: Oh, everything, everything. He advised on everything. I mean, you never knew what they were going, what the subject would be. He would be talking about protein structure or he'd be talking about small-molecule structure. He was interested in research projects in alloys. Alloy structure, the unit cell, was, before proteins, that was the largest unit cell in crystallography, the most complex problems. And Pauling could solve those because he understood packing and he understood a lot about the kinds of bonding that might be involved. He used a lot--there's a lot of knowledge that went to solving those structures. So that was the second thing he did. Then he was interested in immunology. He had a whole program. When I say he only had four or five people, I mean students. The rest of the Cal Tech chemistry department faculty essentially worked on problems related... They were independent people who worked on

problems where he generated a lot of the ideas.

Park: I see.

Felsenfeld: Yes. And there was no faculty member, even members of the National Academy, who didn't value a suggestion from Pauling as to what they might work on. So there was a whole immunology group. He had ideas about how immunological specificity arose, which were probably wrong. And he became interested, while I was a student--and that's what I ultimately worked on--he became interested in ferromagnetism as part of his interest in the solid state. And what he did, what this senior postdoc, he explained to me, was that I would receive every week two or three memos typed by Pauling's secretary telling me things he thought I could work on or should work on, and that the trick of not going crazy was to ignore all the ones I didn't like or thought were wrong, because one's judgment even then was important, and then find the one I liked, stick with it, and then ignore all the notes afterward. And Pauling would never remember because the ideas just came into his head, he dictated them, and that was it. Then he was on to something else. So I decided to work on ferromagnetism. He had a theory. I worked out the theory, and I really can't remember very much of what I did, or understand it probably, if I even have a copy anywhere to look at. But I did learn to think about quantum mechanics, and I actually had some original ideas. And then, at the end of my second year, it became time to think about leaving, only

three years for a graduate student. And four was more usual, maybe three and a half to four, but three was not uncommon, and five was very long for chemistry. So at the end of my second year, I began to look for a postdoctoral position...

Park: Already.

Felsenfeld: Already. And I didn't really have a... Actually, my whole thesis came to me in one week, after the beginning of the third year. I had something, but I got a much better idea, and I scrapped everything and I wrote my thesis in a very short time, the material for the thesis. And, meantime, I went to Pauling to talk about where to go for postdoc. Then I thought, "Now I know enough of physical theory. I need to do something experimental if I'm going to do biology." I want to go to [unintelligible] who was the great Danish protein chemist. He was in Copenhagen. And Pauling said, "I don't think you have enough training. I won't approve going for your postdoc in a lab like that. You have to go for another year of training in quantum mechanics." So I said, "Okay." I mean, in those days, you took the advice that was given with great care and concern. That was his advice, and I trusted him. In any case, I knew he wouldn't write me a recommendation for the other place. So, then he told me where I had to go. He said I could go to a man named Longuet-Higgins, who was at Cambridge, or I could go to Slater and I actually applied to go to Slater, and I could go to a man named M.H.L. Price who was a physicist at

Oxford, and I actually applied there. But Price then moved to Bristol and I wasn't interested in going to Bristol. So, another person who was okay was C.A. Coulson, and I went to work for him. And I had an interesting year. Again, by that time, Karplus had gone ahead, and he was working for Coulson. So when I arrived, I again had a roommate. We took rooms together. And that was a great year because, in Coulson's lab, visiting, were William Lipscomb who eventually won the Nobel Prize for his crystallographic stuff; a man named Walter Hamilton, who came along from Cal Tech at the same time, now dead, but he was a distinguished crystallographer in his time; and a man named Don Hornig, who was an infrared spectroscopist who eventually became, he was professor at Brown at that time, he became President Eisenhower's... No, next president, some republican president's science advisor. *[N.B. Lyndon Johnson's science advisor]*

Park: Right, I know.

Felsenfeld: Many were republicans.

Park: Very important in providing AIDS funds to the developing countries.

Felsenfeld: Oh, really?

Park: And South Korea is one of the recipients.

Felsenfeld: Really? He became president of Brown University. And I saw him recently. He's retired now. Anyway, that was the group who were there, and one of the most pleasant things I recall was, that was the year Pauling

won his Nobel Prize in chemistry, and there was a big party at Francis Crick's house in Cambridge. We all went, and Crick and Peter Pauling was there. That was Linus's son.

Park: Right.

Felsenfeld: And all of us, and we had a great time celebrating this event. This was before Crick won his own Nobel Prize.But, of course, in the middle of my graduate work came the double helix.

Park: Right, right.

Felsenfeld: And Watson came and spent some time at Cal Tech then, and that's when I first got to know him. And then Crick came, and there was a big meeting that I think David Davies maybe had a picture of.

Park: Yes. He showed me a picture.

Felsenfeld: I attended that meeting. I wasn't a participant because I was only a student. I met Crick then, and then I've known him all these years also. In those days, senior people, new students, there weren't many students. And so what happened in the meantime that was important was that, just before I finished my degree, I was about to be drafted. When I went home to New York for a holiday, I had to go to see my draft board. I had an interview with them. I explained that I was finishing my Ph.D. I had been exempted for some years while I was a student. And I said I had a fellowship, a National Science Foundation fellowship. They came in while I was a graduate student, and they were enormously helpful. I

remember that the Cal Tech graduate chemists, the graduate students, I think we got a very large fraction. There were only about 16 fellowships offered in chemistry in the country the first year, and we got some very large fraction. It was a marvelous time. And, anyway, the draft board people said to me that they would let me go, but the chairman of the board said that while I was away, there was something he would very much like me to do, and that was to get myself a commission, because if I didn't, as an officer in some military organization, because if I didn't do that, then they were going to just draft me as a private in the Army. So, that was it. So I went for my year, knowing that it was my last year, and I then began to think about places I could go. I knew some people here, and I was offered a commission in the Navy to work across the street at the Naval Medical Research Institute. And also, at Cal Tech, I had made the acquaintance of Alex Rich, a professor at MIT. I'm sure you've heard his name from David. And Alex offered me a place in his lab, and he also offered David a place in his lab. David had gone back to work in industry in England, but I kept in touch with him in England. I was at Oxford.

Park: Yes.

Felsenfeld: So, at the end of my year, I came home and I got my commission, and I think there was a little period when I worked at the Navy across the street on an extension of my NSF fellowship because my commission was ending. I had to do some paperwork, and I worked there with a man

named Terrell Hill, who is a statistical mechanician, and I did some statistical mechanics. But when I came here, which would have been, let's see. I finished my Ph.D. in 1954. I didn't actually. it wasn't awarded until '55 because I finished back in the summer. But it was done in '54, and it was '54 to '55 that I spent in England. I came back here in late '55. I began my work here, and that's when we began work on some nucleotides that led to the discovery first of the three-stranded nucleic acid structure, which happened... It's just marvelous. It happened in my first year.

Park: And your first year...

Felsenfeld: Of experimenting. I had had all those years…

Park: It was published in 1959?

Felsenfeld: Fifty-seven.

Park: Fifty-seven.

Felsenfeld: I suppose '55 to '56, yeah. It must have been early '57. So, somewhere here I even have the notes from those days.

Park: Oh, really?

Felsenfeld: Mm-hmm, because... I'll have to find them. I put them away someplace. But if you want them, I'll...

Park: Yes. I'd like to get everything, is this original?

Felsenfeld: In those days--yes--we used to keep the records on paper, on a clipboard, with carbon copies, because often David and I were working together. And then there's a marvelous one in 1958, which I love, and I'm sort of

reluctant to part with that because it shows--we were making a large prep of polynucleotide phosphorylase, and the notes are in my handwriting, and then comes a certain date in June, and the handwriting changes to David's, and that's the date of the birth of my first child, my daughter, who's now a little over 40 years old. And then two days later, because in those days men didn't stay home with their wives for two weeks the way they do now, two days later the handwriting was my handwriting again.

Park: Only two days later.

Felsenfeld: Yeah, uh-huh. I'm not proud of that, but, certainly, it was not considered unusual. Anyway, yes, I have all those notes, and they bring back a lot of memories. But the memory I have that's the most vivid is, I had been doing these things where we mixed poly-A and poly-U and I measured the decrease in absorbance, the so-called hypoglycemic effect, that comes from the formation of an ordered structure in the stacking of the base pairs, the reduced optical absorption. So you could follow the reaction. And when I did that, I found that I formed a 1:1 complex, which was what I had expected and everyone else. It should be just like AT in the deoxy series. But then, as I let it sit, something happened, and a bump appeared, and this--I couldn't fit this anymore to 1:1. And finally, I started to draw it out, and it came to 2:1, and I said--David had the best back-to-back and I said, "David, is there any way in which there could be a third strand, a second strand of poly-U?" and he said, "I don't know. Let's go next

door." And I think that's just marvelous because you didn't have computers, you know. What you had were these great big cut-out bases of sheet metal and then backbones made of those metal rods. So we took one of these sheet metal U's and he started putting it around, and what he found, what he discovered at that point was the Hoogsteen, so-called Hoogsteen base pairing, which, I mean, it got that name much later, and that was it. That was the model that we proposed ultimately for this three-stranded structure. But you don't have thrills like that anymore for a lot of reasons. Everything is so much more complicated for that kind of direct feeling of discovery. So that was--it was good to have that at the beginning of one's career, a long time. Anyway, so that was the first thing.

Park: What was Alex Rich's role?

Felsenfeld: Oh, he was the person who actually decided that we ought to be working on these structures, and he negotiated and got us the materials, and he was a collaborator, really, in the whole thing. I mean, he was the section chief, and he certainly made a critical contribution to all this. He just didn't happen to be there at that moment. And we weren't, any of us, expecting that result. Up to that time, I was more or less showing that we had a two-stranded structure, and there were all kinds of very funny things that happened. I remember one day coming in. I was a physical chemist, of course. So I was going to measure the heat of the interaction--but we had

infinitesimal quantities of material--by raising the temperature and looking and using the Van 't Hoff relationship, which gives you the relationship between the equilibrium constant and the heat of the reaction. The heat of the reaction is... The equilibrium constant is a function of temperature.

Park: Right.

Felsenfeld: And one day, sitting in my chair, was Leo Szilard, who was at that time an advisor to the NIH.

Park: Oh, really?

Felsenfeld: Yeah. And he was not... Informal is not the word. Rude would be closer to it, but all right. And he asked, "I'm here to find out what you're doing," he said. Famous man, so I told him what I was doing. He said, "Why don't you measure the heat by putting a thermometer in, mix them, measure it?" So I said, "That would be nice, but the peaks of reaction are pretty small and we would need more material than there is in the whole world by the factor of 10,000 probably, very expensive to make." And he said, "Nonsense!" I said, "I'm doing it using the Van 't Hoff equation," and he didn't know the Van 't Hoff equation. He told me that it was nonsense. He had no idea where I'd gotten such an equation from--very revealing. He was really a smart man, but sometimes even smart people can be foolish. Anyway, so that work continued, and Alex and David did the original fiber diffraction structure. I was the person doing the chemistry. That was the division of labor. And Alex thought of the

project, and they were doing the x-ray crystallography. I was doing the solution chemistry to kind of see what relationship that had.

Park: Was there any problem in communicating between, among the persons of different backgrounds, your physical chemistry, x-ray crystallography...

Felsenfeld: Well, no, because we had all been at Cal Tech. Rich was also a student of John Edsall's. As an undergraduate, John Edsall had been his tutor, so we had that in common. In fact, Alex knew about me and I knew about Alex because of Edsall. So, we were friend; we were friends at Cal Tech.

Park: Could you tell me more about your first impression at NIH, about 1955? Nowadays, NIH is well known and it's a big institution and a research institution for biomedical research. And in the 1950s...

Felsenfeld: It was, for this reason, that many very smart people had been here because, just as I came here to avoid the draft, I was not an M.D. If I had been an M.D., I would have been here even sooner. All the M.D.s who had any interest in research tended to end up here because the doctors' draft was a great deal more stringent than the normal person's draft. They really needed doctors, so doctors couldn't escape, and they didn't get deferred for very long. As a result, you had, people like Arthur Kornberg here and many, many others. It was just a great training ground for, a great training ground for people who went out then afterward and became... The first generation of professors of medicine who were really scientists were the professors of biochemistry, who were trained vigorously. This was--that

was perhaps the golden age at NIH.

Park: It was also called the golden age or crucial years of NIH.

Felsenfeld: Yes. It's...

Park: So, before coming here, you already knew that this is going to be an exciting place.

Felsenfeld: Oh, yes. I had no doubts that this was a very good place to be.

Park: I see.

Felsenfeld: For me particularly.

Park: How many years were you supposed to be here?

Felsenfeld: Well, I got a commission in the Public Health Service, and it could be renewed indefinitely. And had I chosen to stay, then there would have been no problem to get a continuing commission. But what happened was I decided to leave, and as soon as my training time was up, I could have stayed on, but there was no real chance to expand, I think, at that time. So I went to the University of Pittsburgh, which had one of the few biophysics departments, and there I continued my work, and the work was on the physical chemistry of nucleic acids in solution. I was interested, not so much in the ordered structures; I became interested in the disordered structures, in the single-strand structures, also on how ions interact with nucleic acids, metal ions particularly. I was interested in metal ions because my undergraduate work was on, remember, I said, for example, copper histidine and copper imidazole interactions, so I had an

interest in metallic proteins.

Park: I see.

Felsenfeld: And that also--there was something I missed, but the summer after I finished college, Edsall arranged for me to spend the summer at Woods Hole Oceanographic Institution, where his former teacher, Alfred Redfield, who had been chairman of biology in the early 1930s at Harvard but became director of research at Woods Hole Oceanographic, Redfield was working. And Redfield's main interest and great contribution was in the study of hemocyanin which are proper proteins. They are the respiratory pigments of squids and mollusks and crustaceans like lobsters and crabs, horseshoe crabs, which are somewhat different, but all have different kinds of hemocyanin. And I actually, before I started graduate school, I actually did one experimental study of the binding of copper to hemocyanin which I published solo while I was still in graduate school. I had in my mind all through my graduate years; I should have said that I would probably work on metallic proteins. An the reason was that metallic proteins, I could see, would allow one to combine interesting quantum mechanics through the heavy metals and their chemistry with proteins and biological action. I thought here's a place where you really can apply quantum mechanics and a physical method to biology, and that was the problem. You had to think very hard to imagine. Other than hemoglobin and its oxygenation curves and things like that, there was

really very little. So, actually, when I went to Pittsburgh, I had two... By that time, of course, by the time I went to Pittsburgh, I was tremendously caught up with the nucleic acids. That was something I couldn't have guessed when I was in graduate school, when the implications of the double helix were still only for those few who were really interested in biology. So, at Pittsburgh, I have two sets of projects, the one I'm describing, which was with nucleic acids, and the other having to do with hemocyanin, actually, one of my students and I discovered how to make mitomycin, which had never been made before, which is... hemocyanin is a Q-press [sp.] complex with oxygen, and you could, with peroxide, I speculated that because there were two coppers, there had to be an oxygen bridge across the coppers, and that peroxide, therefore, would fit in there exactly and then oxidize those and that's exactly what happened. Furthermore, that happens with the first mole of peroxide. If you add a second mole of peroxide--remember, peroxide can either reduce or oxidize--the second mole actually restored the metahemocyanin to active hemocyanin, which was a wonderful thing. And I was very pleased because the last person to work on that had been James Bryant Conant, who became president of Harvard. That was the last thing he did as a professor of chemistry at Harvard, and he'd gotten it completely wrong, completely. And, you know, I think he was an icon for me also. I knew Conant a little as a student. So, that amused me. But what was becoming

clear was that you couldn't really--the nucleic acid stuff was too consuming and too important and really offered the kinds of opportunities to do physical chemistry that I was interested in. So that was really--that hemocyanin study was the last thing I did in the metallic proteins. I should also mention that while I was at Coulson's, I did write a paper that started at Cal Tech as a suggestion from probably this guy, Ken Hedberg, who had been giving me advice, but I tried to use crystal field theory to study the conformation of metal complexes. And just about that time, someone published a paper on the structure of Q aniline, which turned out to be a flattened tetrahedron. So what I did at Coulson's was I calculated the d orbital splitting of the copper ion, Q-pick [sp.] ion, in a tetrahedral field as a function of the shape of the tetrahedron, whether regular or flattened. And at the same time, you have the electrostatic repulsion of the chlorides counterbalancing that because the more you flatten, the more you split the d-orbitals that will result in filling the orbitals at lower energy, so it's favored that it should flatten. But the repulsion of the chlorides as they get closer together prevents that from going all the way, and when I calculated the equilibrium point, it was within half a degree or less. It was the observed angle. And that was probably the first application of crystal-field theory to molecular structure. Nobody had done that before. And, actually, every once in a while--I haven't done this in 10 years or so, probably--I go to look in the field, the literature, to see, and it seems that

people still cite this, which is interesting, because in biology, aside from maybe Watson and Crick's paper, you don't expect to see a paper from... That would have been 1955, 45 years ago.

Park: You must be very proud of it.

Felsenfeld: Yes, I am. I wouldn't tell you otherwise. Yes, I am proud of it.

Park: Right, right. And I have a question. Crystal-field theory is also called ligand.

Felsenfeld: Ligand field theory. It got that name later.

Park: Yeah, I see.

Felsenfeld: Got the name later. No one used it for that. I may be wrong, but I'm pretty sure that was the first one. It got used for more sophisticated things, actually.

Park: Right.

Felsenfeld: It was called crystal field theory because, I mean, it was, in fact, used to calculate energy states in crystals, I guess. Now, to go back, at that point, I wasn't enjoying Pittsburgh. And after about two years, of course, I kept up all my contacts; I had all my friends here. David was here and Martin Gellert was here. You haven't met Marty, maybe, but he's just down the hall and Gordon Tompkins. During the three years I have been here, two and a half to three years I have been here, I have--I think that was when I taught the course. Is that when I taught the course? Yeah. I think it was then. Or was it after I came back? I can't remember. So let's leave that

out for the moment. But I did get to know Gordon Tompkins quite well. He was quite friendly with David in particular.

Park: You and Dr. Davies were at the Mental Health Institution?

Felsenfeld: Yes, that's right.

Park: In Building 10.

Felsenfeld: Building 10. We were the first people to occupy those labs. Alex Rich had got there the year before, but many desks were not used, and it was brand new. It was like nothing else anywhere, state-of-the-art, marvelous.

Park: Do you have any picture of that time?

Felsenfeld: Photos, you mean?

Park: Yeah, photos.

Felsenfeld: I'm not really sure. I don't think so. I'm not sure if I have. I'll look for them. I'll try to think where they might be.

Park: Gordon Tompkins was at NIAID at the time?

Felsenfeld: Yes.

Park: Even though you and Dr. Davies were in the Mental Health Institution, you had frequent contact?

Felsenfeld: Oh yeah, yeah, and partly, I think, because Gordon was nearby, was a neighbor of David's, and they used to drive, carpool to work. And Bruce Ames I knew from Cal Tech because he was in the biology department as a graduate student when I was there as a graduate student. Todd Miles I met at about that time. He's across the hall. He's just about to retire. I'm

trying to think who else was here. And Harvey Itano. You know this name?

Park: Yes, I know Dr. Itano.

Felsenfeld: The discoverer of sickle cell…Pauling's lab. I had met--David and I met Harvey at Cal Tech. So that's more or less the group of people. And the rest of them are here. I was in Pittsburgh feeling very lonely, and there was a meeting. I remember there was a meeting in Pittsburgh organized by Paul Flory, who was then in Pittsburgh. And they came to it. David, I think, and some others and someone said to me, "How do you like it here?" and I said, "I hate it!" And immediately someone said, "Well, there's going to be a new laboratory forming. Maybe you should come." And the next thing I knew, I had an invitation, and I took it right away. There was no hesitation. And I had my own section. Can we stop for a second?

Park: Sure.

Felsenfeld: So, I was offered a section with a small amount of room. I can't remember exactly how much, but enough for me, for sure, then.

Park: Do you have a letter of invitation?

Felsenfeld: I'll have to look in my old papers to see what I have. I'll do that. I was overjoyed to come back. And, in fact, we were, of course, in Building 2. I came back as soon as I could, but the labs weren't ready. They had to be--Building 2 was renovated for us. So I actually then went for two or three

months with my family. They said I could go anywhere in the world, but we were just moving once and I already had two children, so we decided to go to Dartmouth for that time, where I had a very good friend, Peter von Hippel, who is a distinguished physical chemist. He was, even then, a very... He was a little younger than me. I had met him when he was across the street at the Navy because he also had to serve his military time, and he went to the Navy. And then afterward, he moved to Dartmouth, and I went there and we worked together on various things having to do with nucleases. He had been just working on proteins until then, and after that he did many, many important things with enzymes that worked on nucleic acids over the years. He's still a very active professor at the University of Oregon. That's where he moved. Anyway, when I came back here, my lab really still wasn't ready, so they put together some old lab furniture in an empty room and I set up shop and I started to work. I got my equipment going. And then, gradually, the rooms, the real rooms got ready and I moved into the room--it was just temporary. I moved into my final quarters. Everybody else came along and we had just a great time. And what I remember most vividly is that there was so little known. By that time, molecular biology had been--that's why we got the name Laboratory for Molecular Biology. It was very early. It was a new kind of name. And we all really understood each other's work, and we used to have marvelous seminars where people would talk about their work, and

everybody had something interesting to say. Everybody could make a suggestion. Bruce Ames was working on what he called coordinate genes. He had discovered quite independently the operand. He discovered it in histidine operand. It came to be known as the *Ames test.* It's a series of enzymes involving histidine biosynthesis in salmonella, and he made the observation that they all seemed to be controlled by a few regulatory regions, maybe even by one. I can't remember anymore. But the important link is the principle is that there was a single regulatory domain that caused the whole group of enzymes' involved in a single pathway to be turned on and off coordinately. So that was very exciting. The thing is, we all understood exactly what he was doing. We knew the literature, the other literature, and so we could say all kinds of intelligent things. The same was true for what I was doing. People could give me lots of help. And we all just felt as though we were the smartest people in the world. It was a great feeling.

Park: A history of molecular biology is not kind to this group, actually. Probably you have some history. And recently, there is a book out by a French biochemist, and it's *A History of Microbiology.* And many years ago, there was a book published by...

Felsenfeld: Oh, I know that one.

Park: *Eighth Day of Creation*.

Felsenfeld: Yeah. Well, I wouldn't say, I mean, that's not inappropriate. To say it's

not kind, I mean, it's simply that the handful of truly important discoveries, I have to say, in those fields that have to do with regulation of gene expression were not made in our Laboratory of Molecular Biology. Other things were done here, but not those that were the kinds of things that attract the scientists now. It's rather different. For example, the structure of the immunoglobulin gene doesn't figure in Horace Judson's days of creation because it's not inside his range of interest. Neither would my work on the structure of nucleic acids. It may later because only now is it becoming clear how these multi-strand structures are important. Only now is it becoming clear... I've worked for years on chromatin and the organization of DNA in the nucleus. Now, suddenly, that's turned out to be the basis for regulation of gene expression. So, that has to be, take a long view of these things. I'm not impatient.

Park: So, at that time, in the early 1960s, you were among the smartest people in the field.

Felsenfeld: Yes. I mean, I don't think if you'd asked us then what we are doing comparable to discovering the double helix the first time. No. Our pleasure wasn't in being... Maybe I would be giving you a mis... Our pleasure wasn't that we were doing the greatest work ever done. Our pleasure was in discovering, our pleasure was in making... These were important results. But it was the pure joy of discovering, which doesn't really have to do with how many people are going to give you prizes. I

mean, the fact of the matter is, although the historians may not be, I think we counted up how many members of the National Academy were either members of our staff or had been postdocs here. It's 16.

Park: Sixteen.

Felsenfeld: That's an enormous number when you consider that we don't have a very large group over the years. There isn't turnover every two years.

Park: Right, right.

Felsenfeld: So we've had a very large influence on how biology is thought about in this country.

Park: Was Marshall Nierenberg one of the original members?

Felsenfeld: No. Marshall was never a member, and the reason was, he was offered something here because he had been in Gordy's section, but at that time he had just made his discovery, and he had lots of offers, and he said, "I'll only stay if you give me this amount of space," and the amount of space he wanted was so great that there would have been none left for us. And we saw our laboratory as just a group of young people. We were just... In 1961, I was 32, and so we were really quite young.

Park: Right, right.

Felsenfeld: And what we decided was to advise Hans Stetten that...

Park: Right. He was the acting chief of the laboratory?

Felsenfeld: No. He was... Well, he was acting chief just as an official status. He was the scientific director of the Institute of Arthritis.

Park: Right.

Felsenfeld: And he--we advised him that what he should do is try to get Marshall to stay at NIH by seeing what other institutes also were willing to make him offers. And the fact that other institutes made him an offer so that he could stay, and then we decided it simply made no sense, that he should move because he wouldn't be happy with what we could offer him, and we would be very unhappy with what we could offer him because there would be nothing left for us.

Park: Right.

Felsenfeld: And that worked out very well.

Park: I've got interest in the excitement of the early 1960s, of young people, a new laboratory, new name, and exchange of good ideas and comments and criticisms. And how could you compare that atmosphere with, in other words, the NIH laboratory with the university laboratory?

Felsenfeld: Well, first, I think I'd better compare it with other NIH labs. It's become clear over the years that the experience we have had in NIH is not necessarily the experience a lot of other people have had. I think this institute in particular is very unusual in supporting basic research without interference. It's less true in some other institutes, anyway. But many people in other institutes don't report, you know, people my age don't really report having such a great time as we did. The secret for us was that over the years, when we could easily have split into three or four labs, it's

not usual; we have in this laboratory now Martin Gellert and David Davies and myself and Kiyoshi Mizuuchi are all members of the National Academy. It's not usual that a member of the National Academy doesn't have a lab of his own, a lab, you know, of which he's the laboratory chief. Until two years ago, we shared this. We governed the laboratory--we still do--we govern the lab as a group, and we always managed everything very well. And when we wanted something, we left it to the director's approval, which made it very hard to refuse us. So, in that way we kept together and we got what we wanted, and we were always very well taken care of. We never asked for anything foolish, so people trusted us. And over the years, we have had an idyllic existence, I would say, in terms of being able to focus on the science, being trusted to choose whatever was the best subject, and being supported. We were very crowded physically until we moved to this building. That was the one difficulty.

Park: In Building 2.

Felsenfeld: Yeah. It was really unpleasant, and we couldn't persuade people that that was causing us pain. It was. But we managed anyway, of course, and the move here was our eventual reward.

Park: From the beginning, you know, except Gordon Tompkins, all of the section chiefs had a common experience at Cal Tech: Harvey Itano, you, Bruce Ames and Dr. Davies. And does that have anything, mean anything?

Felsenfeld: Well, I mean, it meant that we were friends. The most important thing here is that we were friends. We saw each other socially and we knew each other well and respected each other. So that makes a big difference. And we never had any kind of fight, argument, any arguments or hard feelings between us over the years, at least nothing that didn't very quickly get. And I've always thought, you know, over the years, to come to work every day and never to think, this is going to be difficult because of personalities or some fight or someone I resent, it just didn't happen among my colleagues.

Park: I see.

Felsenfeld: And there was no kind of rivalry you hear of in universities, none of that. And I don't think that's the same at other NIH labs. We were just very fortunate to have found each other, and we were friends when we formed the lab and we just stayed friends.

Park: Right.

Felsenfeld: And that's an intangible that makes it so much more pleasant to do one's work.

Park: I was curious how this lab has been protected from the pressure of outside and inside from doing something practical, something biomedical.

Felsenfeld: Nobody ever asked us.

Park: Nobody?

Felsenfeld: They wouldn't dare!

Park: They wouldn't dare.

Felsenfeld: Yes. I think that's about right. Nobody would ask. I mean, the fact is that many practical results have come out of what we do. Martin Gellert discovered DNA gyrase, Nelson discovered DNA ligase and also discovered the mechanism of recombination that leads to antibody diversity. The discovery of gyrase is connected with a whole series of antibiotics, which are the most important antibiotics we now have, ciprofloxacin, levofloxacin things like that. Those are all inhibitors of DNA gyrase. That's how they work. And so there's just that. I mean, there's all of David Davies' work on proteases, which leads to the protease inhibitors, which leads to the work on HIV protease inhibitors. It all stems from his original structures, and, I mean, long before he started to work on integrase complexes, inhibitors of integrase and things like that, integrase binding to DNA. So I think our belief, our strong belief is that there is a direct connection. Actually, I'm very involved with the National Academy of Sciences in a study of how various discoveries that are practical, how, when you trace them back; you find the basic research result. It stands at the base. And how the people who did the basic research were looking for something else and certainly could never have guessed that this is what was going to be done with it. So, and it's true. At the Academy, it's a major program at the Academy for public understanding of science. And I think we are an example of that also. So nobody--no one has ever asked

us, and yet nobody in our laboratory has ever been reluctant to exploit whatever they can. I mean, we're two things. We're fundamental scientists, but we're also quite interested in applications because we're also people. We're taxpayers, so we want to see... And we want to see and we're proud of anything that we do that can be used. It's not that we're ashamed of it or we would like to suppress it. Quite the opposite. So we're sure to tell people anytime we have a discovery that's likely to have practical importance. Nowadays, the NIH has very good mechanisms for connecting.

Park: So, that has not been changed since the 1960s up to now?

Felsenfeld: Not for us. Other institutes. Yes. You know, when we took in Harvey Itano, the reason he came here, he was in the Cancer Institute. The Cancer Institute didn't want him because they said, "Finding the cause of sickle cell anemia is of no interest to us. It has nothing to do with cancer." That's what they said. And our institute had a different belief, which was that everything has to do with cancer, which is, of course, proven amply, and that the very first example of a mutation leading to a protein with an altered function, I mean, it's the very, very model of what we think is the cause of cancer. But I can remember that, having an argument as a postdoc in, it must have been 1955 or 1956, with Dean Burk, who was the senior biochemist in the Cancer Institute, in which I suggested to him that DNA and mutations in DNA might have something to do with cancer, and

he said that was just nonsense, it was all proteins. It was a metabolic defect of proteins, whatever that meant. Of course, I didn't know what I was talking about either, but I was right and he was wrong. The main thing is that they were looking backwards, and it took a very long time. They were very much toward application. And I remember coming into Hans Stetten's office when he was still director of our institute, and he was--he'd just put down the phone and he was smiling, and he said, "I just spoke to my counterpart in the Cancer Institute, and I suggest..." There had just been something, some report from an investigator in the Dental Institute that was--I can't remember what it was, and it was some hormone. It's not important. But he said, "I just told the director of the Cancer Institute that I thought it was just as likely that the cure for cancer would be found by the Dental Institute as it was that it would be found by the Cancer Institute." And he said, "And it got him very angry," and he was laughing. And then I was laughing because I agreed with him. In those days, that's what you thought. You don't think that anymore. But in those days, only this institute and maybe one or two others really supported basic research, I think, without reservations.

Park: Was that--did that have to do with the resistance of Hans Stetten or administrators?

Felsenfeld: I'm not really sure. I've often asked myself, but it's what we call an epigenetic phenomenon. It's not in the gene, but it's in something. In this

case, once you have a group of basic research scientists who come up through the ranks and then make the decisions, so our scientific directors are all, so far have been people who were alumni of our institute, they have that tradition, so they keep it. Their idea of what our institute should be comes from what they have seen that it is. So there has been a tendency to maintain this tradition of strong basic research. I don't mean that there isn't good basic research at our institute. There is.

Park: It's about 10 minutes.

Felsenfeld: We can talk for another 10 minutes if you want. About 3:30 I should go because I have another meeting coming.

Park: Right. Well, we can stop here. And can I come back?

Felsenfeld: Yes. You can see I love doing this.

End of transcript