National Cancer Institute
Oral History Interview Project
Interview with Lloyd Law
Conducted on January 30, 2001, by Peggy Dillon
In Bethesda, MD

PD: Good afternoon Dr. Law.

LL: Good afternoon. I'm happy to have you here.

PD: Thank you. I'm happy to be here. Today I would like to talk with you about your work at the National Cancer Institute and your contributions to cancer research. And I would like to start by asking you about your background before you joined the National Cancer Institute in 1947. Could you tell me a bit about your upbringing in Pennsylvania and your education at the University of Illinois and Harvard?

LL: I was born in Ford City, Pennsylvania, which is western Pennsylvania, on the Allegheny River near Pittsburgh. And after . . . where I was born, within the first month, my mother decided she wanted to live in California. So, we went to California.

PD: When you were a month old?

LL: Yes. And I went . . . we stayed there until I got through kindergarten. And the reason we came back is . . . when I was six or seven . . . the reason we came back was my father

sustained a bad burn, so we came back despite the objections by my mother. She didn't want to come back to western Pennsylvania.

PD: You returned to Ford City?

LL: Ford City.

PD: Okay.

LL: Because my father was a railroader and he wanted to come back here and do the railroad, which he did. He got a job at the Pittsburgh Plate Glass Company and we started to school, the elementary school there. So, in a two-room schoolhouse, grades one to four and grades five to eight. And we didn't have running water at that time, which wasn't unusual. So, I graduated from high school and, fortunately, one of the people I got to know very well was the coach of the track team. And he was thirty years old. He never graduated from high school, but somehow he got admitted to the University of Illinois. So he invited me to apply and I applied, seventy-five dollars tuition a semester. And when the time came, we hopped the train for Urbana-Champaign. I had never been more than, except the trip to California, I had never been that far. Illinois was about 400 miles from Ford City. So, I got there and got a job at a dollar an hour, working in the football training room and graduated from the University of Illinois, I think, in 1931.

PD: How did you decide to study science?

LL: I liked it in high school. I liked it very much, especially chemistry. And Illinois was good for science particularly. I took a premed course that had all sorts of biology, physics, math and chemistry. So, I graduated and went home. I don't know why I did that. Of course, that was a bad time, you know. People didn't have jobs. They didn't save money.

PD: Did the depression influence your choice of career right after college?

LL: Oh yes. I really wanted to go to med school at the University of Illinois, but you had to have a certain amount of money and I didn't have it. So, I taught school for three years, when I got through the University of Illinois at Charleston, Illinois, which is right smack in the middle of Illinois and near Mattoon and Paris. And I stayed there for three years. It was wonderful, although the little money I made, the bank failed and I ended up not having any money at all. But the third year in teaching in Illinois, I noticed this . . . that Harvard University gave teachers a scholarship. There was a name to it—Austin Fellowship—so, in the third year of teaching, which I didn't want anyway, I went to Harvard. They gave me six hundred bucks plus tuition. And I went to study genetics. I liked genetics very much. And I went to work with William Castle. Unfortunately,

Castle didn't tell me that he was retiring next year. So, I liked it this one year with Castle and then I transferred to a botanist, Edward East, who saw me through my three years . . . four years . . . at Harvard.

PD: What sorts of research did you do at that time? Mouse genetics?

LL: Mouse genetics. And he chose a very good subject, the inheritance of size in mice. And, of course, he had many different inbred strains of mice which could be used, and he steered me to this, which took all of three years to do. And, most of the time, I was situated at the Bussey Institution, which is at the periphery of Boston. And, but the rest of the time, I had an apartment in Cambridge, so I could take courses.

PD: So, at one point did you work with E.C. MacDowell?

LL: I never worked with him.

PD: You did not?

LL: The only connection I had with MacDowell was to get C-58 mice from him, and continue inbreeding. And I was the source of C-58's after MacDowell retired. So I remember sending C-58's all over the place. That was the only inbred strain that had spontaneous

leukemia. The only . . . afterwards, Jacob Furth had an inbred strain called AKR, but we found out that he hadn't inbred them, so I didn't want them . . . C-58 was the good strain.

PD: So, you were working on leukemia research at Harvard?

LL: Well, no, I didn't.

PD: When did that start?

LL: It started when I came here to NCI.

PD: Okay. I don't want us to get ahead of ourselves. So, after graduate school, what happened then? You went to Jackson Laboratories?

LL: After graduate school?

PD: Yes.

LL: Well, I, you know, they were looking for Army buddies, and I had a low number . . . number eight, in Bar Harbor. No, that couldn't be. That's because . . . what was the question you asked?

PD: I was wondering what happened after you went to graduate school. You went to . . . you then went on to Bar Harbor, Maine, to work at Jackson Labs?

LL: Oh, yes. No. I went to Stanford University. They had a fellowship from Harvard, a Sheldon Fellowship, which I won. It paid $1500. And, at the time, George Beadle, who was an associate professor at Harvard . . . and I took a course from him . . . decided that he wanted to go to Stanford, so he drove across the country, and I with him, because I had a fellowship at Stanford, which, for me, wasn't good. Because Beadle and I didn't get along very well. And, he was sort of a selfish guy and he was in the process of getting a divorce. So, I went with him and we stopped at his home in Nebraska, called Wahoo, Nebraska.

PD: Where he had grown up?

LL: On a farm. And we met his father and his sister, who was a nurse. Apparently, his mother died. So, he went to the University of Nebraska and then went to Cornell University. You know, he finally got a Nobel prize in physiology and medicine, which he deserved. He was a very bright person.

PD: So, you two arrived in California . . .

LL: We arrived in California, and they had his lab all fixed for him and he started right out doing work. He worked, at that time, on Drosophila melanogaster. So, the man he had working for him got me a room in Palo Alto, Stanford. I was there a year . . . not very happy year. So, then I came to Bar Harbor.

PD: And then who did you work with up there? And what did you do?

LL: Well, I met . . . when I was at . . . before we went to California, Beadle worked at Cold Spring Harbor with a man by the name Sturdevant, who was a professor at Columbia University. So, I made arrangements to drive with him, and, in the meantime, I met C.C. Little . . . Clarence Cook Little at a lobster party in Cold Spring Harbor.

PD: In Maine? Bar Harbor?

LL: No. No. Where they went in the summer . . . not Cold Spring Harbor, but . . .

PD: . . . so this was in Woods Hole that you met him . . . that you met C.C. Little?

LL: Yes, Dr. Little. And he told me that if I needed a job at any time, to contact him. So I did that, because I wasn't happy with Beadle, and he immediately got me a fellowship to go to Bar Harbor, which I did. I drove from California to Bar Harbor. That's when I got in

trouble with the Army/Air Force. They had wanted me as a private. So I found out that they had a position for Ph.D.'s called aviation physiologists. And you had to go to Randolph Field in San Antonio for six weeks and take the course there. Well, in the meantime, I got married and it wasn't long that I was on the train going to San Antonio. And my wife had the car, and she stayed around Bar Harbor a little while and then she drove home, to the middle of Iowa, Marshalltown, Iowa. In the meantime, we had been married.

PD: So, you were in the Army . . . Army or Air Force?

LL: Well, at the time . . . at that time, it was called the Army/Air Force, you know, before it was called Air Force. So, I was in the Army/Air Force for four years. After being trained, we were assigned to, you know . . . we were in Texas and Colorado, Utah . . . anyplace they had B-29 Air Force. That's where we were as aviation physiologist . . . training crews to fly at 38,000 and also how to ditch their plane. It's a huge plane which wasn't too good, and a lot of them crashed. Most of the time we spent in Clovis, New Mexico, and that's where our first son, Bill, was born. And we trekked around Utah and Colorado, and Texas. It was nice. It was nice to later see green things. Okay . . .

PD: So, after that, you came back. After you finished your military duty, didn't you return to Jackson Labs as a scientific researcher?

LL: Yes, I returned to Marshalltown, Iowa, my wife's home, because a person had offered me a job at the University of Minnesota. And I went to look at it and I didn't want it. So I came back to Marshalltown and then I went to Bar Harbor for a year, the same old job as also the scientific director, whatever that meant, because we had only about ten people in the Jackson laboratory.

PD: Had you worked . . . had you started working on chemotherapy by this time? What was the status of your research interests?

LL: No . . . four years in the Army/Air Force. You know, we didn't . . . we didn't do anything in research. But I got right on joining research. The peculiar thing about Bar Harbor was nobody bothered you. They didn't tell you what to do or where to live or anything. So I was on my own, and I was interested first in carcinogenesis. And I got hold of a compound they call azo . . . azo compound. And it was interesting because I had a summer student there whose uncle was in cancer research. I can't think of her name . . . Rosenthal, I think. And she finally went to Johns Hopkins University and stayed in cancer research as a pathologist, which I like. And she did very well the summer that I had her. So, after that, I don't know . . . I think I was still interested in carcinogenesis, but the fire came along and wiped out all of the mice which I had set up to send to Bethesda. And, so, there I was in Bethesda without any mice.

PD: So, when you joined the National Cancer Institute in 1947, your mouse colonies had been destroyed?

LL: Yes.

PD: How did you deal with that when you got there?

LL: Oh, I had a person by the name of Walter Heston and Howard Andervont and all of the other people worked on mice. That was the animal of choice. And they got their mice from the Jackson laboratory, which . . . C.C. Little had worked when he was at Harvard . . . he worked on mice and he was one of the first to inbreed mice, which means brother times sister, every generation, and has figured out when all the mice will be alike genetically. But . . . C.C. Little was responsible for that. I don't know why. He was always loaded with bourbon [laughter]. So . . .

PD: How did you join the National Cancer Institute in the first place? Who suggested that you apply there, or how did that come about?

LL: Well, when we moved to Bar Harbor, a very good friend, who was developed in Bar Harbor, was Walt Heston. He was a geneticist who had been prepared for the NCI. They had about ten people training in Boston, set up for the NCI, to move to Bethesda in time.

And he was sent to Bar Harbor. But the other people trained in Cambridge and Boston at Harvard University. I think there were ten to twelve people that were transferred to Bethesda.

PD: So, when you got there, you recreated your mouse colony . . .

LL: Yes.

PD: . . . and you began working as a geneticist in the Lab of Biology with Walter Heston. Is that correct?

LL: Oh yes. Right. He was . . . the head of the laboratory was Andervant, and Heston was under him, as a geneticist, and a very good one. And when I moved there, of course all of those people in Boston transferred to Bethesda. And also, they had a unit at the University of California, San Francisco, who did clinical work. I don't know what they did . . . not very much. But they came . . . so all of that was the root of the Cancer Institute . . . the people who were trained. And I, of course wasn't trained. I had Heston get me a fellowship. So, when I first came here, I was on a fellowship.

PD: When you arrived, what kinds of research did you do? Did you start doing chemotherapy research then? Or, how did that come about?

LL: No. I was interested in gonadectomy and leukemia, so we were interested in the . . . in testicles and ovaries and the relationship to . . . that's when we used the C-58 . . . animals. I got those again from . . . what's his name . . . MacDowell, who was at . . . he was in New York . . . at Cold Spring Harbor.

PD: Okay.

LL: So, I got what I wanted from him and also other mice from various people at the NCI. And they all worked with the mice at that time.

PD: So, tell me how you got into leukemia and chemotherapy research.

LL: I don't know. I don't know . . . except we were interested in the genetics of leukemia . . . you know, susceptibility. And I used C-58 for that.

PD: Okay.

LL: And that was . . . a lot of the mice that got burned were C-58. I had hundreds of mice to ship. In fact, you know, Heston did all of his experiments with hundreds of mice. Today, you couldn't do it. They wouldn't have space for it [laughter]. But despite the interest that Heston had in what I was . . . I was doing, we never did any work together.

PD: Really? I wonder why.

LL: Well, there were various reasons. One reason they moved us out of Building Six . . . that was the Cancer Institute, and everybody set up in Building Six, which still exists. And I moved to Building Eight, which is a building next to Building 1, because they had . . . we had space . . . laboratory space and space for the animals. So I moved there from Building Six . . . that separated us. At that time, though, you didn't do much collaborative work. You know, there weren't that many people . . . and they were very good pathologists and radiologists and geneticists . . . they were limited in what they could do, you know. So, I was surprised that, in the work that I did on development of resistance to antimetabolites, it took hundreds of mice to do that. And it was nice that we were at the National Cancer Institute.

PD: So, tell me what research was like at NCI when you first arrived . . . what the facilities were like . . .

LL: Very good. I was situated in the attic of Building Six. That's where they wanted me. And I had a lab there, and mostly animals. You know, you had to check the animals all the time. And everybody had . . . was interested in cancer research. What they did was dependent upon what they were trained. As I remember our pathologists were extraordinary . . . that good. And [Harold] "Red" Stewart had, over the years, got some

young pathologists in which we didn't work with because, you know, we had to know whether we were dealing with a lymphocytic leukemia or not. And I remember this person I worked with closely . . . Thelma Dunn. She was from Virginia and she was a very good . . . interested in mouse leukemia. And she was the first one that classified the leukemias for Potter and for me, and also there were new young pathologists. Clyde Dawe . . .

PD: Dawe?

LL: . . . D-A-W-E, which we did a lot of work with. He was Ph.D., MD from Johns Hopkins and I did work with him because he was one of the first at the Cancer Institute or anywhere else that grew tumors in-vitro. You know, there were . . . we worked with nice leukemias, but you had to transplant them from mouse to mouse. And people had to develop in-vitro. So, one of the first things I did was hire people who were interested in in-vitro development. And I remember we had a man from Wistar Institute on the fellowship and we had two people from Australia on fellowships, just to work on the development of in-vitro passage.

PD: Anybody else who stands out in your mind from those early days?

LL: Oh yes. Then, of course, with time, then you knew what people were doing and what they wanted to do, so we, besides working with people there at the NIH, such as virologist, Wally Rowe and the people in pathology, we got fellows in, to spend one or two years. And we had people from Australia, from Sydney. We had people from Israel, Nathan Trainin, who spent two years with us. And I would say we had ten to twelve people who came as fellows. And one type of fellowship we liked was Eleanor Roosevelt type of . . . and we had a man from Sydney who spent two years and a man from Israel from the Weizmann Institute [of Science], who spent two years here.

PD: So, you had people from all over the world coming . . .

LL: We had pretty . . . and not only that, but they really wanted me to come talk about my work in England and Stockholm and France . . . all over the world. And, you know, cancer research was just beginning at that time.

PD: What was known about it? Was there . . . was it pretty wide open?

LL: It was wide open. And one thing that we had to develop right off was a biological system that would divert, you know? And we got one of the transplantable leukemias, 1210 . . . L-1210 . . . that we developed from all of the in-vitro and in-vivo work. And that is one thing that Thelma Dunn was very interested in, classifying leukemias. And we developed it. And soon it was all over the world. And we lost our transplant. We had it by

microbiological assistants here in Cambridge and they lost it. So, we could always get it back, but it wouldn't be the same thing.

PD: It was you who developed the L-1210 right?

LL: Yes. "L" means "Law."

PD: Did you do that by yourself, or were you collaborating?

LL: Well, you know, we had technicians who always helped. And we had a man by the name of Miller, who was from Millerstown State in Pennsylvania. And we had a name by the name of Boyle who was from a little school in Hamline, Minneapolis, who was here. And then we had people who took care of the mice, who developed skills. No one person removed a thymus or removed . . . and if they . . . so, it . . . they were interested and they did a lot of work. As I . . . I remember, Jim Miller, who helped me with the studies on resistance. He worked very hard. And I sent him to Yale University to get his Ph.D. because I knew Beadle did very well and he had connections with Yale. And the guy flunked out. He didn't pass his French reading exam.

PD: So, if it was wide open . . . if the area of cancer research was wide open, how did you hone in on this particular area?

LL: You mean cancer research?

PD: Chemotherapy research for leukemia.

LL: Well, you know, the problem that we faced at one time, which Jim faced and . . . what's his name . . .

PD: Dr. [Joseph] Burchenal?

LL: . . . Burchenal and the people here, we were faced with children getting lymphocytic leukemia and dying. And that was a big problem. And it was a problem that the Cancer Institute faced with Tom [Emil] Frei and Emil Freireich and several other people who were made clinical associates. You know, they could spend two years of their military here in the public health service, and that's how all of these people started . . . six or seven of them. There's a man . . . I can't recall his name . . . who is at the . . . St. Jude's . . .

PD: [Donald] Pinkel?

LL: Pinkel.

PD: Yes.

LL: Yes. He was with Frei and Freireich, and also the man who wrote the book, *The Cure of Childhood Leukemia*.

PD: John Laszlo?

LL: Laszlo. Yes.

PD: Hold on just a second Dr. Law. I'm going to turn the tape over.

[End Tape 1, Side A]

[Begin Tape 1, Side B]

PD: Okay. Go ahead.

LL: We had that problem of leukemic children dying and they had these people . . . they didn't know what to do with them, so they finally set them to work curing leukemia, under the supervision of . . .

PD: Gordon Zubrod?

LL: . . . Gordon Zubrod, who just died recently. But Gordon Zubrod had all of these young people work on curing leukemia. They didn't know what they were doing, but at the time, the . . . at the time, two sets of antileukemia agents, folic acid antagonist and purine antagonist, were developed by these people at the . . . I can't think of the pharmaceutical company . . . they worked for. Gertrude Elion and the man she worked for . . .

PD: [George] Hitchings?

LL: . . . Hitchings . . . George Hitchings . . . were in upstate New York and developed . . . and they first contacted Joe Burchenal because they had these . . . I don't know why they thought they'd be interested in leukemia, but they used 6-MP, an antipurine and what they called amethopterin at the time. It was called amethopterin and methotrexate since then. But they used it on the kids. And Burchenal, I think, was the first to use it. I could never figure out how Joe fit into this whole problem. But Frei and Freireich and Jim . . .

PD: Jim Holland?

LL: . . . Jim Holland . . . they used these compounds and they found an amazing response of the leukemic kids to 6-MP, especially one to methotrexate. And this is the first time that they cured childhood leukemia. And I think somewhere, somebody ought to reduce that

in writing. You know, how they used the compounds, how many people, how many children they used and what the response was. Nobody has done that. And I would think the person who is capable of doing it is Tom Frei. I think he was the scientist of the group. So, but they . . . Zubrod and these people . . . and we had a laboratory of biology and I didn't have, really, too much contact with Frei and Freireich. And Holland and I became fast friends, because he liked to get lamb patties and come into our place and cook them [laughter]. He was divorced at that time. So . . .

PD: Well, I have a question about just what a typical day in the life is like for you while you were working with these people. Or, were you pretty much in the lab and they were somewhere else? Or were you interacting constantly every day? Kind of walk me through a typical day.

LL: You mean Frei and Freireich?

PD: Frei and Freireich . . . Dr. Holland . . .

LL: I saw very little of them, because they were in the, you know, in the clinical part of it. The clinic had just been finished in 1953 and shortly after that, I think Zubrod got his people together. But I, you know, I knew Frei and Freireich. We lived side by side and

we talked a lot. But some of those people didn't have much to do with curing leukemia, like Laszlo.

PD: He didn't?

LL: No.

PD: Well, tell me what a day was like for you then. I mean, you would get in early . . . I mean, just, you know, when would your day begin? What would your usual schedule consist of?

LL: Well, there was a time when you didn't have much money for travel, you know. And the first time we came here, when we came here, we had to use . . . we had to live in a house . . . a room in a house, for eight weeks.

PD: You and your wife and your children?

LL: Yes. Well, one . . . Bill was about two years old then. But I remember eating out at the Marriott every night. There weren't any places. And finally, they developed some apartments on Bradley Boulevard that was only for Army retirees and Army/Air Force,

Navy and so forth. That was the first indication that we could get anything . . . Bradley Boulevard.

PD: Well, tell me a little bit about the response in the scientific community to these discoveries regarding combination chemotherapy. Wasn't there a lot of resistance among other scientists to the idea that you could use a combination of drugs to cure leukemia?

LL: No, I don't think so. I don't think so. It was that people hadn't done it. You know, they had done it in bacteria . . . in salmonella . . . [Sal] Luria and [Max] Delbruck did it. But that was easy, you know. When you came to doing it with mice, it was very difficult because of the numbers of mice, where you kept them and took care of them, and somebody to look at the leukemias and decide what they were.

PD: You mentioned that Dr. Freireich lived next door to you?

LL: Freireich, yes.

PD: I read a story that it was during backyard conversations, while your children were playing, that you and he came up with the idea of trying your findings in mice on humans. Is that true?

LL: You know, that's cutting out Frei and Holland and so forth. And I think Holland was the person to push, you know, collaboration. Frei was a good scientist, but Holland pushed. And they, with the new clinical facilities there, and they money that they had . . . they had a straight shot to curing leukemia. I don't know what Burchenal was doing at that time. Burchenal did a lot with mice, as well as human beings. So, but, I don't think he was related, in any way, experimentally with these people here, you know.

PD: Okay. Right. He was in New York.

LL: Yes.

PD: A year after you came to NCI, individual drugs started to be used for acute lymphocytic leukemia. Did your research help play a part . . .

LL: Oh yes.

PD: . . . in their being discovered?

LL: No.

PD: No?

LL: No. I . . . the organic chemists, Hitchings and Gertrude Elion did that on their own. What they had to tell them that, you know, biologically they are accurate, I don't know. But I do remember talking with George Hitchings and he wanted always to send new drugs to treat, to test.

PD: An experiment for which you are especially well known is the fluctuation test. Could you tell me how that came about and what it proved?

LL: Well, we have found that some leukemic clones would respond, and some wouldn't respond, to, I think aminopterin. That's the one that took so many mice and . . . hundreds of mice . . . which I did with this man Jim Miller, who I brought from Bar Harbor. He had a bachelor's degree from Millersville State in Pennsylvania. He was very good. But we noticed that some clones . . . clones that . . . when you're taking off groups of cells . . . some clones didn't respond to methotrexate, and they found that some of the kids weren't responding to what we call aminopterin at that time. So we decided we should look at cells which are selected by drug, and which aren't selected by drug, as to what they did. So, you know, we had to use twenty or thirty mice for each little clone. And we found out that the methotrexate (aminopterin) really didn't have anything to do with it, and with the clone not responding to aminopterin. And when we looked closely at it, we found that true, that you had . . . you had clones which didn't respond, that had no previous . . . the aminopterin had no place in it, you know. We were using a fluctuator test which

Luria and Delbruck had used for salmonella when they studied for resistance to salmonella. So, it was a matter of what you selected, how many mice you used and what you were looking for. And that's why Frei, Tom Frei, couldn't believe it, you know. But it was there.

PD: So, in the fluctuation tests, were your results the first compelling evidence that combination chemotherapy might be effective where individual agents would not?

LL: I would think so, yes. Because we used antifolics plus antipurines and antipyrimidines. And that, especially 6-MP and methotrexate really told us what was happening.

PD: And then not long after you conducted the fluctuation tests . . .

LL: That's the fluctuation test.

PD: That was in 1952.

LL: Was it?

PD: And then the next year, you successfully cured mice of leukemia using combinations of these new drugs.

LL: Yes.

PD: So that was on the heels . . . directly on the heels of the fluctuation tests.

LL: I think we used different antifolics and antipurines there. Not one, but several, which we saw the compelling evidence that two or more antileukemic agents . . . we used many of them. But one of them that worked very good was methotrexate . . . again, aminopterin, plus guanazole . . . 8-azaguanine. But unfortunately, 8-azaguanine didn't work with children.

PD: It didn't?

LL: It didn't work. But all the others we did, including 6-MP, in children . . . but 8-azaguanine, which was so good in mice, just didn't work in kids. But that's the . . . but that has happened many a time in the . . . in treatment of leukemia.

PD: James Holland was assigned to apply your findings with mice leukemia to human leukemia. Tell me about your working relationship with him.

LL: I didn't know that he did that.

PD: That's not true?

LL: I don't think so. But if it's true, he would be an ideal person to work with. But I don't think he ever had a mouse in his hands.

PD: I think it was 1954 you were promoted to head the carcinogenesis section of NCI's laboratory of biology?

LL: That . . . those promotions didn't mean much. It meant that you got a little more space and got more help, you know. But it really didn't make that much difference. People were very helpful all the time, here . . . people who worked here and people who worked . . . Henry Kaplan, for example, who worked at Yale, and Kirschbaum who worked elsewhere in Minnesota . . . they were always writing and looking you up, and suggesting things that . . . and that's true of people in, especially, Stockholm and France.

PD: So, you would hear from fellow researchers all over the world, on things you might try, and . . .

LL: Oh yes, or meeting them at meetings and suggesting . . .

PD: What were the ethical and scientific guidelines at the time for moving from animal trials into human trials? Did any such guidelines even exist?

LL: No. I mean, the kids were dying of leukemia. And they had these six or ten clinical associates that were wanting something to do. And Zubrod put them at work curing leukemia.

PD: So how did you judge when a treatment was deemed effective enough to move it from mouse trials to human trials?

LL: I don't think we ever looked into that, except, you know, like 8-azaguanine, which was so good in mice . . . it just didn't work in human beings. But I don't . . . you know, it worked in mice, so you tried them in human beings. But I think . . . you know, you said someplace, under the guidance of Zubrod. Zubrod was strictly a clinical person. And I never talked with him very much.

PD: You were not that . . . you didn't come into that much contact with him on a daily basis?

LL: No, because he was in the clinical center and I was in Building Eight.

PD: You moved buildings?

LL: Yes, Six, Eight, the clinical center, back to Eight. It depended upon how many people we had and how much space we needed.

PD: So that's why people would go back and forth between Six and Eight?

LL: Yes.

PD: When did you move from one to the other?

LL: I don't know. [There was] very little moving. And I always got along with the people who, you know, the directors. They were always nice for what you wanted.

PD: Do any of them stand out in your mind? Ken Endicott or Carl Baker?

LL: Well, Carl was trained as a chemist, you know, at the University of Louisville, but he started working with mice and found that he couldn't work with mice. So, I was close to Carl, yes, and Endicott. Endicott was trained as a pathologist, and the reason they got these other jobs was they got more money. We're thinking about people . . . well, Thelma Dunn, who worked in the lab, stands out, and Red Stewart, another pathologist, and Clyde Dawe . . . they all were interested in what happened in the lab, and they didn't

really have much to do with human pathology. You know, that's what they wanted to do. So, it's been a good place to work, you know.

PD: You studied a couple of different areas . . .

LL: Yes, the area that we are discussing was the first area . . .

PD: Yes. Tell me about how you moved into other research interests.

LL: Well, because of people, you know . . . and what was happening. People were interested in viruses . . . polyoma virus, which we did a lot of work with, with Wally Rowe and then we were interested, for a long time, in cell antigens which have to do with immune system, which we spent an awful lot of time on, in mice. Because at that time, we had developed in vitro methods and we had also a person from Stanford University who was interested in H-2 cell markers, because he spent two years with us and . . . trying to characterize those normal antigens. And he went back to Stanford. His name was Sam Strober. But he did a lot of good work.

PD: Well, on the subject of virus oncogenicity, what would you say your major contributions were in that area?

LL: Well, in conjunction with Wally Rowe and Clyde Dawe, we defined the conditions necessary for production of tumors by polyoma virus and also by the leukemia viruses, which we found were effective. So, it was what they wanted to do and what we wanted to do together. It made things interesting. And all these people were wanting to collaborate. They sent Heston and Andervont and I never got together.

PD: The three of you never worked together?

LL: No.

PD: How about your work on immune mechanism . . . cancer induction and immune mechanisms?

LL: Well, we used some tumors that were induced by the chemical called methylcholanthrene or 910-Dimethyl, which developed in mice and we had found several of them were immune to just antigens that you prepared by solubilizing. So we did a lot of work for that, and also with Vincent Hearing on the melanomas recently we did in attempting to characterize these antigens which we got by the usual methods of solubilizing antigens. And that all turns back upon the man Strober who came to us from Stanford University, who was interested in the H-2 system of antigens, which he solubilized. So that worked out very well his two years. That was the beginning, I think, of when we used sarcomas, melanomas in attempts to . . . in attempt to get active material.

PD: To get what kind of material?

LL: Active material.

PD: Oh, okay.

LL: Yes. Most of the honors that I have for that, are for immune system. The first one was especially to resistance.

PD: Which honor?

LL: Rosenthal.

PD: The Rosenthal Award?

LL: Yes. That was early.

PD: Okay. The Anne Frankel Rosenthal Award, in 1955. What was the particular discovery that, for which you won that award?

LL: The fluctuation tests.

PD: Okay.

LL: And the rest of them came as . . . in specific things.

PD: Specific discoveries?

LL: Yes.

PD: Such as . . .

LL: Eli Lilly, for example, that had to do with immune systems. That was one. I don't remember . . .

PD: Eli Lilly.

LL: Eli Lilly is given by the American Association for Cancer Research.

PD: Yes.

LL: I remember having to go out to Indianapolis to give a talk.

PD: In 1970, you became chief of the new laboratory of cell biology.

LL: Yes, I don't know why [laughter].

PD: Well, you had the post for twenty years.

LL: Really?

PD: Why were you tapped, do you think?

LL: Well, I don't know. Because afterwards . . . not too long afterwards, Michael Gottesman was the . . . he was appointed chief. I guess I had to resign then. So I resigned and they made me an Emeritus.

PD: Well, that was in 1990 after . . .

LL: Oh really?

PD: . . . but when you took the position in 1970, you oversaw research into cell growth and development using the techniques in immunology and biochemistry . . .

LL: I guess that's when we started looking at the antigens, which would be solubilized there . . . in 1970, yes.

PD: Was technology changing at that time? Was molecular genetics coming on to the scene?

LL: No. Molecular genetics had nothing to do with it. But, you know, you would always have things that happened. I don't remember what happened then, but it was at a time when immunology played a good role, you know.

PD: What would you say were the positive aspects of being at NCI during your many years there? What were the highlights of your career?

LL: People. People who did things, and discussed them. There were good scientists. The NCI tried to get the best that they could get, and it was very difficult to get a job . . . a permanent job at the NCI or NIH, but particularly NCI. And also the NCI had more money than any other institutes.

PD: Even from the start?

LL: Even from the start. You know, a person who had quite a lot to be in and quite a lot to do in developing the NCI was Clarence Cook Little.

PD: Did he?

LL: Yes. He was very active in developing the NCI.

PD: Any other particularly positive aspects of your time there?

LL: Well, no. I guess the people . . . Thelma Dunn and Wally Rowe and . . . people I don't think you'd meet any other place, who were quite willing to collaborate with you, and a good place to work, you know. I finally moved to Building Thirty Seven, which was a wonderful place for the laboratory of cell biology.

PD: Not long after you became head of the lab of cell biology, the National Cancer Act was passed. Were you present at the signing of that?

LL: Yes.

PD: You were there?

LL: Yes.

PD: What was that like?

LL: Oh, a lot of interesting people. We had a meeting and then we signed. That was it. We had a discussion for several days of what we were doing and what we expect. And I remember meeting people I had seen before at this meeting. They had a meeting like that last year in France. They invited everybody back to sign something, that they would spend all their time and money on cancer research.

PD: It was sort of the modern equivalent of the National Cancer Act?

LL: Yes.

PD: Or, what were they talking about?

LL: Yes, but they stressed curing cancer. Why they did it in Paris, I don't know.

PD: Did the passage of the act affect your research at all?

LL: No.

PD: Nothing changed?

LL: Well, you know, we had several days. We discussed what was important, where it was happening and the . . . and that way was sort of targeted research. You know, who was involved and so forth. It was held over in Virginia at one of those places. So, we went and stayed overnight. It was nice.

PD: What did you think of the claim that cancer could have been cured by a certain date?

LL: I don't know. I guess there's some people who still believe that . . . the man from Harvard, the surgeon. Do you know what his name . . .

PD: No, his name doesn't come to me.

LL: He's the chief surgeon at the Children's Hospital. The way I know him is because the man we had here for two years is the deputy now . . . the surgeon at Children's Hospital . . . Folkman . . .

PD: Oh, Judah . . . Judah Folkman.

LL: He really . . . he got the Cancer Institute to give him lots of money and I don't think he ever got anything.

PD: Let me just change the tape for one minute . . .

[End Tape 1, Side B]

[Begin Tape 2, Side A]

PD: This is tape two, side one, of the oral history interview being conducted by Peggy Dillon of History Associates in Rockville, Maryland, on January 30, 2001, with Dr. Lloyd Law, for the National Cancer Institute oral history project. Dr. Law, I just have a few more questions for you. What is the proudest accomplishment of your entire career?

LL: Oh, I don't know. I don't know, except it has been pushed a lot for an awful lot, is the response to antipurines and antifolics combined. Because, besides the curing of childhood leukemia, it has worked very well, especially 6-MP aminopterin plus a few others for other cancers. And it is used today.

PD: What other cancers? Hodgkins?

LL: Non . . . whatever they call it . . . Hodgkins. Hodgkins especially, and also some breast cancers. There . . . I think there are a few others . . . 6-MP and methotrexate.

PD: What other people would you suggest we interview for this series?

LL: I have one person that you should. You should interview, because he's had the same honor that I had . . .

PD: What's that?

LL: You know, the Cancer Institute saying that you've done well.

PD: Who is that?

LL: His name is Waldmann.

PD: Waldmann?

LL: Thomas Waldmann.

PD: Okay.

LL: Yes. He's the boy who came from the University of Chicago and Harvard Med., who never had a day's practice in experimental medicine, and who has done very well . . . Thomas . . . what did I say?

PD: Waldmann.

LL: Waldmann. Yes.

PD: Okay. Have you donated your papers to any particular organization or institution, or are you planning to?

LL: No. What I plan to do . . . I have all these bound and preface it with a biological sketch and put it in the library which bears my name.

PD: The library at the National Cancer Institute for . . . that they named for you?

LL: Yes. I have never seen it.

PD: Okay.

LL: But the, I . . . invite Gottesman, invite Hearing and invite Appella to do the same thing . . . then they have all the reprints . . . and with the biographical sketch . . .

PD: That's great. What are you ties to the National Cancer Institute right now? Aren't you an Emeritus investigator?

LL: Yes. That means they give you a little money and they give you a place to work and also a place to park . . . and they're good. They're good . . .

PD: Do you go in much?

LL: No. I used to go in about two or three days a week, but recently, with my legs, I have difficulty walking. So maybe I'll get that fixed up.

PD: Any final thoughts that you'd like to share that I haven't thought to ask you?

LL: You can come back and ask. I'll think about it.

PD: Okay. We'll do that. Well, thank you so much for your time today.

LL: You know, it couldn't be better, what has happened as far as my life scientifically is now, because everything has turned out wonderfully. And I just remember today of going

through a huge apartment in Paris by this French scientist named Lacassagna, who I got to know very well. But he invited me and somebody else to have the best roast lamb I ever had, in his apartment in the middle of Paris. And there are so many things that happened that way, you know?

PD: It was a very good career?

LL: Yes. But I'll think of the special things.

PD: All right. We can revisit them another time. Thank you very much.

LL: You can come back.

[End of Interview]

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