This is an interview with Dr. Lois Salzman on June 29, 1998, in her office at the National Institute for Dental Research (NIDR), National Institutes of Health, Bethesda, Maryland. The interviewers are Dr. Victoria Harden, the NIH Historian, and Dr. Ruth Harris, a contract historian for the National Institute of Dental and Craniofacial Research (NIDCR). The interview is part of the NIDCR Oral History Project and the NIH AIDS Oral History Project. *Note: in October 1998, "Craniofacial" was added by Congress to the name of the institute.*

Harden: I'd like to start with your growing up and how you got into science and how you got to the NIH. Could you tell us a little bit about where you grew up, what your parents did, where you went to college, and how you got into microbiology as a professional field.

Salzman: I was raised in Philadelphia, Pennsylvania, in an area called Mount Airy. My father worked for the Pennsylvania Railroad in the Real Estate Department, and my mother worked at Sears Roebuck. School was very easy for me. I had an aptitude for doing academic work that resulted in very good grades and in being pushed forward by people. I went to the Philadelphia High School for Girls, which was a selective, citywide academic school for girls. When I graduated, my standing was high enough in the class to let me receive a full tuition scholarship to the University of Pennsylvania from the Philadelphia Board of Education. The University of Pennsylvania was a superb learning institution. Science had always been a great interest to me intellectually, and I enjoyed it. And so I became a science major at Penn. The faculty was very good, very

supportive, and very interested. And they were also interested in the fact that I was a woman at a time when it was very unfashionable for a woman to be involved in the sciences. I did extremely well at the University of Pennsylvania, graduated with honors, and was faced with the world and what to do next.

Considerations were medical school or graduate school; so I applied to a great number of places and was offered a very good scholarship with full tuition and maintenance money at Columbia University in New York to go to graduate school. My parents were certainly not able to afford the graduate education. Even though it was cheaper at that time, they could not afford it. So I went off to New York City and entered the graduate department there and worked first with a man named Frances Ryan, a drosophila geneticist. He was well known, and I had a very good experience. I also met my husband in New York--at Columbia Law School. I came to Washington with him after he graduated and came to Washington for a clerkship. And when he decided to go back to New York, I went back to New York. Instead of going to the undergraduate campus on 116th Street at Columbia, I decided to get medical training at P&S [Columbia College of Physicians and Surgeons], where they offered me a very handsome postdoctoral scholarship. And I remained there for two years. When my husband again moved to Washington, I came down here with him. I then attended Georgetown University.

Harden: I want to divert just a moment because, as you said, you were a most unusual character at this point, a woman pursuing a serious career. Would you comment on whether there were any particular mentors you had in undergraduate or graduate school? Were they male, were they female? And did you face a lot of opposition, or was it fairly supportive?

Salzman: It was very supportive at the university. There were no women in faculty positions to be my mentor. The men were very supportive, and very supportive in a way which didn't take into any account the fact I was a woman. I was just a student. And I must confess that, in this day and age, I know all kinds of things to complain about as a woman, but most of my education has been superb, without sexual harassment at all, and I enjoyed that very much. The faculty was just very good.

There was one professor at Penn, Professor Nelson in developmental biology, who was very supportive. He gave me extra attention, extra credit assignments, and he encouraged me. I remember taking his course, and even after his course, he was very supportive. There was another staff member who was a parasitologist—I can't recall his name right now—who was also very supportive. But I found the developmental biology more interesting.

Harden: Looking at your CV—at your graduate thesis, your Ph.D. thesis--I see that you were working on genetics and microorganisms and the isolation and purification of the chemicals they produced. Could you talk a little bit about what was happening in microbiology and the movement toward

molecular biology at this time?

Salzman: My thesis work was based on biosynthesis of an antibiotic, actinomycin. I worked with enzymes, isolation of the enzymes, and the substrates involved in the biosynthesis of active products. This involved a lot of what we now call molecular biology techniques. It was the very beginning of molcular biology. At that time isotopes were not as easy to come by or as widely used. I dealt with a lot more colorometric assays. The answers were there, but it took a long time to get them.

Harden: You came to the NIH in 1965. Marshall Nirenberg must have been finishing his genetic-code work, and it must have been a very exciting time to be here.

Salzman: I met him and the people who worked with him, such as Maxine Singer. I remember going to their section lectures many times.

Harris: I would like to know of any influence on you by Georgetown's Estelle Ramey, who was very ardent in urging women to go into science and who also was concerned about including women in scientific studies. Did she have any influence on your career, or did you have communication with her about your experience?

Salzman: Estelle Ramey was in the Pharmacology Department, which was a separate department from the Microbiology Department that I was in. She was situated on a different floor. And my contact with her was rather limited, I must confess, although I did go to her lectures, and it was well known that she did support women in science. I did not get to know her on any real

close, beneficial way.

Harden: Let us come back to when you arrived at NIH. You were initially supported by the National Cancer Institute [NCI], but you worked in the laboratory in the Arthritis Institute of Dr. Arthur Weisbach. Could you describe the climate for research at the NIH when you first came?

Salzman: Dr. Weisbach is a biochemist, well respected, and an excellent man. He worked with lambda phage and the biochemistry of phage infection.

Harden: Dr. Salzman, let's move to the time when you began to work with Dr. Norman Salzman, Chief of the Laboratory of Biology of Viruses, National Institute of Allergy and Infectious Diseases [NIAID]. You worked with him for a good period of time. In fact, you were there when the first publication on AIDS appeared. I'd like to know what was going on in that particular laboratory and what kind of work you did during this period.

Salzman: I was a virologist. At this time we began to get a feel for molecular biology, which was constantly changing and becoming much more well known. I worked on DNA synthesis of a parvovirus, KRV [Killam rat virus]. I did this work at a time when not too much was known about DNA or DNA sequencing. I sequenced part of the genome of the KRV virus, which is a single-stranded DNA virus. Little was known about how such a single-stranded molecule could replicate in the cell. Only double stranded DNA replication was known and the replication of a single- stranded DNA virus was not understood.. Retrovirus replication [RNA to DNA] was not known.

Both I and someone from Dave Ward's laboratory at Yale independently discovered that the end of the KRV single-stranded DNA molecule could flip back and bond with itself, thus creating an area of double-stranded DNA.

Harden: This is especially interesting to me because of the foundation such work had for later research on AIDS. When we interviewed Dr. [Abner] Notkins, he discussed the building up of detailed knowledge about viruses during the 1960s and 1970s. Would you like to comment on that?

Salzman: The mechanism of how these viruses functioned was not known, and I contributed some of the early work in that field. I showed that the DNA was indeed able to bond with itself at the end, therefore creating an area of double-stranded DNA, which could be used to initiate DNA synthesis of a double-stranded molecule. It was another way of synthesizing DNA. What it did was make apparent that DNA could be replicated in more than one way. And I think anytime you do that, you open people's minds to look for different ways of replicating DNA. It came with the virus--it came with the single-stranded molecule--and I, therefore, think it was a worthwhile contribution.

Harden: Do you recall when you first learned about the disease that came to be known as AIDS and what your thoughts were at the time?

Salzman: My background was in virology. I was interested and tried to follow the literature in virology, and it simply became apparent that there was a disease out there in the early 1980s that we didn't know anything about.

The epidemiologists, I think, made a tremendous contribution to science by being able to tell first by epidemiological methods that the disease was associated with homosexual men. That didn't come from laboratory science; that came from epidemiology. It was not known what caused the disease, and the pathology of the disease was not understood at all. Nobody knew anything. So the race was on to find the cause. And, of course, that race was very attractive because the disease was affecting a whole group of people, a huge number of people.

Harden: I want as many details as you can give me about this. You were still in Dr. Salzman's laboratory in 1981, but by 1984 you were into administration. I want you to tell me about your personal transition during this time and about your perceptions about AIDS as a scientist. The first meeting here at NIH on AIDS was in September 1981. It was organized primarily by the NCI, but NIAID was also involved. Did you attend that meeting?

Salzman: Yes.

Harden: Could you talk a little bit about it.

Salzman: As a virologist, I attended that meeting. It was not known at that time that AIDS was caused by a virus. It was a "feeler" meeting: We have these symptoms, these people. What the devil is causing this disease? And various disciplines participated in that meeting to try to get some feeling or some focus of where we were going and what we should be looking for.

The reason I had left the laboratory and gone into administration was that John Seal, the NIAID deputy director, had said to me at one time,

"Lois, you're a rare combination of a scientist and a person who gets along with other people. And I would like very much for you to come into the administration." John Seal was someone I had known for many years. I met him one day when I had just started here at the NIH as a postdoc and did not know him at all. Would you like to hear about it?

Harden: Yes.

Salzman: I was driving through Bethesda in my Volvo car, in a residential area, and there were two people who looked as though they were drowning—it was pouring rain. They were standing beside a Mercedes. And I had an NIH parking sticker on my car, and John Seal got out in the middle of the road and flagged me down. And he said, "You're from the NIH, we're from the NIH. I am with a guest speaker. Will you take us to the campus? My car has broken down." I did not usually pick up middle-aged men in my car, but he didn't give me much of an option; so I picked him up, and we chatted on the way. That was the first time I met John Seal. He was with a visiting Indian scientist who was scheduled to speak at NIAID, and he was trying very hard to get the speaker there. John Seal never forgot that I picked him up and delivered him to the NIH. We were friends for many years, and, consequently, he could come to me and speak to me in that manner about coming into the NIAID administration.

And so I had been in research a number of years and had been publishing at fairly regular intervals. I had postdoctoral students, and I was well supported. Norman Salzman's philosophy was like that of other lab

chiefs and administrators at NIH: I give you a room; I give you money; do your thing. That was the end of his interest. Once a year we would give a talk on what we were doing, what we'd accomplished, and that is how he found out what I was doing. Otherwise, he was really a hands-off person.

I was in the same laboratory and on the same floor as a very distinguished group of people. I was with Bernie Moss; Malcolm Martin; and Jim Rose, who was also working with a parvovirus. And we were very friendly, a very good group, and we met at least once, probably twice a week for journal clubs and daily in the hallways. It was a very fruitful and wonderful time.

Harden: And established, too, the personal kinds of interactions that we have heard about already from other people when they started dealing with AIDS. They called their friends who were experts here, there, and yon around the intramural program.

Salzman: It was a different program at that time; it really was.

Harden: How so?

Salzman: Well, I can remember that someone working with Bob Channock [Dr. Robert Channock] was trying to grow a virus, and I don't even remember what virus, but he couldn't get the virus to grow. And we all took our cell lines and grew them up and took them over for him to try to grow his virus on any of those cell lines to see if any of them would be receptive. That was just the way one acted to help other people for no reason other than just because that was science and we were here to learn about science. And

I think that's very different from what you would find now.

Harden: Do you have any explanation for the change?

Salzman: Well, partly, I think it's the need now to have collaborators, because the various disciplines are very intricate and very involved. At that time you worked very much on your own; although if you wanted anything, you could get it. And people worked together, and it wasn't as important to publish, although, of course, you did; but it was rather that we were all working for the same thing, to advance science, and that's what we did.

Harris: With regard to AIDS, was there any organized effort where you were working, or, for various reasons, did people just take up an investigation into what this was all about?

Salzman: Because of the number of people that were infected with AIDS, even early on, it was readily apparent that this was something that we had to face immediately. It was like the plague. I mean, it really had to be held down. People approached the problem from all avenues.

I remember that Ken Sell's [Dr. Kenneth Sell] laboratory thought they had an agent that could cause AIDS, a yeast, and he had done a tremendous amount of work. It looked good for a while that AIDS might be caused by a yeast. It turned out not to be. But researchers tried everything: viruses, bacteria, anything they could get their hands on to see if it would cause AIDS. And they tried again, all cell lines, to try to grow out agents. They tried infectious material from patients and tried to isolate something, anything that could possibly be the causative agent. And they

were working under pretty difficult circumstances, because you certainly couldn't take the material you grew up and then put it back into a human being. You couldn't do that. And there wasn't a good animal model. It was very difficult. They tried everything.

Harden: This brings us, then, to that meeting out at RML [NIAID's Rocky Mountain Laboratories in Hamilton, Montana], which centered around finding an animal model, as I recall.

Salzman: Actually, I think the main focus of that meeting was to look at everything we could. We looked at all the animal infections that resembled the pathology of AIDS. Then we compared the causitive agents. I set up the meeting, and there were people there from many disciplines. There were people who worked with viruses of owls who were invited. By that time it looked as if AIDS was caused by a virus. Probably the reason it ever got it tied down as a virus was the superb work that came out of Bob Gallo's [Dr. Robert C. Gallo] lab.

Harden: The meeting at RML was in the fall of 1984, I believe, after Gallo had announced his findings.

Salzman: Yes. The meeting was concerned with animal models of retroviruses and their relation to AIDS. We were looking at that time at avian viruses. The lentiviruses of sheep were also of great interest. Everything had to be done in tissue culture, and there were some rather unsatisfactory animal models.

Harden: Well, now, Bill Hadlow [Dr. William Hadlow] at RML had worked on the

scrapie agent, which we now think of as a "prion" but at that point was called a "slow virus." Can you explain to me the difference between lentiviruses and these slow viruses or prions?

Salzman: Well, the lentiviruses were a well-known class of viruses, and there was some information on growing them in animals. And we were very much interested in doing that. Little was known, as I recall, at that time about prions.

Harden: But they were considered as a possible cause of AIDS?

Salzman: Oh, absolutely. But they were impossible to grow. Absolutely impossible, at least with the animal models, and that's essentially what the meeting was about. Here was a whole group of animal models that was perhaps related to this virus causing AIDS. And this was what the experimental detail has shown us with these animal models. Were any of them relevant to what was occurring in humans? We were interested in both the effect of viruses on the animals and their ability to grow in the animals. As for prions, nobody knew what they really were.

Harden: One of the criticisms of NIH leveled early on was that people moved too slowly, people didn't get along; the agencies didn't get along. Would you comment on this?

Salzman: That was not my feeling at all, and I don't know much about the budgets of other institutes. But I think it was readily apparent that this was affecting a whole group of individuals, a large group, not one in a million individuals. And I thought the response of the NIH was absolutely wonderful.

Anybody who worked with viruses was trying to see if their virus was involved. Originally, anybody who worked with anything that was infectious was looking.

Tony Fauci [Dr. Anthony Fauci] should be congratulated over and over again because his institute got very little in the way of funds to support this research. But he still poured what he had into this research, realizing its importance, and being such a fine physician, clinician, laboratory person himself, he poured money into it that he really did not have for this purpose. And the response at the NIH--it was just super. Everybody tried. I even tried my little parvoviruses to see if they might have some relationship to AIDS.

Harden: You then moved into administration and you were working as a special assistant with Ken Sell, the NIAID Scientific Director. Do you recall any particular conversations about trying to encourage individuals in the institute to look at AIDS or trying to find ways to support particular lines of research in this early period when money was very tight?

Salzman: They had special meetings all the time.

Harden: Who were "they"?

Salzman: Ken Sell set up a laboratory with Tom Kindt [Dr. Thomas Kindt] to search for agents that could cause AIDS. They devoted hours of research to attempt to find the causative agent. Dr. Sell would have meetings with all the members of this laboratory and with the members of all of the other virus laboratories. They would get together and they would discuss this

peculiar situation.

Harden: But he did not dictate who was to do what, correct? He continued to encourage investigators to pursue their own best ideas?

Salzman: Originally, there couldn't be any direction because nobody knew what was up. The idea was to try anything; try everything; try it.

Harris: Did this apply to other institutes? Because I know that in NIDR, according to the annual report for 1982, somebody was looking at viruses as a possible cause of AIDS.

Salzman: Harold Löe [Dr. Harold Löe, NIDR Director] was a big supporter of AIDS research at NIDR. There was no additional money supplied; so research money was diverted from other sources. It was a special challenge to find funds and personnel and make time for research while keeping the existing lab programs going. I was amazed at the energy that went into this, and the people who say that NIH did not respond, in my experience, are wrong. NIH responded. You can't drop everything you've done for years. AIDS was taken on as extra work.

Harden: Is there anything else that you can recall about the NIAID response to AIDS during the administrations of Dick Krause and Ken Sell [Dr. Richard Krause, NIAID Director, 1975-1984; Dr. Kenneth Sell, NIAID director of Intramural Research, 1977-1985]?

Salzman: Dick Krause was also very much interested in supporting AIDS research. Aside from knowing that the director's office supported us, I don't remember much about Dick Krause's activities.

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Harden: When we interviewed him, he had talked about the problems of going to Congress. One year he had told them about NIAID advances in treating bee stings, which is very important if you are likely to go into anaphylactic shock because of a bee sting. But the Congress was not terribly impressed. Bee stings were apparently not considered a major disease threat like cancer. Dr. Krause felt rebuffed. And so he said that when AIDS appeared and affected a relatively small percentage of the population . . . .

Salzman: Homosexual.

Harden: He did not go as far as to say that, but he did say that he believed he would be rebuffed by the Congress if he argued the case for funding research strongly at the beginning when AIDS affected such a small number of people. Do you think it was was homophobia that the Institute had to deal with in Congress?

Salzman: Oh, I think Congress was very much aware that AIDS was "a homosexual disease." I think that there was a reluctance on their part because members of Congress are responsible to people back home, and they tend to react the way they think those people would want them to react, at least in some circumstances. And I think AIDS was very early on shown to be a disease that was associated with homosexuals, and many people in this country felt that homosexuals were a special group of people, and that AIDS was a manifestation of God's wrath against them.

Harden: When Dr. Krause and Dr. Sell left the institute, Dr. Fauci became director; and after Dr. Sell left, Dr. John Gallin became the director of intramural

research. This was the point in time which you moved to the dental institute. Do you have any comments about the efforts of the early Fauci-Gallin administration to address AIDS in the period before you left and before the money began to be appropriated by Congress? The money was freed up in 1986, I believe.

Salzman: Dr. Fauci found money. I don't know where he got it. He took it away from other projects, but he found the money. And we owe a great debt, I think, to Dr. Fauci, because he recognized how important AIDS was; and he found the money to put into it because he recognized its gravity.

Harden: Knowing that you are married to a judge and knowing that you personally have given a great deal of consideration to the legal questions involved in medicine, I want to ask you the following question. Do you think that the Congress and the courts have gotten it right with AIDS in the way they've treated people?

Salzman: I think we were very, very slow. I think they were slow to recognize it was a disease, to recognize the prisoners who had this disease. Prisoners should perhaps have had medicine available to them because of their health status. Congress and the courts were very slow to appreciate the danger of this disease. Their actions probably reflected the public attitude about the fact that AIDS involved a homosexual population (which is probably not a very political thing to say).

I can remember that in the court system once they would find out that a prisoner had AIDS, on came the gloves. No court official would

touch a prisoner with AIDS without gloves on. There was really quite a bit of isolation. And when you don't know how the disease is being transmitted, perhaps there is just an occasion for that kind of a response. But they certainly made the prisoners with AIDS know that they were different. They treated them differently, and they would put them in a single cell. It was a very different way of treating prisoners. They were afraid.

Harden: The rulling handed by the Supreme Court yesterday stated that HIV infection should be considered a disability from the moment of infection. This is interesting because it underscores Dr. Fauci's assertion that there is no latent period in AIDS when it is harmless. It supports the idea that HIV is destroying the immune system from the beginning.

Salzman: At first they didn't know that.

Harden: That's right. They didn't know that. But now they do. Is this the first infectious disease that has been designated a disability in this way? I'm not sure about tuberculosis, for example.

Salzman: As I understand the court's decision, the suit was brought by an asymptomatic person, and if the person is asymptomatic, I'm not quite sure what the disability is.

Harden: I believe it was a question of whether their infection with HIV might cause them to be fired from a job or cause them to be refused treatment by a health-care provider. In the case before the court, I believe, a dentist did not want to treat a patient who was infected with HIV in a regular office

visit. The dentist wanted her to go the hospital so that special precautions could be taken. Am I correct?

Salzman: Yes, the dentist specified a hospital where they could maintain sterile conditions, because, as we now know, AIDS can be spread by blood. I do not know what treatment the patient required, but it was obviously going to involve blood, and the dentist felt more secure if the work was done in the controlled setting of a hospital.

Five years ago, I had a root canal done in a dentist's office, and when he found out that I was involved in research on AIDS, he had lots of questions because there was a paucity of information. I think dentists and M.D.s don't all read the literature, which is confusing at best, and they're dependent on the newspapers. He told me that he had had a patient who came in and who told him he had AIDS, and he treated him in the office. But after the patient left, he gathered up the instruments and destroyed them, hundreds of dollars worth of precision instruments. And I said to him, "That's not necessary. It's a fragile virus. Treat it with 12% Clorox and you'll kill it. So he called me a week later and he said he had had a patient who had had a medical condition, so he had spoken to the physician who was in charge of the medical problem to see if it was all right to treat the patient, and the medical physician had told him the person also had AIDS. So he treated the person and, having listened to me, he thought if 12% was good, he would do even better to sterilize the instruments in 100% Clorox. But that destroyed his instruments, so he lost hundreds

more dollars. I mean, it cost him a lot of money to treat people with AIDS in a manner that made him and his patients feel protected.. And I said, "No, 12% is enough. It won't destroy your instruments." After that he said, "But the problem is that I don't know who has AIDS, and 99 percent of the people will not tell me."

Harden: But then, where does the responsibility lie? Does it not lie in the public health officials to advise dentists and health care workers that 12% Clorox is enough to sterilize instruments? If 12% will do it, then should he not feel comfortable treating patients, treating all patients that way?

Salzman: I think the dentist also—and I perhaps have my dating and timing off a little bit—but dentists had suffered tremendously from hepatitis B. It became a disease that dentists caught from their patients.

Harden: They were afraid.

Salzman: They were afraid. They're human beings.

Harden: Of course.

Salzman: ...and afraid, and AIDS patients died.

Harden: Right.

Salzman: And besides that, they died with a stigma attached to them. And we're human beings.

Harden: But physicians and dentists also choose their careers, do they not?

Salzman: You can say that. They choose their careers to help people. And I think you have to understand human beings. They don't want to kill themselves.

Harden: Of course not.

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Salzman: And certainly, if you get AIDS from a patient, that's what you would do. And so I think that you have to respect this as an honest fear.

The root-canal person I went to treated people infected with the AIDS virus in his office, and perhaps his reaction with the instruments was extreme, but he did treat them there. He worried about his other patients, too. What happens to the next guy who comes in, and I use equipment I can't destroy on that person? And I have all these people I don't know that have AIDS who may come in because once it became known, through the grapevine, that there was a dentist who would treat HIV-positive patients, other HIV-positive people would go to him. They didn't necessarily identify themselves as HIV positive.

Harris: How do you view the problem of funding targeted research, which is now what is done with AIDS? A specific amount of money is put aside for AIDS research. This is opposed to NIH's previous policy of stressing basic research without paying particular attention to a targeted kind of research.

Salzman: In my opinion, I think that is one of the big changes that has hurt the NIH. The fact is that you now have to take into consideration your research program, the mission orientation of research. That was not true when I first came to the NIH. You have the room, the money. You have shown that you are bright enough and can publish. Do something, anything you want, and consider it a worthwhile addition to the advancement and understanding of infectious disease, and the understanding of science. That is no longer the atmosphere. I think when people started off with the

AIDS research, they took it on as an addition to their own research, and their own research was first. But the AIDS research was important because of the involvement of a lot of people. Since the AIDS research was taken on as a second project, some scientists might get a postdoc and have one postdoc work on it. They always kept their own research interest more active. I don't think that's true anymore. I think that targeted research is pledged to get money, to get support. Congress likes it, and people have to consider that when they choose their research projects.

Harris: Would the AIDS research be where it is today if there hadn't been a lot of basic research done in the first place?

Salzman: Actually, maybe not. It is my understanding—and I don't know Bob Gallo that well—that it was only because of the work that he had done with the retroviruses in the laboratory that made him consider that a retrovirus might cause AIDS. It was only because he had already worked with viruses in that particular group that made him realize it could be. And if he had not, I don't think that it would have been just another virus group that he could have tried. So basic research was very important to AIDS.

Harris: Now, when you were with NIAID, were you aware of any collaboration between NIDR and NIAID AIDS research?

Salzman: Not that I can remember, Ruth, not at all. But that's probably because Allergy [NIAID] has such a robust program that it was hard enough to keep up with what was going on in Allergy. But the feeling was, at the NIH, that we were all here together, and I think that if there was a program at NIDR,

there would have been a lot of people who would help out.

Harden: In the earliest years of AIDS, I think the main interaction between institute personnel came in the Clinical Center. If Tony Fauci, for example, had an AIDS patient who had an oral manifestation of the disease, he could have contacted a clinician in NIDR to help. I know the primary physicians for AIDS patients did this with the Eye Institute, and I believe they did this with Dental. The contact was informal. I don't know of any early collaboration in the laboratory.

Salzman: I do.

Harden: Do you? Okay.

Harris: This brings up the question of whether or not the work done by Phil Smith [Dr. Philip Smith] and Sharon Wahl [Dr. Sharon Wahl] that led to the finding that infected monocytes played a role in HIV infection was a collaboration with NIAID. Originally it was through a clinical relationship between Phil Smith and people in NIAID that they got the samples from HIV-infected patients at the Clinical Center.

Salzman: The only way that one could get clinical samples at this time through the Clinical Center was through using the samples from the AIDS patients that came to the allergy and infectious disease institute, and because the work was done with shared materials, it was considered a collaboration. Regardless of the amount of personal collaboration on the research that there was, NIAID considered it a collaboration with respect to publication. There is controversy about this decision

Harris: I have a follow-up question on this monocyte work, which, in my view, turned out to be quite important. I went through the science citation index in depth and found that Phil Smith's and Sharon Wahl's work was cited over 200 times in the next decade. Did this monocyte work have any effect or influence on NIAID? You were at NIAID at the time that their publication came out in 1984. I notice that NIAID later on set up a separate lab with a similar title to the one that Sharon Wahl still has. So, do you know of any influence on NIAID that the Wahl-Smith monocyte work had?

Salzman: Sharon and Phil did make a very important contribution to AIDS research. It was an extension of the research that was going on in their laboratory--working with monocytes. Consequently, they were very well prepared to take on slightly different approaches with the AIDS virus. And this is the way a lot of the AIDS research was conducted at the NIH, as a separate project from the regular research program. Having gotten samples from Allergy and Infectious Disease, they found something very important. The role of the monocyte for a long period of time was downplayed because people did not know where it fit in. But it is now recognized, certainly, as a very important part of the AIDS disease.

Harris: But did this have any effect on the course of research or the organization of NIAID in pursuing the AIDS research?

Salzman: I think so. As it became more widely recognized that monocytes were important in AIDS research, Dr. Fauci had sufficient funds and resources to

put more people onto this project. Sharon Wahl tells me that only she and Phil were working on the monocyte project. When the importance of the monocyte became apparent, the big fellow with money and people stepped in and took it over.

Harris: Can you tell me your version of what happened when Phil Fox [Dr. Philip Fox] in the Clinical Center led a team that was investigating a possible anti-HIV substance in saliva? Do you recall just what the circumstances were surrounding that research? It was controversial. Dr. Notkins was scientific director at the time that this was being done, and he asked that work be done to replicate this in a more, I guess you would call it, scientific fashion. Did the controversy erupt before the first article appeared in *The American Dental Association Journal,* or did it come up after the article appeared?

Salzman: Yes. I remember the series of incidents, very well. Dr. Fox made a fundamentally important observation about the effect of saliva that had not been recognized or even approached before. We knew very little about saliva and its components at that time. Phil Fox reported his findings in a way that a clinician might find satisfactory, but he was reporting about a substance which is concerns molecular biology, and yet he did not set up his experiments in such a way that a basic scientist would take credence from them because he had few controls. They were not what was required for an experiment from which you can draw an unambiguous conclusion. He reported it as an observation, but the way he wrote it up was as if it were the result of rigorous experimentation, and I think he was missing

most of the controls that were required for that kind of experimentation. There was an attempt to aid Phil in trying to set experiments up so that he could rule out many variables and could say that what he found was true. I think Phil felt as though getting down to the lab bench and doing that kind of experimentation was not something he was trained to do. It was at that time that Sharon Wahl became involved because, obviously, she had the background as a laboratory scientist to run controls, to look at the proteins, and to do all of those basic types of experimentation.

Harris: Was it after the first article was published by Phil Fox that Sharon Wahl got into the picture?

Salzman: Yes. And it was a collaboration between them--or at least that was what was tried–with her supplying all the things that Phil's laboratory did not have at that time.

Harden: I'm interested in this from a broader perspective, too, because you were working with Dr. Notkins, the scientific director at that time, were you not?

Salzman: Yes.

Harden: What did the administrators in this institute, particularly Dr. Notkins and you, believe was your responsibility with respect to publishing these research findings? Here you have a scientist wanting to publish data that saliva inhibits the transmission of AIDS when you have excellent data that saliva is a good transmitter of most other viruses. If you allow this to be published and it turns out to be wrong, you could put many people in jeopardy of acquiring AIDS. How did you and Dr. Notkins view your

responsibility as administrators of intramural research as this project moved along and acquired new data?

Salzman: I think because of all these things, as you so well have put it, we felt that before it could be published, the report had to present very clear evidence that there was a substance in the saliva that inhibited AIDS. And it is my memory that at that time the components of saliva were not really known very well. This left you with a big black hole in understanding so that you were forced to say that there was something in saliva that we don't know anything about that is having a suppressive effect on the AIDS virus, and "we don't know anything about" is too vague to be reported as anything other than just an observation.

Harden: Was this component the SLPI [secretory leukocyte protease inhibitor] protein that Sharon Wahl is now working on?

Salzman: SLPI is a natural component.

Harris: But it was not known at the time.

Salzman: It was not known at that time. So little was known. It was just so vague. For those of us who had spent years in basic science, it was unsatisfactory to report this as an entity.

Harden: This also highlights, then, the messiness of medicine versus the exactness that scientists in the laboratory want to get to.

Harris: You were telling me about the number of organisms, the different kinds of organisms in saliva the other day on the phone. Would you repeat that?

Salzman: Well, it is well known that there are probably 300 varieties of bacteria and

300 to 400 varieties of microorganisms present in saliva in a normal healthy mouth; and that on a tooth, a single tooth in a normal healthy mouth, you may have more microorganisms than the human population of the world. The mouth is really what I would call a sewer. These microorganisms are kept in check by the components of saliva. There is no other place in the body where you have such a tremendous concentration of potentially infectious organisms which do not result in disease.

But saliva had received so little emphasis and we had so little understanding that we did not know the components of saliva. And to take saliva--this collection composed of bacteria, viruses, protozoa, yeast, everything you can imagine--and to add it to a virus preparation and then to see that this virus seemed to be inhibited in growth is something that you can report as an observation. But it is not basic research until you know more about what you are doing. I think that's a valid statement.

Very early Phil realized that he had some limitations, and that is why Sharon Wahl took over this basic work, to find out more about the saliva and to find out more about a particular protein that might be involved in this inhibition. As it turns out, SLPI is not specific for the AIDS virus. It is a very general protective device. SLPI covers a large area on the white blood cell, and, consequently, the virus cannot get into its receptor. But it is a broad device that would affect many organisms, and saliva may and probably does have many other such protective devices that we still do not know about because it keeps this population of microorganisms under

control.

Harris: In this particular period of time, you came from NIAID to the National Institute of Dental Research.

Salzman: Yes.

Harris: Can you tell us what led you to move from one institute to another? Was it because of your connection with AIDS, do you think?

Salzman: No. The reason that I left Allergy and Infectious Disease was that Ken Sell left Allergy and Infectious Disease as scientific director. That produced a general upheaval in the office. Gordon Wallace [Dr. Gordon Wallace] was already the deputy scientific director. The position in the dental institute opened up, and I met to discuss it with Dr. Notkins. I had a tremendous respect for him and for his research. Although I was working in an administrative capacity, I was and am a scientist. I just thought he was super-duper, and we talked about things we could do together, and I found it exciting.

Harris: So we have you now at NIDR. Now, Dr. Notkins' laboratory, as I have mentioned before, was the Laboratory for Oral Medicine.

Salzman: He is part of a group headed by Sharon Wahl.

Harris: As early as fiscal year 1982, somebody in that laboratory was searching to see if he or she could find a virus that was causing AIDS. They were suspicious. It was already called AIDS then. Then, at the same time, they were concerned with viruses in general in that laboratory, and several people were working on developing a transgenic mouse. Now, what do

you recall about the work on trying to develop a transgenic mouse that would serve as an animal model for AIDS research? There were several people involved.

Salzman: Dr. Notkins was well versed in what was needed in science and had a tremendous foresight, being able to think of what the intramural program needed to develop in order to keep it first-rate. He decided that one of the areas in which there was no emphasis at all but was promising because of the information it could provide was the area of transgenic animals, inserting external DNA into the animal genome. So we took discretionary funds from the Office of Scientific Director and decided to set up a transgenic facility. At first it was under his laboratory's direction because that was the best place to put it, it was felt, because of his knowledge and his understanding; but it was to be a general facility for the whole intramural program. We advertised for a veterinarian and interviewed a number of veterinarians to come into the intramural program because we had been operating without a full-time veterinarian. When I came to the NIDR we had just a part-time veterinarian on loan from Veterinary Resources. We had someone in the position who was ill and had a lot of difficulty in the position and did not move it forward and decided to leave. And so we looked for another veterinarian, and that's when we decided on hiring Joe Bryant [Dr. Joseph Bryant].

Harris: Can you describe what Joe Bryant contributed toward the Institute's animal research?

Salzman: I think our choice of Joe Bryant was a very fortunate one because I think he is a superb veterinarian. For small animals, he absolutely is one of the most knowledgeable people I know. But more than that, he has an intuitive sense of animals and illnesses. To see Joe operate is to fill one with a lot of respect. He's not afraid of the animals. He picks up the mice and he looks at them. He understands their needs. He can see when something is wrong. He is a superb veterinarian.

In the field of AIDS he was able to see the differences in some of these animals who were born of HIV-positive mothers, and he could observe that. He could see that, and he could see it repeated. It is only because of his dedication to these animals that the observation about human choriogamatotropic hormone was ever made. He had people to go to and talk to, but he made the observation.

Harris: Now, quite a few people in the Laboratory of Oral Medicine appeared to be working on developing or trying to develop a mouse model. You have mentioned the growth of mice born with HIV DNA. Can you elaborate on how that contributed to knowledge about AIDS?

Salzman: One of the problems with AIDS is the fact that you can not test your results in the host animal, which happens to be human beings. And you can't even easily test them in the closely related non-human primates because that type of experimentation is prohibitively expensive. So it was felt that transgenic animals offered a possibility of either adding genes or subtracting genes so that you might be able to understand some of the parts

of the AIDS picture and put them together. Observing the effect that an added or subtracted gene has on a transgenic animal may lead you to some information of what effect that gene may have in human beings. I think the findings from working with transgenic animals were productive in many cases.

Harris: Now, I'd like to turn to SLPI. What is the significance of Dennis Torchia's [Dr. Dennis Torchia] nuclear magnetic resonance studies on proteins related to AIDS?

Salzman: Dennis was supported and given money, I think, from the NIH Office of the Director. In a time when we knew that this three-dimensional structure of a protein was important in its interactions and in its interactions with drugs, Dennis was going to take protein from HIV and determine its three-dimensional structure. He had to work out the fundamentals on a related protein because there was an insufficient amount of the HIV protein for him to work with. They couldn't get it in large enough amounts. He did work for a number of years on a representative protein so that he could work out its technology until that point in time in which they could come up with enough HIV protein. And I think it has been borne out that you have to know the three-dimensional structure of a protein in order to really understand how the protein can interact either with drugs or with a receptor. That was the way he was going to proceed, and that's why he was supported with funds from the Office of the Director of the NIH.

Harris: In 1996 Dr. Frank Robey and his team shed some light on how GP-120, the

large protein on the surface of HIV, adheres to its target CD4 receptor on lymphocytes that become infected with HIV. Can you please comment on the relative importance of that work to the AIDS research?

Salzman: Well, I think in Frank's case there is no controversy at all with the fact that if you know what portion of the virus protein is reacting with the CD4 receptor, the receptor on the T cell, then you have a tremendous amount of information to use in trying to prevent that interaction. Frank has pursued that with a very small group in a very careful manner. A lot of other laboratories are also working on the interaction between a virus and infected cells. I think that Frank had a lot of difficulties along the way, but he was very careful about pursuing this.

Harris: What do you consider to be the most important accomplishment at the NIDR since your arrival at NIDR?

Salzman: My answer will be based on just the intramural program, which is certainly the area where I have more expertise than the extramural program. I think the intramural program developed into a body of people with diverse interests who worked very well together. I had not seen such interaction as existed at the NIDR between people and how they helped each other since I came to the NIH. I think that contributions with SLPI--just making us aware that they are protective proteins in saliva--is very important. The work on collagen is superb, and [Dr.] Hynda Kleinman and [Dr.] George Martin and that group have done something unique, something that was important to science and to our understanding of collagen and hard tissue.

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It is a wonderful accomplishment. And it's still very productive. They have found, just recently, an anti-angiogenic protein. Very, very fine work and very well done, and something that we in this Institute should be very proud of.

I think the work in diabetes that comes out of the Laboratory of Oral Medicine is recognized around the world as being a significant contribution to our understanding of diabetes and perhaps to a preventive test. We have bone, we have the diabetes work. And the contribution that we're making in AIDS is or certainly was of great interest to the field. The involvement of the macrophage really belongs to this Institute. Although it may not be perceived, in retrospect, by the AIDS community as such, I think the work done here was of great significance.

Harris: What is your view of the SLPI discovery?

Salzman: I think it is important because we knew so little about saliva and its components and how it performed in keeping infection from the oral cavity, I think the observation by Phil Fox was an excellent observation. And the molecular biology that's been carried forth by Sharon has been extremely well done. I think the finding that SLPI is a general protective protein that's in the saliva is a very good contribution. I think most people acknowledge that that probably is protective of moieties in the saliva or is probably the reason that it is not readily transmitted, if transmitted through the oral cavity except in these rare occasions, or appears to be, although I do not doubt that the virus is there. It is dispatched or taken care of by the

saliva. And I think that's an important thing, not only to dentistry, but to the whole AIDS research field, because there had to be some explanation why, with the frequency of oral sex, the virus was not readily transmitted that way. If it had been, the whole darn treatment of the AIDS virus would have had to be different.

Harris: If AIDS had occurred before 1954, how do you think the response would have been by the biomedical research community?

Harden: What we're asking is pre-molecular biology. What could have been done before we had techniques to isolate and study retroviruses?

Salzman: I think the victims would have died. I think we would not have understood what was killing them. I do not know whether the scientific background would have been there at that point to have isolated a virus or to have even understood the disease. It would have been like the black plague. It would have killed off a huge number of people, until it killed off the people that were involved. I think the epidemiology could have been done, and perhaps even could have found the association with homosexual people primarily at the beginning. And, consequently, any kind of preventive or protective policy would have had to treat AIDS like leprosy used to be treated--isolate the people who are infected and wait for them to die.

Harris: Do you think that there will be a cure or a vaccine created against AIDS?

Salzman: Oh, I think that we will be able to come up with some kind of protective device. Yes, I do. I'm not sure that the protective vaccines they're looking at now will be satisfactory. But I do think that we will eventually come up

with a protective vaccine. Plagues are not unique to AIDS. We have always had them. But they have always been able to burn themselves out—by infected people dying, unfortunately. And I think that's probably what will happen to AIDS.

Harden: Is there anything else that you would like to say before we stop? Any other observations either on NIDR in general or on AIDS in particular?

Salzman: My association with the intramural program has been a tremendous learning experience for me in fields in which I had no expertise or background. I found that both satisfying and very interesting. I really did, and the people were great. I find that in the work I do now, I am constantly learning more, and that appeals to me. That's what I like.

Harden: Thank you, Dr. Salzman, for speaking with us.