Abstract

Dr. Edward P. Gelmann, formerly of the National Cancer Institute, discusses the work of Robert Gallo's laboratory at the NIH and the early information on immune deficiency in AIDS patients. He describes the development of research to determine if AIDS was caused by a retrovirus and the contributions of researchers in Gallo's laboratory. Gelmann discusses the growth of clinical programs at the National Institutes of Health involving AIDS patients and his work in connection with these. He also comments on the value of the NIH intramural program, NIH research funding, and the organization of medical science research more generally.

This is an interview with Dr. Edward P. Gelmann, formerly of the National Cancer Institute, presently employed at the Georgetown University School of Medicine. The interviewers are Dr. Victoria A. Harden, Director of the NIH Historical Office, and Dennis Rodrigues, program analyst. The interview took place at Dr. Gelmann's office at the Lombardi Cancer Center in Georgetown on 1 May 1990.

Rodrigues: Why did you decide to pursue a career in medicine?

Gelmann: That goes back to considerably before AIDS. I was raised in a medical household and was exposed to discussions about patients every day. It was just something that I was brought up in the midst of and it was very natural to me. I suppose along the way I had questioned whether I wanted to go into medicine, and had thought about doing science exclusively, but when it came right down to it, I never really deviated from the goal of going to medical school. I trained in a

scientists' training program and was introduced to retroviruses when I was in medical school, working with [Dr.] Henry Kaplan, who has since died, but who was the father of radiation treatment for Hodgkin's disease and who also was the discoverer of one of the original murine leukemia viruses.

Rodrigues: What school was that?

Gelmann: At Stanford University.

Rodrigues: So, retroviruses were an interest of yours very early on? Was that after you received your degree or during your training?

Gelmann: During the years of getting my M.D., I spent three and a half years in medical school working in Kaplan's laboratory, I published several papers, and that is how I became interested in retroviruses. I committed myself to go to the NIH when Bob [Dr. Robert] Gallo came out [to Stanford] to give a seminar. We were working with mouse viruses, and he was talking about a human virus that, at the time, was thought to be HLV23, but turned out subsequently to be a contaminant and not a human virus. But what impressed me was the fervor with which he described the topic and went after it. I decided that I wanted to go to the NIH after my house staff training to work on human retroviruses.

Harden: So you came to the NIH right out of medical school?

Gelmann: No. I applied right out of medical school, but I first did my house staff training and then went to the NIH to finish my clinical training. After I finished a year of clinical training in the Medicine Branch, I went to Gallo's laboratory in 1979.

Harden: What were you working on when you first arrived at the NIH?

Gelmann: Most of my work was with different viral and human oncogenes. I was one of the first people to get involved in gene cloning in Gallo's laboratory. In those days, it was not as simple and store-bought a technique as it is now. There were a number of technical hurdles that had to be overcome. I had, from previous research experience, done a substantial amount of work with bacteria. Since you had to know how to deal with prokaryotic systems, I got involved in setting up gene cloning. Once we succeeded in getting the techniques to work, we began to clone different animal tumor virus genes. From the animal tumor viruses, we obtained oncogenes and used the oncogenes as probes. We cloned a number of human proto-oncogenes and we published a number of papers in that area. That was just about the time when [Dr. Bernard] Poiesz and [Dr. Francis] Ruscetti had identified and isolated HTLV-I [Human T-cell Leukemia Virus, type one]. The reagents from that work were being spread around the laboratory for other people to investigate different aspects of it. We were supplied with virus particles and nucleic acid to try to clone a piece of HTLV-I. Because of our success with the animal viruses, we were provided with the material to try to isolate that. But, actually, I was never successful at that. A postdoctoral fellow named [Dr. Vittorio] Manzari finally cloned a small piece of the cDNA of HTLV-I. But that was only after the Japanese had cloned the whole thing and had sequenced it. It was a technical tour de force. The scientists were [Dr. Mitsuyaki] Yoshida and a

graduate student doing his postdoctoral work [Dr.] Motoharu Seiki.

Harden: This background explains why your interests seem to span a number of fields--virology, genetics, and oncology. You have been investigating a number of fields in terms of bringing it all together.

Gelmann: When I went to Bob Gallo's laboratory as a postdoctoral fellow, that was what I was told to do, so I started doing it.

Rodrigues: In 1979, you started working in Gallo's laboratory. The first CDC [Centers for Disease Control] reports [relating to AIDS] came out around mid-1981. Were you aware of those reports?

Gelmann: Yes, we were aware of the reports. There were these whisperings about the strange patients who appeared to have Pneumocystis [carinii pneumonia, PCP], and, of course, we knew what that was, as well as Kaposi's [sarcoma]. This was mentioned and some discussions were held. Very early on, Gallo, to his credit, seized upon this as a human analogy for the immunodeficiency induced by feline leukemia virus. He felt very early on that the agent [causing the disease] would be a retrovirus. That is rarely quoted and rarely cited, but in informal discussions in the halls and at laboratory meetings, he was very keen on this idea. It was because of the similarity of the symptoms with those caused by the feline leukemia virus. We did not know at the time that there would be a monkey model as well--the simian immunodeficiency virus was not yet discovered. That whole topic developed more or less simultaneously with the development of AIDS and

was done by the people at the New England Regional Primate Center.

Rodrigues: Some of the people we have talked to characterized their first reaction to AIDS as being a problem that was probably something unique to the gay population, related somehow to the lifestyle of gays. They thought that, because of this, AIDS would probably be a transient, localized problem as opposed to something that would eventually turn out to be a global problem. Different people seem to change their perspective on this matter at different points in time. Some people saw the implications of AIDS very early on, and other people were a little more conservative about the implications of this new disease problem. In your first exposure to this problem, did you incline more to the former view or did you think that AIDS could possibly be an infectious disease?

Gelmann: I really thought that we were just seeing the tip of the iceberg. My views on that came from the initial CDC information on the demographics and the characterization of those patients, when there were about a hundred patients or so. The CDC was very interested in their sexual practices. The patients were largely homosexual and there was a use of nitrites. There were sexual practices that facilitated transmission. Basically, there were very few common denominators amongst those who were ill except for the fact that the very first patients were amongst the most promiscuous, having many, many sexual contacts in a day. When calculated out, it was more than a thousand a year. If you want to spread a new virus, that is the population to do it in. It is like getting a thousand blood

transfusions in a year. It was apparent that this was just a group of people whose behavior facilitated transmission of a rare agent amongst many of them.

Harden: Did you think of it as a new agent--something that had not been around or was it just an unknown?

Gelmann: Certainly it was not known in the Western world. The fact that all of a sudden, young men started walking into emergency rooms with Pneumocystis pneumonia was not subtle. It appears now from studies that this disease problem had been going on in Africa for some time. But, yes, I think in the Western hemisphere, most of us were convinced that something had changed; that there was something new to contend with.

Harden: How did you feel about the assumption that it might be caused by a retrovirus? Did it sound reasonable?

Gelmann: Yes. Actually this idea appeared somewhere in the literature very early on. Bob [Gallo] and I speculated about that and I was one of the people who tried to get involved with that research very early. The way we did it, was by looking for viruses that were similar to the known one--HTLV-I. That was the only handle we had into human retroviruses. My work with HIV [Human Immunodeficiency Virus] was not even known then. But with the AIDS question, when I was in Gallo's laboratory, everyone was doing molecular studies trying to identify viruses in infected and noninfected tissues that were similar to HTLV-I. That effort did not succeed and I left the Gallo laboratory about a year before HIV was

discovered, after [Dr. Luc] Montagnier had published the initial description in Science in parallel with the papers from the Gallo laboratory.

Rodrigues: My research indicates that you did give a talk in April of 1983. It was at the first workshop that NIAID [National Institute of Allergy and Infectious Diseases] put on. It was titled "Search for the Etiologic Agent." I think Gallo was originally scheduled to speak but apparently you stood in for him. Do you recall that particular workshop?

Gelmann: I gave several talks presenting some of our molecular data and one talk which was a little bit more speculative. But one, I think, was up at NYU [New York University], one was at the Masur Auditorium, and one was at Cold Spring Harbor. I actually got to talk several times in public about it. I do not know exactly which one you are referring to, but I did give several talks.

Rodrigues: It was a meeting which Dr. Albert Sabin attended.

Gelmann: I do not remember. I know what Albert Sabin looks like; I just do not remember the specific meeting.

Rodrigues: Amongst those various meetings you attended, were there any that stood out in your mind as being particularly stimulating or provocative, helping people's thinking move in the right direction?

Gelmann: In those days all the meetings were stimulating, because everything was so new. Every time you had a meeting the epidemiologists told you what was new about the next hundred patients. That is where all the real data and all the hints were

coming from. No one really knew what the virology meant, if anything, at the time. Also, Max [Dr. Myron] Essex's people had been doing a bunch of serology with HTLV-I reagents and had come up with a number of positives. The other group that I remember, with whom I actually collaborated, although we never published any papers, were the people at the New England Regional Primate Center. We heard about these macaques that had developed lymphomas and an immunodeficiency that was apparently transmitted to other members of the colony. I visited the center; gave a seminar and talked with [Dr.] Ronald Desrosiers and Norm [Dr. Norman] Litvan, both of whom subsequently were involved in the isolation, identification and cloning of SIV [Simian Immunodeficiency virus]. That seemed, at the time, to have great potential. Once again, we took samples from those monkeys, and screened them with probes that were related to HTLV-I to see if any material could be found in the monkey samples that related to the human virus.

Rodrigues: The process by which people began to move in the direction of doing AIDS research as opposed to something else is something that varies from place to place and from individual to individual. Some individuals said that they were not working on anything else at that moment and that AIDS seemed like an interesting problem. Other people said that it fitted in and dove-tailed exactly with where their research was going, so it was a natural extension of their work. Some described it as a process where someone galvanizes other people and

begins to direct others to attack different pieces of the problem. How would you describe the process in Dr. Gallo's laboratory?

Gelmann: I hesitate to say what went on in Dr. Gallo's laboratory. I cannot represent what went on there or the general procedures.

Rodrigues: Could you give your perspective?

Gelmann: It was an interesting problem. It had to do with humans and T-cells. We had reagents that were relevant. It was a fascinating issue. It was something new and different, and there was always a tremendous support and enthusiasm in that laboratory to look into what was new and different, as long as it was related to human viruses and cancer. So we had some unique reagents to deal with that, and an interesting problem. It was just a matter of trying to get specimens, which eventually began to come into the laboratory in 1982 and 1983, and then of working with them. Also, I went out and sought blood samples from hemophiliacs at a hemophilia clinic, because it had become evident, from the work of Jim [Dr. James] Goedert and others, that hemophiliacs were receiving infection in their blood products.

Harden: You have talked about giving these names to the CDC. Can you comment on the interagency cooperation, or lack of it, among the CDC, NCI, and NIAID and any other such groups?

Gelmann: Bob Gallo's laboratory always worked more or less as a sole agent, relying on collaborators who brought in samples. There was not a whole lot of collaboration

with the virology laboratory at the CDC which was headed by [Dr.] Cyrus Cabradilla. If he did not head it, he was intensely involved in it. There were other collaborators who brought specimens and exchanged materials with Gallo, but there was no extensive collaboration with the CDC. I think the big exchange of materials or activity went on after I had left the laboratory. This famous story is told about the 200 samples which Gallo was given blinded. He was able to identify them based on the new serologic tests which had been developed from the viral reagents that [Dr. Mikulas] Popovic and [Dr. M.G.] Sarngadharan had isolated.

Rodrigues: We have come across your name listed next to a series of different projects that the NIH was initiating, some of which had to do with an efficacy study of human lymphoblastoid interferon in Kaposi's sarcoma. Could you comment?

Gelmann: What happened in the middle of 1983 was that I was in the process of making a career move, regardless of AIDS. It happened to fall right in the middle of the AIDS excitement. This was just after we published our papers in Science and had gone to the meeting in Cold Spring Harbor. I was packing up my stuff and moving to Building 10 when [Dr.] Françoise Barré-Sinoussi was visiting the laboratory after the Cold Spring Harbor meeting. She had come down to Bethesda and brought samples with her. I had made a decision completely independently to take a senior staff position in the Medicine Branch and return to a little clinical activity. Because of that move, my activities changed from doing

laboratory research in AIDS to being involved in some of the clinical programs at the NIH. There was a desire to establish clinical programs, like those in which I was involved in the National Cancer Institute. So, we decided to focus our activities on the cancer aspect of AIDS, which was Kaposi's sarcoma. I was involved in those trials, when they began, while I was still in Gallo's laboratory, and had a commitment to go to the Medicine Branch. We also felt that it would give us an opportunity to collect our own patients and that those patients would provide us with the ability to learn about the disease and to collect samples. Since interferon was being used in Kaposi's sarcoma, we thought it would be a good idea to test whether it had any antiviral properties as well as antiproliferative properties. I became the principal investigator for that trial and then we began to accrue patients on it. I continued that Kaposi work when I moved to Building 10.

Rodrigues: About how much longer did you pursue that?

Gelmann: I was involved with clinical AIDS work for about a year or two after I moved to Building 10. That work was very much of an inter-branch collaboration. We had a large number of patients in the clinical studies and also a number of on-going ancillary laboratory studies. There was a cadre of research nurses, Fellows, and other people who were interested in the patients' care. Every week, Cliff [Dr. Clifford] Lane, [Dr.] Henry Masur, and I sat down in a large conference room with all of the ancillary staff and went through the records of each and every patient who was part of the various studies at the Clinical Center, NIAID, and

NCI. When patients were done with one study and were appropriate for another, we exchanged them. Laboratory workers from the FDA [Food and Drug Administration] and from elsewhere would come and give reports on viral testing, on reagents, what we needed to do, what we could give them, and so on. That was a very rich and fruitful time for collaboration.

Out of those activities, basically ad hoc, an AIDS working group sprang up out of nothing. That was strictly from the initiative of Lane, Masur, and myself. We got together and started seeing patients on the ward, but then it would become overwhelming so we sat down in the room once a week. Out of that came, for me, nearly fifteen or twenty papers. It was just a tremendous collaboration and it is where all that stuff in my C.V. [curriculum vitae] comes from.

Rodrigues: Maybe you could say a little more about how that AIDS working group evolved. It was confusing when we looked through the records since there were many different groups of people that seemed to come together for different purposes.

Gelmann: From my point of view, it evolved strictly out of the needs of clinicians trying to deal with the increasing number of patients. Henry Masur was quite an expert in clinical management; Cliff Lane was working with Tony [Dr. Anthony] Fauci and had some new reagents that he wanted to try; and we were collecting our own patients to look at Kaposi's sarcoma. The clinical aspects of AIDS were pretty new and we did not know that much. So, we were constantly consulting with

each other while seeing patients on the ward.

But, as more and more patients came, the burden became so overwhelming that we just had to sit down and do it in an orderly fashion. In addition, so many other investigators were asking for blood, urine, and other samples, that we felt that the best thing to do was to coordinate this through a single meeting. That way, various protocols and requirements for the acquisition of different samples could be met, patient care would be optimized, and then patients who were done with one study could go to on to another if they were eligible. It was really a grassroots event which sprang just out of the needs of the people who were involved.

Harden: What about your staff--the nurses, technicians, and other people? Were you getting any particular feedback from them in terms of their concerns about AIDS and direct patient care?

Gelmann: Amongst the research staff, everyone in this working group was dedicated and I guess we just accepted by observation that this [disease] was no more contagious than hepatitis B. We were careful, but not paranoid. Certainly we dealt with these patients and materials relating to them carefully, but basically in the same way as we would for a patient with hepatitis. There was greater concern amongst the general nursing staff and it was addressed directly in meetings. The one thing we did early on was to proscribe contact of pregnant medical personnel with patients, because we knew that the patients were carriers and shedders of

cytomegalovirus. That represented a direct threat to a fetus. There has been much written about regulations in handling and universal precautions. There has been a lot of adaptation and things coming out of the CDC, but fundamentally not much has changed for us, since we followed certain procedures from day one. Fundamentally, AIDS still has a similar transmission pattern to hepatitis B.

Harden: What about the patients as people in their behavior?

Gelmann: It was something to which we adapted. In my recollection, in our clinical activities there was not any specific support or focus on psychosocial aspects of AIDS care. I do not remember whether we did not have the personnel or whether we were too busy.

Harden: Were the patients generally cooperative?

Gelmann: Immensely. They were one of the heroic stories of the whole AIDS saga. Initially, most of those patients were homosexuals and one of the great stories of the AIDS saga has been the response of the homosexual community: active, well-informed, cooperative, supportive to each other and not particularly enjoying dying young. It is my personal belief that the AIDS activists, in terms of the experimental drug issue, have done all of us a favor, and cancer, sooner or later, is going to benefit from the model of the AIDS activists. In fact, now there is a cancer survivors' group being formed and it is becoming more vocal. It was the AIDS activists who taught us how to do that.

Rodrigues: As the work on AIDS began to expand, were there problems for you and your

staff in terms of support, or did you find that the resources you needed to carry out research and to expand this effort were forthcoming?

Gelmann: Intramurally, there was always too much money. For a while, my personal viewpoint--it is strictly my opinion--was that extramurally, there was also too much money. This is a tremendous problem. People had to throw money at AIDS, because only then did the bureaucrats and legislators think that something was being done, and then the money came too fast. We could not adapt; we could not learn how to spend the money as fast as it was coming.

Rodrigues: Was this true even for the intramural programs at that time?

Gelmann: It is my personal view, that for the extramural programs, when all of a sudden there was a tremendous expansion of the AIDS dollars, a lot of money went to projects that were not properly conceived. It takes time to figure out how to spend the money and what experiments to do. But the public demanded that money be spent; that the problem be solved. That has changed. We went through a growing period, things evolved, and there has been some incredibly useful work coming out of the studies of HIV at many levels. The funding has tightened up, now. But, in the beginning, there was a huge waste.

Harden: To ask a philosophical question about the public's view, physicians, and scientific medicine. Do you think that we can just pour the money into disease problems, that the solution must be forthcoming and, furthermore, if it is not, then anger is justified?

Gelmann: The understanding is forthcoming, and you do not need AIDS for that. I mean, look at sickle cell anemia. We understand that down to the atomic level. So, the understanding is forthcoming. AIDS patients certainly have benefited. For example, AZT [3'-Azido-2',3'-dideoxythymidine] basically came out of the intramural NCI program. AIDS testing of the blood supply is, after all, essentially safe. Just think, right now if we had no serologic tests, we could not guarantee our blood supply. What a disaster! So, there have been some major, major advances from this. We are learning about this virus. We have known about influenza much longer and have yet to be able to figure out how to make a permanent vaccine. We have to re-vaccinate people. We may have to wind up re-vaccinating people for the AIDS virus once we figure out which people we should vaccinate--it is tricky. But, we have learned a lot, in general, about retroviruses from the work on AIDS. The technical expertise that has poured into this work and the biotechnology is wonderful. The knowledge gained will have ramifications for many different fields. This is not only just AIDS. When you get down to such fundamental issues in biology, there is always spill-over.

Rodrigues: You can get an idea of where research will go in the future, in terms of what can be learned by looking at AIDS. The other factor that many people tend to discount is the work that was done immediately preceding the emergence of AIDS. Look, for instance, at all the work on HTLV-I and the techniques of cloning genes.

Gelmann: I am glad that Montagnier had the virus, but I am certain that there was no place

in the world which was more ready to analyze its import, and to prove that it was the causative agent of AIDS, than Gallo's laboratoy. Gallo had all the pieces in place; he had all the machinery to analyze new retroviruses, and it was what he had been trying to do for fifteen years. His people learned how to grow the retrovirus. Mika Popovic learned how to grow it. Once they knew how to grow it, and make enough of it to get reagents to study, then they knew what tests to do. That was the one place in the world where the virus needed to be to get things done fast. There is no question about it.

Harden: Do you think that the [John] Crewdson articles are tilting at the wrong windmill and, in a sense, splitting hairs or is there some justification for Crewdson's claims?

Gelmann: Crewdson was trying to analyze personal behaviors, individual actions at particular times of some day of a week, and make a pattern or develop some understanding of it. I am not sure that I can understand those events in the same way that Crewdson did. Science works in funny ways and much of it is opportunism. If Bob Gallo gets the Nobel prize, which he should, it will not be the first time that someone, who other people think is a bastard, wins the Nobel Prize. That is part of life. Mika Popovic had spent twenty years working with retroviruses. He came from the institute in Prague, one of the cradles of retrovirus research. Sitting in his little back room, he applied techniques that were twenty years old, trying to grow this thing. In a very ancient and European way, he

would puff on his pipe, put his pipe down, and do some work and pick his pipe up again. The biohazard people would have shot him. But, he was involved in a critical breakthrough in terms of growing viruses.

In fact, at that time, viruses were just not there; making enough virus for anyone to prove it and to figure out what it was meant learning how to grow it. The French did not know how to grow the virus; they grew it in culture on fresh cells, and the virus did what it was supposed to do and killed the cells. So, every two weeks they had to start their cultures all over again and they were never able to collect any and save it for the winter. Popovic derived the cell line which was resistant to be killed by the virus. Therefore, you could grow and produce the virus and you could collect it in studies--protein studies, nucleic acid, make antibody tests out of it, and so on. There were all the people in place to do the mass testing, to take the blind samples from the CDC, and prove the association. Gallo was ready.

Harden: It sounds as though Dr. Gallo's personality becomes the focus for many people's opinion of him.

Gelmann: Throughout his career; throughout his career.

Rodrigues: I think that part of the problem is that people expect physicians, in particular, and probably scientists, in general, to be individuals who are somehow beyond those weaknesses and frailties that we see in others. We are unforgiving when we see these in them. The expectation is that someone in that kind of position is more

than human.

Gelmann: It is hard to meet those expectations.

Rodrigues: One of the points you mentioned before was about how the AIDS patients and the AIDS activists helped not only their own cause but also patients with other types of diseases. Has any of the activism about AIDS hampered any effort or discouraged people from becoming involved with the research? It seems as if the federal researchers particularly, according to some of the articles, were cast as villains by some of the more extreme activists.

Gelmann: Yes, they cast Gallo as a villain, whereas he should be a saint, as far as they are concerned. He has taken a terrible beating from the gay press. I have no idea why; it is beyond me. It really is. There have always been extremes with activism. I do not know that any of the extremists have dissuaded anyone from research. In fact, I can not think of an instance where anyone has been dissuaded; the activism certainly politicized AIDS. AIDS is a very political field. I think some people decided not to get involved because they did not like the politics. You like to go to your annual meeting. I go to the Cancer meetings; hear about things and talk to colleagues. If you go to the AIDS meeting; it is a circus. People are lining up on the streets; policemen are wrapping up people and taking them away; there are protests in the back of the room. You can not give a scientific talk. It is a three-ring circus. The real AIDS meeting was Gallo's laboratory meeting. It had its roots years ago when he brought everyone out to

Rockville or wherever the contract laboratory was just to get away and to hear about the data for two days. Those started long before AIDS. I remember doing that in June and having pizza in the afternoon. Now, they are international events. The real--the official AIDS meeting is a circus. That is distasteful to some people; some people just do not want to bother. What keeps people in AIDS is the money; there is grant money if you apply for it. The money is a tremendous determinant of the kind of research that gets done. The NIH announces, "We are giving out $20, $30, $50, $100 million dollars for this; give us proposals." They will get proposals. The peer review process and the granting process is superb. It gets the job done.

Rodrigues: Now if we could return to your own work once more. We left off the discussion at the time when you had moved over to the Medicine Branch and you were working with interferon and other therapeutics. I believe you said you did this for about a year and a half?

Gelmann: It may have been two. I could, if you really needed the dates, get the dates for you. I still have some for the publications, for the clinical trials. I continue to keep the records, because these days, who knows what people will try to dig up and complain about. Actually, I have all the records of the clinical trials.

Rodrigues: I just want to trace how your work developed. Did you continue working with AIDS patients?

Gelmann: Yes. I continued to work with AIDS patients for the next two years. Then AZT

appeared, and Sam [Dr. Samuel] Broder, who was my boss, two levels above me, was at that time director of the Clinical Oncology Program. His laboratory had generated AZT and then gotten other analogues, nucleoside analogues from Burroughs Wellcome and were doing clinical trials. The focus of the NCI effort shifted away from Kaposi's and the cancer aspects of the disease to the anti-viral aspects. Sam and his colleagues were perfectly appropriate principal investigators of those trials. I focused my interests elsewhere. I then got back more into cancer for cancer's sake. I have gotten out of work on AIDS almost completely.

Harden: When did you move to Georgetown?

Gelmann: I moved here in October of 1988 at the time when the old Medicine Branch basically de-materialized and everyone left, except for a single investigator. Three senior scientists went to Fox Chase and, I think, five or six came to Georgetown. By that time, I was out of AIDS completely.

Rodrigues: You have mentioned a number of people, to some of whom we have talked. Other than those people to whom we have already spoken, are there any other individuals that you think might provide some new insight, into these questions?

Gelmann: You are interested in early things? Geographically, at the NCI, there are Cliff Lane, Henry Masur, [Dr. Hiroaki] Mitsuya. Mitsuya is in some ways a Prometheus. He is a very, very gifted man with a mission and he accomplished a huge amount of work. He is the real father of AZT. Certainly, Sam Broder was a driving force, and intellectually is without peer. But Mitsuya did it and deserves

tremendous credit, which he has received.

Harden: Considering the organization of science and of who gets the credit for the work, you have already mentioned a number of people in Gallo's and in Broder's laboratory who actually did the work, but the credit seems to go to the laboratory chief. Would you like to comment on that?

Gelmann: That is a sensitive matter. I am a laboratory chief myself. I do very few experiments and have many people working for me. It is the way science works and it is different. I think Mitsuya has made a tremendous contribution and has received his due. I do not think Sam has shortchanged him. I am not sure that he could have done it without Sam. I think there was an important collaboration between the two. But Mitsuya has been very successful. Bob's [Gallo's] laboratory is bigger; Bob has always been criticized for having more difficulty in sharing credit. I think that he has tried hard over the last five or six years to hear some of those criticisms and to change a little. His treatment of people like [Dr.] Beatrice Hahn, [Dr.] George Shaw, and [Dr.] Lee Ratner has been different from his treatment of Bernie Poiesz and Frank Ruscetti. Night and day. He really squired Ratner. The disagreements with Poiesz and Ruscetti were legendary. Everyone knows about them. It is a sensitive subject, but it is certainly not a secret. But I think that Gallo was very kind to some of the younger people. Although they are funded, investigators in HIV research are doing well. There has been a change.

Harden: The reason I would like you to comment on this matter is because we are trying to communicate to people how science works.

Gelmann: Working in the laboratory and being a postdoctoral fellow or being the junior person is partly a training, even though no one knows the experiments better than the person who does it with his own two hands. No matter how slight, there is always a technical creativity in getting the experiments to work and in publishing reproducible results. But unless there is someone who is very bright and very gifted, and there are such people, it is usually a collaboration of a junior person with a senior person with some more perspective. The senior person has the insight, although the goal may change before he or she reaches it, or the people who are working towards it might change. That is the way most of science happens today.

Scientists like [Dr.] Barbara McClintock, who have been working by themselves for thirty years, are becoming increasingly rare, partly because of the technical challenges. Everything is so specialized and technically difficult. There are people who closet themselves in the laboratory, if they can fund themselves with one or two good grant proposals. There is a handful of people like that in the United States today. But barely a handful. I am on the outside of the intramural program looking in. I am a funded investigator; I have an RO1 [investigator-initiated research proposal]; but quite frankly, I feel a little uncomfortable unless I have a grant application pending somewhere. I always like to have one iron about

to go into the fire. You have to pay all those people sitting in the laboratory.

Harden: From your experience both in the intramural program and being at a university, would you comment on what you think is the value of the NIH intramural program? Can it be done elsewhere or is it a unique set up?

Gelmann: There is no question that it is unique. It is probably too big; probably inefficient; and it is probably abused. Big deal. Nothing is perfect. Nothing will run perfectly. Science is inefficient and expensive by its nature. But there are things that you can do at the NIH that you just can not do anywhere else. Where else are you going to get [Dr.] Jacob Maizel with a big super computer concentrating on certain problems? Where else can you get together the collection of young scientists to concentrate on something to produce? There are branches where huge million dollar efforts have turned into nothing. God knows what will become of Steve [Dr. Steven] Rosenberg's immunotherapy. But, you have to try. You do not know until ten or fifteen years down the road whether something has worked or not.

The NIH is a unique place for that reason. You can have well funded, goal-directed work that comes out of the investigator's imagination and creativity. Clinically, I think it is unique also, although I see a continued erosion of the clinical activities in Building 10. That is, you can easily and quickly do pilot trials of agents in humans at the NIH, which you basically cannot do anywhere else because of the restrictions on human experimentation. No testing in this

country can be done quickly in people, except in Building 10. Most drug companies, when they have new experimental agents and want to get some quick pilot trials, do not bother to do them here; they do them in Europe. The Europeans are reliable investigators and good people who do not have the regulations we have. We are trying very hard to get some experimental drugs because there is a demand from the patients for this. The drug companies by policy do not want to bother. But still, intramurally you can do it. Boy, do I miss that. I would say that I miss that more than anything. Grant writing is not bad; it focuses you; it subjects you to the criticism of your peers. You learn from that. And there was a lot of stuff we did intramurally that was really a waste. I have notebooks full of good stuff, but even more notebooks full of complete trash that will never be published. Maybe a good attempt, if you are a fast learner. You have to be more focused in your thinking on the outside.

Rodrigues: That is one of the problems that we have had, trying to describe all the different work on AIDS and looking through the literature. People were quick to publish work that had panned out and had positive results. But so many efforts ended up with negative results or with no results.

Gelmann: Of course. [Dr.] Linus Pauling spent a long time trying to which ascertain whether protein was the genetic material. Is anyone dinging him for it now? You expect it in a career; you are going to publish something that is going to turn out to be dead wrong. You cannot be embarrassed about it. You make an honest

effort; you make an observation. Either things are reproduced by other scientists and the field moves on, or the idea just dies there in the literature. Certainly, Bob Gallo has had more than his share of that. He has had a tremendous public beating. I am not on his payroll, but I recognize that he went through tremendous personal tribulation and that in the end, he came out with something.

Rodrigues: Was anyone from the FDA involved in AIDS research?

Gelmann: Jerry [Dr. Gerald] Quinnan was involved in the FDA. He had a large group in which several individuals were working on different viruses. Some of them were co-authors on papers. He was doing a lot of research at one time. I do not know whether he is active any more.

Harden: Was it in the early period that the FDA did this work?

Gelmann: Yes. Quinnan was working with another man and they were trying to culture Kaposi's [sarcoma] cells and he was talking about the cooperation of EBV [Epstein Barr Virus] and CMV [cytomegalovirus] in causing Kaposi's sarcoma.

Harden: This brings me to another question. I have been doing some research on Koch's postulates. It was stimulated by [Dr.] Peter Duesberg's challenge to HIV as the cause of AIDS. He does not believe that HTLV-I causes cancer, either. What did it take to convince you that this retrovirus [HIV] was indeed the cause of AIDS?

Gelmann: I think the fact that it can kill cells <u>in vitro</u> and the serology were the two convincing things for me. It was interesting to see that it was a lentivirus, and that it was similar to other lentiviruses which did these things in animals.

Harden: You have done some work on Burkitt's lymphoma and I believe, that Duesberg was saying that someone had recently found the Burkitt's lymphoma was not caused by a lentivirus.

Gelmann: In my studies of Burkitt's lymphoma, there has been the involvement of an oncogene called myc. I think what Peter was quoting was that it was thought that in every case of Burkitt's lymphoma, if you looked at the detailed molecular pathology of the myc oncogene, you could find that one of the two copies--we all have two copies of every gene--had a mutation, or some change. About that time I was studying a particular case of Burkitt's lymphoma, which happened to be in an AIDS patient, but that was irrelevant to the issue. There was a published paper in which it looked like there was a myc gene which looked normal. But then, when we looked at our gene, we found an interesting change which was in a region that was unexpected. We went back and looked at that one and found it did have mutations. To my knowledge, today, there is still no normal myc gene in a Burkitt's lymphoma or there is no Burkitt's lymphoma without an abnormal myc gene in it. I think that in terms of myc and Burkitt's, it is the second best example of an oncogene being very, very closely associated with a specific cancer. The best example is abl-oncogene in chronic myelogenous leukemia, where Koch's postulates have almost been satisfied.

Harden: Thank you, Dr. Gelmann.

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