

This is an oral history interview with Dr. Edward P. Gelmann, formerly of the National Cancer Institute, and now professor of medicine and oncology at the Georgetown University School of Medicine. The interview was conducted on 1 May 1990 in Dr. Gelmann's office at the Lombardi Cancer Center. The interviewers are Dr. Victoria Harden, Director, NIH Historical Office, and Dennis Rodrigues, Program Analyst.

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

Gelmann: That goes back 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 it and had thought about doing science exclusively, but when it came right down to it I never deviated from the goal of going to medical school. I trained in a scientists' training program. I was introduced to retroviruses when I was in medical school, working with [Dr.] Henry Kaplan, who has since died, but who is the father of radiation treatment for Hodgkin's disease and also is the founder of one of the original murine leukemia viruses.

Rodrigues: What medical 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 studies?

Gelmann: During the years of getting my M.D. I spent three and a half years in medical school working in Kaplan's laboratory and published several papers, and that is when I got interested in retroviruses. I committed myself to go to the NIH when [Dr. Robert] Bob Gallo came out 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 HL23V, but turned out subsequently to be a contaminant and not a human virus. 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 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 got there?

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 today. There were a number of technical hurdles that had to be overcome. I had done, from previous research experience, 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 take on 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 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. That was [Dr. Mitsuyuki] Yoshida and a graduate student doing his postdoctoral work, [Dr.] Motoharu Seiki.

Harden: This explains why your interests seem to span a number of fields—virology, genetics, and oncology. So you had been investigating a number of fields in terms of bringing it all together.

Gelmann: When I went to Bob'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 in 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, and, of course, we knew what that was, as well as having 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 that the agent would be a retrovirus. That is rarely quoted and rarely cited, but in informal discussions in the halls and in laboratory meetings, he was very keen on this idea. It was because of its similarity with 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 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 and related somehow to their lifestyle. They thought that because of that it would probably be a transient, localized problem as opposed to something that would eventually turn out to be a global problem. Different people seemed to change their perspective on this at different points in time. Some people saw the implications very early on, and other people were a bit more conservative about the implications of this new problem. In your first exposure to this problem, did you hold more with the former view or did you think it could possibly be an infectious agent?

Gelmann: I 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 epidemiologists were 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 except for the fact that the very first patients were among the most promiscuous, having many sexual contacts in a day. It calculated out to more than a thousand a year. If you wanted to spread a new virus, a group within the gay population was the most fertile environment at that time. It was 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 among 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 not 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 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 a retrovirus? Did that sound reasonable?

Gelmann: Yes. Actually, it appeared somewhere in the literature very early on. Bob 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, since the only handle that we had into human retroviruses, was by looking for viruses that were similar to the known one—HTLV-I. 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 non-infected tissues, that were similar to HTLV-I. That 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: I noticed that you gave a talk in April of 1983. It was at the first workshop that NIAID [National Institute of Allergy and Infectious Diseases] put on. The talk was titled "Search for the Etiologic Agent." I think Gallo was originally scheduled to talk, but apparently you stood in for him. I do not know if you recall that particular workshop.

Gelmann: I gave several talks presenting some of our molecular data and one talk that was a little more speculative. But one, I think, was up at NYU [New York University], one was at the Masur Auditorium [at NIH], 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 on the subject.

Rodrigues: It was a meeting that 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: Of those various meetings were there any that stood out in your mind as being particularly stimulating or provocative, helping people move in the right direction?

Gelmann: In those days they all were, 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, [Dr. Myron] Max 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, was the people at the New England Regional Primate Center. We heard about these macaques that had developed lymphomas and immunodeficiency that was apparently transmitted to other members of the colony. I visited up there, gave a seminar, and talked with [Dr. Ronald] Ron Desrosiers and [Dr. Norman] Norm Letvin, both of whom subsequently were involved in the isolation, identification and cloning of SIV [Simian Immunodeficiency retrovirus]. That seemed, at the time, to have great excitement and potential. Once again, we took samples from those monkeys and screened them with probes that were related to HTLV-I to see if there was any material that could be found that related to the human virus in the monkey samples.

Rodrigues: Something that varies from place to place, from individual to individual, is the process by which people began to move in the direction of doing AIDS research as opposed to something else. 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 dovetailed exactly with where their research was going, so it was a natural extension. Some described it as a process in which 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: Just 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 from a hemophilia clinic, because it had become evident from [Dr. James] Jim Goedert and others, that hemophiliacs were receiving the 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 thereof, among the CDC, NCI, and NIAID and any other groups?

Gelmann: Bob'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 that was headed by [Dr. Cirilo] Cy 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. There is this famous story told about the 200 samples which Gallo was given blinded and how 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: Another thing that we have come across in our research was your name listed next to a series of different projects that NIH was initiating, some of which had to do with an efficacy study of human lymphoblastoid interferon in Kaposi's sarcoma.

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 doing a little more of

clinical activities. Because of that move, my activities changed from doing laboratory research in AIDS to being involved in some of the clinical programs.

There was a desire to establish clinical programs like those I was involved in 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 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 disease and collect samples. Since interferon was being used in Kaposi's sarcoma, we thought it would be a good idea to test whether it had some antiviral properties as well as antiproliferative properties. I became the principal investigator of that trial and then we began to accrue patients. I continued that Kaposi's 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 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 their care. Every week, [Dr. H. Clifford] Cliff 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 on the various studies of the Clinical Center, NIAID, and the NCI. When patients were done with one study and appropriate for another, we transitioned their care. 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. An ad hoc AIDS working group sprang out of those meetings. That was 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 where all those publications in my curriculum vitae come 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 was quite an expert in the clinical management; Cliff 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 way to do that was to coordinate this through a single meeting. That way, various protocols and requirements for different sample acquisition could be met, patient care would be optimized, and then patients who were done with one study could move on to another if they were eligible. It was really a grass-roots effort that just sprang 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 direct patient care and their concerns about AIDS?

Gelmann: In the research staff, everyone in this working group was dedicated and I guess we just accepted by observation that this was no more contagious than hepatitis B. We were careful, but not paranoid. Certainly we dealt with these patients and their materials carefully, but basically in the same way as we would for a patient with hepatitis. There was some greater concern among 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 potential threat to a fetus. There has been a lot written about regulations in handling and universal precautions. There has been a lot of adaptation, and also recommendations have come out of the CDC, but, fundamentally, not much has changed for us, since we took precautions from day one. Fundamentally, AIDS still has a similar transmission pattern to hepatitis B.

Harden: What about the behavior of the patients?

Gelmann: It was something we adapted to. To my recollection, there was not in our clinical activities, 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 homosexual men and one of the great stories of the AIDS saga has been the response of the gay 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, there is now a group for cancer survivors being formed and becoming more vocal. It was the AIDS activists that 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 that you needed to carry out research and to expand this effort were forthcoming?

Gelmann: Intramurally, there was always too much money. My personal viewpoint—it is strictly my opinion—was that extramurally for a while, there was also too much money. This was 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 was came too fast. We could not adapt; we could not learn how to spend it as fast as it was coming.

Rodrigues: Now, you say that was true even for the intramural program at that time.

Gelmann: It is my personal view, that for the extramural program, it was true that when all of a sudden there was a tremendous expansion of the AIDS dollars, there was a lot of money that 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. It has tightened up, now. But in the beginning, there was a huge waste.

- Harden: We can take this one step further for a philosophical question about the public's view, the physicians, and scientific medicine. Do you think we can just pour money into a problem and a 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 have certainly 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! There have been some major advances with 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 vaccine that is useful for more than one season. We may have to wind up re-vaccinating people for the AIDS virus once we figure out which people we should vaccinate. But we have learned a lot in general about retroviruses from the work. The technical expertise that has poured into this and the biotechnology is wonderful. This will have ramifications for many different fields. This is not just AIDS. When you get down to such fundamental issues in biology, there is always spillover.
- Rodrigues: You can look at the spillover of where things will go in the future, in terms of what we are learning, by looking at AIDS. The other part that a lot of people tend to discount is the work that was done immediately preceding the emergence of AIDS. For instance, look 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 prove that it was the causative agent of AIDS than Gallo's laboratory. He 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, namely 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 it needed to be to get things done fast. There is no question about that.
- 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 them?

Gelmann: Crewdson was trying to analyze personal behaviors, individual actions at particular times of some day of a week, and make a pattern or make some understanding of it. I am not sure I can understand those events in the same way that Crewdson did. Science works in funny ways, and a lot of it is opportunism. However, the sinister and conspiratorial aspects of Crewdson's account are perceived and were not real. If Bob Gallo gets the Nobel Prize, which he should, it will not be the first time someone, whom other people think to be difficult, 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 virus stocks were just not available. Making enough 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 it. 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 that was resistant to killing 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's laboratory was ready to do that.

Harden: It sounds as though Dr. Gallo's personality becomes the focus for a lot of people.

Gelmann: Throughout his career.

Rodrigues: I think that part of the problem people seem to have is that they 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 such things 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 things you mentioned before was about how the AIDS patients and the AIDS activists helped not only their own cause but also other types of patient areas. Has any of the activism about AIDS hampered any effort or discouraged people from becoming involved in the research? It seems as if the federal researchers particularly, if you read 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 have been recognized as a saint. 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 extremes have dissuaded researchers. In fact, I cannot think of an instance where anyone has been dissuaded; it 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. In the 1980s, the AIDS meetings were a political and media circus. People were lining up on the streets; policemen were wrapping up people and taking them away; there were protests in the back of the room. You could not give a scientific talk. The real AIDS meeting was Gallo's laboratory meeting which had its roots years ago when he brought everyone out to Rockville just to get away and to hear about the data for two days. Those started long before AIDS. I remember doing that every June. After AIDS they became international events.

What keeps people in AIDS is the money. That 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 are superb. They get the job done.

Rodrigues: Now, if we could jump back to your own work once again. I think we left off when you had moved over to the Medicine Branch and you were working with interferon and other therapeutics. I think you said you did that for about a year and a half?

Gelmann: It may be two. If you really needed the dates, I could get them 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. I have, actually, all the records of the clinical trials.

Rodrigues: I just want to follow what work you did. Did you continue working with AIDS patients?

Gelmann: Yes. I continued to work with AIDS patients for the next two years. Then AZT came on, and [Dr. Samuel] Sam Broder, who was my boss, two levels above me, was at that time director of the Clinical Oncology Program. His laboratory had developed a drug testing assay and had obtained AZT and other nucleoside analogues from Burroughs Wellcome. When antiretroviral trials began, the focus of the NCI effort shifted away from Kaposi's sarcoma and the cancer aspects [of AIDS] to the anti-viral aspects. Sam and his colleagues were perfect investigators for those trials. I focused my interests elsewhere. I then got back more into cancer research.

Harden: When did you come to Georgetown?

Gelmann: I moved to Georgetown in October of 1988 at the time when the old Medicine Branch basically broke apart and everyone left except for two investigators. Three senior scientists went up to Fox Chase Cancer Center in Philadelphia and, I think, five or six came to Georgetown. By that time, I was out of AIDS research completely.

Rodrigues: You have mentioned a number of people, some of whom we have talked to. Other than those people that we have already spoken about, 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 gifted man with a mission and he accomplished a huge amount of work. He is the real father of AZT. Certainly, Sam was a driving force and, intellectually, is without peer. But Mitsuya developed the assays and deserves tremendous credit.

Harden: In the context of how science is organized and the issue of who gets the credit for the work, you have already mentioned a number of people in Gallo's and in Broder's laboratories who actually did the work, but the

credit seems to accrue to the laboratory chief. Would you like to comment on that?

Gelmann: That is a sensitive topic. I am a laboratory chief myself. I do very few experiments and have a lot of people working for me. It is the way science works and it is different. I think Mitsuya has made a tremendous contribution and has gotten his due. I do not think Sam has shortchanged him. I am not sure that he could have done it without Sam. I think that was really an important collaboration between the two of them. But he has been very successful.

Bob's laboratory is bigger; Bob was once 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. I think his treatment of people such as [Dr.] Beatrice Hahn and [Dr.] George Shaw and [Dr.] Lee Ratner has been different from his treatment of Bernie Poiesz and Frank Ruscetti. He supported the careers of some of the most prominent HIV virologists in the United States. The disagreements with Poiesz and Ruscetti were legendary. It is a sensitive topic, but it is certainly not a secret. But I think that he was very kind to some of the younger people.

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

Gelmann: Working in a 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 them 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 except in the rare instance where a young person has made a unique observation, the work is usually a collaboration with a senior person with more perspective. The senior investigators are the ones who keep their eyes on the goals and keep the research focused. That is the way most science happens today.

Scientists like [Dr.] Barbara McClintock, who worked by themselves for thirty years, are becoming increasingly rare, partly because of the technical challenges. Everything is so specialized and the experiments are technically demanding. There are people who closet themselves up in the laboratory, if they can fund themselves with one or two good grant proposals. There are 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 with RO1 grants [investigator-initiated research proposals]; 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 in the intramural program and from being at a university, would you comment on what you think the value of the NIH intramural program is? 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 in the NIH that you just cannot 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. Who knows what will become of [Dr. Steven] Steve 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. It is a unique place for that reason. You can have well-funded, goal-directed work that really 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, which you basically cannot do anywhere else because of the restrictions on human experimentation. No testing in this country can be done fast in people, except in Building 10. Most drug companies, when they have new experimental agents and they want to get some quick pilot trials done, do not bother to do them here; they do them in Europe. They are reliable investigators and good people [there] who do not have the regulations [to deal with]. We are trying very hard to get some experimental drugs because there is a demand from the patients for this. The drug companies do not want to bother. But still, at the Clinical Center, you can do it. 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 the process. And there was a lot of work we did intramurally that was really a waste. I have notebooks full of good material, but even more notebooks full of complete

trash that will never be published. 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 efforts and look through the literature. People were quick to publish things that had panned out and that showed positive results. But there were so many efforts that ended up with either negative or no results.

Gelmann: Of course. [Dr.] Linus Pauling spent a long time trying to ascertain protein as the genetic material. Is anyone dingling 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 your results are reproduced by other scientists and the field moves on, or your observation just dies there in the literature. Heaven knows, Bob Gallo has had more than his share of that. He has taken 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 there anyone from the FDA involved in AIDS research?

Gelmann: [Dr. Gerald] Gerry Quinnan was involved at the FDA on the Bethesda campus. He had a large group with several individuals who 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 work on AIDS?

Gelmann: Yes. Quinnan was working with someone and they were trying to culture Kaposi's 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 all stimulated by [Dr.] Peter Duesberg's challenge to HIV. He does not believe that HTLV-I causes cancer, either. What did it take to convince you that this retrovirus was indeed the cause of AIDS?

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

Harden: You have done some work on Burkitt's lymphoma, and I think that Duesberg was saying that someone had recently found that Burkitt's lymphoma has no lentivirus involved.

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 had a mutation. About the 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 that was in a region that was unexpected. We went back and looked at that one and found it did have mutations. So, 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 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.