Dr Robert Gallo Interview 3 June 8 1995

Interview with Dr. Robert Gallo

This is the third oral history interview with Dr. Robert Gallo of the National Cancer Institute concerning the history of AIDS at NIH. The interviewers are Dr. Victoria A. Harden, Director, NIH Historical Office, and Dennis Rodrigues, program analyst, NIH Historical Office. The interview takes place on 8 June 1995 in Dr. Gallo's laboratory in Building 37, Room 6A11.

Harden: Dr. Gallo, it has been some time since we conducted the earlier interviews. We will try to pick up where we left off last time. We were talking about your laboratory's research on the basic molecular biology of HIV. I am interested in some of the spin-offs of the research. I know that you found one or two new human herpesviruses which might be cofactors in AIDS. I would like you to describe the whole idea of cofactors and whether these new herpesviruses are now viewed as cofactors in HIV infection.

Gallo: Just talking generally, the spin-off in terms of the herpesvirus actually did not come out of molecular biology; it came more out of virology/biology experiments with a design, in fact, a plan, to discover new herpesviruses. As usual, the general idea bears fruit, but it is never for the reasons that you predicted. I will come to that in just a second and then we will talk about cofactors.

But, in terms of molecular biology spin-offs, I think the biggest ones are the discovery of new genes within HIV, within the genome of HIV, that have rather novel molecular mechanisms of action, that have, in fact, contributed to molecular biology. Some of those new genes have also become targets for people trying to interfere with HIV replication. Some of them are genes, the *tat* gene being an example, essential to HIV replication.

Let us turn to the issue that you wanted to talk about, the cofactors. Many people have the idea that if you do not always get a disease from a microbe that causes the disease, then either the microbe does not cause the disease, or something else is required as a cofactor. But this is not true. A microbe may cause disease in a very small percentage of people. That is usually the case. In fact, the usual case is that it causes no disease at all. The determination of whether somebody gets disease or not from a microbe depends on a very large number of factors.

The number one factor is, of course, the nature of the microbe. Some are efficient in causing disease, some are not.

Second, it sometimes depends on the host. Most of the time it depends on genetic factors in the host. Sometimes it depends on chance events–the dose–and if that seems trite, there are experimental examples that actually prove that in a number of systems.

Staying with retroviruses, it is clear that in nature–I probably used this example in earlier discussions, but I will use it again–when a cat gets infected by the feline leukemia retrovirus, it usually does not get leukemia; it is usually carrying the virus without leukemia occurring. My belief is that if cats lived long enough, let us say, for 100 years, the majority would get leukemia. There is a chance of genetic events occurring due to the integration of the provirus that eventually leads to leukemia. But it is known that if you inoculate the right dose in a young enough kitten, you get leukemia all the time. This is typical. The same is true with chicken leukemia retrovirus. If you inoculate newborn chicks with a proper dose, most will get leukemia. But, in nature, when chickens get infected as adults, it is unusual for them to get leukemia. So, it sometimes depends on the age of the individual, or on the age of the organism, or on the dose of the microbe. These are chance events. People often do not appreciate that.

The third is that sometimes it depends on the genetics of the host and how it handles a given microbe.

The determinants, for example, of HIV, are still unknown, but it could be that there is so much virus variation that different variants may have different virulence. But all the other factors I have just listed may be important.

Now, in my mind, when we talk about cofactors, we have to give a definition. Most people, when they think of cofactors, start to believe that you mean something that is absolutely required to get the disease. I would divide them into categories. I would say that there are essential and non-essential cofactors or, maybe it would be better, to call something a cofactor if it is truly required. Other things are just catalysts or promoters of the probability of getting disease and of the probability of the disease being more rather than less vicious, or more acute rather than it taking a long time to develop the disease. Let us go directly to HIV.

Many people have proposed cofactors for AIDS without data, and sometimes without even ideas; just claiming that there must be cofactors. But there is no evidence for any cofactor. Can HIV alone produce AIDS? I believe so.

Have we ever argued for a possible cofactor? Yes, with the qualification I just told you, that it is obvious that some things will promote progression and some things will inhibit progression. One of those things may be the genetics of me versus you. We can say dose is a factor that can lead to progression, or lack of it, and at a greater or lesser rate. But we have argued for certain herpesviruses as possibly being a factor in promoting AIDS progression. Several groups have argued for cytomegalovirus because it does do things and it does activate more HIV in some subtle settings.

In the middle of the 1980s, we became aware that the lymphomas that were associated with HIV infection were perhaps one-third of the time EBV-positive. Epstein-Barr virus, as you know, can immortalize some B cells and, when you have EBV-positive lymphomas, generally they are the kind of lymphomas that, more or less... If they do not require EBV, EBV makes the probability of getting a lymphoma much greater, because the cell cannot die easily. It is immortalized. Other genetic events are needed to develop the lymphoma, but the immortalization of the cell is perhaps a key factor that makes it probable that it will be an EBV-containing cell that is the one that will become a lymphoma.

What about the two-thirds of lymphomas in HIV-infected persons that were not EBV-positive? We wondered if there were herpesviruses yet to be discovered. We looked in the B-cell lymphomas of patients with AIDS who were negative for EBV and we discovered the first new herpesvirus in 25 years, and the first herpesvirus of man that targeted predominantly the T cell.

We had a new herpesvirus, but it was not involved in the lymphoma, at least not as far as anybody knows, even today. We even misnamed it. We called it HBLV, because we found it in a B-cell lymphoma. Then we studied it more intensively and determined that it primarily infected T cells, not B cells, which was an unexpected finding. We learned that it killed T cells when it replicated. Then we learned that it infected natural killer cells and, when it did so, it made those cells attack other natural killer cells. We learned that it could infect the same cell as HIV and activate HIV expression. Next we learned that it infected CD8 cells and activated the gene for CD4, the only known biological agent I am aware of that activates the gene for CD4. Now, the CD4+/CD8+ cells could be targets for HIV.

It was at that stage we proposed that the herpesvirus might be a cofactor for progression of AIDS. It was then that I started to be careful of the use of these words and called it a “catalyst” for progression, that is, a nonessential cofactor, but something that makes disease progression go faster and also makes it more probable that immune deficiency will develop.

We put that idea out and it got a little bit of a reception by [Dr. Larry] Corey in Seattle, and by [Dr. Donald] Don Carrigan at Wisconsin. But then [Dr. Harold] Jaffe published a paper, the data of which we already had in hand. I think that paper–by Jaffe and his colleagues at the CDC [Centers for Disease Control and Prevention]–was not a sophisticated look at the problem. Namely, they said, “Look, everybody has antibody, so how can it be a factor in progression?” That is like saying a cytokine like TNF [tumor necrosis factor] is not important in disease pathogenesis because everybody has it. The question is, if 90 percent of the human population has it, they also have EBV, but EBV can cause Burkitt's lymphoma under certain settings. The question is, does it get activated in an immune-suppressed individual?

We put the problem aside for a while because we did not have a quantitative assay to measure the amount of herpesvirus; only this antibody that indicated a previous exposure to the virus, which everybody showed. We argued, however, when we presented it, that we needed to have a quantitative assay for virus in blood and the amount of human herpesvirus-6 [HHV-6] DNA in lymphocytes circulating around.

At this time we learned of Carrigan's work. He reported in a few clinical papers, that sometimes in immune-suppressed people, following transplantations, he saw an enormous amount of human herpesvirus-6 replication and that he believed it was responsible for some of the bone marrow abnormalities in such people. He showed a lot of virus in bone marrow. Second, he pointed out and emphasized that interstitial pneumonia is the cause of death in 10 percent of the deaths of HIV-positive people. No one knows the cause of that interstitial pneumonia, and he found the lungs of those who died loaded with human HHV-6. He presented at our laboratory meeting that he thought it was very likely that HHV-6 was the cause of those deaths.

Meanwhile, before this, Japanese workers had shown that HHV-6 was the cause of *roseola infantum*, also known as *exanthem subitum*, a disease of infants, with fever and rash, but usually with not much more.

So now what is new? I have discussed with my colleague [Dr.] Paolo Russo that the only way we are going to get any proof of this, or get stronger support, is if we get a specific inhibitor that does not inhibit HIV, inhibits HHV-6, and as far as we know does not inhibit anything else, is relatively non-toxic, and then show that patients do better rather than worse.

Another way of doing it would be to find an animal model not infected with a parallel virus to HHV-6 which can be infected by SIV [simian immunodeficiency virus]. SIV can induce some immune deficiency–not the acute sort–but there are monkeys in which SIV induces nothing, there are monkeys in which some strains of SIV induce an acute AIDS, and there are monkeys where some strains of SIV induce a disease more similar to the human disease, where it takes time.

We used such a system. This is not published data. With the SIV alone, there was a little immune deficiency, and with the HHV-6 alone nothing, but with the two together they got it. I think we have proven the point with that rhesus virus and that we can publish that soon. So, I believe human herpesvirus-6 is a factor in AIDS progression.

Harden: Thank you. I would like to turn, for a moment then, to another...

Gallo: But wait. One last sentence about this, and to jump away from it, it will be interesting. There are other people who have suggested things [as cofactors], like Montagnier suggested mycoplasma. He has absolutely no evidence for it, nor it appears has he made any attempt to get evidence, and that has been going on for six or seven years. That is where we need a little more critiquing in the field. You cannot just keep talking about what could be, or what is theoretically possible. Mycoplasma can do things in culture, but so can anything; so can acid and certain things you are exposed to many times. If you put a lot of bacteria in a culture, it will kill the culture. This is not meaningful. You need to do the epidemiological studies, because the mycoplasma is not ubiquitous, like the herpesvirus, so you could certainly do a prospective study and prove it one way or the other. Basically there was not any more reason to suggest it than that. It is a common tissue culture contaminant and it is a common contaminant of an immune-suppressed person. But no one has ever shown that these things have any immunosuppressive activity *in vivo*, and the effects *in vitro* are very mixed. There is no epidemiological link and there is nothing else, so the idea sits there.

I do not even know right now what are the other claims for cofactors. I do not believe there are any that I can think of. Some people argued for the Kaposi's sarcoma drugs, the etoposide, but the epidemiologists tell me none of those data hold up.

Harden: Let us move then from herpes to Kaposi's sarcoma, which you have also worked on extensively. Maybe you can begin by briefly describing how Kaposi's differs from other tumors. Apparently it has characteristics suggestive of an infection. People have called it “perhaps” an immunological disease. Then I would like you to tell us how AIDS related Kaposi's sarcoma differs from other Kaposi's.

Gallo: The latter is easy enough. AIDS-related Kaposi's sarcoma differs from the others in not too many ways, except that many clinicians say it is one of the most aggressive forms. Obviously the link with HIV infection and maleness is a peculiar factor among all Kaposi's sarcomas, but even more so in HIV-Kaposi's and the strange story of gay men. They have much, much more Kaposi's. That is what is special about it. That is easy to answer.

The first question about the nature of Kaposi's sarcoma, what it is, and all the interesting things about it requires a longer answer. I find myself, if I am talking to a general audience, saying that if you start with the emotional side, it is bad enough to have a tumor, but when you have to watch it disfigure you and grow on your face and body, it adds an extra dimension of horror. This sarcoma has an unusual aspect that way.

If you can put aside the emotion of the disease, it offers us a host of enigmas that are fascinating. It comes across as the most fascinating tumor, I believe, that one could think of, and there are many reasons for that.

We can begin with the strange localization of the tumor. It starts on the skin and in the mucus membranes of the bowel. That is unusual.

We can proceed to say it is unusual in its composition. A lot of blood vessels proliferating? That is unlike any other tumor. You could say, “It is a tumor with blood vessels.” Perhaps, and perhaps not.

Another strange feature is that the cellularity of the early tumor is mixed. It is not the sea of homogeneity that characterizes most cancers, because it has fibroblasts, white blood cells, and endothelial cells. All these new blood vessels are all mixed together in what looks more like a granulomatous reaction or an inflammatory reaction. As you said, that is giving rise to the notion by some that it is more like an infectious disease reactivity phenomenon, with cytokine-milieu overplay. I think much of that is true in the early stages.

We come to another fascinating aspect of Kaposi's sarcoma. Is it cancer or not? Or is it only what you just said? If it is a real malignancy, or a true sarcoma–let us get away from the word “cancer” because that implies carcinoma and this is sarcoma–but if it is a true malignancy, what is the tumor cell? That is also interesting.

It is also peculiar that humans are the only species to get Kaposi's sarcoma. There are four epidemiologic forms. There is the HIV form; the African endemic non-HIV form; the transplantation, usually of the kidney, form; and the so-called classical form in older Mediterranean males, mainly Greeks, Jews, Spaniards, and Italians. That is who gets it.

Those are all oddities, every one of them. Then why is it in gay men so much, and why so much in males? Many of these things are strange. Which one is the most interesting?

Harden: Also, with regard to the latest finding about, perhaps, a pregnancy hormone that inhibits it?

Gallo: That finding is from our laboratory.

Harden: Let me ask you then to talk about this new finding and what role it may play in Kaposi's sarcoma?

Gallo: I think that this is an interesting time to talk about Kaposi's sarcoma, to take a breath, pause, and look at it, because many findings have emerged in the last few years. I cannot say they have come together. It is just that there are developments in at least three different areas that merit really aggressive pursuit. Which one of these will yield the most fruit, I am not sure, but before we discuss the hormone and this may be helping to answer part of the question, let us take what I think are the three areas that are coming together.

First of all, beginning around 1987, we started the first systematic culturing of the cells of Kaposi's sarcoma, the reasons being: we were convinced that it was an interesting tumor; we are in the [National] Cancer Institute; and, it was not being studied by virtually anyone. There was nothing in the literature about culturing Kaposi's, or almost nothing, so we set out to culture systematically what we hoped would be the tumor cell. We spent several years doing that, and I think we now have a summary of what those results mean, or where we are with them anyway.

Those studies indicated to us that the bulk of the tumor cells, or the bulk of the cells, I should say, that are proliferating and that can be grown in the laboratory, are hyperplastic, not cancerous. They are normal diploid chromosome cells. They are cells involved in responding, I think, to emergencies, like in wound-healing. They make and respond to many growth factors. They stimulate angiogenesis. They are probably some kind of primitive endothelial cell of the blood vessels themselves.

You can also grow–and some laboratories have–fibroblasts from the tumor called Kaposi's. I now think this is an epiphenomenon. There are two ways of looking at it. This hyperplasia, this proliferation or stimulation, that is occurring may be a forerunner of the malignant cell. This may cause the malignant cell because their growth leads to an accident in some people, transformation malignancy. But you can look at it the reverse way too. It may be that the malignant cell is there in small numbers, like the Reed-Sternberg cell in Hodgkin's disease, and the malignant cell, which appears for reasons I cannot even dream of yet, is secreting cytokines that creates the reactive hyperplasia. I am not sure which is the father and which is the child; the hyperplasia leading to one of those cells becoming a malignant clone, or the malignant clone secreting cytokines that create the hyperplasia? That is the problem that we are stuck with now, but we may have ways to answer that soon. I will tell you why.

Anyway, if I summarize all that work, it indicated to us: that early Kaposi's sarcoma involves many different hyperplastic cells; that what is producing that hyperplasia is ironically the product of chronic immune activation. AIDS being an immune deficiency is also immune activation. Some of the cytokines from activated cells are able to activate these endothelial-like cells, or endothelial-related cells, to grow, proliferate, and themselves secrete cytokines which produce the blood vessel angiogenesis and other things as well.

We discovered during that process that, at least in early Kaposi's sarcoma, a key cytokine that was produced by these growing spindle cells that are probably endothelial is basic fibroblast growth factor. Once they have been activated and have proliferated from activated immune cells, they are making lots of basic fibroblast growth factor. Basic fibroblast growth factor, we discovered, synergizes with the *tat* protein of HIV in promoting blood vessel growth again and promoting growth of themselves. We published a long article in *Nature* about the mechanism of this and so on.

At about this time our laboratory, it was predominantly a visiting scientist from France, Yanti Lunardi-Iskander, described it. And a laboratory in Israel, working with classical KS, and us working with HIV KS, have both succeeded in isolating, from a total of only two patients, malignant cells for the first time. This data now powerfully argues that Kaposi's does have malignant cells. But now comes the question: are they there at the beginning or did they develop later? But now that we have them, we hope to develop molecular markers and go back and look at all Kaposi's sarcomas to see if such a cell is there buried within the mess of hyperplastic cells which we have been studying and which are really an epiphenomenon. That is where we are right now.

New data that argues for neoplasia has also come from the epidemiology group at the National Cancer Institute, [Dr. William] Bill Blattner's branch, involving [Dr. Robert] Bob Biggar, and from a group at Johns Hopkins, involving a man named [Dr.] Charles Rabkin, also of NCI. They have shown, in three out of three cases, at least, that indeed late-stage Kaposi's sarcoma had cells that were clonal, derived from one papa. If that is true, it is a malignancy. So, this is now coming together.

During the studies of the malignant cells, [Dr. Joseph] Joe Bryant, at the Dental Institute [National Institute of Dental Research], our collaborator, was putting those cells into nude mice, immune deficient mice, and they developed a big malignancy which metastasized and killed the animals. We were having a certain amount of experimental fun with that model when Joe observed that one group of animals did not get the tumor and he found that those animals were females that were pregnant. They got pregnant by accident. That is, he housed male and female infant mice together in the same cages. I never really talked to him about why he did that. I think it was probably a mistake. But the pregnant animals did not get the tumor. Then we went after what the factor was. To make a long story short, we found that it was the serum in the first trimester of pregnant mice and women, chorionic gonadotrophin, a hormone of pregnancy that targets the gonads, but God knows what other functions it might have. We found the bulk of the activity resided in the beta-chain that was blocking Kaposi's sarcoma cell growth i*n vitro* and in the mouse. We have learned that it is not blocking growth; it is killing those cells. So, if you want to make something physiologic of it, there are two things to think about:

Is there a normal cell that it is killing? What would the normal cell be? Embryonic, maybe. The first trimester, the molding of the infant, the hands, for example, maybe there is a cell that is related in lineage to the cell we call the Kaposi's sarcoma tumor cell? That is a thought.

The other theory it gives rise to, at least in my mind, is that since the beta-chain was 85 percent homologous to the luteinizing hormone betachain, and we have shown that luteinizing hormone also has this event, perhaps that is why women get Kaposi's sarcoma less.

This is now in clinical trials. We will be able to talk about that probably–or maybe–during the laboratory meeting in late August [1995].

Rodrigues: Dr. Gallo, about a month ago, there was a series of articles in the popular press about a child who apparently cleared an HIV infection. I think in the paper they noted that there had been a few other such cases reported, but this particular one, according to the articles, was very well documented. I wonder if you are familiar with that case.

Gallo: I am not familiar with it other than by reading about it in the newspapers like you. I have asked others about it and, if others are accurate in what they tell me, I do not think that the researchers showed that the lymphocytes that harbored virus were of the sex of the child. If they were female, the mother's lymphocytes circulate in babies. That has been shown long ago. How do the researchers know that they just did not look at the mother's lymphocytes circulating in the baby, which eventually get destroyed and that the baby was never infected? That is my answer.

Rodrigues: Around the same time, actually I guess it preceded that somewhat, there were also reports in the newspapers about the new understanding of the role of CD8 and T cells in suppressing the HIV infection. We were curious whether or not you thought that this implied that we understood more about what was happening in cases of long-term non-progression of AIDS?

Gallo: No. I do not think we have any notion whatsoever why some people progress less rapidly. Maybe it is HHV-6. I am sure that is something that has not even been looked at. Not that I predict it is, but I do not think it has been looked at properly. One person may have better control of HHV-6 and it may not be replicating as much. That is an interesting idea. Some researchers cannot distinguish what is the cart and what is the horse. They look at the lymph nodes and they are worse in the person who is doing poorly than in the person doing better. What would you expect? So, is the lymph node not being in good shape the cause of progression or, if it is in good shape, the cause of non-progression, or is that just symptomatic of the fact that a person has much more virus when AIDS is progressing and destroying the lymph node, or the immune system is destroying it? The real problem is to try to prove what is cause and what is effect, and nobody has done that yet.

Regarding CD8, I do not know of any new data that says it is important. There has been a factor that suppresses HIV replication that was described by [Dr. Jay] Levy back around 1986-87. The horrible frustration is that there has never been a report of the identification of the factor or its gene cloning or any publication on what it is; only what it is not. In fact, that has led, in the last year, out of frustration, one wanted to have the time to do something with it, to others getting involved in the problem, including our own laboratory, and we know that there are at least two such factors. There are at least a few factors secreted by CD8 cells which are anti-HIV replication. CD8 cells can also be, as you know, cytotoxic killer cells and can kill by mechanisms that involve the so-called “kiss of death.” There are many ways in which CD8 cells may be important. There is no doubt CD8 cells are important in immunology, therefore you can conclude that they are important in AIDS. But whether they are what is responsible for the difference in survival between one group and another group is a question. I am sure they are helpful to both groups, but whether I am marked, if I am not doing well because my CD8 cells have some predetermined way of fading out earlier than yours, who does not go as fast, is far from clear. There is no evidence for that that I know of.

Rodrigues: Apparently it is rather difficult to design experiments that can look at that?

Gallo: Yes. I guess it is. I think so.

Harden: Let us move a little away from specific questions and see if you will give us an overview on the current prospects for developing a successful vaccine against AIDS?

Gallo: I believe that the development of a preventive vaccine is totally unpredictable. I do not see anybody being in a position to say whether we should, or should not, go forward with trials of anything. As you know, I do not like to be diplomatic very much, but I can be sympathetic with the argument this way, and I can be sympathetic with the argument that way. In other words, if you argued one way, I would argue the other. If you would say, “We should go forward with trials,” I would argue that it is crazy, because you will cause reactions in the field, [and] lack of faith in the science, and you will make it impossible to go forward in the future. You will mark those people with an immune response and it will be hard to tell in the future what is happening with them. They will not be available for other trials. We do not have proof these vaccines are really ready. You might even produce enhancing antibodies that facilitate infection. There are many negatives.

On the positive side, many of the things that are currently available have given reasonable immune response in animal models. The animal models are virtually impossible to predict one from another. The way to go forward is in human testing. Enhancing antibodies have not been demonstrated in the work with the protein in the Phase I trials that have already gone on. The data is not outstanding in any one, but there is enough evidence that sometimes you get protection in animals to be tempted to go forward.

I guess, if I had to weigh in on one side or the other, I would like to see the testing of the vaccine, because I am 58 years old and I want to see some results and know what is going on.

No. To be serious, I think I would lean towards having some trials go forward. But no one is in a position to predict the outcome. We talked previously about [Dr. Ronald] Desrosier's argument for the use of live virus vaccine. I said that I did not like this argument and I said that to Desrosier early on. You have probably seen that subsequently to that [Dr.] Ruth Ruprecht at Harvard has shown that with that approach baby monkeys got AIDS. I did not think a few years was long enough for Desrosier to wait with the other, nor did I think he could predict from SIV to HIV. Nor did I think he could predict ten years down the line of the population at large all developing a cancer of some kind. Yet I know the argument. The argument is, if your back is against the wall and you are in some special place and there are so many infections, what can you do? It is one of those real “catch-22s,” but I think the dangers far outweigh the argument to go forward. I believe approaches through vectors like the adenovirus or the canary pox virus, or the NYVAC from Virogenetics that we are collaborating on, have given enough at least reasonably interesting data to go forward with vaccine trials in humans to get some baseline data. But I cannot predict that there will be a successful vaccine next year, or two, five, or ten years from now, or ever. I think there will be one.

Harden: You think there will be eventually?

Gallo: I think there will be. I would not take Albert Sabin's approach, that there cannot be a vaccine, because we cannot imagine the science that is developing. There are all kinds of new things happening. I am attracted by some ideas that [Dr. Myron] Essex has been promoting recently in the model systems that he has talked about with cat leukemia. There are brand new types of experimental approaches. My former coworker here, [Dr.] Jonathan Gershoni, who is now back in Israel, has some interesting approaches that no one has tried before. I think there is so much going on right now...But the downside of all of this is that the companies are getting out of vaccine research, and obviously the companies are needed. Whereas in research we often hear from the lay public how cooperation is needed and competition is bad, usually the opposite is true, sometimes we have almost too much cooperation. Competition is good–it stimulates fields–but in this case, for an AIDS vaccine, there is no question that we need total cooperation. We need, I think, government's involvement, or some kind of world leadership, an agreement where everybody comes together and perhaps gives a certain percentage of their GNP [gross national product] towards the research. I am not certain, but I think the companies fear lawsuits. They do not have incentives, the research is expensive, there is no assurance of success, and so they have real difficulties in deciding to stay in vaccine research. Most are not, as far as I can tell.

There are people out there trying to promote research. I know that in Connecticut and in New York there is a group trying to raise a very large amount of money by multiple different mechanisms predominantly for a preventive vaccine. The Sabin Foundation, in fact, with Eloise, Albert's wife, is involved in this and I think it is headed by a man named H. R. Shepherd from Connecticut. He has talked to me several times and I think it is a very exciting endeavor. I hope he succeeds, because, if they get the kind of money they want–they are trying to raise half a billion dollars or more, $600 million dollars–they should fund three or four centers, rather than giving out grants to support basic research or clinical research by thousands of investigators everywhere. They should gamble on three or four centers and say, "Here take $25 million dollars, take $50 million dollars, take it for five years–you do not have to publish–just come back once a year and give a report and, at the end of the five years, we hope you have something" and maybe force them to work with one of the major industries. Something like that is going to be needed to develop a vaccine unless we are very lucky.

Harden: The other approach to dealing with AIDS, besides vaccines, is, of course, therapies.

Gallo: Yes.

Harden: Perhaps you would comment on the hydroxyurea therapy, the prospects for gene therapy, and give an overview of other forms of therapy that you think might become available?

Gallo: Let us maybe back up. As you know, we probably have touched on the fact, to some degree, that the standard approach to HIV therapy right now is the targeting of enzymes of the virus. Those are what can be screened. That is what companies can get into most easily. That is where the most information is available. Reverse transcriptase, protease, and, ultimately, probably the integrase. Some of these proteins have been crystallized, their structures are known, and molecules can be designed to fit those structures. Companies can screen because they can do an enzyme assay. Also, you can just screen large numbers of compounds.

Part of that work has led, early on, to the nucleoside analog approach, to AZT, ddI, and ddC. All these are reverse transcriptase inhibitors. The problem with this approach is the escape mutations. It looks like these therapies will never be highly effective.

We were all hopeful that the protease inhibitors would do a lot, and they have; they can greatly reduce virus. However, it looks as though there is escape pretty rapidly from those protease inhibitors. That is disappointing. In my mind it is extremely disappointing. I think that sets people back. I would not give up on the protease inhibitors. I think they are a powerful class of antiviral compounds. But it does mean it is probable that we need to invent other approaches.

There are a large number of other approaches and a large number of investigators involved. With therapy there is more commercial incentive. There is less likelihood of lawsuits and less likelihood of doing damage, because the person is not normal. With a preventive vaccine, you are involved with normal, healthy people. With therapy there is also something to sell. A company does not go broke. It is not only for the Third World because, speaking in reality, much of the urgency for the preventive vaccine is in the Third World, as you know. So there are incentives here. This is not the problem. As I said, you could talk all day about the myriad approaches to therapy being taken by academic investigators and by the pharmaceutical industry, but the predominant industrial approach still remains targeting the enzymes and the problem still remains of escape mutations in patients and sometimes, though not always, toxicity.

To speak specifically about my laboratory, we are focusing on about four different approaches. One is what might be called a molecular approach. That is, the antisense [RNA], which is a collaboration with a company in Massachusetts called Hybridon, that Paul Zamichnek got me started in many years ago, I think in 1986. We have been working with that company on and off since then. We have a smaller, similar collaboration with Lynx in San Diego, on the antisense approach.

Now an antisense can be given subcutaneously. Hybridon is trying to develop a form to be given orally. But it can also be delivered with a liposome, perhaps, or, by the means you asked about, gene therapy. You can use antisense in gene therapy too. What do we mean by gene therapy? Yes, we are involved in it, and yes, I think it is one of the few theoretical chances for a home run for AIDS, but it has its problems. I do not see a home run this year or next by any means. But gene therapy will certainly go forward this year and next. It is going to take time to work out major bugs which, hopefully, can be worked out.

Gene therapy is a new way of delivering something. In AIDS usually, but not always, we think about it as delivering a gene, which, when put into a cell, will protect the cell from being infected. But there are other imaginative uses of gene therapy going on–for example, in Seattle, by [Dr. Philip] Greenberg and colleagues–that augment the immune system, let us say. But the approach that we have focused on and the one most people are focused on has been to inhibit HIV from being able to infect a cell. You put a gene in and you say, "Never will that cell get infected." Now, what cell would you like to put the gene in? Since we know that T cells and macrophages at least can be infected, we would like to get the gene into the stem cell which gives rise to macrophage and T cells. One problem is getting enough stem cells cultured in the laboratory. The second problem is getting efficient transfer of the gene into the cell. Barring that–it works beautifully in the laboratory in small-scale studies–I believe, and I think most people believe this, we would be able not to have to take bone marrow out, work with isolated stem cells, and infuse them back into the patient's arm. This is hardly something that is going to help the Third World. But it would be wonderful if we could just give it the gene once intravenously and, say, go to the stem cell, hit 90 percent of them. If we can do that I think it will be a potential treatment for the Third World because, although gene therapy for AIDS in the Third World sounds like it is too fancy, it is the perfect therapy. A person does not have to keep taking pills all the time. One inoculation and it is over. That is a dream.

It is theoretically doable, but the problems are not solved. In theory, you could draw something on the board and say, "Here is the idea and here is how it should work, et cetera." But we are not there yet. You can safely predict that it will be in clinical practice next year or the year after. You can safely predict that we will improve the way we target cells, including stem cells. How soon that will be, I do not know. How efficient it will be, I do not know. But, ultimately, this could be one major way to get on top of the problem.

We have also suggested–this has been an idea we have championed in a way–the idea of targeting cellular factors because they do not mutate like the virus and, as we talked about once earlier, the virus needs cellular factors to replicate. It does not readjust itself. It does not have a metabolism. Rather, I should say it "cannot" readjust itself. You cannot put a virus in broth and say, "Go replicate," as you can bacteria or a parasite or a fungus. A virus will just sit there until it is finished because, as you know, a virus is made up only of genes and proteins, so it needs more of them to reproduce. It gets them from the cell. If you can find things in the cell that you can interfere with without too much toxicity, you may be able to block HIV replication.

To investigate this kind of idea, we focused on hydroxyurea because it is known, available, can be given orally, and is relatively cheap. People know how to use it. It targets a cellular factor that HIV needs to continue its replication. Unless you want me to, I will not go into details on that. It is in clinical trials in France. Some interesting results were reported recently in *The Lancet*. If I have something to say about a running a clinic, which I will soon, hydroxyurea will be in clinical trials in this state [Maryland]. So will some of the antisense [RNA]. And so will modulation of the immune system with cytokines.

I will come to the last part of what we are doing, and that relates to the HCG [human chorionic gonadotropin] from the anti-KS effect. We believe HCG has much more to offer than that, and it is getting us into hormone research. It is something that I dread because I do not know anything about hormones, and there are many people who do. It is something we will just have to keep learning about.

Rodrigues: You have been telling us about some of the therapeutic possibilities for AIDS. Our understanding of HIV has given us these opportunities to design new therapies. Do you believe that there are other aspects of the basic life cycle and pathogenesis of HIV that we still need to learn about before we can get more therapeutic opportunities?

Gallo: The idea that there is more to learn and that it will give us more ideas for therapy–of course, we are not at the end of the road. One would be the study of some of the so-called "auxiliary" genes like *vpr* and *vpu*, things of this kind, *vif*, *nef*. All those things are giving new ideas for therapy as we talk. Yes, there is still more basic information that needs to be generated which will give more ideas about therapy. That is not just antiviral therapy, but also with the immune system. But that does not mean that we should not pursue what we know in practical ways with speed.

Harden: We wanted to ask a few questions that were less scientific and perhaps more organizational and political. Various groups have made suggestions about how one might best coordinate AIDS research, and I am sure you recall these various ideas. With regard to intramural research here at NIH, how would you organize it for the optimal outcome?

Gallo: Certainly it takes benevolent, good, and yet strong, leadership. I would have everybody in one large institute devoted towards research on AIDS. But that does not mean I would pick on research in other institutes. I would not over-fund every institute on AIDS. But I think having people under one roof is not a bad idea for cross-fertilization and exchange of information. So that is one way.

I would try to get rid of redundancy. No director likes to tell scientists what to do. It is rough, and it is also wounding to the person who is on the receiving end of being told what to do. But there comes a point in a disease like this where some of that direction is necessary, I think, if there is too much redundancy, or if there is too little of something, that you try to fill in the gap.

What if everybody here was working just on the blood test. What if we became insane and we all said, "Let us all just do the assay for the blood test." You would certainly stop this if you were the director and say, "We have a blood test already. Why are you all working on a blood test?" There comes a time, I think, when the director has to step in. Maybe I would look at the totality of it [the research being conducted] in some retreat. NIH is so big it is hard to grasp that. But maybe everybody working at least 40 percent of their time on AIDS could be organized to present their program at one hearing for three or four days with an NIH group of three to five people looking at it carefully. If you did this, you might get a sense of what is redundant, if something is, and you might get a sense of what you are not doing enough of. Somewhat closer contact between the people who have the money, or control the decision making process and the people who actually are doing the work and most of the thinking would be what I would want to see.

Harden: I get questions from time to time about the justification for funding particular diseases, including AIDS. What is your evaluation of the extramural funding for AIDS and the impact it has had on funding levels for research on other diseases? Is the funding out of balance?

Gallo: I have no way of being able to answer that question because I have never looked at such things. I am not in a position to do much about it, unless I knew that funds for AIDS research were greatly lacking, and then I would be screaming. But it is hard for me to know whether if more money is given here, there is less there. Usually that is not the case. In my experience at NIH, when people argue, either out of jealousy or fear that they are not going to get funded, it ends up that both are hurt in the end. It reminds me, as I mentioned to you once, about when the National Cancer Act was passed and I was called by a famous scientist who said that his son was a good scientist but he could not get funded, and also this and that about the National Cancer Act. I was a relatively beginning person here. I was startled that I was called. I was in the laboratory and I did not know anything about it basically. But I just said, "Why didn't he get funded?" Well, he had applied to the National Institute of General Medical Sciences, and I said, "Why not just apply to the National Cancer Institute. The project could fit with NCI's research program, even though it is on *E. coli*, its replication, with DNA." The scientist's son did and he got funded.

I feel it is a mistake for scientists outside to argue against funding anything, because Congress responds to crises and Congress responds to crusades. That is a simplistic statement, I know, but it is generally true. If they put a lot of money in for some crusade, it is a mistake to fight it, I think, because there is obvious spillover and there is obvious justification to fund research in many different areas that are not directly AIDS related. I do not think–from what I have usually seen–that if the money does not go to AIDS it will go to the Heart Institute [National Heart, Lung, and Blood Institute], or something like that.

But putting aside that kind of politics, to evaluate whether AIDS research is over-funded versus another field is not easy. It is simplistic and, frankly, I think it is stupid to use the numbers game, "There is more of this disease than there is of that, and therefore this is more important that that." That precludes any discussion of is there as much morbidity here as there, is there as much involvement of young people here as there. As you know, my mother died a few weeks ago of a stroke. She was 92. You could argue that many more people die of strokes than almost anything else. We have this problem. Now, which way do you want to die?

Let us say that you got rid of strokes, and everybody died of heart disease. Let us say you got rid of heart disease; everybody will die of cancer. I mean, something is going to happen. That is clear cut. I do not like the idea of hypertension and stroke in somebody of age 30, 40, or 50, but at 92, is it a bad way to die? How do you compare that to an infant born without parents because they died of AIDS at 25 and now the infant is infected too, or something like that? How do you compare it to a 16- or 17-year-old dying of AIDS?

I am not arguing for more AIDS money. I do not know what balance there should be. I only know that you cannot play numbers games, and particularly since the number of people with AIDS continues to grow. The stupidity comes right down to that. With the numbers of AIDS patients there were 10 years ago, you would have said, "AIDS is the least important disease." Now, all of a sudden, it is very important. But it was important then too; just as important as it is today.

The thing about AIDS that you can argue for is that you have the cause in hand. You have quite a bit of understanding about it. You have a chance to get rid of it and go back to work on the more complex diseases. AIDS sounds complex. The virus is terribly complex. But, on the other hand, it is much less complex than many of the more subtle chronic degenerative disorders, and so it would allow us to get back to them.

This is a sort of strangely chronic emergency situation, and the danger is complacency, because we cannot really predict what is going to happen in the future. So, I do not know. The answer as to whether AIDS has too much money versus something else is yes if there is over-funding, if there is a lot of bad science, if there are no ideas, if there are too high a percentage of the grants being awarded, that kind of thing. If that were the case, then I could answer it better. I think there are also many spinoffs from AIDS research to other areas, to cancer certainly, to basic immunology, and to molecular biology. AIDS is in the forefront in virology now. It will be for antiviral therapy and it is likely to be a leader in vaccine efforts as well, I hope, if everybody does not run out of the profits.

Rodrigues: Recently you announced that you will be leaving the NIH to create a new Institute of Human Virology at the University of Maryland's Medical Biotechnology Center. I wonder if you could tell us about this episode in your career, how you came to the decision, and the context in which you made the decision?

Gallo: Sure. The decision was gradual, over a long period of time. Actually, before AIDS, I started thinking that there should be centers of excellence in virology in the United States, and there were none. In fact, the trend was in the opposite direction. There were medical schools getting rid of microbiology departments because they were not needed anymore; everything was molecular biology. I felt, on the contrary, that certain chronic viral diseases were threatening, potentially on the rise, and that centers of virology should exist in America, as they do in Europe.

Many virology experts, or, let us say, the centers of excellence in Europe were not even focused on human virology; they worked on any kind of viruses. Certainly that was true in the United States. You could argue that Rockefeller [University] was certainly a great place for virology, but the research was mixed. It could be animal viruses, it could be plant viruses, it could be anything. That was fine. That was good basic science. But I also felt that nowhere in the world was there a unique center of human virology. That belief began in the 1980s and certainly was greatly fostered by the AIDS epidemic. So I thought someday, if I left NIH, that would be my dream, to form a center of excellence in human virology. I have thought this since roughly 1982, the year before–or at–the time of our first AIDS experiments. But I remember thinking it even before I knew AIDS existed, maybe in 1981.

But I never got that serious. It was not time to think of leaving. The relationship to NIH was too tight. Like most of you here, I thought I was immortal, that everybody else would get older, but not me, and so there was plenty of time. Then, all of a sudden, time went by and around 1988–I think it was 1987 or 1988–I had the first real push to look around. That was when two sets of individuals came into my life and offered me a large amount of money to leave the NIH to do exactly that, found a center of excellence in virology, and that was because of AIDS. That crystallized my thoughts greatly. Even though some of the offers were quite dramatic, and more than I have right now, I could not quite get myself to do it, thinking I still had plenty of time.

When I got everything I wanted, it was for an institute, on the NIH campus, which was a fusion of government, industry and university. To show I was not doing it for financial reasons, I was to stay. I was ready to accept that, and it got approved by the Scientific Director of the NIH during [Dr. James] Jim Wyngaarden's tenure. But then the person providing the $60 to $75 million went from black to red and then dead, and that was Robert Maxwell. You remember the problems. At the same time, the Blech brothers in New York were offering me large sums of money to do something very similar. I learned a lot in that period, so it was not a waste of time, but the project never really came to fruition.

Time now provides a very big demarcation point because, on 1 July [1995], I will have been 30 years at the NIH. On July 1, I can retire with benefits. Any time I leave after July 1 is, in a sense, a loss of money. Money is not my main purpose for leaving, however, but the timing is appropriate. The thing that stimulates me is that the old idea never left my mind and now there is opportunity to realize my dream. Most important, the last five or six years have been very frustrating to me because I could not go to the clinic very easily and I could not be, shall we say, master of my own destiny. I cannot determine what goes from here, to there, to get to the clinic at NIH. I am in the hands of the pharmaceutical industry's positions and patents and I have CRADAs. If it is the NIH, I am not in the position of saying what goes to the clinical person here, or administrative person there, and it depends on their interest. In my new position this will depend on my interest and my colleagues in the institute we form. A biotechnology company will be part of this new institute too. The purpose of that company will be to feed the institute financially, but also to help develop movement from the laboratory to there, to go to the clinic.

I am not criticizing the NIH for that, because I chose to be in a basic science building and to have a laboratory that was focused on laboratory science rather than clinical applications. I do not think that you can just walk into the Clinical Center one day and say, “I want this ward, or that ward, and I am going to do this or that.” But it has been a frustration for these last few years.

Furthermore, those years of dilemma that I went through certainly make it psychologically easier to leave NIH, if you understand what I mean.

Finally, the move is only up the road [to Baltimore] and therefore, in a way, I do not feel exactly like I am leaving. I will have many memories, lots of nostalgia, and lots of love for this place. As I told you before, I do not believe I could have achieved anywhere else what we have done here, so I owe everything to the NIH. I will still have friends and collaborators here and I will be not moving my home. I will live and stay in Bethesda. I will maintain the collaborations, the friendships, and the dinner meetings here. The way I look at it, I will just have added access, with collaborations throughout the University of Maryland system and, in part, with Johns Hopkins, where I will be an adjunct professor of biology in the graduate school.

Rodrigues: The last time we were talking to you, you mentioned many of the administrative burdens that detract from your ability to focus on science. I imagine that in your new position you will probably try to restructure things so that you can focus on science.

Gallo: In the new position, if I have money, the administrative structure will depend on me. I will determine what administrative help I get. Here, I cannot do that; I am told what it is. Here, at NCI, Dr. [Vincent] DeVita gave us an administrative helper. That is, we could have a scientist who was not doing as well scientifically any more, who could be our scientific administrator. Dr. [Samuel] Broder did not allow that. Where I am going, you can be sure I will have administrative help, and plenty.

Harden: Can you flesh out a little more the organization in your new institute that you anticipate now. What roles will you, Dr. [William] Blattner, and Dr. [Robert] Redfield have?

Gallo: Yes. This institute is novel in two ways. It is novel, according to Governor [Parris] Glendening, in its structure in relationships with the state and the city [Baltimore], and with the University of Maryland. It is not the University of Maryland Medical School, it is not UMBC [University of Maryland Baltimore County]. It is housed in the Biotechnology Center, but it is affiliated closely with the Medical School and the biotechnology part of the University of Maryland and the hospital. There is this partnership with the city and the state. So, this is novel.

It is also novel in that, to my knowledge, it is the first Institute of Human Virology. For certain, it is the first Institute of Human Virology where laboratory science, a large epidemiological program–or a modest program, whatever it turns out to be–and a clinic are together. In part, that will all be under one roof.

The Institute will be divided into three programs: population studies–and prevention as well–essentially it is epidemiology and prevention, Blattner; a clinical program, Redfield; a laboratory science program, me. Each will have its own little committees of scientific advisory groups within the Institute or its surroundings at the University of Maryland.

There will be a Board that will be freestanding, at least one day it is supposed to be freestanding. The Institute has its own scientific advisory board, as well as a very impressive–I am hoping it will be [impressive]–Board of Trustees.

People are advising me on this now, but at this moment I cannot properly, ethically, get too involved in that. But, I trust the people helping me and, from what they tell me, it sounds extremely exciting. I just cannot report it to you.

There will be very close relations with the hospital. We want to have a relationship with the outside community in Baltimore too. This [Institute] is in the Empowerment Zone, so we want to have programs for people in the minority community for training in technology, jobs in short. [Dr. Joseph] Joe Bryant will join me, and Joe is an African American. He will play a close role in working with minority colleges in training programs and grants for AIDS. This is the direction he is going to go. He is a veterinarian, as well.

The Maryland governor and I hope, obviously, that the biotechnology company will also be economically useful for the State of Maryland. I believe that. I expect in time there will be more than one biotechnology company.

We will collaborate throughout the University of Maryland, hopefully, and we will certainly collaborate with Johns Hopkins's AIDS people because, after all, we are partly funded by state and city. As I told you, I have a position at Hopkins and some of the AIDS people there have talked about some linkage, and I hope to have that with them.

We will surely go for philanthropic help and certainly industrial help and, of course, we will try to have a partnership with the NIH. I have already spoken, as much as I can speak, to people in NIAID [National Institute of Allergy and Infectious Diseases]. I cannot be specific because I cannot be fundraising just now. Doing things like that is not right ethically at this moment. Obviously my hope would be that we will be partnered with NIAID and with Dr. [Anthony S.] Fauci, personally, in some of his research programs, in particular, perhaps, in vaccine and therapy aspects with being part of the program here and, in Kapos's sarcoma, probably with NCI, or certainly with NCI.

Harden: You stated in one newspaper article that one feature attracting you to this new post was the direct access to patients that you lacked at the NIH. Did you mean lack of access to patients, or to clinical trials in general?

Gallo: Everything. When I came to NIH, I was in Building 10, the Clinical Center, and there was not much competition for patient samples. Over time, the Clinical Center has been shrinking. The number of people who want the same patient samples has grown, and I am no longer in Building 10. Even obtaining clinical specimens, let alone getting into clinical trials, is not so easy here. It may be tougher here than any place in the world, because there is a tremendous population of scientists on the campus so, no matter who you are, no matter what you have done, it is not easy.

Look at whom I collaborated with. Look at the HCG paper–Paris, Belgium, West Coast. If you look, even in our 1984 papers showing the etiology, there is Redfield at Walter Reed, North Carolina, Georgetown, and I cannot remember where else, but they are all over the place. They, Broder and others, were also here at that time too.

So, I will have a clinical program at the new Institute. I will have something to say about clinical specimens. Redfield will be the boss of the clinic, but we will be talking every day.

Harden: We want to go back, as we start to wind up this interview, to some of the things you said when we first talked to you. One of these was the comments you made about the scientific climate when you first came to NIH.

Gallo: I am sorry. I forgot one thing related to the question of leaving the NIH. The other thing is, I would like to leave some kind of legacy when I am ready permanently to leave this place we call Earth. At the NIH, what I see is that when people retire often there is nothing there any more. The laboratory is sometimes dismantled, and I do not know whether there is change, but there is certainly nothing to indicate anything ever was there.

This is one of those rare moments in the history of the NIH where anybody is talking about permanence, or a legacy, or a record of scientific accomplishment. Maybe the NIH is more conscious of that now than it used to be, but let us consider some people that were thought to be pretty great during their time here. I think they just disappear into the walls.

[Dr. Robert] Huebner was a great virologist. He had an illness. He is gone. There is nothing left of his laboratory, and you would not know he had been here. I think that I have become a little Europeanized by spending too much time in Europe. As I told you before, every Rue, every Piazza, every Platz, whether it is in, say, Germany, Italy, France, or Britain, or wherever, has the names of artists, philosophers, musicians and scientists. Here in America everything is named for a politician or a money donor. This is fine, and I will be doing the same thing, I suppose, but one would just like to know that there would be also something more than the wall that was inside there. It would be nice to be able to say, “That is a great institute; I helped build it,” and to know that it is there. If I walk out of here, I do not know what is going to be here.

It is the government. I mean, it is government. It is not personal. It is everybody. Everybody has this problem at the NIH, and what you do depends on your psyche or your position. If you are in a position to do something about it, you do something about it, if it bothers your psyche. It bothers my psyche and I am in a position to do something about it. But I am 58, and so would I be able to do something about it 10 years from now? It is now or never.

Harden: Going back then to when you first came to NIH, you described the climate for research for a young investigator and how exciting it was.

Gallo: Yes.

Harden: From your perspective now, how do you see the climate for young investigators at the NIH who are just beginning?

Gallo: I told you that one of the great difficulties for me–and I do not mean this to be funny; it is true–there is a variable that we cannot account for, and the variable is age. You would have to ask me this question and turn me back into a 27-year-old, or a 26-year-old, the age I was when I came here. That was 30 years ago. Anything I say now is biased by age. There are two variables: the real difference, and the difference in me. I am more cynical now and a little more perceptive of weaknesses and holes, and I know that not every laboratory chief here is a monument. I had my mouth open and my eyes wide when I first came to NIH, and I was impressed by everything. That is a difference. It is hard for me to say what the climate is for a young investigator.

I do not think there is the same level of enthusiasm and idealism as there was when I came. Now, I do not like to say that, and I may be wrong. It may be because I am older and I do not see it. But it is my impression. Part of it is, I think, that I do not see as many Americans here and, to me, as an American, coming here at that period of time... Although it must be that I am partly right, because in that period of time everybody talked about the NIH and you had to go to the NIH for two to three years before you could become cool to academia. I know there are two changes in America today: first, fewer people who go into academia think they have to come to the NIH; and second, there are fewer people going into academia, period. Those are two facts. So, I am certainly partly right. Part of it is not just getting older. I think I would conclude that there is less enthusiasm and less idealism among the young people now related to NIH.

But that does not mean there is none, or that it is a crisis; it is just not as much as I think there was when I came.

Can you recapture it? That is the added corollary. I do not know. There is much more competition for the NIH now, and there is going to be more.

Harden: You have said that many young investigators have applied for a position in your new institute and that you were contemplating how many to take from your own laboratory. Will this laboratory go on? Mostly, at the NIH, laboratories are created for the person. Will the Laboratory of Tumor Cell Biology continue when you leave?

Gallo: I do not know. I hope so, because it has been part of my existence, in a way, for so long, for my whole career, and so it is funny to see it over.

Harden: But you named this laboratory. This laboratory did not exist before you.

Gallo: That is correct. But it is not always true that a laboratory dies when somebody leaves. It could. The decision has to be made, I know, on the basis of the plans of what the NIH's future is going to be: what it can afford in the new climate, what its direction will be, what the new director wants. So, I do not know what to say. I do not know if it will continue. I will not be taking everyone from the laboratory. I will take some, surely. How many I take depends on many factors, including the nature of the applicants I am now receiving and how much money I can afford to spend at the beginning, things that I have to calculate and deal with yet. I will not know the answer to that until the fall. But some people I will take.

I would like some to stay, even for the reason of continuation here, for maintaining some collaboration and the existence of the department, or the branch, or the laboratory.

Harden: You will have senior people, then, who will also stay here?

Gallo: I hope so. I think so.

Rodrigues: You mentioned before how after some very prominent scientists who worked in the intramural program departed, there was nothing to indicate that they ever worked there. You mentioned Dr. Huebner. In a small way, our museum is attempting to remedy that.

Gallo: It is not a small way. It may be a very big way because, if there is almost nothing now, that having the museum is infinite improvement.

Rodrigues: Rather than asking you a question at this point, I want to make a request. If you come across anything in the act of departing that you may think would be appropriate for the museum, we would like for you to offer it to us.

Gallo: Do you take things that include pictures?

Harden: Yes. We certainly do.

Gallo: In 1984 I had major discussions in this office and a visit and it was photographed by this Brazilian photographer and I have the pictures with Albert Sabin. Right in back of you there is a picture... After the leukemia viruses were discovered, that is Ludwik Gross, who discovered the first mammalian leukemia viruses in mice, and he is an historic figure. Scientists that are in virology know him, but almost nobody else does. He was funded by the Veterans' Administration Hospital. But, certain pictures that will bring back... But it is hard for me to tell you... As I told you, I dumped so much stuff.

Harden: Perhaps later we can extend our conversations about your Federal records, personal records, and pictures. Dennis and I are also very keen on collecting laboratory instruments, technologies, objects, and articles.

Gallo: Then I will tell you, I would talk with Evelyn in the office, and Anna. Anna and Evelyn, not Gail. Gail has moved. Anna has been with me a long time doing manuscript typing. Evelyn has been around here a long time too. I would talk to both of them. You might want to mark that down. Then I would also consider speaking with Marvin Reitz, with Veffa Franchini here, and Sarang and Markham, who are off-campus but are close collaborators that we have seen twice a week for all these years. They have closely collaborated throughout, since 1970, which is 25 years of collaboration. They are much better in the record game because they keep it for the company, a lot of stuff. Then, other than myself exploring around, I would talk with Popovic, who is now in the Karolinska Institute, Flossie Wong-Staal at San Diego, and a few of the technicians, Ersell Richardson, who is still here might be one, and a few of the other long-term technical people. There may be things that I just am not thinking of that they would be helpful on.

Harden: We will get back to them. There are several people whom you mentioned that we will be interviewing also for the AIDS piece, and we certainly would like to follow up on this. We are more or less at the end of the interview, but I wanted to ask you if there is anything else that you, personally, would like to say before we stop?

Gallo: No. I do not think that there is anything I can add to all the questions we have been through–science in the future–and so forth. It was a very good opportunity for me and I thank you for it. I congratulate you because it is the first time, as I told you, that I knew that anybody cared about this kind of thing. I used to think that if Marshall Nirenberg ever had a heart attack or something then...

Harden: We lost [Dr. Christian] Chris Anfinsen. We hope to interview Dr. Nirenberg.

Gallo: I know. I was in the same department with Chris Anfinsen. He was one of the people who instigated my being in the department at Hopkins. I was just thinking, what is there after, you do not even know, whereas they [the French] built angels with swords around [the tomb of] Pasteur and of Dr. [Emile] Roux, his assistant. It is very dramatic, night and day. America is funny that way.

I have many thoughts about what I went through and certainly disappointments about leadership, not so much here at NCI, because I do not know if here we could have done much, although a little bit here, but higher up the ladder. I think that is a story in itself, but I will save that for another interview when I am a little older.

Harden: We hope to talk with you again. Thank you so much.