NCI Laboratory of Molecular Biology
Oral History Project
Interview with Dr. Max Gottesman
Conducted on September 26, 2008, by Jason Gart

JG: My name is Jason Gart, and I am a senior historian at History Associates Incorporated in Rockville, Maryland. Today's date is September 26, 2008, and we are in the offices of the National Institutes of Health in Bethesda, Maryland. Please state your full name and also spell it.

MG: This is Max Gottesman, G-O-T-T-E-S-M-A-N.

JG: Thank you. I want to briefly mention the interview scope: Established in 1970, the Laboratory of Molecular Biology, Center for Cancer Research, National Cancer Institute, National Institutes of Health, commonly referred to as LMB, currently has among its ten groups four members of the National Academy of Sciences. LMB has trained many other prominent scientists and its researchers have contributed to both basic science and to novel applied cancer treatments. LMB has initiated this oral history project to capture the recollections of prominent scientists currently and formerly associated with the laboratory.

Talk about where you were born, your interests as a child, and your move into university.

MG: I was born in New York City and went through high school in the city, went to Swarthmore College where I majored in philosophy, and then went to Yale Medical

School where I got my M.D. degree and where in fact I first met Ira Pastan. He was my resident when I was a medical student on some rotation. After receiving my M.D. degree, I enrolled in a Ph.D. program there and got a Ph.D. in pharmacology.

JG: Just to backtrack a second—so at Swarthmore College you were a philosophy major?

MG: That's right.

JG: Why did you decide to study philosophy, and then, what caused you to switch to the study of medicine?

MG: I loved the logical aspects of philosophy and putting ideas in order, and I think that that training has served me well over the rest of my career. But at the same time it was like playing chess. I did not feel it had real impact on the world and that there was really no progress in philosophy. It's kind of circular. I did not have a clear idea at the time that I went to medical school that I would do research. In fact, I did not think of that at all. That was pre-Sputnik after all and there was no funding for research. However, as soon as I got to medical school and I began to work in a research lab, I enjoyed it incredibly and I realized that's what I wanted to do with the rest of my life.

JG: What year did you graduate Swarthmore College?

MG: Fifty-six.

JG: Fifty-six. What was it like to be at Yale in the late 1950s and early 1960s?

MG: In the medical school? Remember, it is not Yale, it is the medical school, which was separated from the rest of the campus by a bridge over which it was dangerous to cross. I did not think it was a great place to be, quite frankly. They had not understood that there was a revolution in molecular biology going on. They were very old fashioned. They did not appreciate genetics. There were a few exceptions, people with whom I was friends, but for the most part I thought it was not an exciting place to be, that the real action was going on elsewhere. But I was there, so I continued to stay there.

JG: Was it common to do an M.D. and then to go back for a Ph.D.?

MG: No, that was quite rare at the time, although several members of my class did that.

JG: What was the reason for you? What were the skills that you thought you were missing and hoped to get from the Ph.D. versus the M.D.?

MG: I needed real close attention in the laboratory; I had to learn laboratory techniques. Remember, I was a philosophy major as an undergraduate so I was not terribly well prepared. But basically I loved doing research, and being a graduate student was fine.

And I did fill in lacunae in my training a lot. I took a lot of chemistry which I had not taken before. I took . . . yes, mostly chemistry which was missing.

JG: How did you see your career progressing? And also—you meet Ira. What are some of your first impressions of him?

MG: Ira was not doing research. He was a physician, of course, and my first impression—this was a presentation of a patient, and I was the one who was presenting. Ira was sitting at my side, and my first impression was his overwhelming exasperation with my presentation, which was terrible. I got in an argument with the Attending, all of the things that you are not supposed to do as a medical student. Nevertheless, I went to Ira's lab and spent many happy years there.

JG: Talk about some of your mentors during this period and how they helped you move along.

MG: I got my Ph.D. with Van [E. S.] Canellakis at Yale, and he was a biochemist and had made some interesting discoveries in RNA metabolism, DNA metabolism, so that sort of got me interested in that aspect of nature and biology, DNA, and RNA. After my Ph.D. I did a Postdoc with Fritz Lipmann at the Rockefeller where in fact I worked on polypeptide synthesis for two years, and then came to NIH in the Arthritis Institute.

JG: Rockefeller University is a leading center for biomedical research. What was it like to—

MG: At Rockefeller University?

JG: Yes.

MG: I did not enjoy myself there. [Laughs] It was a place that hired big egos, and there was very little communication among the different labs. The labs were locked at night, so you locked your notebooks away. So although there were a lot of good people there at Rockefeller, I really did not interact with them. There was very little interaction among the labs—unfortunately because there were so many good people. It was also not really a university. They had very few students, so it was basically not a cheerful place to be. And that contrasted greatly with NIH when I came here and I saw how interactive everybody was. It was a great relief.

JG: Watson and Crick had described the structure of DNA in 1953. When did you first take an interest in the emerging field of molecular biology? When did you start to really think that this was an area that you wanted to pursue as a lifetime career?

MG: When I was still an undergraduate at Swarthmore, I was aware of these revolutionary changes in science—the birth of molecular biology. In addition to philosophy I was taking some necessary basic biology/chemistry courses, pre-med courses so I could go to

medical school. And I just happened to wander into a meeting in Cold Spring Harbor, still as an undergraduate, and saw in one room at that time all of these people—Jim Watson, all of these great scientists, Sidney Brenner, and they were talking about what they were doing and I did not understand a single word. But there were numbers on the blackboard and logical constructions so I thought my Lord, this is really fantastic, that you could actually approach biology quantitatively and logically instead of cutting open frogs and trying to draw their livers. So that just by happenstance, wandering into Cold Spring Harbor during one of their meetings was a big inducement for me to head in the direction that I have.

JG: What was your impression of Watson?

MG: Watson and I got along famously. He is quite eccentric, as you know. He was not bizarre, but he was eccentric.

JG: How so?

MG: I was mostly interested in talking about molecular biology, about DNA. He was interested mostly in talking about girls and how to find them, and he was singularly unsuccessful. He was extremely awkward.

JG: Did you meet Crick at all?

MG: I met Crick later at Rockefeller. Crick and Watson were entirely different. Watson was quiet and nervous, and Crick was very expansive. He could just think on his feet in a way that was extraordinary, grasp things instantly, and had great ideas. He was really quite a remarkable person.

JG: So you are at Rockefeller and the position at NIH opens up. Were you looking at clinical opportunities? Were you considering teaching or did you want to do basic research at this point?

MG: No, I always wanted to do basic research, and the reason of course that NIH was attractive in the beginning—one of the reasons—was that it was a way of getting out of Vietnam. NIH was full of people called "yellow berets," who were avoiding going to Nam and doing their alternative service here.

JG: And this was the Uniformed Commissioned Corps—

MG: U.S. Public Health Service Commissioned Corps, yes. There were a couple of labs that I looked at at NIH, and the one that appealed to me the most was Michael Yarmolinsky in Arthritis. He was working on phage lambda, a very simple and beautiful system. He accepted me and I was looking forward to going there. After a brief contretemps—I was a security risk—and that had to be cleared up first and then I joined his lab.

JG: Why were you considered a security risk?

MG: At that time *The New York Times* was running advertisements—five hundred scientists against the war in Vietnam. I did not think anybody read these advertisements, but the FBI did, and so my name got on this list. At that time at NIH, they had an office of . . . not security, but an office of patriotism, and you had to pass through this office and show that you were not a security risk. What they wanted from me was a promise never to sign an advertisement for *The New York Times* again against the war. So I accepted, got into the corps, and as soon as I was accepted, I signed another advertisement. There is the First Amendment and you can't do anything about that.

JG: What year was this? 1961?

MG: When I came here? No. It was later than that. Let's see, I got my Ph.D. in 1964, so 1966 I believe.

JG: Were you politically active?

MG: Here I was, against the war in Vietnam, and there was very little political activity when I came here. People were intimidated basically, and that was—

JG: Intimidated by working at a—

MG: At a government institution. They thought they didn't have the privileges of an ordinary citizen. That turned out really not to be the case. And so as the war dragged on, sort of everybody became antiwar, even stockbrokers. And so then the NIH scientists for the most part came along, too.

JG: What was Bethesda like in 1966? You arrived from New York City; Bethesda is the South in a sense. What were your impressions?

MG: It was quite rural. Very few restaurants, the beltway had not been built so it was not so easy to get around, you had to go by East-West Highway. Bethesda itself had no . . . it did not seem that South; it was neither one nor the other. But if you went outside of this region, it was quite a racist environment. I remember incidents where I had black scientists with me, and it was not easy. I did not feel comfortable, and people would insult you and so on. So at that time it was pretty bad, but things changed very quickly. It is certainly not that way now.

JG: Are you married at this time?

MG: I was married.

JG: Speak about some of the first projects you did at NIH. Who was your benefactor here and how did you see your work progressing?

MG: The first work that I did here, almost as soon as I arrived, was . . . I worked with bacteriophage lambda and showed that lambda made a particular enzyme called integrase, a nuclease that cut bacterial DNA and allowed the lambda phage to integrate into the DNA. I showed this by isolating mutants of lambda that could not do this, and then went on to do some of the biochemistry with Susan Gottesman. At the same time, or maybe a little bit later, I was working with Ira—I'm not sure of the chronology exactly—on catabolite repression in bacteria, CRP for example. Ira with Bob Perlman had shown that the growth rate of *E. coli* was controlled under certain circumstances by cyclic AMP, which had only been known previously to work in mammalian cells. And he had found mutants, mutants in CRP, and then I collaborated in mapping these mutants. Where they were . . . . So that was my contribution. So it is two years with Michael Yarmolinsky and the Arthritis Institute, and then I came with Ira when we moved to Building 37.

JG: Before you moved to Building 37, are you a fellow at this point? What is your position? You are a young researcher—

MG: Yes, I finished the two years in the corps, and then I switched out to become a civilian civil servant, which in retrospect was a mistake. [Laughs] I should have stayed in the

corps. It didn't really matter, and in those days I was called something which I forget, but it was not difficult to stay on if you were doing good work. NIH was expanding.

JG: Speak about your first publications and your first presentations at conferences and things of that sort. Had you published anything before you got to NIH?

MG: Oh yes. I published things that I did for my Ph.D., both of them on DNA or RNA metabolism. We had found an enzyme that could add deoxynucleotides to the ends of broken strands of DNA, any kind of nucleotide, and that enzyme subsequently became useful for cloning, although we did not see it at the time that it was in fact the way to clone things. Then with Fritz Lipmann I published a paper showing that peptide bond synthesis did not require soluble factors, that it was innate in the ribosome, and you could wash the ribosome and wash the ribosome and it still could carry out this reaction. Again, I did not think far enough ahead to understand that in fact you could wash away all the proteins and the ribosome would still be active. The RNA would carry out the reaction, but if I had written that down in my paper, it would never have been accepted at the time. I wasn't even thinking in those terms . . .

JG: What was it like at the NIH at that time? You mentioned before that the Yale School of Medicine and Rockefeller University were unpleasant—Rockefeller locked its labs at night. What was it like to be here?

MG: Just the opposite, of course, and everybody was covered with chalk dust because they were at the blackboard explaining things. The labs were small, there were no large groups, everybody was interacting with everybody else, everybody was working in the laboratory. There were no people who were just sitting at the desk writing grants. Everyone was working with his own two hands. Everybody was extremely into what they were doing. It was not one step removed. And it was filled with these just wonderful scientists. This was Building 2. The group was extraordinary, and we had NIH-wide meetings of people who were doing molecular biology called Lambda Lunch, which is still going on after all these years.

JG: Describe the social aspects of being a scientist at NIH? Did everybody socialize on the weekends together? I saw an 8mm film that Ira had and you are all very young . . .

MG: That's right. Yes, we socialized. Everybody was married and had children. And of course we all lived in suburbia around here, so there were barbecues and the usual stuff. Yes, it was a time of social interaction.

JG: How did you think about your career at that point? Did you think that this would be someplace you would like to stay?

MG: I did. I had looked at other places, had interviews, but I never saw anyplace that came close to NIH at that time. In a sense, it was very early in the molecular biology period,

and other places were not caught up in it. I wouldn't say that they did not appreciate my work, but I think they did not grasp where science was going. So there was no reason to leave NIH. I was not too serious about moving anywhere.

JG: Ira works here, and prior to your move to LMB, describe your interactions with him. Did you ever play tennis with him?

MG: I think on occasion, but he was too good. [Laughs]

JG: I guess you met at Yale, and did you remain in touch?

MG: No. We met at Yale and then again here just by coincidence, so we did not remain in touch. I can't remember exactly when we started to collaborate, but that went very well. I enjoyed the collaboration. I thought that Ira was generous in doing this, because I had not done that much really, just mapped the gene, and then that collaboration led to other aspects. So my work was really in two sections. It was working on lambda, and then working on cyclic AMP and the operons that are controlled by cyclic AMP. We had a bunch of papers. It was a good lab in the sense that we had both genetics and biochemistry going on.

JG: Why is cyclic AMP so important?

MG: Bacteria can live without it, but they are handicapped and they can't respond to the environment very well. It is extremely important in mammalian cells for all sorts of signal transduction pathways which are involved in differentiation and also response to the environment. I have continued to work on cyclic AMP in animal cells over the past twenty years, I guess.

JG: You are recruited by Ira to join the new laboratory he is setting up. Talk about that change and walk me through your decision to leave the Arthritis Institute.

MG: It was certainly a good offer, and I liked Ira and got along with him. We were already collaborating, it was more space, it was a Section I think at that time or soon to be a Section, and that gave me some opportunity to bring in people, which I did not have in the Arthritis Institute. I was unable to bring in people and that was a problem. Coming to the Cancer Institute was challenging. I think I was the first one to actually physically move in. The Cancer Institute was a terrible place. There were very few people there who were doing any good research. When I moved in, my lab was dark because there was no light bulbs. I went next door, somebody was sleeping, and I said I have no light bulbs. He said take this, he gave me his light bulb. It was really a very sleepy place. And Ira was one of the first people to change this . . .

JG: Why so? Why had it been left behind?

MG: I do not know why they did not attract good people, but they had not. There was a lot of dead wood.

JG: Is this before the war on cancer?

MG: When was the war on cancer?

JG: I guess about 1971.

MG: So probably before, right? When did I move here? In 1972?

JG: Yes.

MG: No, it was before the war on cancer.

JG: Talk about the recruiting effort and some of the people you brought here. How did you convince them to join? How did you describe the aspirations of the lab and what you thought the group could accomplish?

MG: It was easy to get people to come here. It was a really good lab. The lab was divided into animals and vegetables, and by that time I think Ira was mostly working on the animal part, he was certainly recruiting into animals. The vegetables, we had full

support, they could do what they pleased. They came and they fit right into the program that was going on. Sankar Adhya came early, Susan Gottesman passed through the lab, Don Court passed through the lab, and all these people stayed at NIH in one capacity or another. And we just did great things. It was the first cell-free system that responded to cyclic AMP. Susan was involved in the first biochemical demonstration of integrase.

JG: Talk about the skills that each of them brought—Sankar, Don, and Susan. How are they different as scientists or researchers? What were your first impressions?

MG: Well, they all brought this terrific intelligence. They had all been trained very well. Don and Sankar by Allan Campbell, Susan by [Jonathan] Beckwith. So they came in with great background in genetics, super intelligent, and then the lab here had good biochemical capacity. People could make extracts and things worked, so it was a perfect marriage for everybody. Everybody benefited enormously. It was a very well-meshed group. So particular skills it is hard to say but everybody was very polymath.

JG: There is confusion because there are three people with the same last name. Describe how that plays out?

MG: [Laughs] So, Michael, Susan, and myself, we would get invited to nice meetings and interesting places, or not so interesting places. I think that all that mail went through Michael first, and he just selected the nice places and went there, and I got to go to

Newark and Pittsburgh and places like that. I think we benefited because everybody thought there was only one Gottesman, so we got credited for three times as much work.

JG: Is there any relation at all?

MG: Susan has prepared a genealogical chart, which you should see, showing the Ur-Gottesman, the first Gottesman, and how we derived from that creature. You have to go back a long way.

JG: What interested you about cancer research?

MG: While I was here, I was not terribly directed towards cancer research. I understood that the integrase enzyme was important because HIV has an enzyme like that and that could be of interest. But basically I didn't become really interested in cancer research until I left here and went to Columbia [University Medical Center] and became the director of the Institute of Cancer Research. I brought some people, or at least one person from NIH with me, and then set up a lab that was—I continued doing what I was doing in terms of lambda, but also did research on cancer.

JG: So your work here was primarily basic research?

MG: Yes, right.

JG: In the early 1970s as the laboratory begins there is the recombinant DNA controversy. Talk about that and your standing offer to drink . . .

MG: [Laughs]

JG: I've done my research.

MG: Well obviously I thought it was all a lot of nonsense.

JG: Walk me through the controversy.

MG: This is a very biased view you will get, of course.

JG: That is what history is all about.

MG: There were at that time a group of quite radical scientists, Beckwith and Signer—

JG: Maxine Singer here at NIH?

MG: Not Maxine Singer. She wasn't radical. She was involved in this—but I am talking about Ethan Signer. Maxine was a driving force in this moratorium, she and Paul Berg I

think. I thought the basis of it was just not thought through, and it was never comparable to the atomic scientists where there was a real danger of some research going awry and falling into the wrong hands, which unfortunately I think it has, but there was never any danger I felt from recombinant DNA technology. The moratorium just seemed stupid because people were doing all the research, they just were not publishing. I do not think it was effective, and I thought it was silly. I think I went to France at that time, and I do not think anybody honored this moratorium. Everybody was cloning. It was a very important phase in molecular biology and biology in general that you could clone things, and trying to stop it was dumb. What was supposed to happen during this year? What kind of experiments were supposed to be done to prove that it was safe? That was never made clear.

JG: What were the other views in the laboratory?

MG: I do not remember anybody being enthused about the moratorium.

JG: How did it impact your work? Did you just go on and—

MG: I just went on, of course, but I was not cloning human viruses or human genes. I was cloning bacterial genes into phage lambda.

JG: What was the standing offer to drink recombinant DNA?

MG: You know, I do not even remember this?

JG: You offered to mix up any cocktail of recombinant DNA and drink it.

MG: [Laughs] That was provocative of me, but I do not remember the details.

JG: Describe some of the publications that emerge in the 1970s with the group?

MG: I should have done my homework and looked at my CV. With Sankar, we began to look at the *gal* operon, and that led to the isolation of the *gal* repressor. And I think also Sankar was involved in the establishment of the cell-free systems that could recapitulate control of these operons, if not early, then later on. Susan as I said joined me in describing a cell-free system that carried out lambda excision. We were the first to do that. Don was a little later. I can't remember who—it was such a meshed group that I can't remember who contributed to what exactly. But we began to explore with Sankar then the antitermination reaction and how that worked. That was also a momentous time. We published a paper that showed that lambda had a system for suppressing transcription terminators. Sankar and I wrote a review on how polarity in *E. coli* works and that it involved, again, transcription termination. Those were important papers.

JG: Do you recall a notable failure and how that impacted your career?

MG: Well, everybody has projects that do not work out. Mine did not take too much time, happily. You have to know when to hold 'em and when to fold 'em, so I did not spend a huge amount of time on some hopeless project. I had them, but I knew when it was time to abandon them.

JG: How do you know when to fold them? Is it just a gut instinct that this is not working? It could be three, four, five months down the line until you realize. . .

MG: It could be, but for example, in setting up the biochemistry we knew that it had to work, that integrase worked. We knew from the *in vivo* from the genetics that things had to work, so we knew it was just a question of working with an *in vitro* system to get it to go. With genetics, you do not have a huge stake in something. It is easy to do the experiments, and you can test your hypothesis very, very rapidly, so you are not likely to go off in a direction that is a total disaster, unlike working with trying to purify some enzyme that it turns out you can't do, or these days making a mouse that takes a year or more to make and does not have any of the characteristics that you set out—total failure. So in genetics there is not much of an investment because the results come quickly.

JG: When you were in medical school and your Ph.D. program how did your mentors describe scientific success and scientific failure?

MG: You have to remember at that time there was not much competition. Funding was very abundant. As soon as Sputnik went off, science was a favorite recipient of funding. So an immediate success or failure did not impinge as it does today on your funding. It really impinged on where you were going to end up, what university and so on. I must say I never thought there would be any problem.

JG: You leave NIH in 1984?

MG: Eighty-five.

JG: Walk me through the 1980s and compare and contrast the laboratory in 1985 to 1975.

MG: I thought that the NIH in general was going through a downhill path at that time. There was no more war in Vietnam, the yellow berets were gone, they moved on elsewhere. It was hard to get American postdocs to come to NIH. I think it was beginning to—the expansion was slowing down. I thought the quality of postdocs was decreasing. There were no more Susan Gottesman, Sankar, Don Court ,and so forth. I felt at that time before leaving here that it was not as fun a place as it was when I first came, and it was not clear it was ever going to come out, but in fact it did come out. On the other hand, the offer at Columbia was terrific. It was directorship of a large space, and again there were very little funding problems at that time. So that is what was going on at that time.

JG: Were you recruited or were you looking at that point?

MG: No, I was recruited. I got a call from Richard Axel who had been here at NIH and who had moved to Columbia, and he asked me if I was interested in looking at this position. At first I was quite skeptical. I did not want to move to New York again. New York was not a prosperous and happy place, but I looked. He is very persuasive. Indeed, he went on to win the Nobel Prize. And eventually I took the position.

JG: Before we talk about what you are doing now at Columbia, I thought we could capture some of your thoughts on a broad range of topics: How has technology changed over your career?

MG: Well it has been an enormous change. When I started in genetics, there was no sequencing, so it was much more of a challenge in figuring out what your mutation was. Now, of course, you have a sequence, you have a database, you know what your gene does by—its annotated most of the time. You can move very rapidly. On the other hand, all of this information can be a bit too much, and it is possible just to be overwhelmed by the information that comes from all of this technology, from the sequencing in particular, and other things. It is not to say I do not use it, obviously. I use it as much as I possibly can. But it does lead to an overwhelming amount of data which is not hard to gather, but it is getting away from hypothesis-driven research.

JG: How do you manage all of this information? There are much more journals today than there were. There are more papers being published. How do you keep relevant in the field?

MG: Computers make life extremely easy. I do not think I have been to the library in five years or so, so you can quickly pull out of PubMed any publication that is relevant. So that is very important.

JG: What about the serendipity of going into the library and paging through journals?

MG: I don't know people who do that. [Laughs]

JG: But you would have . . . .

MG: I would have at that time.

JG: And if you were trying to find this article and flipping through . . .

MG: I do not do that. The serendipity comes from going to meetings and hearing people who are doing other types of research and describing technology that you did not know about. Serendipity comes from talking to people on the telephone, it comes from being invited to give a lecture somewhere and meeting everybody in the department. And of course a

place like Columbia has a huge number of seminars, so every day there are at least two or three and you can pick those, and often I will go to some seminar that has very little direct relevance to what I am doing and be surprised.

JG: How about the social enterprise of science? Describe the importance of collaboration and contrast that to the view of the lonely scientist off on a bench somewhere.

MG: I guess that does exist. I myself have been very much into collaborations. I can't do everything. I never had a huge lab anyhow. I think almost all of my papers, recently anyhow, have been collaborations with other labs, especially now when I am collaborating with structural biologists who are solving the structures of proteins, something I could never do myself.

JG: Is there a scientific etiquette on collaborative work? Do you collaborate with people that you just feel comfortable with? Or do you seek out people that bring a certain expertise?

MG: Well, both. Certainly one would not collaborate with somebody whose judgment you did not trust, whose scientific ability you were suspicious of. That would be a disaster. So it is people that you trust or at least that you get the raw data from so that as best you can you can evaluate it. And then it is this. You collaborate with somebody who has an expertise which is not yours. Structural biology, for example, that is very specialized.

JG: What are some of the challenges that you have seen over your career with women and minorities in the sciences? Ira mentioned that Susan was brought here. What are some of the success stories that you have seen?

MG: Susan Gottesman and Susan Wickner are both here. I am not sure the NIH has been so behind the times in recruiting women. I am not sure. I do not have the statistics. But out there in the universities, it is a big problem. At Columbia, we do not have women chairs.

JG: And still today—why is that?

MG: It is hard to say.

JG: Is it just generational?

MG: I would think that my generation by now would not have this issue, but it is just a fact that is out there.

JG: Talk about the role of publications and their importance in science.

MG: I think that maybe fifty years ago you did not have to publish. There were people who just did their research, nobody asked them to publish. Now of course you must publish, and you must publish frequently, and the funding often depends on people just counting

the number of publications without actually reading them. So this is not so great, and what it leads to is a lot of publications have a phenomenon called the LPU, the least publishable unit. So they publish just a small part, and another paper with another part of it. So grand synthetic papers you do not see much anymore.

JG: How has that impacted the sciences and research?

MG: Publishing papers quickly is hazardous, I find. I think there are probably more retractions now than there used to be. It is hard to say how much of an impact this has had on the quality of science.

JG: Can a researcher or scientist spend months thinking about an issue—or are those days over? You know, months investigating a hypothesis and then another year or two preparing to publish?

MG: That is why the NIH was founded. It was to permit this kind of research that didn't have immediate application or immediate payoff. It dealt with research that was quite speculative but important, and people came here to do that. They may not have published for a long time, but they were doing things that eventually turned out to be fantastic. Now at least I think parts of the NIH are still built that way. I think it is still more supportive of speculative research than out there. Out there you do not have that luxury. The way the system is now with a very low funding rate, you have got to publish and

publish and publish. You can't even switch fields because you do not have a track record in the new field, so it is not very good out there.

JG: How did we get here? Is it just because of decreases in funding for the sciences and thus you have more and more people chasing after the same pot of money?

MG: Well that is true. I think that is a good call. If there were abundant funding, then people could spend—

JG: Like the post-Sputnik period.

MG: Yes. They could go off and do things that might not lead to a publication for a couple of years. I think there is that. I think a lot of the money that the NIH has gotten has not been I think applied productively. As you know, there is a lot of pressure on NIH from groups, breast cancer groups, prostate cancer groups, this and that, who want their money funneled in certain ways, and those particular diseases may not actually be ripe for research and not require the amount of money that these groups wish to have devoted to it. So I think there is not much money and part of the problem is the targeting of this money may not be optimal.

JG: Speak about the influence of scientific stars. Are there people that because of their research or success get funding and can switch careers, and then if you are a new researcher or scientist, you are more limited. Is that a problem?

MG: Well the superstars are fine. They are superstars for a good reason and a lot of them are supported by Hughes.

JG: HHMI [Howard Hughes Medical Institute]?

MG: Yes. So they have a lot more leeway I think than the NIH-supported R01 [Research Project Grant] supported research. So no problem with that, although they get a huge amount of money, and some of that might be better spent for other people that are not under Hughes, but that is another issue. What is a real issue is that now for a young scientist to go into a department, people do not look at what he is doing. They look at whether it is fundable and that is really a perversion of the system, I think. So a new scientist has to continue what he did as a postdoc, really, in order to get funding in some reasonable period of time. It has got to be related to what he has been doing for his postdoc work, so he can't switch. For me, for example, I switched entirely from ribosomes to lambda genetics. That is not a switch you could make now.

JG: Peter Medawar wrote a booklet, "Advice to a Young Scientist," in which he argues that the most important decision a young researcher makes is their first topic. The selection

impacts where they get funding and where they will eventually go. Isn't this the antithesis of the whole concept of basic research? That you should research what interests you, and what you think might be important ten, twenty, thirty years from now, as opposed to what is directed by funders and benefactors?

MG: Yes, I think that is true. What he says is right. The startup scientist has to have a five-year plan. He has got to come in, he has got to get funded quickly, and he has got to remain funded. Universities now are, if your funding level drops, they take your space away and that can be an irreversible down spiral.

JG: Where are the professional organizations—what is their stance on this? Is there a discussion going on among senior scientists like yourself about this? Is it considered an issue?

MG: Well, there are science lobbying groups out there, and they try to get funding for science and they are pretty effective. And I think that is really all that they can do. If the funding level went up, I think these things would be resolved for the most part.

JG: Describe your responsibilities to younger scientists and your mentoring over the years, first at NIH and then at Columbia. How do you teach scientific ethics? How do you make sure that young postdocs scrutinize errors and are also creative in their research?

MG: That is a very good question. Ethics, I have not had any problems with anybody in that area—you have to take an ethics course now in order to get your Ph.D. I think. I think that anybody who has half a brain understands that if you are not ethical in your science, if you fake data, you are going to get caught, and I think that people who fake data are nuts. I have known people who faked data, and they are nuts because they are going to get caught. I do not think that is a big issue. Developing them as scientists and letting them develop as scientists, I do not know what the trick is there. You give them confidence, you let them mature as quickly as you possibly can, you do not treat them like technicians, you treat them as fellow scientists, and you do not put them on impossible projects, vanity projects. So a lot of talking with them. I, myself, work in the lab and I think that is very useful, because if you are in your office and the door is locked, you do not have the same contact as if you are on the next bench next to your student or postdoc.

JG: What about the need to be creative as a scientist? You started your career as a philosopher, very logical, but what about the creative aspect of it?

MG: Creativity is a gift from the gods, I think, and I do not think you can teach that. You can have creative people who are not using their ability because they are stuck in some particular location and working on some hopeless project and some obscure bacterium. So the creativity of a person is often very site-specific, so if this person would move to Harvard or Columbia or someplace like that and interact with other people, their

creativity could bloom. It is cryptic, inert. But some people will never be, no matter what their environment is. They just can't. It is a leap from being a postdoc to being a scientist, or maybe a graduate student to being a postdoc, where everything is done for you, protocols are written for you, the project is all laid out, so the realization that you have got to think on your own and come up with your own ideas and your own directions, and some people just can't make that leap.

JG: How does your profession continue to attract young students into the sciences?

MG: The students that I see just love science, and they understand that the chances of success now are not great, that they may have to take several postdocs, may have to write grants over and over again, and they may end up not doing what they want to do, they may not end up in academia, they may end up in a company or going into something else like patent law or something. But they will give it a try because they love it.

JG: We spoke about this earlier. What is your view of science today?

MG: I think despite the problems and the handicaps, it is really a time of incredible scientific progress. All of the leaps in technology, the database, the ability to find out things that were hopeless not so many years ago, it is an incredibly exciting time to be alive and to be a scientist.

JG: What are you currently working on at Columbia?

MG: I am continuing the work on transcription termination, very basic research. I have a couple of other projects. One is DNA repair, going all the way back to how DNA is repaired and that is a project in—it is biochemistry, frog egg extracts, Xenopus egg extracts that recapitulate DNA repair, working in that system with DNA that has been damaged by crosslinking agents which are used in cancer treatment. We have set up an *in vitro* system that efficiently repairs these crosslinks, and at the same time the system detects the crosslinks and tells DNA replication to stop until the crosslink is fixed so that you do not incorporate a mistake into your DNA. So that is pretty exciting stuff, and we have just sent a paper off yesterday. I have two other collaborations, one on bladder cancer, and that is related actually back to cyclic AMP, believe it or not, looking at how cyclic AMP signaling works in eukaryotic cells, and that has led to some very interesting observations on a marker in bladder cancer which may be an interesting biomarker as a screen for bladder cancer, which is a big health problem. So those are the general areas that I am working in, DNA repair and cyclic AMP signaling in mammalian cells. Monday morning I am going to meet with some urologists actually to discuss this gene as a biomarker.

JG: What are some of your outside hobbies, outside of the sciences?

MG: Figure skating. I started that here and continue to do that as my major outside interest. That is one of my major outside interests, and poetry. I write poetry and I read it to groups.

JG: Have you published any of your poetry?

MG: Sure.

JG: Last question. If you have one piece of advice, one lesson learned that you would like to pass on to a future scientist or researcher operating ten or twenty years in the future, what would that be?

MG: A couple of things. I would say be skeptical of current information. Not all of it is correct, and it is never complete even if it is correct, and there is always more to be uncovered and there is no reason why you can't do it.

JG: Thank you very much.

[End of interview]