NCI Laboratory of Molecular Biology
Oral History Project
Interview #2 with Dr. Sankar L. Adhya
Conducted on October 8, 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 October 8, 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.

SA: Sankar Adhya. S-A-N-K-A-R—A-D-H-Y-A.

JG: Today I would like to first walk through some questions that came up from the last session. Then we will switch from a chronological to a thematic approach and talk about the role of publications in science, the practice of science, and what has changed.

SA: Okay.

JG: When we last spoke we were talking about your election to the National Academy of Sciences in 1994. I had a question about the twentieth anniversary reunion. I had the opportunity to watch the videotape of the evening and saw that you gave Dr. Pastan a dinner bell. What was the significance of that gift?

SA: Ah, yes.

JG: Can you explain the significance?

SA: I think what happened was that we had a weekly seminar on data club and journal club. At that time there was only one group, everybody participated, both the eukaryotic people and prokaryotic people participated in the same seminar. Later Dr. Pastan divided the groups into two. One was called the vegetables; the bacteria people. The other was called animals; the eukaryotic people. Originally, there are people coming late to the meeting. It used to start at 12:15 pm historically. He would call, "It is seminar time," "It is seminar time," and people would come out of their labs and go to the library where we used to have the seminars. I thought instead of him yelling and peeking into labs he could use like cow bell, that if he rings the bell and walks from his lab to the library, everybody would know it is seminar time.

JG: Did it work?

SA: It worked. He used to use that and people got the message.

JG: When I did the interview with Dr. Susan Gottesman she spoke a little about what those seminars were like. She mentioned that early on they were more—not contentious—but people would debate the topic and now that has changed a bit. I wonder what your reflections are on the seminars and what their value is to a lab like this.

SA: As I mentioned before the lab started as an integrative biology lab in the sense that people of different expertise got together and discussed with free exchange of ideas. These seminars were based on that kind of idea. It was very useful for postdocs to learn different ideas from different expertise. Like a geneticist or a clinician and so on. We learned from each other, both the senior and junior people, and I thought it was very useful in everybody's mind. It was a free flow. We used to interrupt, argue, and used to joke, kid, and so on, and heckle each other—I mean in a very, very friendly way—and it was very useful. Things have changed over the past years. The joint seminars have become a little more formal as time went on. Mostly because, in my mind, the junior people who came later, the young postdocs and so on, they are afraid to present raw data in front of other people and defend their ideas. They try to present more formal, finished data, and therefore you don't interrupt, which is not the way it used to be. I liked it free flow, discussions, interruptions and so on. My memory is that speakers, even visiting speakers, we used to have the same format. The invited person, whoever that person is, would stand there and two people in the audience, X and Y, would argue with each other about the subject. I think it contributed greatly to develop intellectual capacity to discuss and think about science, and I liked that. Things have changed. Now it is more formal and I am not in favor of the current situation. But this is only time in our laboratory wide seminars.

JG: Do you have meetings separately with your own section?

SA: Yes. I think most every section has its own so-called group meeting where we try to practice free flow interactions; there is no time limit, and people interrupt and challenge. In my group, I follow the old format.

JG: When we were talking last week you mentioned that bacteriophage was actually used by the Soviets and Russians. They were using this therapy to treat infections in the 1950s and 1960s but it never really took off in the U.S. for some reason. I wonder what your thoughts are on this?

SA: Actually, it did not start in Russia. Phage was discovered as a so-called antibiotic by [Félix] d'Herelle who was a French-Canadian and a British health officer. I think it was in the 1930s and early 1940s. He discovered phage and found this has an antibiotic potential. He did not call it an antibiotic. He did not know what phage was; he did not know about DNA, or anything. He found that some bacteria secretes some material, which can be propagated by infecting new bacteria, which were killed. He made bacteria-free preparations. He used to inject humans infected with bacteria. They killed bacteria. He used to travel as a British health officer to India and Egypt, and here and there, whenever there was an epidemic—cholera or dysentery—and so on, and it used to work. It started that way really. After antibiotics was discovered in 1944 or 1945, penicillin, that was the death nail of so-called phage therapy, in the Western world that included the U.S.A. and Europe.

In the meantime what happened was that Stalin actually hired d'Herelle—the discoverer of phage—there was another discoverer, but he was not interested in phage therapy, [Frederick] Twort—to establish a phage Institute in Tbilisi, Georgia. I think people have the impression nowadays that the Institute was established to develop, so-called "bioterrorism," to grow pathogenic bacteria and so on. Part of the Institute also started working on phage therapy. Even today, they use phage therapy in Georgia. There was a meeting three months ago and I was there visiting the Institute. It is actually called Stalin's Institute. There is a real name for the Institute, I forget the name, [George Eliava Institute of Bacteriophage, Microbiology and Virology]. Because of Soviet dominance in Eastern Europe the phage therapy was being practiced in Poland, Czechoslovakia, and many Soviet republics. Still today they are using phage therapy. I have some samples of phage that they use.

JG: There is a lot of talk today about antibiotic resistance. Does phage offer an alternative to that?

SA: We became interested because of antibiotic resistance, widespread multiple-drug resistance. Carl Merril who used to be my collaborator at the National Institute of Mental Health, he has since retired, and I got together to reinvent phage therapy, to try to bring it to Western medicine, because of antibiotic resistance. We started working on that around late 1990s and we found out that, in animal experiments, phage therapy works. If you inject the right kind of phage, it works. The problem . . . Let me go back a little bit. The phage therapy died not just because of antibiotic discovery but also because when phage was used as a treatment there were problems because people at the time did not know that there was a specificity—you had to use a certain kind of phage for certain kind of bacterial infection. They did not know that. D'Herelle's original mixture had a lot of phage in the same preparation. It happened that a person, for example, in Bombay, India, during a cholera epidemic was injected with some dysentery phage, Bacillus dysentery phage, and it did not work. The person died. It was because they did not know that phage was specific. Another thing was that sometimes phage therapy killed patients even if they used specific phage. The reason was traced back to the fact that fresh preparation of phage has toxic effect; old preparation did not. So what happens, the phage are grown in pathogenic bacteria, and they had endotoxin released into the phage and the toxin has deleterious side effect on the injected people. They found out that old phage preparations was more effective than fresh ones.

Those were the things that were working against widespread use of phage therapy. In Kolkata, India, where I was born, it was being used in the 1940s, 1950s, and so on. Knowing these facts it is now easy to use phage therapy, that is use of purified phage, specific phage and so on. The second thing we realized that phage therapy works in animal experiments very well, except you need tremendous amounts of phage. Phage are foreign bodies and rejected by the innate immunity inside mammalian hosts and ejected out through the spleen and liver quickly. We isolated phage mutants which stay in the body for a longer time by using a genetic selection process. That phage works much better with a lower dose. Another problem that some people are saying is that there will be phage resistance, which is true. We tried to use a cocktail that uses more than one phage of a given bacteria. There is more than one available phage for a given bacterial strain so you can use two strains. If it is resistance to one it can be killed by the other. The third thing we did—I am not continuing on that project at the moment because Carl retired and I do not have the animal facilities—that were in the process of trying to construct an engineered phage with more than one type of tail, which is responsible for bacterial infection.

JG: Are other researchers also working on phage?

SA: Yes, absolutely. At the time we were working on phage, we also got involved in collaborations or consultations with several phage therapeutic companies, small companies. Then also we had some CRADA [Cooperative Research and Development Agreement] partnerships; they gave some money for a postdoc and so on. We made great progress, but now NIH does not allow us to consult. Recently a company, I can't remember the name of the company, has been approved by the FDA for use of phage for preventative use in the poultry, meat, and cattle industry, and so on. They have FDA approval. They are doing well. Several companies are now interested in Sweden, Holland, and Denmark. Phage are used for prophylactic purposes.

JG: Talk about the antibiotic resistance. Is this an issue that the U.S. and the world will have to deal with?

SA: Absolutely. Because the most effective and prevalent antibiotic is vancomycin and right now a lot of vancomycin resistant bacteria have been found all over in the hospitals, particularly *Staphylococcus aureus* which is a major problem in many hospitals. People go for treatment in hospital, where they are going for surgery, and they come back being infected with staph bacteria. This is a major problem and something has to be done. Phage is one way.

JG: Walk us through some of the significant projects that you have worked on since 1994.

SA: Well, one is I was very excited to develop phage therapy which I worked for about seven or eight years. We published quite a few papers on that. We also have some patents on those things. This project I discontinued simply because at the moment I do not have the animal facility and Carl retired. NIH also prevented consultations. Another related project we developed which I am still doing is use of phage for detection purpose. Many times when people get infected you go to the doctor's office. They give you some broad-spectrum antibiotics, and at the time, send you for a blood test. You come back two or three days later to get the report, and they give you specific antibiotics or whatever they want to do. I think sometimes there is some bacteria which rapidly invade and develop, it is too late. We developed a technique where you can detect bacteria in clinical samples, blood or urine, using engineered phage quickly—in half a hour or one hour while you wait in the doctor's office. The idea is that we have labeled the phage. When they infect bacteria in the clinical samples the phage that comes out has fluorescent signals that we can detect with a fluorescent microscope. Phage grows in about half an hour to one hour.

All phages grow within that period. You have the results while you wait in the doctor's office, so that is the idea. We have done that, we have patented that, and now we are also trying to use the same concept to detect cancer cells.

JG: Let's talk about—

SA: That was one of the things. Second, my major interest is regulation of gene expression and eighty percent of my time is spent on those. It developed slowly. Initially we thought, everybody thought that there is a DNA and there are RNA polymerase which transcribe genes. There are signals of initiation of transcription which turn gene on and off. We spent a lot of time studying biochemical details as to specificity and their mechanisms and how genes are transcribed and how they are regulated. It looks like more and more that all the genes are connected in one way or another to each other in some way that is called systems biology. So we are now looking at structure and function. DNA has to be organized in a given way to be able to be transcribed or expressed. The DNA could become silent even in bacteria; they become silent and it is not accessible. DNA has to be given some signals to change its structure before the regulatory proteins can have access to those genes.

JG: Where do you see the work progressing over the next ten years?

SA: I think we are progressing in understanding structure-function of the genome as a whole. Because of technology we can study not only a specific gene but many genes together and therefore their interconnection through their products or substrates and so on. We call that functional genomics; we are looking at a global scale, and the byproduct of that is we find ways to manipulate, either to inhibit or to activate, certain gene functions or their products. This would be of great therapeutic value for controlling diseases.

JG: I want to ask you a strange question. I have asked everyone this—how do you deal with a notable failed experiment. What happens when you have a hypothesis that is incorrect and it has consumed months of your time? How does that disappointment affect you?

SA: I know it disappoints some people; particularly young people; they get frustrated. For me, I have the opposite view. If an experiment failed and it was designed properly—the whole idea is that you set up a hypothesis and set up an experiment to test that hypothesis—if you do it properly the negative result means that hypothesis is not true. That is a great contribution to science. How things work: A, B, and C, if you prove that C is not the right answer that is a great achievement in my mind. Then we will move on to A or B. I do not think that is a disappointment even if it takes months to disprove a given model. That is the way I look at it all the time. Negative results, if done properly, if you are hundred percent convinced that the negative results are not because of bad design of an experiment, or somebody made a mistake, or something, but if done properly they disprove hypotheses. That is the way I look at it.

JG: Your publication record . . . You have approximately 198 publications? Talk about the role of citations in science and how they are connected to the career of a scientist and to funding and to things of that sort.

SA: Well things have changed.

JG: How has it changed?

SA: Things have changed. It used to be something called *Science Citation Index*. Your paper is referred by other papers and there used to be a hard copy *Science Citation Index* volume and if you are interested you can go to the library and find out how many of your papers have been cited how many times. I have checked that when I was much younger once in a while—not many times. I found out one thing is that some papers are cited many, many times, although they are not very, very important papers, and some papers have not been cited although I think they are very important papers. It is just that people are not interested. So you have that knowledge that you are not doing something which is very popular or people care about. That is one way to look at it.

But those are old days; now things have changed dramatically. Now it is called impact factor. People are judged by how many papers they have published in high impact factor journals. Journals are rated nowadays by the criteria, if I am right, how many times a paper published in a given journal have been cited by other papers. It does not matter whether it is your paper or not, but how many times papers published in, for example, in

Nature have been cited by other journals. If *Nature* papers are cited many times then *Nature* is a high impact journal. Young people are now very crazy about publishing in high impact journals simply because nowadays grant applications and people's performance and jobs are evaluated in many places by how many papers you have published in high impact journals. The journal has an impact number; they add up the numbers. You have to have more than 30 points to get a job or to get a grant or so on. I do not quite agree with that system but that is the way things work. Another thing is that people have moved on from basic research to something which are more so-called fashionable research, that is, a popular topic. If you are working on a global fancy system then you have more visibility than studying some mechanism of a given specific process and that is less popular in terms of both funding and finding a job.

JG: Can a researcher or scientist still spend years looking at an issue or topic that might not make it into a high impact journal?

SA: Yes. That is true and I think we do that. We do that. We work on things which are not very popular and publish in a journal that are not that popular. I value research. That is the way I was trained and I am interested in what I am interested in researching. What is interesting to me is not necessarily what other people are interested in. Of course, I understand the funding issue but I am very fortunate to work at NIH where we have that freedom and therefore we follow our nose.

Going back to the modern way of doing science, I have in my lab many people who are postdoc's from another country. Many of them have gone back and have good jobs. I talk with them. One time I had a visiting scientist. He was here for a year. He said he needs . . . He was at the time an associate professor in that foreign university and he thought doing a sabbatical here, and publishing a few papers, he would be able to get a full professorship promotion. I said, "What do you have to do?" He said, "I need to publish papers." I said, "How many?" He was supposed to be here for only a year. He said, "Well, it doesn't matter how many he needs thirty impact factor points." If he published one paper in *Cell*, for example, which at the time had a rating of 32, he will get a promotion. If he was to publish in *Journal of Bacteriology,* which is one of our favorite journals, the impact factor is less than five and he would need to publish six papers in one year to get that promotion. He preferred to publish a paper in *Cell*, of course. I said, "Why is that? Why do they look at impact factor of journals and not your performance? He said in his country they are not very many experts to evaluate everybody in different areas of science, all the candidates, applications, promotions. This is the way they decide, let journals decide, and their admissions is based on somebody else's decision. I said then, "Why you need letters?" For example, if you have these numbers, they add up the numbers by the impact factor, then a secretary can look at the applications and give you the appointment. "Okay you made 32—fine, you have an appointment." You do not need a committee, you don't need evidence of scientific expertise, or applications. He laughed but that is the way it worked. He was able to publish . . . I think he stayed for another year or two years and he was able to get thirty points and he got his promotion by publishing a few papers.

JG: Is there a scientific elite in each profession? I guess not elite—maybe scientific stars. Those that win the Nobel Prize in Medicine or Physiology, or get elected to the NAS very early, or become editors of *Nature*. What is their role in the profession?

SA: I do not know . . . You call them elites but they are renowned scientists. Most of them are renowned scientists and they definitely play a role in directing science because they are frequently members of the granting agencies, councils, and editorial board that direct what papers are acceptable, or not acceptable. The younger scientist has to follow that guideline to get published in a good journal, to get a grant, and these are decided by those people you mentioned. There are recognized scientists who influence science, yes.

JG: What about the role of scientific worldview—that is not the word? I think of science as always trying to find truth but sometimes a person's worldview could negatively impact the pursuit of science?

SA: Of course, dogma—dogma.

JG: Dogma, thank you.

SA: Sometimes people are dogmatic. I know people could be dogmatic. It is bad in science. There are dogmas which dominated the field of biology—I do not know much about chemistry or physics—that turned out to be wrong later. A classic example, if I might cite one, is DNA replication. It was mediated, we were told, by an enzyme called DNA polymerase discovered by Arthur Kornberg who got a Nobel Prize for discovering that enzyme. It turns out it is not the enzyme—it is a DNA repair enzyme. So textbooks were corrected, but Kornberg was the first one to change his mind after this discovery by somebody else and moved on and he did a much better job later.

JG: You have served on the editorial boards of some notable publications, *Virology, Journal of Bacteriology*. Talk about the responsibility of being on an editorial board and what that is like. How does it improve you as a scientist and a researcher.

SA: Certainly it helps because you try to think about, read other people's paper, try to evaluate, and also many times you get enlightened by new ideas. You are reading manuscripts—you are privileged to read manuscripts which have not been published yet. On the negative side it takes a lot of time. The older you get the more responsibilities you have to bear, and which I struggle all the time.

JG: What are the other responsibilities?

SA: It is more and more reviewing grants, reviewing papers, and making decisions; sometimes if you are the editor you read the reviewers' comments; many times reviewers do not agree with each other for a given manuscript. You have to make a decision, and that is a job, and you have to read the background to make a fair decision and that takes a lot of time. But somebody has to do that. I do not like much to get involved but I have the responsibility because somebody is doing the same thing for my papers, okay.

JG: Speak about the changes in computing technology over the last thirty years.

SA: It is enormously helpful to science, the whole computing technologies, advanced science exponentially. People can handle a lot more data and look at things globally, which is impossible to manipulate manually. Unfortunately, I am not a computer freak or computer competent, so it takes a long time for me to use computers for my own purpose. I usually get help from other people. I get to the postdocs to help me, but that is my incapability. Computers have moved science forward in an astronomical speed, really. We could not think about the kind of levels of science people are doing—that we are doing—I could not think about that fifteen years ago. The other aspect of that, we are doing, for example, genomics and studying gene expression of the entire organism under given conditions and the data you generate are enormous. It takes a long time to go through that, to sort out, to make some meaningful conclusions, and so on. It occupies your mind also although the computer helps you.

JG: When you first arrived at NIH were there PCs or computers in each lab?

SA: No. There was no such thing as PC. In fact, I remember at the time in my Ph.D. course we used to use a mechanical electric calculator to add things up or to determine the specific activity of many enzyme assays. I had to use that. They are all in my thesis.

When I came to NIH, Dr. Pastan bought for the lab an electronic calculator. There was only one I think—there may have been two. One in his own office and one was put in the library and everybody would play with that and take it to their own room. Dr. Pastan decided to have it chained to the table so nobody took it home. It was a very interesting thing but there was no such thing as computer. Computers came around 1970s. It used to be one or two computers for everybody. Slowly it became as it is today.

JG: How about e-mail? Talk about the changes in the 1990s with e-mail?

SA: E-mail again has pros and cons from my viewpoint. The pros is that the communication is very fast. You can quickly find out something about manuscript submission, it is electronically done, and you get an answer by e-mail quickly. In older days, they used postage—frequently manuscripts got lost in the system. E-mail on the other hand . . . The e-mail itself I do not like simply because you get all kinds of junk e-mail. You have to go through that, answer that, and when people have access to e-mail they bother you a little bit. They write a letter, you have to respond, although you don't like to entertain those kinds of letters. Just the enormity of the process. I still like . . . I print out anything important coming in e-mail and I read it rather than reading it on the computer and that is my feeling about computers because I was not trained to deal with computers.

JG: We spoke about this a few minutes ago. You have five patents and seven or eight pending?

SA: Quite a few pending, yes.

JG: Describe the role of patents in molecular biology.

SA: When I was studying biology it is only for curiosity in science. Physicists and chemists and engineers, the physical sciences, they get a job, they have a qualification. They get a job in industry. Biology is only for researchers. They are interested; there is no money there. You have to accept a faculty salary or something with these things. You do not make money by studying biology. But because of booming molecular biology and biotechnology things have changed enormously and people are patenting biology code. Maybe people should have patented penicillin in those days but I don't know any basic findings like discovery of genetic code being patented or the discovery of DNA synthesizing enzyme RNA polymerase being patented. Things have changed because you can patent any thing that may have commercial applications. Biotechnology is influencing the economy nowadays.

JG: Has that had a negative impact on doing science or has it just changed things?

SA: No, it just changed because it became multidisciplinary. Integrated science gives better biotech products. Second is that biology has been able to attract physicists and chemists and engineers and mathematicians and I think that is . . . Many companies, many, many biotech companies are developing technology which involves instrumentation, all kinds of fancy gadgets and that involves many areas of science. There is a commercial aspect.

Many postdocs from NIH have jobs in these biotech industries who are developing instruments and products.

JG: Because you work for NIH does the government ultimately have—is the patent awarded to you but then licensed or given to NIH?

SA: NIH being in the government has a little bureaucracy. It comes with the territory. At universities, I am told . . . I know some colleagues who have discovered something and patented something and they are free to deal with the commercial concerns without too much of a bureaucracy. NIH has a different set of guidelines and I am not quite familiar with those guidelines and rules. They change once in a while. My experience is that the government requirements in dealing with industry are very strict. Many small industries cannot afford to deal with the government so they are discouraged. I have experienced this in phage therapy because phage therapy at the moment is done by very small companies, start-up companies, and venture capitalists. NIH, in particular, demands a lot of money from them. They cannot afford to pay them. NIH owns something if it is done at a NIH lab and NIH has the authority to give it to whoever has first right. The small industries do not want to touch government. That is my experience. I do not know much about the many people that are doing very well being at NIH and dealing with the drug industries.

JG: Reflect a little bit on how the lab has changed in the sense that experiments are larger today than they were?

SA: Yes.

JG: I guess they take more people and there is more of a need for collaboration, not just within the NIH but then outside the NIH scientific community.

SA: Absolutely. Things have changed. A lot of science have become larger because you can attack a given problem or try to answer a question of a biological problem from many angles. It used to be genetics and biochemistry, now there are all kinds of physical techniques available. You get the help of physicists. We do get help from physicists also. Mathematicians are getting involved in mathematical modeling of evolution and organism development. It is a larger science so you need a lot more manpower and certainly as you mentioned it needs collaboration because one scientist was not trained to deal with all these different angles. I had in my background chemistry and physics and math but it is not to the level that I can handle all the problems in doing research in those areas. I have collaborated with mathematicians and physicists. Collaborations, I get help from them. Of course, there is the manpower you need a lot of people.

JG: Talk about lab etiquette or collaboration etiquette. Is it difficult to successfully work with others? Do you only pick collaborators that you feel comfortable working with?

SA: Can I go back to the previous question. One thing you asked and I did not answer. Fortunately at NIH we have collaborative expertise and we collaborate inside more than we go outside. Of course I have outside collaborators but there is a lot of expertise at NIH you can collaborate with. People do. I know that. Coming to your second question. What was the second question?

JG: Talk about the etiquette.

SA: Yes, personalities. Of course, you have to collaborate with somebody who you have similar philosophies of science. You just cannot fight all the time and do collaboration. It does not work out. There is some personality issues and so on. In my own life I keep the personality aside. I have collaborators who do not get along with many people. I do because I just have a way of dealing with people. I deal with them in a humorous way and so there are difficult personalities but I have no problem. I have gotten along with many, many people and have collaborations and I will not name names but they are all my collaborators and we have been highly productive.

JG: Talk about career building. In a sense it is not just for an individual but it is also for a lab. Over time labs become more notable. That is particularly true for LMB.

SA: From my experience, and for many other people, just doing science you get recognized, you attract people, and you build up your lab and career. It happens that way. Things have changed slightly because of the highly competitive nature. There are a lot of people that are fighting for the same money and jobs. There is also something called mentoring. People have to be mentored properly to survive in the modern world. In the old days, I know many scientists—many, many renowned scientists, my role models—they hardly express their thoughts. You cannot understand what they are saying either because they are a foreigner or foreign accented scientist or because they do not speak well. It is hard to understand what the message is. That was the way life was. Now you have to communicate well. Today you have to be mentored how to give a good seminar and how to present your data in a clear fashion. You cannot say "um, um, um." What career path should you follow? If you want to be an academic scientist or a government scientist you have to follow certain rules and you need many publications and need some references to present yourself in a manner and that is called mentoring. Our LMB has produced lots of good people around the world that are very successful and apparently this lab does good mentoring.

JG: Talk about the revolution in the last ten or fifteen years with poster sessions.

SA: Ah!

JG: We missed that when we were speaking about publications. It is different then it was. There are posters everywhere—in the labs, in the hallways, everyplace.

SA: The concept of poster sessions in general did not exist when I started going to meetings. There was no such thing as posters. They developed later because more and more people were coming to annual meetings and wanted to present. You cannot accommodate everybody as a speaker that is why the poster sessions developed. I remember that when

I used to organize some meetings many people thought presenting posters is not a proper recognition. People would like to present a talk rather than give it as a poster—it is demeaning. I remember I did a trick one time to make more people motivated to give posters. It worked very well. I asked my senior colleagues, renowned scientists around the world coming to that meeting to present posters and said the students were to give the talks. That worked very well because it showed that poster presentations were not second rate presentations. I asked Frank Stahl, Hatch Echols, and Alan Campbell and many other people to present posters. And they did, they were happy. A poster is also good—you can have a more detailed conversation. Now posters are kind of an official thing. It used to be an informal thing, now they are more official. The poster presentations have become also an art nowadays. You have the fancy PowerPoint presentation and you can do much more in an organized way. Our lab is very large and people really do not know what is going on from one section to another and I think Ira had the idea to have poster presentations. Put your posters which you have presented in a meeting, which your next door colleagues may not know, in the corridor and people can stop by and read, and they do. Once in a while we have a poster presentation session in our lab seminars. Instead of seminars they have people that can present some posters and have pizza and so on.

JG: Talk about the challenges that women have faced in the sciences and how that has changed over time?

SA: Absolutely. No question about it. Well I hope it is much better nowadays. It used to be very few women in science. In biology from the day I started—not enough, but more women than in physics and chemistry. I think that has changed a lot and particularly in microbiology. There are more female renowned microbiology scientists in our field today than ever before and they are doing very well. I do not think it is complete equality yet. I think it needs much more improvement.

JG: What do you say to young postdocs or research fellows that are women that come through your lab? Do you have to prepare them in a different way?

SA: No, I do not think so. I do not do that. I think everybody . . . In real world women or men should not get any special preference. They have to fight out. I mean they get the opportunity. I do not discriminate, and I do not think anyone discriminates when selecting a postdoc, whether it is a man or woman, that is totally a non-issue. You train them like I mentioned before. You have to mentor. It does not matter whether it is a woman or man.

JG: Talk about funding and how that has changed. You mentioned that when the laboratory first started there was one pot of money and now it is done differently.

SA: Yes. I think it used to be that when the lab was smaller or at the beginning of the lab . . . It was not just this lab every laboratory chief got a budget and there was a common account number. Anybody who wants to buy something, spend some money could do that, except the postdoctoral slots were not like that. It used to be fixed and assigned to a particular PI. As the labs have grown larger . . . Usually nowadays the lab is reviewed.

Every lab is reviewed every four years or so by a site visit committee. When the lab was born, the lab was evaluated as a whole, after listening to the individual presentations or performance, but labs have gotten diverse in different areas and it is not possible to evaluate them in an integrated fashion. I think there was a time that outside committees felt that each individual should be evaluated and given a budget separately away from the lab. It is possible that—our lab never had the problem to my knowledge—some people in the lab are not doing very well but the lab as a whole is doing well so they are sneaking by without performing. I think the current system is better from that viewpoint and I think it is working very well.

JG: How about different presidential administrations and what is going on in the broader economy? Has funding gone up and down for the NIH?

SA: I am not quite . . . We do not see much of that in the sense that the presidential politics or appointments do not trickle down to our level in a specific fashion but overall of course it influences who is the director and so on. I think that to my knowledge when Bill Clinton was president he wanted to double NIH's budget and started doing that in his second term and he gave ten, fifteen, twenty percent raise every year but he did not finish when he left the office. I think Mr. Bush continued that doubling program for a few years. The NIH budget, from a newspaper report, went from $13 billion to $26 billion. Now the budget is tight again.

JG: How about lobby groups? There are breast cancer awareness groups and lung cancer awareness groups that want funding to go to—very well meaning groups—that want funding to go to a specific issue. Is this a problem at NIH?

SA: Well, people call those political diseases. Some diseases are earmarked by Congress to have special amounts of money. Of course people who are not working in that area think that their money is taken away to give to the other guys because the total money is not really increased. Congress does not necessarily give extra money all the time. Sometimes they do, to fill up that mandate that is earmarked, or whatever it is. I should say that whether it is HIV research or breast cancer research or aging—that is another popular thing—people doing basic research also get a share of that. They can write a good grant under that umbrella and frequently get funded. I know that. Recently NIH got a lot of money for biodefense after 2001. I got a piece of that money to try to develop detection of pathogenic bacteria which I mentioned before. I applied for a small amount of money. They share money frequently. I know breast cancer research program—many people doing basic research got money from that program so it is not really bad.

JG: We touched on this last time, and a bit today, your responsibilities now include overseeing staff and writing grants. What percentage of your time is still doing basic research? Do you carve out certain days? How do you manage your time successfully?

SA: No. I am very bad at managing my time because I spend most of my time . . . I try to spend most of my time trying to think about science and talking to people who are working with me. There is always other responsibilities—reading manuscripts and applying for extra money you need and that kind of thing. It takes some time which are quite justified. I have no problem with that. I do have a problem with NIH is that there is so much guidelines like ethics committee and you have to pass ethics tests and all kinds of things we have to do which, in my mind, they can be severely cut down. You cannot do this, you cannot do that, financial disclosures, ethics guidelines. You cannot give a lecture and get funded by somebody else and all kinds of other things. It is not just restricted but also the fact that we have to take courses and trainings. Those are the things that really—

JG: Has that become worse over time?

SA: Yes. In my mind I have to say that they have become worse and worse.

JG: I want to explore mentoring and teaching for a couple of minutes. I know we touched on this before. What do you think your responsibility is to younger scientists, postdocs, and fellows that come through your lab?

SA: My responsibility? Well my first responsibility has been all the time is that to engage them in doing a good project, first thing, that they like. It is not that they come and I tell them this is what I want you to do. I discuss various possibilities and I find out . . . I try to study their mind which one they would like to do. Otherwise they cannot be creative. If they do not like the project I do not think they can be creative. I think they have to like something about it before they can think on their own and spend their time. That is first my job. After they start something . . . The way I look at that is I try to really argue with them all the time. Many times I know they are right but I argue with them. I encourage them to tell me that I am wrong. There are some people who I enjoy talking to enormously. They are always trying to disprove me. That is the way things go. I like to challenge people and that is what I try to do. Other than mentoring about how to present a seminar, what you have to do to find a job, and that kind of thing, I think to instill inside them to think about a project and challenge their standard the concept is the main thing I try to do.

JG: How do you teach the need to scrutinize errors and create good hypotheses and good experiments? Is that a difficult thing to do?

SA: No. I think from my experience the best thing to do is—I hope I understood your question—don't accept something until, whether I said it or somebody else said it, it is proved. I think the best thing I can tell them is to prove it. Whatever you want to say, prove it by designing an experiment. I will help to design experiments and do that and come with the results to say something. You just cannot say that somebody is not right or—put the money where your mouth is. Is that the right phrase?

JG: Yes, quite. You mentioned creativity a moment ago? Talk about that.

SA: Right. I think generating data is not doing scientific research. You are doing something in science but it is not doing scientific research. I think you have to do something creative and something nobody thought of before and something new and something exciting. You know people nowadays in many labs generate a lot of data because of the technology—massive data and they hope that something will come out at the end which is interesting. In my mind that is boring science. Something may not come out. If you find a problem, why it is so, or how it works, and try to set an experiment to test your idea or propose some idea on how it might work—one, two, three, four—there are four different ways and try to test with some creative thinking, first of all you have to propose some hypothesis, how it works and how it is working, and say how you can test that idea.

JG: Are there people that are just natural scientists?

SA: Absolutely. Some are not. [Laughs] Yes, that is true. Some people are very creative and very entrepreneurial and they have a knack for science. I think I have seen some at very junior level. We have the summer students program. We get high school students or college students. I think this is where mentorship is a little bit over sold. They follow certain paths, that is, you should do this, you should do that. You come at the high school stage to do work in the scientific lab and this is to pad up their CV for future career that I worked at NIH and therefore I know this and that and they move on in their life. Frequently I find that they are here only to pad their CV. There is no interest in science. You have to be naturally . . . I don't know whether it is genetic or not but I think it comes with the person whether they are scientifically oriented towards doing science. I have seen young people who are natural scientists.

JG: Talk about some of your successful postdocs and fellows that have come through your lab. What are some of the things that they are now working on in their own careers?

SA: I mean more than half of my postdocs are from another country and many of them went back and are very successful scientists. Many of them are directors, chairs, and all these things which I am proud. Some are working on pathogens and some moved to genomics and some doing gene therapy and also one of them—one of my very talented recent postdocs who left, he is Hungarian, and he went back to Hungary, and he did microbial genetics here in my lab and he integrated that to mathematics. After he went back he is working on a project which he is going to give a poster in the upcoming reunion on osteoporosis which is very surprising to me. They have found, the team has found that deer antler, the bone, the head, this huge gorgeous antler, somewhere in the Russian-Hungarian border, it falls off in the winter and they grow back in the spring again from scratch. They are doing genetics of bone development. Interestingly, the deer eat the tip of the grass only—not plants, and grass, only the tip. A growing plant, I am told, has more calcium in the growing tip part than in other parts of the plant. They need in bone development a huge amount of calcium so they know by nature. That is the only thing they eat and they grow rapidly. After they become very heavy and at a certain time they fall off. They have identified many genes which are involved in antler bone development. What is interesting is that when they are developing the antler bones their skeleton bones become very fragile because they are not getting enough nutrition. Most of the body's nutrition, calcium, and other things, are going there. When they fall off, in winter time, the skeleton bone gets the nutrition and becomes stronger. They identified genes which are involved in bone development and found that many of them are homologous to genes in humans.

They have applied for money to study osteoporosis. This is the first time that I have heard that somebody is doing genetics on osteoporosis. What happened is that they wrote up a paper about their findings and sent it to me to communicate to the *Proceedings of the National Academy of Science* [PNAS] which I declined because I have no idea. I know the story, they tell me, I believe that. I sent it to the proper geneticist here and they loved the subject and Jim Crow, I sent it to Jim Crow at the University of Wisconsin-Madison, because he is a renowned geneticist. He said it is so interesting but he doesn't find a reviewer who can review the paper. The paper has been sent for review. He finally found somebody and the paper has been reviewed. I do not know the updated news but this is something I am so proud that Szabolcs [Semsey] changed his thinking from bacteria to human bone development. It is just genetics. It is all genetics and they identified the genes using modern technology.

JG: That is interesting.

SA: Very interesting.

JG: Talk about professional associations and their role in the sciences?

SA: American Society of Microbiology, for example, which I am actively involved. There are many, Genetics Society of America, Biochemical Society, and so on. They play a role from historical time. They organize meetings and they bring people together and they are the ones who also attract young people by organizing the right kind of sessions and meetings and talks and seminars. Young people go there and they get attracted to that area. They find the proper labs. That is one of the purposes of the meeting to connect students and postdocs to future mentors. Secondly, it is a nice chance to talk to each other and discuss things with each other. Formal meetings are very useful.

JG: Do you make sure that all of your fellows and postdocs attend?

SA: Well, I prefer that they go to smaller meetings and not larger meetings. In larger meetings mostly there is not much chance to discuss things with others. You only listen. Maybe if you are courageous enough you can stand up in a huge audience to ask a question. For younger people that is hard. Smaller meetings, like small microbiology meetings, phage meetings, those that Cold Spring Harbor sets up here and there. If you have much smaller meetings maybe thirty people, I like them to go there. There they are forced to interact with people—sitting at lunch, and discussing and sitting at the same table, and that is much more beneficial I know for my life than these big meetings. There are many small meetings and I encourage them to go to those meetings and they do.

JG: Michael Borange writing in *A History of Molecular Biology* argues that there are a number of problems in science that are important but have been avoided Only scientists with the luxury of being at the end of their career, those with a lot of success, or a young scientist can approach them for fear that their reputation might be harmed. Do you agree with that statement?

SA: I do not know what kind of science people avoid and only pick up later in their careers. You are talking about something like gender, intelligence, race?

JG: Well, no. I do not think he meant that. I think he meant that there are scientific questions that are not being investigated. There is a bandwagon and many will not risk their career to look at non-traditional questions unless they are a well-respected scientist who can pick and choose what you want to investigate or a young naïve postdoctorate who has not realized there is a career path they need to be on.

SA: Yes, I think I understand. Well there are people who avoid mainline science or popular science or bandwagon science because they will be done anyway. Very smart people I know they like to do something which is not popular and left alone. Funding is an issue I understand but for older people funding is not an issue because they can get some funding on some context and do something else as a side business. I heard a story that might answer your question. Oliver Smithies was a Nobel Laureate last year. He was a professor in Wisconsin who got the Nobel Prize and he moved to Duke University later. There was a reception symposium honoring him two months ago and I was invited to go there to participate. There were a few speakers and he gave a talk about this whole thing and I think he dealt with the question you are asking. When he had a grant, and he was doing routine science, that is what most of his associates were doing, he himself was doing something which was not popular, something nobody cared about. He did not have the proper funding for that so he would go and borrow things from other labs, his colleagues. They would say, "Why you are doing that? You are wasting your time." His colleagues said that to him and he mentioned that in public. So therefore to avoid embarrassment he showed some notebook pages . . . He would come on eight o'clock on Saturday and Sunday mornings to finish before the other groups arrived to avoid answering questions about why he was doing this. But that got him a Nobel Prize later. So he is a very good example that you do not have to do popular science or something on the bandwagon. He said to the younger people, he had a message, he said pursue your nose and pursue what you like to do. Funding is an issue but he said he avoided that by having a mainline research funding with the students and he used to go on his own with the help of technician and so on. Something he really liked and it brought him a Nobel Prize later. Is that something like what you are talking about?

JG: That is exactly the issue. What about the research topic that young postdocs pick. Are scientists and researchers able to switch gears very easily today? If someone picks a topic and then they decide they want to go off and do something else is that easy to do? We talked about publications and the need to be published in high profile journals.

SA: As I said I try to get somebody involved in the beginning with a project that they would be interested in and creative. As they go along they read journals, they hear seminars, and they hear all these buzzwords nowadays and they have a tendency to move along to do some so-called popular science where they think they will get a job easily which might be true to some degree because people like to hire in these areas. A given university or department will hire in new areas like bioinformatics. I don't think they always succeed. I had two students who were doing some biological experiment in gene cloning and transcription but had a nose to do bioinformatics and I found that out and they are doing very well. They are switching to something which is more popular because I realize that they are creative and they are doing that. They got a job—one at NIH and another one moved to Miami, Florida finding that kind of job. You have to have that kind of knack to switch. You have to be able to easily switch and adapt and learn. Not everybody has that—the ability to do that.

JG: Talk a little bit about the mapping of the human genome. It was quite an extraordinary undertaking and what was it like to be at NIH during the period?

SA: Well, I was never directly involved in Human Genome Science or any such thing but I know that it was a big achievement first of all. NIH played a serious role in achieving that goal and I know, the one person I knew, was Jim Watson who was hired from Cold Spring Harbor to direct that but he did not get along with the then Director of NIH so he left. But he was a person who was widely recognized as a Nobel Laureate scientist and was a big voice and he was able to get money for NIH from Congress to fund that research. I think he played a great role while he was here at NIH. He left, but he did the initial groundwork to get the money to get the human genome science. I know some stories which I won't tell now about him here at the NIH.

JG: Let's speak about the lifestyle of the scientist. You have a lot of freedom to organize your work. How do you balance both your professional and your family obligations and things of that sort.

SA: As scientists you have to play some juggling role because it is not a nine to five job. We take home our thought processes and, you know, homework. I do a lot of writing and correcting and this and that at home. You have a family life that you have to balance with that but the freedom is that if I am needed for family reasons I can take an hour off in the middle of the day to take care of something. That is our freedom. I really enjoy the privilege to have that freedom and that is the way we can maintain the balance. If you are working actually eighteen hours a day doing science only the family suffers. I have always sneaked out of the lab to take care of something with the family and come back and so on. I think about science while I am driving and on a vacation time. My vacation is usually doing nothing—some of my colleagues do vacation and they do this and then they will do hiking and all kinds of physical things and for me vacation means doing nothing. But I have found out that scientific thoughts creep into your mind while you are lying on a beach or relaxing. [Laughs] I am doing science mentally. It takes a lot of time. It really consumes your life and you have to maintain a balance. Some people are very good in those and some people are not.

JG: Do you have any children?

SA: I have one daughter.

JG: Are you urging her to be a scientist?

SA: No. She is already . . . She is a therapist, a children's therapist. She started as a social worker, has a Master's in Social Studies, and now she has a private practice involved jointly with her friends working on taking care of children with problems. She enjoys that. She did an internship one summer with the NIH in a department but she is not a scientist. She does not . . . She is totally opposite. She is very good with children and she is very good with people and people skills. She has great people skills. She likes what she does so I am happy.

JG: Talk a little bit about science today. How do you characterize the health of the profession here at NIH and then also in the broader community?

SA: Science, particularly biology, has exploded last several decades beginning in the 1970s. In my mind 1960s was very, very booming time in terms of knowledge in biology and biology combining genetics with biochemistry thanks to phage research. The real boom started after DNA sequencing and restriction enzyme discovery and gene cloning and nobody could visualize at that time what biology would be ten years, fifteen years, two decades later. It is an enormous amount of information that is available now in biology. You know a lot, lot more than we knew before. The rate of progress in the old days was very slow. Now the rate of progress . . . That is why it is attractive. There are a lot more biologists working today than ever before. I calculated this. It is disproportionate to the population increase. It is not related to population. More people are becoming scientists nowadays than proportionate to population increase and you know that has spread all over the world. They are doing first rate science and getting Nobel Prizes nowadays.

JG: How do we attract young students into the sciences? In the U.S. I would say that there is not as many young people that want to move into the sciences.

SA: The teaching has changed. They do science teaching very early in schools and kids are inclined to do science. I think there was a time, I don't know exactly when, when people became more interested in earning money than doing something creative. They are going mostly to law school, business school, and not so much into basic science. The deficiency in science was made up in this country by importing from other countries. We had all these talented people from other countries coming in, but I think recently, things are changing. People get more applications of high school students nearby who want to do science in the lab. Not all of them are going to do science but some of them are. At least they are exposed to do science. They get the opportunity. If they are not going to be scientists they at least find that out. In other countries the scientific interest among young people is enormous. I visited Korea, India, of course, Hungary, Denmark.

Western countries have always some good scientific community but the explosion of biotech is everywhere.

JG: There has also been a shift with biotechnology firms. Biotechnology firms are no longer just on the West Coast. How does that impact the NIH?

SA: There are two kinds of biotech industries. One I would call service-oriented biotech industries. They make products to serve scientists. They do some innovations but not major innovations. There are a lot of them around NIH, on the East Coast, around Boston area and Bethesda area. Many biotech companies who started doing biological research, fundamental research, and developed products, like Genentech, which became a big company, they are mostly on West Coast. I don't know what is the idea, because people I know who founded them, are used to be in the California area, or the weather was there. I don't think labor is cheaper there to have industry. California is expensive. Genentech and many other firms I know, my phage associated companies, are all in California.

JG: What do you do outside of the laboratory? Do you have hobbies?

SA: I do a lot of reading. I do not have much of physical activities. I used to play soccer very well and I used to play goalie when I was young in India. My vision was not that great. I stopped doing that and then after that somehow I became a scientist and my time is consumed. I do not have much hobbies other than I like to go hiking in the mountain area. Beach—my family likes water and so on and I am not very interested in those but I find a place where nobody is around and you can hike. I have a small retreat home in West Virginia and that is where I go mostly on weekends. I maintain to some degree my real hobbies, if you call it hobbies, stamp and coin collections. I have that private hobby and enjoy that. The reason is that I started this very young, when I was very young, and maintained that because I learned a lot of history and geography by collecting stamps. Why one stamp was published and made and one coin was made. Those kinds of things. I have a quiz for you. I have a quiz for young people, or some historians, or anybody. I will ask it, okay?

JG: Okay.

SA: There was an event in the history of world, not long ago, when coins of many countries, fifty countries had to be changed. Something with the coin design had to be changed. The inscription or something.

JG: Fifty countries?

SA: Well many, many countries. I don't know, many, many countries.

JG: Well, when the European Union came into being I know coins were changed?

SA: Nine countries—fourteen countries.

JG: Okay. The fall of the Soviet Union would affect all of the satellite countries?

SA: Yes, but that was only seventeen Republics and three East European countries—about twenty altogether.

JG: What else would—

SA: I do not want to waste your time on this. When India became independent from British colonies, all over the world, Canada, Australia, all over the British Empire, which was fifty, sixty, eighty countries, little countries, Africa and the Caribbean. The coins used to say "Emperor of India." Every country's coin said Emperor of India and when India became independent they had to remove it the coin. [Laughs]

JG: I will now use that to quiz other people when I get back at the office. [Laughs]

SA: The books I read, mostly I don't read much of fiction, unless my daughter tells me something is funny. I read mostly historical books. I like history, reading history, even personal life of Winston Churchill, or this and that, or country's history, that I enjoy and that is what mostly I read.

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

SA: I think to be satisfied as a scientist, to enjoy being a scientist, they have to choose a project that they have some inclination to solve and they can be creative and there is something that attracts them. There is a mystery and they need to find out. The nature of the mystery must attract them. Otherwise, I think it does not work very well. I mean people are successful doing good science, but from my viewpoint in science they can be creative only if they have a curiosity of identifying a project and trying to find out why it is so.

JG: Thank you very much.

SA: Well thank you. Thank you for your time.

[End of Interview]