Bruce N. Ames, Ph.D.

October 29, 2003

Interviewer: Buhm Soon Park, Ph.D.

Note: this transcript is a rough edit and portions were unintelligible

Summary:

This is an interview with Dr. Bruce N. Ames on October 29, 2003, at Dr. Ames's office in Children's Hospital, Oakland Research Institute, Berkeley. The interviewer is Dr. Buhm Soon Park, and we are going to talk about the history of NIH after World War II, focusing on Dr. Ames's experiences at NIH as an intramural researcher and as a Berkeley professor after 1968.

Buhm Soon Park: Thank you very much, Dr. Ames, for giving me an opportunity to talk with you. I usually start an interview by asking questions related to training and education backgrounds, but since you already talked about it in your reflection article, I will just keep that part. Could you tell me, however, a little more about your research at Cal Tech and your search for places for you to do postdoctoral years around 1953?

Bruce N. Ames: I did my undergraduate at Cornell, and I was always kind of half a geneticist and half a biochemist. I majored in biochemistry, but I was always interested in genetics, so I took courses, and then took a course in biochemical genetics and got very interested in that. I went to Cal Tech for my Ph.D. because they were sort of center of biochemical genetics, Mitchell [H.K. Mitchell] was chair of the department. He had started isolating biochemical pathways. Somehow I never did. And I was lucky. My thesis work worked out very quickly, so I got my Ph.D. in three years. I was 24 and I had my Ph.D., and then I looked around. I was looking around for where to do a postdoc, and I was thinking of going to Europe, but a particular fellow I wanted to go with had gone somewhere else, so I ended up applying to work with Bernie Horecker at the National Institutes of Health.

Park: And Europe, did you think about going to a Cambridge school?

Ames: No. I thought of going to work with Van Calcar who was in Denmark, who was, again, a leading biochemist. Actually, it's just as well I didn't so when I came to NIH, there were a lot of first-rate biochemists, but I was the only one who really knew about genetics and knew about the interface between genetics and biochemistry, what later became molecular biology. I feel I had some influence on that place, bringing genetics in there. In fact, I remember a group meeting. Kornberg had started these group meetings, and I went to them, where people presented a paper from the literature, and I remember I presented a Watson-Crick paper that had just come out soon after I got there. Our chemists were very skeptical, very speculative and all of that, and they said, "Hey, you guys just shut up. This is the paper of the century!" And so I knew it in my bones because of all my training in genetics and biochemistry. This was the big breakthrough. So I had to try and convince them that it was really important.

Park: Why were biochemists there skeptical about Watson and Crick's . . .

Ames: Biochemistry is so complicated. What biochemists . . . And people made so many wrong, and you do the right controls. So the whole Kornberg, Horecker, Stadtman -- that whole school tended to be very tough-minded. They first looked at the experiments: Were they done right? Did they do every possible . . . And then they see it. Well, were the conclusions really justified? They were just very hard-nosed about all of that. And this was much more speculative than they were used to. But I think they didn't have the background to realize why it was so important but they came around.

Park: When you applied for the fellowship at NIH, did you know that Arthur Kornberg was supposed to leave soon?

Ames: I don't even remember anymore how I ended up with Horecker and whether I . . . I just don't remember the details about why I picked that group. I knew they had a very good reputation. I think also, that was the Korean War was around then, and at one point they were going to draft me when I was a graduate student, and I had an Atomic Energy Commission fellowship because they were interested in something like that. And so I asked them if they'd write a letter getting me deferred, and they wrote a letter that sounded like the country would fall apart if they drafted me, so… It was a very good letter. My mother could not have written a better letter. That kept me out of the army for a while. And then, by going to NIH, I could get a commission, commissioned officer, which I did, and that kept me out of the war.

Park: I see. So you took an exam and . . .

Ames: No, it was not an exam, but it was -- I forget what it was. But I was a lieutenant in the U.S. Public Health Service. I was a Ph.D. scientist, and that kept me out of the military.

Park: And your obligation was to stay at NIH for three years?

Ames: Right, that is what it was, but I stayed there for 15 years, so it didn't matter. I felt what I brought in was this knowledge about biochemistry and genetics, and genetics is the tool. I had used mutants to work on a biosynthetic pathway, and we were working out how the genes in this biosynthesis got turned on and off using, isolating mutants to do this. So I brought in that kind of expertise, and soon it started spreading around NIH.

Park: Do you remember in what building you worked at NIH?

Ames: Gee, I can't . . . When I first came, I worked with Horecker. That was in Building 3? I just don't remember.

Park: And?

Ames: Maybe I worked in the [?]. I don't know. And then I was with Cantoni and then Tabor gave me a kind of a job where I could do what I want, so I went over to Tabor's place. Later, when Tompkins came and had a laboratory, he asked a few people around NIH to join him, and that was one of the ...

Park: I see. So your first job was with Cantoni?

Ames: Yes. Horecker's group is more like a year's postdoc, and then I joined Cantoni's group, but Cantoni wanted me to work on his project and I wanted to continue the project I had started, and so I switched over to Tabor, who let me do what I wanted.

Park: I heard that NIH biochemists were very close and that they had a lot of interactions socially and intellectually.

Ames: Oh, yeah, oh, yeah, tremendous.

Park: And could you, if you can, could you describe a little of that atmosphere and how was it possible at the time?

Ames: I think Kornberg had started some of that. They were all learning biochemistry and a lot of them were M.D.'s. And they were very serious and very -- each one brought knowledge, and we just had that kind of tradition and I was quite friendly with the Stadtman's and used to go to parties at their house and have them over. So there were a lot of activity.

Park: And the scientific directors at the time joined in the social interactions? James Shannon or . . .

Ames: I didn't know those people very well when I was young. Ed Rall who was eventually associate director of research, he was palling around with the scientists.

Park: And what about interactions with other biochemists in other institutes, like NCI or Dental Institute or Mental Health?

Ames: There was that also. So the biochemists would all know each other, and if you needed -- there's a lot of art in biochemistry, and if you needed to know some technique, there was somebody who knew it. You went over and you learned it. So there was a way of keeping up on all.

Park: Did you teach courses?

Ames: Yeah, I think I did a course.

Park: I was told that David Davis took a genetics course from you.

Ames: Yeah, could be. So the thing that -- they knew a lot more biochemistry than I knew, but coming out of Cal Tech, I also had taken a lot of genetics courses, so I had a very good grounding in genetics and had used isolating [?] for working out biochemical [?] in my thesis. So I think I was the first one at NIH who had that kind of background, so people were always coming to me to ask about that. That was before molecular biology, after Watson-Crick genetics took on much more importance.

Park: Right, right. In your reflection related to your comment, in your reflection article, you said that, you had to learn more about enzymology.

Ames: Yeah.

Park: And then at NIH, there were many enzymologists at the time. And was NIH *the* place to go if you wanted to learn enzymology in the United States, or somewhere else?

Ames: Wisconsin was very strong. There were other places, but it was certainly one of the good places. Again, there was Kornberg.

Park: Right. It's quite interesting to see that in 1959, Arthur Kornberg got the Nobel Prize, and the next year….

Ames: So that was all NIH. Right?

Park: Yeah, all NIH.

Ames: Well, they were outstanding people. Stadtman is still -- every 10 years he changes his field and does something wonderful, so Stadtman is kind of a biochemist's biochemist, and Horecker had that. And Kornberg had this very strong personality, so wherever Kornberg went, people followed. He influenced...

Park: So these get smaller and smaller.

Ames: Right.

Park: In the 1950s, I found that many scientists at NIH were couples, married couples, both scientists. For example; the Stadtmans, the Tabors, and Arthur Kornberg and Sylvy Kornberg, and Alan Rabson and [Ruth Kirschstein]. And there are a lot of married couples coming in, and I found that your wife [Giovanna Ferro-Luzzi Ames] was also hired.

Ames: Well, she came from Italy as a postdoc to Johns Hopkins, and I met her. Gordon Tompkins took her on as a postdoc for a year, and she stayed on.

Park: Right.

Ames: So I don't know whether it was easier at NIH. Maybe a lot of universities had nepotism.

Park: Did you apply for other jobs?

Ames: No. I wanted to just stay at NIH. I enjoyed doing the research and there was enough money, and we had a wonderful group. Tompkins started thinking about leaving and I started.

Park: Right, right. So, could you talk about your research, scientific research in the 1950s to the '70s, or '60s? How much you did at NIH, how much you [think you were] accomplishing at NIH?

Ames: Well, at Cal Tech, I had to isolate the intermediates of the pathway and kind of postulated a particular pathway. But the next step was to isolate the enzymes and show they were lacking. And when I got to NIH, I started collaborating with Phil Hartman, who was at Johns Hopkins, and he came out of the school of [Milislav] Demerec, who, when they first started using [?], the first organism where they had isolated mutants, amino acids. Lederberg introduced genetics in *e. coli*, and genetics in *salmonella*, and Demerec, who was a geneticist but worked on *drosophilia* switched over to *salmonella*, and Hartman worked with him. Since I had published a paper on histidine biosynthesis, he started work by using all of his *salmonella*. Since he was at Hopkins, we started talking a lot because he had worked on the same pathway. I realized it was much easier to work on bacteria than on [?] which is a fungus. So I gradually switched over to the bacteria. After fishing out the enzymes of the pathway and working out the steps of the phosphorylated compounds located in sugar, I got interested in why the genes were all together, which Hartman had shown the genes were in a cluster. We realized that genes got turned on and off as a group and if you move the bacteria up, a lot of histidine had a low level of enzyme, but if you [start] limiting this, you have a big [?] so I got interested in how you turn the genes on and off, and I switched over to *salmonella* and kept a long collaboration with Hartman.

Park: And at NIH, did you have to justify your basic research?

Ames: No. That's one thing that was very good. At least the Arthritis Institute always had -- they looked for the best scientists around and they didn't care too much about what they were working on [in] metabolic diseases. I was convinced that if a cure for cancer came out of NIH, it would come out of the Arthritis Institute, not out of the Cancer Institute, because cancers were very narrow. They just weren't interested in anything that wasn't directing cancer in people. I remember in the early days, when molecular biology was just getting started, someone in the cancer field said, "*E. Coli* has nothing to teach us about cancer," and I thought that was very shortsighted [where] molecular biology is concerned.

Park: And did you work just by yourself or . . .

Ames: Yeah, I was working by myself. But then I got some very good postdocs. My first three postdocs were Bob Martin, Jerry Fink, and John Roth, a fellow from the National Academy. These were super-smart people, so I was very lucky to have such good people.

Park: Were they all M.D.'s?

Ames: No. Fink and Roth were Ph.D.'s and Martin was an M.D. I picked Martin because I think somebody came in one day with a series of dossiers of -- they had a program where medical students, at Harvard or other places, but had spent a semester at NIH learning some biochemistry, and somebody came in with a stack of them and said, "Do you want to have a student working with you?" and I said, "Sure." And I looked through them, and there was Bob Martin. He had taken quantum mechanics and all these advanced physics courses, and I figured he must be smart, so I said, "I'll take this one." He came down for a semester and Judith had just gotten [unintelligible]. She came down. He liked it so much, we did our sucrose gradient paper with that semester and it became one of the most cited papers in biochemistry. He liked it so much, when he finished, he went back finished his M.D., and then came down permanently, and Judith got a job at the Washington Post.

Park: Right. In the paper by Hofstetter, Bob Martin mentioned that your research was cutting edge.

Ames: But it was more on the regulation, the biosynthesis, one biosynthetic pathway that I just used in genetics. We got interested in how the genes got turned on and off and the fact that turning them off or on [unintelligible].

Park: And he seems to mention that your idea and theory was even before…

Ames: Right, yeah. No. I think I influenced [unintelligible] about it. I told him all the things we were doing, and he never, I felt, gave me quite the credit he should have, but it didn't bother me that much. Bob was more upset than I was. So they were very good marketers. They were good in marketing.

Park: Marketing in science? How can you?

Ames: Well, if you put things in the right way. Anyway, they were good at selling their wares, and they did some key experiments. Anyway, they deserved the credit. It is complicated but we contributed.

Park: But it seems to me that it's an example of how NIH biochemists were there, almost at the major centers of microbiology so it's one example.

Ames: Hartman had a little of this genetic expertise, so Hartman and I [?] a mutant, so all the histidine genes were in a cluster on the chromosome, and I knew that mutants in this gene were lacking this enzyme, and mutants in this gene were lacking this enzyme. Hartman had a mutant like this. It was a deletion of the beginning of this [?] and all these genes were present, but what we showed is they did not function. So that said that all this is, there is some general control over a gene can be there but not be functioning. We started thinking how genes were turned on and off. We knew that when we measured by the amount of histidine you were getting, then you got 10 times more of them, of the protein. We were early in developing that concept.

Park: Right, right. The late 1950s and early '60s, one of the big events at NIH was the genetic code.

Ames: Bob Martin contributed quite a bit to that.

Park: Could you recall, did you stay at NIH or were you in Europe at the time?

Ames: Well, actually, Joanna, my wife, was a postdoc with Tompkins, and Nirenberg was a postdoc, so they shared a small laboratory. We got married and went off for a year to Europe, and there was space in that lab, and Tompkins let Nirenberg hire a postdoc, Richard [?]. It is partly due to my meeting my wife that all that happened. People around NIH knew that Nirenberg was competing with his big group, Ochoa and all of that, so a lot of people went over and just helped him. In particular, I think Bob Martin quite a bit.

Park: So did you hear the big news from here in 1961?

Ames: Yeah. I think while I was in Europe, I would get the messages in various ways.

Park: Did you recall any reactions from the European scientists about that? You know, the NIH was not the big name at the time. The topic is, of course, very big. Francis Crick and other people were chasing after the problem.

Ames: No, I must say I don't remember the details, but I'm sure there were. Sorry. My memory just isn't that good.

Park: So when you came back to NIH, Gordon Tompkins was here?

Ames: I don’t even remember when or what year he started .

Park: Well, officially, it is 1962, but . . .

Ames: It must have been just when I came back.

Park: Right.

Ames: Tompkins was so bright and so charismatic and so charming. He was very funny. He just could charm anybody. Everybody thought he was the rising young star. Tompkins knew about Davies’ work and about Yellen’s work. Tompkins spoke and read French beautifully, so I remember when the first note papers came out, Tompkins saw them in French, came over and started explaining them all, and he knew more about all the details than I did. I mean, he was just so bright, and he read all the French.

Park: Was he a hard worker?

Ames: Tompkins?

Park: From early in the morning to the late evening?

Ames: He was not so much hard working. He was just so – he was an M.D. and a Ph.D., and he remembered everything. You could talk about some movie he saw when he was 12 years old and he would remember the whole plot and the actors. He had this incredible memory, plus he was very original and creative, and it isn’t often you have people with sort of total recall plus that. If he had read some article and he would remember the journal and the page number and what was in it, and so he just had an extraordinary mind.

Park: And he could understand?

Ames: Yeah. He just learned things very quickly. So if he wanted to learn about a new technique, he would read a book on it and he'd understand.

Park: And the microbiologists. Was there any attempt or consensus about all of this?

Ames: They knew that DNA was the sort of master molecule, and came out of merging the techniques of genetics and biochemistry and understanding. But I was lucky. I was in that field kind of before it really started to take off.

Park: Right, right. In that group, there was Martin Geller?

Ames: Yeah.

Park: And Harvey Tuttle.

Ames: Was he in there originally? I knew him, but I thought he'd left.

Park: I saw his name on the list...

Ames: I'm not sure that he was actually part of the group, but maybe he was there right in the beginning and then he left. I don't remember. But he came from Cal Tech before I went.

Park: And Todd Myers ?

Ames: Todd Myers is for organic chemistry. So we had many different disciplines, and genetics was my usual . . . I knew biochemistry, too, but genetics....

Park: And it seems like there are a lot of people who had experience at Cal Tech.

David Davies post-doctoral and also Gary Rosenberg got his Ph.D. at Cal Tech. So was it much easier for you guys to get together.

Ames: Well, Cal Tech had pioneered in all the structural work. Morgan and then Dietel were famous geneticists, and the origin of biochemical genetics was really due to Dietel and Tatum. Dietel was the chair Cal Tech. I just noticed in *Science* that there's a review of the new book about live vaccines. Then there was Heppel [Leon].

Park: Still alive.

Ames: He was an unusual man, very eccentric. Heppel was an enzymologist, and he was working on all these [unintelligible] so people would always be asking him for enzymes. He hated to read mail. He just liked to work. And so he'd have all this mail, get this mail that he put it on his desk, and then every month or so he'd put a layer of brown paper on his desk, so he had the geological layer going down. I remember one very funny story, that Sutherland [Earl] had been working for years to isolate the key factor, which turned out to be [unintelligible] and he would isolate some tiny amount of this stuff, and he needed an enzyme to prove the structure. So he wrote Heppel and Heppel read the letter and described the property, the enzyme. A little later -- but not too much later -- another letter came from Markham who was a British guy who was in the Midwest at the time, that he gotten a byproduct of cooking up ATP, and he has grams of the stuff and it had this peculiar property, and he needed an enzyme. Heppel found that it was the same thing, obviously, and Heppel had these two letters he had dug out, the two letters, and he went running down the hall, "I know, I know! I'm going to write a paper, I'm going to write a paper, and nobody else knows it." He was joking. And then he called up Sutherland and said, "You have to go see Markham. He has grams of the stuff that you're trying to isolate." And Markham -- it turned out he was in the Midwest somewhere, about 200 miles from Sutherland, the two of them together. But anyway, Heppel was funny because he was just so eccentric.

Park: Could you comment on the sense of working at NIH ?

Ames: I think the Arthritis Institute, where a lot of us were, just trying to get the best scientists they could, and they didn't worry that it had direct application to arthritis, and where cancer is just much more goal directed. I always thought Arthritis just had brighter people and stronger expertise. So when viruses came up, then Cancer they would come over to the Arthritis Institute, some good virologist who really knew about viruses. And so -- and, again, molecular biology had lots of ties to cancer, and we were doing it in Arthritis, but they just didn't know it. I think it was more going to good people and then people tended to work on all sorts of different problems. But there was enough interaction so you knew that you were talking to Ed [?] who was working around a particular disease, so there were advances. It was more long-term thinking.

Park: Right. And NCI, as far as I know, there is a group of biochemists.

Ames: Yeah.

Park: And that group had a close relationship with [unintelligible].

Ames: We never, I never interacted with that group. They were just tissue and [unintelligible]. They were very directed. So I was working on bacteria and I was more interested in these general concepts.

Park: At NIH, there are a lot of people coming in. Could you comment on your experiences with them?

Ames: Well, we met lots of researchers, Howard Hiatt from Harvard. [Paul] Marks became head of Sloan-Kettering, so these were young M.D.'s who became friendly with, and we were trying to learn. I think a lot of M.D.'s rotated through NIH and met up with the scientists.

Park: So at NIH there was bridge between [science?] and basic research?

Ames: Yeah. Also the fact that some of us were Ph.D.'s didn't seem to matter much, so there wasn't this hierarchy.

Park: Let's move on to the 1960s, your decision to leave NIH and come to Berkeley.

Ames: Yes. So Tompkins had made a reputation not only at NIH, but even the broader scientific community, and he'd be starting to get lots of offers to be a chair of the medical school. So at one point he got an offer from Yale. He said, "Oh, I'll think about it if you bring along Felsenfeld and Gellar and Ames and Davies," or something like that, and he made this impossible offer for five full professorships or something, and Yale said yes. And then he was kind of stuck. Did he really want to go to Yale? He backed out at the last minute. He said, "No, I'm not interested." I think what he really wanted to do was go to California because he was from California. So, that got me thinking. Tompkins is going to leave soon, and if our group is breaking up, I knew I wanted to go to Berkeley, and I had a friend, Jesse Rabinowitz, who had been at NIH and was a professor at Berkeley. So I mentioned to him that maybe I'll be on the market to move to a university. Pretty soon, Berkeley offered me a job, and I decided. So I was actually the first one to leave.

Park: Did you consider any other places, like the East Coast or . . .

Ames: No. I just decided if I was going to move, where do I want to move to, and . .

Park: Did you want to go back to Cal Tech?

Ames: Well, sure. If Cal Tech had offered me a job, I probably would have considered it.

Park: Right. You left in 1968.

Ames: Yeah, December of '67.

Park: And 1968 is a special year for the NIH because [James] Shannon retired, and John Fogarty, a supporter of NIH had died and another supporter, Senator Lister Hill retired.

Ames: I wasn't involved in that. I never liked politics too much, so I just stayed out of it.

Park: Oh, I see.

Ames: No. Tompkins or other people may have known about all these things going on, but I was really interested in my science.

Park: So your decision was purely on the basis of Tompkins.

Ames: Yeah. It was just that I had the feeling our group was going to break up, and Tompkins really wanted to leave and he'd probably go to the West Coast. So I just had a good job offer and decided it would be a good change.

Park: I saw a number of senior scientists at NIH left in the late 1960s, early 1970s.

Ames: Yeah. That didn't influence me. NIH was nice, that you have the money and what you want, the freedom, and you can have a few people working for you. By then I guess I was a section chief. But Berkeley was a very good . They had terrific [unintelligible], which was considered one of the best departments in the country. And again, I felt I could bring in this whole genetics view that people there -- nobody had expertise, so I brought a lot of genetics to Berkeley. So I felt I was just in the right place when I left.

Park: At Berkeley, it was the Department of Biochemistry?

Ames: Yeah, it was biochemistry. It was in the letters and sciences. The medical school

Park: So you taught pre-med?

Ames: Oh, yeah. Lots of our students were pre-med, but then they'd get their bachelor's degree and they would forget medical school.

Park: Did you like teaching?

Ames: Yeah. I didn't mind it. I don't have a passion about it.

Park: At Berkeley, I guess one of the first things you had to do was to write a grant proposal.

Ames: Yeah.

Park: And how was that?

Ames: Well, I don't even remember the details, but I wrote a number of them and I got some, and so I was funded early on. I was lucky. Twenty years ago, they put in this outstanding investigator grant where you give up all your other grants for one big grant, and I got one from the Cancer Institute. That was $750,000 a year, and I had it for 15 years, and that really saved my neck in all kinds of ways, and I just had all this nice income come in to run the lab.

Park: Right. Before that, your grant application was turned down.

Ames: Yeah, yeah. I had lots of them turned down. Whenever I wanted to do some really important, it got turned down, because when you're making too big a leap forward, people don't understand or whatever. I just got another one turned down. Whenever I know I really have something important, it gets turned down because people don't . . . I think the system works pretty well, but it does -- you pay a price for being too original. I've always felt that anyway.

Park: Did you ever take it as personal?

Ames: No. It's just the system. I think compared to most of the government , it works reasonably well. At least it's competitive. All the other government agencies are monopolies, and their main incentive is to metastasize. But the NIH is competitive and it works reasonably well. But the committees tend to not take risks, and when you want to really advance, you take risks. And so -- but I'm putting my reputation on the line and everything, but it's . . . Sometimes you should get credit for being successful in the past, and they don't do that.

Park: The fact that you're a former credible scientist at NIH, was there any advantage?

Ames: No, I don't think so. They treat everybody the same. When I worked on mutagenesis, I knew that DNA damage was going to be important for cancer and other things, but it wasn't somehow in -- people weren't thinking that way. And the idea that you can detect mutagens in bacteria would tell you something about what was going on in cancer. So the Cancer Institute didn't fund it. But I got money from the Atomic Energy Commission, which was interested in radiation, and so they funded it, the Atomic Energy Commission. So if you don't get it from one place, you try another. I think it's fine that they're skeptical on when people want to take risks, but if somebody's been successful, you'd think they would lean over backwards and let them gamble if they think it's worth it.

Park: One of the literature that I grabbed was written in the 1960s or '70s. It is about NIH's funding system and how it changed the relationship between scientists and universities, and the people at the time talking about, well, the university became a boarding house of scientists, scientists really not loyal to the universities; rather, trying to curry favor with the funding sources.

Ames: Didn't feel that too much. But one's loyalty is to your home institution, but since the money is coming from government... Now it's worse than it was in the old days. Now I think it's much harder than it was.

Park: Because there are many scientists?

Ames: Yeah. The number of scientists has been going up exponentially, and the funding goes up minimally.

Park: Right. You know the scientists worried about government funding.

Ames: Yeah.

Park: They thought that government….

Ames: Well, private financials makes a big difference. When this outstanding investigator grant, when they closed the program at NIH, I had been running my lab on $750,000. That's a lot of money to try and raise, and a lot of grants turned down.

Park: Sure.

Ames: But the Ellison Foundation, which works on aging, luckily, I got a grant from them, and that saved my neck. And there, they ask you to send in a one-page application. So I sent in this one-page application, and then they weeded it down to 10 people and then ask you to send a full application, which is a two-page application, no more. So I sent that in. And then I got in. And afterwards, Lederberg wrote me a letter, asking me some questions, and I answered the questions. I said, "I want to thank you for whatever you had to do with my getting this Ellison's scholar. The easiest grant application I've ever done." And he wrote back saying, "No. It's a difficult one. You took your whole life's productivity into account." And so . . . But a private organization can be very selective. It makes a big difference and also can take a more risky kind of thing. And so I've gotten several private foundation money, which in this time between the ending of my outstanding investigator grant and getting my lab funded, I used a fair amount of private funds. So I think there's a place for both and the government shouldn't crowd out all the private . . .

Park: Right.

Ames: Howard Hughes had a big impact. I think that's a good thing to have. And also, it wasn't all the government monies coming from one pot. So if I didn't get money from the Cancer Institute because they were shortsighted, I could get it from the Atomic Energy Commission or I could get it from the National Science Foundation. There were three or four competing organizations, and that's always good because then it encourages at least some innovation.

Park: The system requires a lot of scientist involvement.

Ames: Yeah.

Park: Could you say a little about your experiences?

Ames: I never spent much time on the study sections, but I would always get asked to be on this committee or that committee, and I don't like to do that too much because my strength is in being creative, in reading very widely and putting two facts together, and I'm not the best at being very analytical. I look to see, does it seem interesting to me? So anyway, I never liked doing administrative stuff too much. But I'd review papers. Some people like the power.

Park: We talked about the government and. What about industry? These days there are biotech companies with a lot of money trying to hire more trained scientists. Is that trend good?

Ames: I think it's just the way it is. It used to be biochemists. Now every professor I know has some little company on the side that he says, "Help me with it." Five of my former postdocs started companies.

Park: Right. So it's another way of getting funding. In the 1970s, NIH politically, put the emphasis on research. As an NIH scientist, and from outside, did you feel the same?

Ames: Well, I've always had a fairly applied bent, so if you can do something and it affects public health, I'd just as soon do that. Sometimes you have to, to do it well, you have to understand the principles, and so I would dig down to understand the principles, but I was always keeping an eye on the public health. So I don't think it's necessarily bad to have some emphasis on actual application. You don't want to go too far, like in the old days the Cancer Institute was just so narrow, they weren't going to solve the problem . But it's a matter again of balance. And if you get money from industry to do a particular thing, nobody really wants to do that if you are not interested in solving that problem. You know, Pasteur was trying to solve a practical problem, so he did all sorts of wonderful things. He was a great scientist.

Park: Interest in how intramural scientists out of NIH, and how NIH and human relations going outside, they ….

Ames: But someone like Kornberg is a very strong personality and all stainless steel and very well organized, no nonsense. When he was working in the lab, nobody was to interrupt him. Nobody, not a phone call anyone working in the lab so he was very tough. So he has a very strong personality, and he was going to be like that wherever he went. So it was more his personality.

Park: I see.

Ames: And Tompkins was just so interactive. He loved talking to people and learning whatever they had to say, wanted to know everything everybody was doing, and he understood it better than they did halfway through the conversation.

Park: Were you happy to see him in San Francisco?

Ames: Oh, yeah, yeah. We kept in touch. In fact, his wife is still a friend of ours. So they were very good friends.

Park: So in terms of research?

Ames: Some. It depends on personal relations. But I've always known a lot of people. But Tompkins had a big impact on turning that into a [team?]

Park: So before that, it wasn't?

Ames: Tompkins, because he knew all the good people in the country, and he's, "Hire that person, hire that person." And then he and Bill Rutter came together. See, Tompkins wasn't such a good administrator because he loved just talking to people and saying yes to people. So he wasn't good to get money from. But Bill Rutter was very good and very smart, and the two of them were friends, so they came together to. Tompkins had all these brilliant ideas, and Rutter could make them happen.

Park: Today, he took me out and I realized that but…

Ames: Yeah. It's an effort to go to him in San Francisco. You go down now; I can go down to San Francisco, but not that often. There are meetings occasionally where you meet Stanford people, but they're all over. A lot of molecular biology came out of those meetings.

Park: That's right.

I have a personal interest. I'd like to know more about the biochemistry and the molecular biology doing similar things saying that this is my area and science and all kinds of territorial debates, especially of old-school biochemists.

Ames: Oh.

Park: And then other people. I'm talking about biochemistry. How do you think about those ?

Ames: Well, molecular biology is a different way of looking at things. Shareef [sp.] was a very good biochemist, but he missed the boat. I mean, he didn't -- he had the base ratios, but he would speculate and wasn't imaginative enough and didn't know enough to understand what it meant, and Watson and Crick did. Soon after the Watson and Crick paper came out, there was an international congress. It was already clear that this was a major discovery. There was an international congress in Vienna, and Sharif [?] was negative about Watson and Crick. He was demeaning to people who'd made the great discovery. So he was kind of bitter.

Park: What do you think about the physicists ?

Ames: That's fine, but biology is different than physics. It isn't theoretical, it's becoming more so, but they have to learn the discipline. That's why I always felt that knowing two fields where there's an interface, like genetics and biochemistry, I always had a big advantage because I saw the problem, but the geneticists turned up and didn't know how to tackle it, and the biochemist didn't know it existed, so you're always eliminating a lot of the competition when you know two different areas. So I've always been fairly multidisciplinary.

Park: As the science goes to specialties?

Ames: Some people get more and more specialized, but there's a group of people who just read a lot and put facts together, and that's how I make my kind of [unintelligible].

Park: Could you say something about NIH in general terms? How do you perceive NIH's impact upon your own career?

Ames: Well, for me, it was wonderful coming here. The whole emphasis was on doing science. So I'd be working Saturdays, go into the lab on a Sunday and you'd see people working away. It wasn't that 9-to-5 kind of thing. People were passionate about it. And then, of course, it was government putting in the money and making it competitive both intramural and extramural. I think they did. U.S. science became the glory of the world of science.

Park: I don't know whether you're familiar with the 1970s at the time who were the outside scientists program going on at the NIH.

Ames: Well, should you have a kind of noncompetitive program where you have the outside being competitive, and they tried to make NIH more competitive. So it used to be good people would leave and take positions somewhere, and then the people who couldn't get jobs would stay. So there is always a tendency, when you have a noncompetitive situation, for it to become not very good. But NIH managed to keep competitive because I think it made higher standards and it had reviews. But there always is a danger when they're not producing [?]

There are lots of good people. I haven't tried to analyze it, how many citations, or whatever you want to measure, per amount of money spent are you getting out of NIH versus are you getting out of academic research. Presumably, people are doing that kind of analysis. I suspect NIH is. And they have the hospital right there, so it is a biomedical research [unintelligible].

Park: When you came to NIH, did NIH have have such a great reputation?

Ames: Yeah. I think it had a good reputation. Whether it's leveled off relative to other, there are lots of good places around the country. But it was a large institution, with good people. There might have been some deadwood there, too, but you didn't hear about it. That goes on based on personal relationships and NIH would just collaborate as an institution.

Park: What do you think about NIH's role in bringing scientists from other countries?

Ames: A lot of scientists from other countries came here and then went back, and it had a big impact on other countries. I know France, Italy, and England…

Park: In general?

Ames: Now, there's always bureaucracy and you see it in universities and you see it at NIH, and eventually it'll kill everyone if it's not competitive, so that there is a tendency to hear people at NIH complain. The government will spend $100 to save a penny, and so, and you do all these extras [that takes] everybody's time.

Park: I was very impressed to see the area for your research.

Ames: Well, yeah. This whole building -- this started . . . A guy named Burt Rubin [?], who's an M.D.-Ph.D., doing research in Children's Hospital on sickle cell, and he started getting NIH money, and pretty soon he talked the hospital into letting him hire somebody else. Pretty soon they had people all scattered over Children's Hospital doing research, and they were bringing in a lot of NIH money. And then this old high school was empty for about 10 years, and the city of [unintelligible] didn't know what to do with it, and Children's Hospital talked them into selling it for $9 million. So they bought it and they spent $14 million fixing it up as labs. And so Burt Rubin is the visionary behind this place, and he got a lot of good people. And when our building on campus didn't meet earthquake specs, I knocked on his door and said, "Can you please give me a little space? and he said, "Love to have you." I came in. I made a huge amount of money from -- my postdocs sold this company, and I owned 40 percent, and so within the foundation, I gave them a present of $8 million to take this part of the building, which hadn't been built up and needed all this work to fix it all up. And then I moved [to a] small lab they gave me here, and then I hoped to hire a few people. I got very good people, and some younger people who came. So these two floors here are due to my work.

Park: Wow. So do you have to teach anymore?

Ames: Well, I still have a course on the campus and I still have a few graduate students, and they're finishing up. But I am teaching this spring, I'm teaching a course on nutritional determinants of aging, cancer, and I'm doing it with Ron Krauss. So I'm still doing some teaching. I'm officially retired from the university, but they call you back in [when it is time for them to] graduate.

Park: Just before closing, because I have been working on the Stadtmans, their research.

Ames: I think he was at Berkeley.

Park: Yes. He was. And he still had a lab [?]. Their research was on the subject of aging.

Ames: Yeah.

Park: And at the same time, your research is aging.

Ames: Right, yes, so we came into aging from different directions, and I see Earl [Stadtman] He's such a good scientist. You always listen to what he says. He's one of these people who speaks slowly and doesn't say much, but always says something interesting. He's still doing good science. I'm 75 in December, but I don't want to retire. I've made lots of money, but who wants to retire? I just want to continue doing my research.

Park: And Terry Stadtman.

Ames: She's very good, it's nice that old people still have a passion for science and want to do it. It's a wonderful field. It's such a big international club, and you're competing, but you're also cooperating.

Park: These days young scientists are having a hard time getting a job and also writing grants, you know, it's a big difference in experiences.

Ames: Well, it's tougher now, I think. I'm not sure I would have made it in this system because my talents are more creative, and I don't think I would have necessarily made it in this system now. It was always fun because we were doing what we liked and didn't have to worry too much about it. If you were reasonably productive, you got the money. But now you have to write lots of grants, and I'm writing lots of grants that get turned down because the people don't see why that's interesting. And so it is more of an effort.

Park: Right.

Ames: Well, it's the same kind of passion you have.That's why I'm glad there at the foundation. I have a better view of something [unintelligible].

Park: Well, thank you very much for your time.

Ames: It's a pleasure. Could you send me a copy of Martin's article?

Park: Sure.

Ames: Maybe just make a copy.

Park: Sure.

End of Transcript