My name is Elke Jordan.

I was the deputy director of NHGRI when I retired.

The only thing I can think of is that I had a very inspiring professor at college who was a geneticist, cytogeneticist, and really got me interested; I was just fascinated. This was around the time that Crick and Watson discovered the structure of DNA, so it was very primitive stuff. But that really led me to go into that field.

The university was Goucher College, and the professor was Helen Crouse. Have you heard of her? No. She worked on cytogenetics in flies. She had a special fly that she liked, I think a fierra [spelled phonetically], it was called. But she taught us widely about genetics. She was just thrilled and excited about it, and had us read McClintock's papers on jumping genes, so I had an early introduction to some of the mysteries of genetics.

Well, there were a lot less buildings. [laughs] When I go there now I have a hard time -- [clears throat], excuse me -- finding my way about. I was in the biology department, which was a mishmash -- well, not a mishmash but contained every kind of biology, from biochemistry, which was rather famous, the McCollum-Pratt Institute, and all the way up to classical genetics on the top floor. The biochemists were on the bottom and the geneticists were at the top, which didn't mean the geneticists were more regarded. I think the biochemists were -- held sway. And the term "molecular biology" hadn't even been invented yet. We talked about biochemical genetics. And then, as I progressed in my career, it became molecular biology.

Oh, that was another controversial event. And at the time, I had no idea what it would lead to, but it's perfectly logical to connect it with the Human Genome Project.

Well, GenBank was just an attempt to collect all sequence data in one place so that they would be accessible. And it was controversial because, at that time, people were just getting used to desktop computers, and they were developing their own databases, and they really just wanted to keep them in their lab or the sequence that they generated. And so there were lots of little collections about all done differently, and the visionary folks thought that we should collect them all in a central, national facility that everybody could get access to, but other people felt that, no, everybody would have it on their desktop, and it wouldn't really be a big deal, and it was not necessary to have a big, centralized effort. Well, in a way, both were right; everybody does have it on their desktop, they have it on their little iPad or whatever, because you can download, and computers have become much, much more powerful. So, that was in the era when the desktop was becoming available. So, the centralized folks won out, and we went through some tribulations with contractors who were not performing as well as we had hoped. And then, after a while, NLM took over and the whole thing blossomed into a whole series of databases, and they really sort of run the market now.

Yeah, I wasn't there very long. They had a program called the Virus Cancer Program, at the time it was believed that if you just have found the right virus, you know, you could understand what caused cancer. Well, it was partially true, there are some viruses that cause cancer, but it was not nearly as -- and they're not the viruses that they were studying. It was mostly DNA viruses, and

they were studying RNA viruses, which they thought were the key to everything. So I sort of had an administrative role there; I never worked in the field. I did learn a lot about it, which was helpful, because, as a molecular biologist, I was working on bacteria, and this introduced me to Mammalian systems and the more complex biological systems.

Well, I worked in the genetics program. I was moved and recruited by Fred Bergman [spelled phonetically], who was the director of the genetics program. And I came to NIH through a program called the Grants Associates Program, which, at that time, NIH had difficulty recruiting people. Can you imagine? [laughs] Because academia was more attractive, so this program was supposed to convert people from academia into the administrative program. And most of the time, the people who came through were not molecular biologists. I was sort of a rare species, and Fred Bergman became aware of that. There was some linkage as to why he knew of my existence, and so he recruited me into the genetics program, where I was able to manage grants that really dealt with genetics.

Well, at that time, the theory was that you wanted to hire generalists; that managing a grants program required many skills, but that the science was somewhat adaptable. That has since kind of gone by the wayside. I think now the focus in the institutes is more in getting specialists in the area to handle the grants. So that was one reason, maybe, why the program eventually was ended. Another reason that people didn't have trouble hiring anymore.

Well, I had moved on in NIGMS by that time; I was associate director for program activities, I think was the title, so I was -- it was more managerial position and less direct handling of grants. But nevertheless, somehow I was -- well, because of my work in genetics and then the associate director position, my name was very well known in the community because I put my name on a lot of documents, you know, grant awards and such. And from my time in research, people in my field knew of me. You know, I was not a brilliant scientist, but there were not that many of us, and not that many women. So my name was pretty well known. And when Wyngaarden was persuaded to establish the Office of Genome Research, and Watson agreed to come and [unintelligible] the head of it, they needed some staff. So I'm told that people went to Wyngaarden and said, "You have to hire Elke Jordan, or this will not work." And I think that was just because the community was agitating for it knew me. They couldn't possibly know everybody at NIH. So they had some comfort in knowing I was one of them. So that's how it happened. I got this call from Wyngaarden, "Do you want to come over and do this?" And I thought, "Oh my gosh," you know, nobody knew whether this would last, whether we would ever get money, and whether the whole thing would work out.

I know that the community was kind of looking to NIGMS to do a lot of this things, just like GenBank, you know, which NIGMS very, very, very reluctantly agreed to coordinate. And initially, in fact, we got contributions from all kinds of people to fund GenBank, because we Ruth Kirschstein didn't want to divert money from grants. So, the community was sort of looking to NIGMS, here's this new idea, and I did have some chats with people like David Botstein, but they realized that NIGMS wasn't going to pick up the ball. They felt they'd done as much as they could with GenBank. So the community next tried at a higher level, and, in fact, came -- somehow came to the conclusion that it was best to do it separate from any institute, and give it its own identity because I guess they were afraid the institutes might corrupt it [laughs]

into something else. So I think that went on for quite some time, that they just didn't get a positive response from NIH, and I don't know how Wyngaarden's arm was finally twisted to say yes.

Well, I thought, you know, he was probably the best person at that point in time, not in the long run, but he had tremendous reputation, people listened to him, the community had confidence in him, so who else could have done it? And he was willing, and that's always the other part. People are not always at a stage in life where they can just pick up and go.

It's somewhat amazing what an influence he had on people, how he was able to persuade people to his point of view.

By phone. He called frequently, and Zinder called frequently too; Watson appointed Zinder the chair of his advisory committee, so both of them were on the phone a lot, and occasionally Watson came in.

Honestly, I don't remember the [laughs] conversations except when the secretary said, "Dr. Watson's on the phone," you know, you dropped everything and talked to him. And same with Zinder; he was often just venting his frustrations.

About?

Watson. [laughter] "He's gone up here and given this talk and got everybody rattled and upset, and now I have to go calm things down," or something like that.

Well, Mark Guyer I met in NIGMS. And I focused on him to take with me when I went to the Office of Human Genome Research because he actually had worked in the technology. He'd done -- I don't know if he had actually done sequencing of any sort, but he was familiar with the current technology, and I felt I needed that because I'd been out of research for some time. And I left before the recombinant DNA revolution, so I was really pretty ancient, science-wise. I thought he would complement me nicely. He had not been in NIGMS very long, so his science was recent and, you know, he still had a lot of career open to him.

It took some persuasion. He was very reluctant at first.

It was a very iffy sort of thing to do to go, to this office which didn't have its own budget yet, hopefully would have some budget in the future, or might disappear in a year or two, and Mark had only just recently come to NIGMS, so I guess he didn't -- and I think wherever he was working folded or something, so he wanted some stability, and not go off on another rash tangent. But he finally decided to come anyway.

He was the best from the NIGMS stuff--you know, I didn't really look all over NIH, but the chances of somebody really being familiar with that area in another institute were pretty remote.

Did you read the book that NIH wrote about her? Yeah. It got her pretty right. I could really see her and hear her because they took all the stories that she told that people repeated to them

and put them in this book, so it gave a very good picture of the person, somewhat idealized. She was -- well, she was very devoted to NIGMS, which was -- and basic research -- which was sort of amazing because that's not the way she came -- that was not the field she was working in. And she sort of became the voice of basic research and research grants, individual research grants. And she did not want, having finally gotten NIGMS around to getting rid of some of the other stuff they had around the edges, she was not about to let it, again, degenerate into all these other areas that were -- that central to the mission. So I think that's why she resisted all these new efforts like GenBank or Genome Project, and the community that was promoting them, you know, felt that there was a lot of resistance there, so that's why they turned to other avenues.

But she was very effective at promoting basic research to Congress and within the department, and, you know, NIGMS did well during her era.

No, I don't know, but I think it was a gradual process as it became more accepted generally and more successful. That's what -- in my mind, that's what brought the community around, which was very resistant to the Genome Project. As soon as data flowed that they could use, it flipped the opinion completely. So, once we put out sequences and people found them to be useful, then they couldn't wait to get more. And the whole issue of "Is this a bad idea?" just vanished. The same with GenBank, when people saw it and started using it, you know, the criticism died away.

A little later. She had worked at NSF, right? And then she came to NIGMS, and Mark knew her; I can't remember exactly why, were they in the genetics program together? Anyway --

I believe so, actually.

Yeah.

Yeah.

He brought her to my attention and thought that she would be willing to move now to NIGMS. [laughs] And, you know, that seemed to work out well.

Bettie Graham I knew. She was also in the grants associate program to train scientists to be managers way back when we all sort of knew of each other. And I thought that she might be interested in a new situation; she was in the Eye Institute, I think. And I wanted a variety of people, not just NIGMS types. So we recruited Bettie.

Craig Venter, of course, had a lot to do with that. And he and Healy somehow hit it off, and came up -- I don't know who came up with what, but somehow this idea emerged that if we patented sequences, the NIH could become rich. That's the way it appeared to us. It was a way of amplifying NIH's budget. So, Watson thought that was nutty, and I think he's been proven right. [laughs] And was very outspoken about it, as he always is. There was this famous hearing we had on the Hill; I don't remember who was hearing. Do you remember what senator?

I think it was Domenici.

It was Domenici? Anyway, Craig was going on about his stuff, and Watson made some rude remark [laughs] and that was sort of the end of that. So then, you know, that was the beginning of the end for Watson at NIH.

Well, I think the conflict of interest issue was used an excuse, but she really wanted to get rid of him. He probably officially resigned, but he was pushed; he wasn't quite ready to go yet. I don't think he planned to stay around forever, but the timing was pushed up.

She did, I must grant that to her, she did recognize that this was a very valuable program and the community was behind it, so she didn't try to kill it, which she could've tried to do.

He somehow interacted with us. He wanted some funding; well, that's usually why people came to us -- he wanted funding for his projects. I don't remember now whether we gave him any or not, but that's somewhere in the record. And the next stage he had the conversation with Healy about patenting. Then he was very much on our minds. And then he left NIH to start a company.

TIGR.

Venter wasn't recognized or didn't feel recognized in his -- by his institute, and so this was the early stage, where we getting -- recruiting people to participate in the Genome Project, and you didn't yet know who was going to come out big winners, but everybody was looking to play a role.

Brilliant.

Well, you have to put yourself in that time when one of the groups attacking the Genome Project were the people concerned about the ethics. They thought using the information to breed humans and engineer humans and do all kinds of unethical things, which were extremely remote from what the Genome Project was really about, but that was the public discussion at the time. That was the tone of the discussion. And by making it an official part of the discussion, I think Watson quelled a lot of that. First of all, it gave those people who were more moderate a chance to get some facts out. He started going to meetings, constantly giving talks, writing papers, being interviewed, and putting a little more factual basis to the discussion, clarifying what we were and weren't doing. It, I think, gave people some sense of comfort that is was being looked at and someone was working on it. And, you know, nowadays, having an ELSI program when you're starting something that's going to have a lot of social impact, it's really the norm. Even when I went to the foundation for NIH and we were studying grant challenges in -- very early on, we established a little ELSI group, too. So I think it was -- that's what, you know, with all his ordering us and peculiarities, Watson does have vision.

What ELSI did was to give legitimacy to the field, provided some funding to people who could establish themselves, and so the whole thing became -- achieved a more solid grounding.

But they provided an outlet for those kinds of discussions in a controlled, reproducible [laughs] kind of environment, not just the press writing pieces in the newspapers, but, you know, scholarly, serious thinking about the issues.

She was a very good public face to the whole issue. She was great at giving interviews and speaking, and, you know, just generally promoting a sane discussion of ELSI issues and the benefits of the Genome Project. Because, you know, while the public was complaining, they were also going to hopefully benefit from having this research go forward. So she was very effective at that. I remember at some of our advisory committee meetings where press and photographers and so forth were present, and she would be surrounded by a swarm of people wanting to talk to her. So she had a lot of charisma, right.

At the beginning, yeah, well, he got the whole thing rolling. He was an academic, and so he gave a kind of legitimacy to the effort for the people in academia. They felt they had someone they could talk to who could understand them, and he did understand them. Later, he was less oriented, let's say, towards practical results, and that's one reason why he left and went back to academia. Especially when Francis came in, I think he was looking for "what have you done for me lately," you know. We need some concrete results; we don't just need scholarship, although I think, initially, having some good scholarship was very beneficial, but Francis was more of a practical results type of person.

Well, before he came, you know, the community rallied around us; this was during the time when Gottesman was acting because Watson had left and Healy was still around. So I would calls from time to time that they were looking around for someone who could take over, that they could persuade Healy would be the right candidate, in a subtle way because it was -- I think they thought if they directly went to Healy and said, "This is your man or your woman," that would never work. So it had to be done by indirection. And there was a plot on how this would be done. And Francis headed one of our genetics centers, so we knew of him, and we knew what kind of person he was, what kind of research he did, and so forth. He was riding on a high because he'd just discovered -- which gene was it?

CF gene. Right. So that all seemed very compatible, and when Healy actually offered him the job, you know, everybody was happy that it worked out. And he came in, and one of the -- of course a dramatic change that brought is that the intramural program was started, which gave the center a much, much bigger presence in the NIH environment, and a lot of new people coming in. So when Francis first came, establishing the intramural program was really sort of the major issue on the table for the center at that time, a center.

Oh vast. Vast. Yeah, and becoming more so. I -- having an intramural program, first of all, gave us a kind of legitimacy on NIH campus that we didn't have before. NIGMS doesn't have an intramural program, and it sort of feels like it's missing an arm or something; it's not in the thick of some of the issues that concern NIH. But also, bringing in the intramural program brought in expertise that wasn't on the NIH campus. And so as his expertise was shared through collaboration or otherwise, the intramural program, as I see it -- and I wasn't in it, I was just watching from outside -- became very integrated into the rest of the NIH intramural program and provided something of value. And it's good -- a very concrete example, but I think in subtle as

well as not so subtle ways, it changed the tenor in the intramural program. It sort of brought them into the modern era in some areas.

Well, there was some developments in mapping, and there was also developments in sequencing before the sequence really began to appear in huge amounts. That was a period when -- I think those Bermuda conferences were during that period, weren't they? When the Bermuda principles were announced, there was a lot of back and forth behind that. The British were very strong in promoting free access and early access, and they kept pushing us further and further in their direction. And the DOE was also very concerned about publishing as soon as possible. The NIH community was a little more reluctant because they weren't used to it. So, you know, that was a step-by-step process; I wasn't as if it was suddenly full-blown and everybody had total agreement on how it should be worded. It went through many stages. The mapping also made progress; I was just thinking about that this morning as I was reviewing your questions. When we started, there were all these chromosome groups. One for most chromosomes, trying to map their chromosome arduously and meticulously. [laughs] And then -- what was his name, Weissen? Weissenbach? In France.

Oh, yeah, Weissman.

Weissenbach.

Weissenbach.

Jean Weissenbach.

That's right.

Jean Weissenbach did a map of the whole genome, a somewhat crude map, but nevertheless, he got the whole thing by using large-scale methods. And that, I think, really changed the thinking of many people. Eric Lander was thinking that way before Weissenbach even published his map, I believe, but he didn't have many people following him. So, you know, when we started the Genome Project, it was kind of a cottage industry, and there was a great deal of emphasis on getting everything 100 percent right. The change in thinking that Weissenbach's map produced was that there's another way of getting at it, which is to do the whole thing and fill in the gaps later. Some of it will be perfect, some of it will be less perfect, but you can then work on the gaps rather than starting at one end and meticulously and methodically going to the other end.

Yeah, well, there are many areas of conflict. I do think that the Genome Project showed that these large-scale automated approaches are valid in biology, valid and valuable in biology as well; biologists weren't used to thinking that way. What was the other side of my thought? Oh, so we had to get biologists to accept that kind of an approach. And then there was the other tension about perfection, the fear articulated mostly mainly by Maynard Olson that we would produce junk because we didn't have very high standards of quality. And so we had to learn -- the community had to learn how to balance those two issues: have good quality, but also speed, and where was the proper balance those two. And that's -- you know, towards the end when there was several years of debate about when shall we say we finished, what does "finished"

mean? Because everybody knew it would not be every single base pair. Maybe at the beginning people thought it would be, but with the hemochromatin being sort of difficult to work with, people soon realized that there wasn't going to be 100 percent of every base pair perfectly situated. So, those were a lot of tensions that a lot of time was spent on dealing with those issues and getting some kind of consensus that people would support.

Yes and no. There was, you know, the Lander vs. Olson [laughs] and Olson "We need very high standards", Lander, "We need to automate and do large scales, we'll get there faster." That was tension was always there. But there was also a lot of skepticism that the Craig Venter kind of approach would be possible. I mean, you have to give it to Craig, he tried something that seemed impossible to a lot of people and found that it did work. And that, you know, when that became evident, it kind of changed people's thinking about this whole issue.

I don't really know. My source was David Botstein. You familiar with him? He talked to me periodically to give me a heads up about what was happening. But I don't think he was necessarily the head of a group. I don't know. Watson probably was involved, Zinder. And I don't know, Eric Lander, whether he was part of the group or not. But, you know, I think the big names in the field were probably communicating. And Francis was thought to be available because he had just gotten a divorce, and they thought he might be willing to move somewhere else and change careers. And that worked out. So you'd have to talk to them. I really don't know, except the little tidbits I got.

And also, it was known that somehow Healy had taken to him. They had met. And that was important. I mean, if she was allergic to the person, it wasn't going to work.

Well, she seemed to me to be on a different planet. Communication with her was very difficult. For a while there we were called into her office quite a few times to explain this or that or be read the Riot Act. And she just seemed to be, you know, it was like she was circling out there and we were circling here, and we just didn't know how to make the connection. I remember one meeting where, I don't remember what the issue was or why Eric Juengst had written something in response to the issue, and she liked it. And, you know, with a typical Eric Juengst kind of thing, sort of theoretical and academic, and very good prose, and so we grabbed on to Eric and said, you know, "If you two can communicate, tell us what the secret it." But I don't know that it helped. But that particular time, they were communicating. She was a terribly hard worker. She read everything that went to Building 1. She would take boxes of stuff home and read them overnight. And when she wasn't in town -- she commuted -- she would have them sent to her and, you know, I think she really absorbed all this material. But she saw it from her perspective. Very strange woman.

He is very nice. Very approachable. Warm, sensitive kind of person. And seems very laid-back, but accomplishes a lot while being laid-back. There's a lot more to him than first meets the eye. He's been, in my opinion, very successful as a director of Intramural. In a quiet sort of way, no fanfare, gets it done.

Well, you have to remember, Watson was part time. His appointment was part time. He was not physically present most of the time, so he did not involve himself at all in day-to-day things. He

didn't care who we hired or anything. He somehow trusted us to make it all work out, or didn't care because he wasn't going to be around. I don't know. But we had a lot of freedom. I mean, the goals were clear, but how to get there, whom to hire, and so forth, even grant awards, he didn't study in detail how much people got and so forth. The internal workings of NIH, he just wasn't interested in, in the whole process. When Francis came, he was full time. He was here physically. So he, being the kind of person he is, he caught himself up on all the aspects of being the government employee and running a government program. At first, both he and the other intramural investigators that he hired were somewhat shocked by the life of a federal employee and all of its restrictions and rules which you have to follow. But he learned to use them to his advantage, as most people do who stick around. So, yeah, the two styles couldn't be more different. Both were very good at getting their message across and very good at promoting the Genome Project, but in a different style.

First time I saw him was at that famous Airlie conference. He was sort of a young and upcoming scientist who spoke up quite a bit and who clearly had very good ideas. And everybody said, "Who is Eric? He's too young to be having such a big voice" and things. So -- but he lived up to his reputation. He, I think, was very much a confidant of Francis Collins. Confidant, also persuader to his points of view. He was, in terms of the large-scale approaches, he was very much ahead of the rest of the field, trying to bring them along. And of course his center produced a huge chunk of the final sequence. He was very effective in that. So, I see him as a very key person in achieving the public sequence.

Eric has worked in many fields and has always been successful, so I would say that implementing the large-scale approach and really making it work, and being able to communicate with the people from all the different fields that you have to bring together to make that happen was a major contribution that he made that was distinct from what the other centers did. And just intellectually, he dominates any group. [laughs] We never put him on our advisory council or advisory committee because he was so dominant and he had the largest chunk of money, and we felt it would look like too much inbreeding. But he was on the Director's Advisory Committee. It was just amazing. No matter what topic came up, he had wise things to say. So he's just extremely smart.

Yeah, he did get a genius award, so I guess he's a certified genius. I'm sure he's a genius. [laughs]

And he's very articulate, too. Not only did he contribute on any topic, but he was able to encapsulate what the issue was and sort of clearly lay out the facts so that anybody could follow it. He really had a gift for that.

Not much of a collaboration, unless you, you know, one-way collaboration that Venter had all our information as well. The real issue that was galvanized people was the availability of the sequence. Our group felt very strongly to a man, I would say, to a woman, that it must be public and readily acceptable by everybody, but that was the way science would progress most effectively. Whereas Venter had this patenting idea, making access to the sequence, depending on money or whatever, so that was considered a major threat, if he succeeded in that. And that really -- that was what the race was about.

What is his scientific legacy? He's not done. He keeps coming up with these radical ideas. But as far as the genome, I think showing us the whole genome approach, given the right circumstances, can work, and it has been adopted. So that is definitely a contribution. And without him, we would have got there, but maybe not at the same time. I think, in due course, the whole genome approach would have emerged anyway, which is true of most scientific discoveries, they would have -- we knew the historians, but my impression is that sooner or later, people would have got it. So I think we would have had that. Maybe Eric Lander would have shown it, but…

Well, as I said earlier, journalists are always looking for some controversy to give their story a little oomph. But I sat here watching the process from the inside. And there was a lot of tension those last two or three years. Not all of it made it into the public press. Some of the journalism was sort of what we would call biased towards Venter, saying, you know, "Why is the government trying to beat this poor private sector person trying to reach the same objective?" And we constantly had to explain, and Francis was good at that, that we had somewhat different objectives, and it was important for us to achieve ours. We're just making it public.

By the way, while we're on that topic of making public, I do think that is another major -- besides ELSI and a few other things, another major conceptual contribution of Genome Project, that sharing the data as quickly as possible was to the benefit of all. That was not the general mindset at the time.

The ex-worm people, Sulston and Waterston, were very strong proponents of that. The British and the Wellcome Trust were just adamant. And they pushed it as far as they could. It was not the norm at NIH. People felt they had a right to data they produced, and mine it and publish before they shared it with anybody else. So, it was true in the worm group, but it was not universal in the field. But I think even that idea of making data freely available is now spreading into other fields where it wasn't done before, like even clinical trials.

Well, there was a need for people to publish something, to have papers, to fill their résumés. And so they felt they should have some period of time at least to do that before the rest of the world could get at the data. And that's why we started out with the six-month period. And I think it shrunk data on, as technology improved. And most scientists would have liked to have more time. But they seemed to have survived.

I'm not aware of any group in particular. But during my stay here at NIH, I've been present at many discussions about this whole issue of when to release data. And it's now common for journalists to require data depositions before something is published. That was another agonizing multi-effort to reach that point. And to reach the point of making journals take some of the responsibility for getting data out, they didn't want to do that at all. So even back when I was in NIGMS, we were fighting those kinds of battles. So I would say it was pretty pervasive to try and hold onto your data.

Well, Ari certainly did act as intermediary. Got Celera and the public project to talk to each other and arrived at some sort of agreement. Yeah, how to describe the DOE role. They were

actually early proponents of data sharing and sort of pushed stuff at NIH. We didn't have any policy as an institution about data sharing. And we knew, from our relationships with OMB, that getting anything in that area officially changed would be extremely difficult and time-consuming. Any change you made to the application, the NIH application, had to go through OMB, and it was a quagmire. So we came up with a way to accommodate by just asking investigators to describe what they would do, and telling them that if that was not part of their priority score, but if we found it deficient, we would negotiate a better policy with them if an award was to be made. So we weren't making a rule as to what they should do, but we were telling them they had to tell us and then we would react to what they told us. And that sort of went under the radar. Nobody complained. So we kept doing it. And it's also now a way of behaving that's become accepted in other areas. And, of course, the investigators knew what the standard -- what the official standard was, what the G5 was saying, and what was published and so forth. So they knew what policy we were looking for. So, DOE did have an influence there. We otherwise might not have instituted this policy until later. Working with DOE was interesting because their culture is so totally different. It's like the difference between biology and engineering, or what it is, I don't know, but the way the department operates, you'd think it was a different government. They -- and the reasons for it are probably that they report to different committees in Congress. The way they work with OMB is totally different from what NIH does. Because NIH, all the institutes go directly to Congress for their budget negotiation, whereas the DOE is all centralized, awards are all centralized. They seem very rigid. It took for -- you know, they had deadlines, the last grant they could make, or they called them all contracts [spelled phonetically]. It would be months before the end of the fiscal year, whereas we could make a grant at the very last minute in a fiscal year. So there were all these things that had to somehow be made to mesh so that we could collaborate on things. And, of course, they could bring expertise in engineering and physics and mathematics and computer science to the table from their intramural labs that we didn't have as readily available. So, for certain areas that we were having meetings on and discussions, you know, they could bring in people. It was sometimes difficult to work with these people because they were living in a different world. But, still, I think they did have an impact in richening and broadening the discussion somewhat, but you're absolutely right. The final contribution was relatively minor.

Well, they selected themselves, in a way. They wrote successful applications. Everything we did was peer reviewed. So, the groups that did well grew and stuck around, where the others gradually died away or went onto other things. And it was this automation thing. Some labs just couldn't manage it, to go up to a suitable scale and invest in the automation. And that could have been temperament, it could have been space, it could have been just skill, or whatever. But they sort of selected themselves in terms of success. Now that's our centers, the NIH-funded ones. The DOE pretty much stuck with their center. They had their own funding, ways of doing things. And the Wellcome Trust put its resources into Sanger, Sanger Center, and kept them going. But they were successful. Definitely. They made sort of intellectual contributions as well as sequence. And many of the other countries wanted to have a little chunk. They wanted to be part of it. It's amazing how once the thing became established, everybody wanted to be part of it. We had delegations from France and from Japan almost annually because their government keeps changing. So they had a new representative and wanting to know how they could participate. You know, we'd give them the spiel and -- so, and Germany didn't really have a major presence in the sequencing phase of things. But initially, it was important for us to

include as many people as possible. There were political reasons for that, and bringing the community along. These people were already working in these areas, and to just say, you know, "Everything that's going on is junk and we're going to do it completely differently" would have just created even more controversy. So, initially, the idea was to somehow stimulate support, encourage the groups that were already mapping to contribute to the overall map. And it was good. I mean, it was quality control, in a way, because they produced very good data, and if your rapid method matched their data, then that was a good sign.

That's when a bunch of government officials and advisors go and visit a site, a lab where the work is going on to evaluate it and try to get information that is beyond what you can get on the written applications. You know, someone may describe a room full of apparatuses doing this and that, but you don't quite get it or believe it until you actually see it and until you talk to the people working on the project in addition to the principal investigator and get a sense of their qualifications and their commitment and their skills. So we had -- as things got very busy, we often had reverse site visits where the leaders of the projects came here. And, of course, you couldn't see the lab, but you could interrogate them and try to get a sense of their thinking, whether they were really with it. It can be very valuable.

Well, I can tell you, every time we went to see Lander -- I participated a couple of times -- there would be lots of skepticism, and then when people got there, we would just be, "Oh, gosh. Gosh, you know, he really does work. He really does do it." So, site visits can very much work in your favor, but also not, if you're not up to speed.

Fascinating. There were conference calls, I think every week, with all the G5 participants. And he ran them very tightly. I think we always had an agenda: things that needed to be covered and people who were not meeting their goals. You know, they would have their goals, and if they didn't meet them, there was a lot of discussion about why and what could be done to fix it up. Sometimes things were moved around a little bit to keep the overall effort going. It was a fascinating process.

I think by personality. He was able to just keep the group together and get any parties that were having falling outs, you know, to smooth it over. That I attribute to personal skills of his in dealing with people. And the fact that they were all going for the same goal. I mean, everybody had bought into the goal. So you didn't have to persuade them that you should go into this goal instead of this one. Everyone agreed on what the goal was. It was just a matter of how to get there as efficiently and as soon as possible. And sometimes he would have private conversations with one or more of the investigators outside the conference call to prepare the way for things.

Yeah, having a clear goal is very, very helpful [laughs] even if it is not as clear as it might seem. And we did not map the whole human genome, or sequence the whole human genome. We sequenced what was sequence-able at the time. But even so, it was a much more clear goal than most research that I've been involved in. It's a measurable goal. Yeah, and the fact that it finished two years early is -- you know, it depends on how you measure where your starting point is.

No, I -- well, when we had our advisory committee meetings, there would be ups and downs. You know, the downs that, "We're never going to make it," especially in a reasonable time. And then there were ups when things were going well, and there was a lot of optimism. So I don't think there was a time point where we felt, "okay, this is going to work." Although, you know, in concept, everybody soon believed it could be done. It was just a question of when, and how much money it would take.

Yeah, in a sense, there was always a Plan B discussion. You know, "If we don't get a hundred percent, is 90 percent good enough" and that sort of thing. Absolutely.

Yeah. It was a large part political accomplishment, because scientifically, the value was incremental. The more sequence you had, the better. So, you know, the business of whether you finish 100 percent, or 98 percent, or 95 percent, scientifically, didn't make that much difference. But people were very aware of their reputation and posterity. And the political situation, you know, how it would be interpreted, that the public project gave up at 90 percent because they couldn't get the rest or something like that. So, yeah, there was a lot of political thought involved.

Yeah, well, that's what was sort of going on alongside all the time. And Francis was very good at explaining what it would do for society. The issue for NHGRI was, "What do we do next?" You know, "Where does this go?" And there were some who felt "Genome Project completed. Maybe we should disband and declare victory." Or, Francis Collins and others promoting that it's not done -- I think, in retrospect it is done, we're now onto another phase. But that really doesn't matter. The fact is that the institute started branching out in more directions, more clinically-relevant directions mostly. And, you know, you could still call it "genomics" because it involves genomics approaches, but it's not the Genome Project as originally envisioned. So there was a little bit of a fight over what we do next at that point.

Oh, I think they have lots of promise, lots of new insights, to HapMap and to evolution of humans, differences between different groups and what they might be caused by. The ENCODE, I'm not that familiar with all the things that came out of it. I just occasionally read about it in Science. It seems fascinating to me. I mean, this is the kind of information that we've been yearning for, and now we can actually see it.

No, considering how [laughs] stuck we are in our racial backgrounds, and how many wars are being fought over these differences. No, I think it's something to approach very cautiously and something that ELSI should be helping us with. And they were involved in the HapMap, right? Yeah, I seem to remember there was an ELSI component. So, I'm a firm believer that real understanding will demystify a lot of things and remove problems that, in the imagination, seem much more complex than they really are. So I'm all for shedding light on these things. And maybe when we all realize that our genomes are essentially the same, and there's only little bits of changes that produce a visible effect, maybe that will be good for everybody.

Well, undoubtedly, eventually, yeah. I think also it will make the information much more widely available, and by that I mean that people are actually eager to have such information in most cases that I observe. The geneticists, and particularly the genetics counselors, were very

concerned about sharing information with patients that might disturb them or worry them. And now that companies offer this kind of thing by mail order, Francis Collins certainly used to be extremely concerned about those kinds of developments. I don't know if he still is. But it seems to be much less of a problem than the geneticists imagined. So I think people are eager. When I talk to my friends now, they're much more into the health history of their families and how that affects them, and they sort of bought into the idea that our genetics is deterministic. And it doesn't seem to disturb them inordinately. [laughs] We all know that we're fated for certain things. And we all know that we are more similar to our families than to other people. So it's just an extension of our experience to date.

Yeah, everything. [laughs] I would never have imagined it. I was a graduate student when the -- when exactly was it -- what was it that Marshall Nirenberg did?

Oh, he basically --

Polyphenylalanine production.

Right. So he figured out how to --

How the code translated in protein, right?

Precisely.

Now, someone predicted at that point that soon we would be able to sequence the DNA. Seemed totally unbelievable at that point. And we had no way of going near that even, and lo and behold, it happened in my lifetime, so it's amazing. I feel very privileged to have had my career in science during this period because so many amazing things happened. So it's very hard to actually point to one thing that stands out. Just the speed with which things have changed and how different doing science is nowadays, doing biology. Or maybe not all biology, but at least this kind of biology. We were working with metal loops and agar plates. [laughs] Got a lot of information out of that. And now you have all this machinery and everything is automated. I sometimes wonder, if I was starting now a career in this area, whether I would like it or whether I would find it too mechanical.

Statistics. [laughs] Nobody in biology that I knew ever studied statistics in my day, but I think it would be vital now. And regardless, even if you're going into clinical sciences, you need statistics. It's genuinely not valued enough, and I have not studied statistics, so that's one thing -- I'm messing with the microphone. First of all, all this sequence analysis is heavily dependent on statistical approaches, and as biology becomes more large scale, always on clinical trials to sequencing, you have to know statistics. So I would recommend that. Computers, know something about programming, even if you don't intend to do it, so you can at least talk to programmers. [laughs] Other than that, I think it's so wide open, what can be done now. It should be a wonderful thing to do.

Well, Watson's initial vision was that the program would be seated in the NIH or some agency of the government that had money that would actually be run by an international group, advisory

group, called HUGO. And he was trying to get the -- no, the Howard Hughes Institute to underwrite this HUGO, which they never did. There was a HUGO initially, and they did have a couple of meetings where nothing happened, as I recall. And it was complete, you know, innocence of knowledge of how governments work. The NIH wasn't going to report to some kind of international group appointed by God knows who making pronouncements about how the Genome Project should be managed. So, eventually, our advisory committee, and I guess maybe DOE had their committee as well, sort of filled the role that was envisioned for HUGO, but HUGO itself never went anywhere. And it couldn't, and it was obvious to us that it couldn't. First of all, to get a voluntary group like that to agree on anything would be extremely hard. It was much easier for us because we had money to back up anything that was decided. But anyway, that was sort of the idealistic vision of scientists that would be run by scientists for scientists. I don't know of any model like that.

Yeah, we went to countless meetings with Howard Hughes. I went with Watson. And he would berate him about giving him money. Cahill was his name, George Cahill? And it never came to anything. Very wisely, Hughes decided not to support this crazy idea. It is crazy, but it was very idealistic, thinking that a bunch of bureaucrats couldn't possibly manage this, it had to be scientists.

Well, you know, they were all the results of meetings, which were sometimes pretty contentious. I mean, you know, you spent 75 percent of the time thinking, "This is never going to work," and then, in the end, something would come together. But finally came to the realization we had to have some quantitative goals, we had to have something measurable. So the plans were made in that way, which was pretty novel, at least for this field, and then at the next meeting, we had something to measure and wring our hands about, "No, we haven't met the goal. Are we going to meet the goal?" I think for doing the Human Genome Project itself, the thing that was finished in 2002, they were invaluable because they kept everybody on their toes and they kept everybody marching to the same goal. So, this is a novel concept to do it that way, but it seems to work. And then even when the Genome Project was finished, the Institute was still trying to do plans. I'm not sure that they were nearly as successful, and I don't know that they're still doing it.