Bob Cook-Deegan:
So, why don't we get started? And we'll start with you, Jim. I would like to know what were the challenges that you faced? How did you get your job? I would like to concentrate today on the sort of thing we're not going to get from public documents any place else -- that you have only in your head. So, I'm kind of curious for each of you, how did you first learn about the job that you were originally going to take here at what became the National Human Genome Research Institute?

James Watson:
Well, it really started with a phone call from Paul Berg to me about our forthcoming 1986 symposium, and Paul suggesting that we have some special session where we talk about the -- whether to go ahead with the Genome Project. So that was -- I really hadn't thought about it. Bob Sinsheimer had a meeting at U-Santa Cruz. And one knew that Lee Hood was -- tried to build a machine to sequence DNA. But it was really Paul's thing that -- then I of course went to it. And I think, obviously, Wally Gilbert's, you know, $1 a base pair and realized it was only $3 billion. And that, you know, over 15 years, that wasn't that much percentage of the NIH budget. And I was already aware of -- you know, there's several DOE efforts to go for the human genome. So, you know, it was clearly -- it could be done. Though I didn't want to count on Lee Hood. And so I visualized almost a genome city with thousands of technicians, you know, using, you know, the old-fashioned technology. And it could be done.

Francis Collins:
[laughs]

James Watson:
It turned out, of course, it didn't go that way. But I did it because I wanted to -- I didn't want to be head of something that would fail. We could do it -- it was doable, even with the old technology.

And so, then we clearly had to follow up with Cold Spring Harbor. And there was present a very intelligent man named Michael Witunski of the McDonnel Foundation. I don't know when he first entered my life, but he came to the symposium. I really thought it had to move to the level of the National Academy of Science. That is, we had to have some committee to, in a reasonable way, look at it. And Michael said he'd pay for it. So often, that's a real problem of finding the money. But we had the money.

And then, Frank Press, who was President of the National Academy -- he was very agreeable to that. And I remember going and talking to Frank about setting up the committee. And I was afraid of opposition from the good scientists; that is, who would see it as a -- you know, Lee who had had 100 people in his lab soon afterwards. And no one wanted to give Lee any more money because there's just something, you know, that -- gives money to Lee, not to -- and so…

Bruce Alberts had just written some opinion piece that, you know, no lab should be more than 10 people in size. So I thought he's the person to be in charge of the committee, because, you know, it's a pretty good rule that 10 is a very good size. And -- though now, you know, people would say 20 because you expect things to move faster. But Bruce was agreeable. The committee

originally I guess included probably both -- I didn't look it up now -- Lee Hood and Wally. And Wally soon after the meeting announced they wanted to start a company too. And he had just -- he had been a starter of Biogen. And he had been -- at one point, its chief executive and wanted to do everything himself; and so they threw him out. I mean, as its head.

[laughter]

James Watson:
Yeah. And so -- but he was on the committee. The only woman was -- we could think was Shirley Tilghman. And --

Bob Cook-Deegan:
So whose idea was it to have an Academy --

James Watson:
Yeah. With enough --

Bob Cook-Deegan:
-- process for this?

James Watson:
-- with enough medical people, so that we weren't -- didn't want to antagonize the human genetics community. So there were two groups. There were the sort of Boston, Baltimore -- the hard-core militia biologists who were, you know, quite happy with their current science and weren't driven by medicine. I think probably Paul and I were driven by medicine, you know, deep down. And if you wanted to do [laughs] you had -- actually, you had to do that. And so, I was -- basically organized the National Academy Committee and found the funding and was a member, but that was -- then there was a --

Bob Cook-Deegan
So that report comes out in February of 1988. And it comes out to a --
.
James Watson:
No --

Bob Cook-Deegan:
-- kind of a --

James Watson:
-- didn’t --

Bob Cook-Deegan:
-- community that's still a bit in turmoil. There's still opposition. The National Research Council has done a really good job of reframing the project to include mapping, and animals beyond the human --

James Watson:
Yeah, we --

Bob Cook-Deegan:
-- and came out with a budget.

James Watson:
-- it was pretty obvious. You're, of course, going to do the human first.

Bob Cook-Deegan:
Right. But it changed the public dialogue. It made the project seem much more sensible. But one of the looming questions is, is NIH going to lead it? Or is the Department of Energy going to lead it? And who is that going to be?

Francis Collins:
Oh, yeah.

Bob Cook-Deegan:
So enter Jim Watson at that phase. How did that process work? The Academy Report comes out at about the same time that the meeting happens in Reston.

Francis Collins:
The Reston Meeting.

James Watson:
Yeah. The Reston Meeting was important.

Francis Collins:
It was.

James Watson:
And I think that was chaired by David Baltimore.

Francis Collins:
I believe you're right. But [NIH Director James] Wyngaarden was there.

James Watson:
Yes.

Bob Cook-Deegan:
Yes.

James Watson:
And --

Bob Cook-Deegan:

And Rachel [Levinson] helped organized that.

Francis Collins
And this is when I first met Jim Watson.

James Watson:
Oh, okay.

Bob Cook-Deegan:
Was that meeting?

Francis Collins:
At the Reston Meeting.

James Watson:
I think I was really rather quiet at that meeting.

Francis Collins:
You were. But I remember, after the meeting ended, Wyngaarden pulled about four or five of us together. And I guess I was the token, sort of, junior human genetics person --

James Watson:
Yes.

Francis Collins:
-- and said, "Who could run this project for NIH?" And we all agreed there was really only one answer to that. And that was Jim Watson.

James Watson:
So, Jim [Wyngaarden] came to visit me in Cold Spring Harbor. And I didn't say "yes," but I didn't raise a lot of objection. So to the --

[laughter]

I hadn't ever -- even at the time of the Reston Meeting, I didn't think of myself as leading it. So it wasn't a hidden agenda of wanting to --

Bob Cook-Deegan:
[laughs]

James Watson:
Anyways, I think the key thing was the conversation between Jim and Bob Windham. Bob Windham was the Assistant Secretary of Health and who had been appointed by Reagan.

Francis Collins:
[affirmative]

James Watson:
but Bob, I think, just totally ignored the illegality of the fact that I was remaining in Cold Spring Harbor. And, for the national good just [laughs] appointed me, though I should have -- you know, when they fired me, they said, you know, "You were illegal. We could arrest you."

[laughter]

And that's what they actually said to me. So they -- you know, the sensitivity of government attorneys.

Bob Cook-Deegan:
So talk a little bit about that transition from Jim Wyngaarden approaching you, and then you walk in the door, you do your first public lecture to introduce yourself to the world as the director of this new Office of Human Genome Research. What's going on behind the scenes in that window between March 1988 and --

James Watson:
Not much, I think. You know, I think, you know, Jim had told me Elke would run the office. So that wasn't my decision.

Bob Cook-Deegan:
So that's Elke Jordan?

Francis Collins:
[affirmative]

James Watson:
Yes. And Mark certainly came in early.

Bob Cook-Deegan:
So that's Mark Guyer.

James Watson:
And we were over in the old library building to start with. My aim at that time was to try and get about 20 genome centers set up -- you know, sub-mapping and some sequencing. And so, we -- I think I appointed because he was a friend and Norton Zinder served as head of the advisory committee. And this way, I mean, you know, it was hard-core more like the biology. Norton knew all the people. So it wouldn't be rumors that I didn't know about but -- and then that Norton would. I think Norton we knew. Because our original operation were -- opposition were our friends. [laughs]

Bob Cook-Deegan:
So, you walk into an office that doesn't really have budget authority yet.

James Watson:
Yes.

Bob Cook Deegan:
And --

James Watson:
So, I'm an advisor for a year, and then the institute will be set up during that year. And -- but it was more or less to try and have genome money go to as many people who wanted it. And the records would say whether we gave money out to 15 or 20 people. But, you know, there was Cox and Myers in San Francisco before they moved to Stanford. And there was -- I don't know when you came in, Francis.

Francis Collins:
Right at the beginning.

James Watson:
Yeah.

Francis Collins:
One of the first centers at Michigan.

James Watson:
Yeah.

Francis Collins:
One of the first six.

James Watson:
And so, I wanted initially, you know, human genetic centers. I mean, I wanted to have the human genetics community part of the effort. I didn't want to have it as an alternative. And so, I think that worked. I don't think there was ever any opposition from the human genetics community or an outside --

Bob Cook-Deegan:
So, one thing that we haven't covered is the Office of Human Genome Research, as it's initially getting started, is a coordination office. And then, in '89, it becomes a National Center for Human Genome Research and actually can spend money and has a council. Its budget is carved out of the National Institute of General Medical Sciences, which is having its 50th anniversary this year. We haven't talked about Ruth Kirschstein.

James Watson:
She was always opposed to the project --

Bob Cook-Deegan:
And what's going on behind --

James Watson:
-- and wanted it to be controlled by General Medical Sciences. And I only remember her presence at a meeting on the Hill.

Bob Cook-Deegan:
That was our OTA meeting in August of 1987.

James Watson:
Yeah.

Bob Cook-Deegan:
Where it was about the costs of the genome. This is a meeting that Paul Berg chaired to lay out the budget for what would become the Human Genome Project budget in the chapter of the OTA report.

James Watson:
And --

Bob Cook-Deegan:
And Ruth was at that meeting. Paul was at that meeting. And John Sulston was at that meeting, among other things.

James Watson:
You know, I had -- I didn't have a personal, you know, dislike of Ruth. It was that, you know, she wanted to preserve her turf. And she had been, sort of, in charge; genetics was under General Medical Sciences. And this was creating money that she wasn't going to control.

Bob Cook-Deegan:
You know, it was partly -- I actually think probably in Ruth's case, it may have -- it was perhaps partly about turf. But I actually think it was also a philosophy of how science should be done with a very strong emphasis on it should be done by the R01 individual investigator. Let it grow up from 1,000 flowers. And here was a project that was almost being defined as being the opposite of that -- of having a goal and having a set of objectives and kind of an element of engineering and whiz-bang high-tech stuff.

James Watson:
But, you see, it seemed to me very natural because of the way the Manhattan Project had been organized. That was a big project, and it was led from the top. It wasn't a series of small efforts coalescing. It was -- it started from the top and stayed that way. And so, you know, I -- some things are big and some are small. The genome was big and it wasn't going to be done by an R01.

Eric Green:
But Ruth eventually came around.

James Watson:
Yeah.

Bob Cook-Deegan:
Yeah. Actually, very much to her credit, she talked to my students and basically said, "I'm really glad that they didn't follow my advice."

[laughter]

Francis Collins:
Yes, true.

Bob Cook-Deegan:
She was very straightforward about that.

James Watson:
So, you know, so it wasn't -- it was never a deep cancer. It never really occupied any of my time. You know, it was just -- Jim had given me the power and that was it. So --

Eric Green:
Did you have any idea how long you'd likely stay? Did you have any sort of plan?

James Watson:
No.

Eric Green:
Day at a time.

Bob Cook-Deegan:
So that -- those crises are hitting at precisely the same time as you're trying to --

James Watson:
Yes.

Bob Cook-Deegan:
-- launch a new federal initiative --

James Watson:
Yes.

Bob Cook-Deegan:
-- and fighting your political battles for control of the Human Genome Project --

James Watson:
So, I wasn't -- after Bernadine fired me in '92, in '94, I resigned as director and created a new position as president [of Cold Spring Harbor Laboratory]. And I think I had done that just from, you know, my observations of how universities function, that you need one -- you can't have someone raise money and fill buildings, et cetera, and be a scientific leader.

Bob Cook-Deegan:
So when you departed in March/April of '92, did it feel like it was the right time to go?

James Watson:
No. But I didn't miss coming down to Washington.

[laughter]

You know, my evenings when I was down here would be -- a lot of them were with Max Cowan, who was then Scientific Director of Howard Hughes [Medical Institute] or with Bob Gallo, which was fun. And Bob, you know, was in -- the big crisis of who had found HIV.

Francis Collins:
Oh, yes.

James Watson:
So -- and --

Bob Cook-Deegan:
So, Jim, can you talk a little bit -- I'm sorry --

James Watson:
You know, I think, you know -- and Cold Spring Harbor was always -- we had celebrated our 100th anniversary in 1990. And it had built a new building which -- I specially designed a, sort of, president's office, and I moved into that in '92. So I was doing something new that I hadn't done before. I mean, it was much of the same. I think one, you know, worried slightly about whether Craig Venter would be chosen by Bernadine. [laughs]

And I think I knew, you know, that there was just no future for me with Bernadine as the boss because we'd had a rather nasty argument when she was at the White House. She was for regulating plant bio-technology. And I was just totally opposed to any regulation. But I just saw her as the government wanting to regulate, even though she was, you know, Republican. And I more or less indicated, "You don't know what you're doing."

Bob Cook-Deegan:
Probably a little more than "more or less." Yeah.

[laughter]

James Watson:
So I didn't treat her with much respect. But, you know, I had gone through that period in the late '70s of recombinant DNA -- and something Bernadine was -- you know, once you -- Monsanto was beginning to, you know, really prosper in the plant part.

Bob Cook-Deegan:
So, did you ever have any thoughts that if you'd --

James Watson:
So --

Bob Cook-Deegan:
-- stuck it out for an extra six months, it would have been okay?

James Watson:
I basically insulted her when she was in the White House Science Office. Okay? And then, she's my boss. And, you know, so -- but I didn't -- you know, I wasn't neurotic about it. I didn't, you know, every day -- when am I going to be fired? In fact, it was -- totally surprised. The one thing which was -- a seedy character and Bernadine really used it as a basis of firing me was that there was an effort for Venter by a man named Frederic Bourke, who had married a Ford, and who wanted to hire John Sulston away from England and set up a lab in Seattle. And somehow, someone arranged for Bourke to come to the Banbury Center. And Bourke and Norton Zinder and I were sort of talking. And at the end, I just didn't like Bourke at all. And, you know, [unintelligible] indicated you have no role with the Genome Project, because I saw him as killing it.

Francis Collins:
[affirmative]

James Watson:
He had been supported by Lee Hood, who -- you should get a copy of the letter from Lee to Bernadine urging I be fired for not supporting industry -- biotech. So Bernadine was --

Bob Cook-Deegan:
So, this is going on at the same time as you are publicly also disagreeing about DNA patent policy and the EST [Expressed Sequence Tag] patents --

James Watson:
Yeah.

Bob Cook-Deegan:
-- that NIH had filed at the time?

James Watson:

But Lee wrote me it about Bourke. Bourke, you know, he ended up going to prison [the US Department of Justice convicted Bourke of bribing Azerbaijani officials in November 2009] as a --

Francis Collins:
Is that right?

James Watson:
Yeah. He was convicted of some financial --

Francis Collins:
Didn't do that follow-up.

James Watson:
And --

Francis Collins:
He was a very smooth character.

James Watson:
He was a smooth character. But I think I wanted him to come to Banbury to see that I also know rich people.

[laughter]

You know? You're not impressive.

Bob Cook-Deegan:
Well, that'll do it.

[laughter]

James Watson:
Yeah. I remember being in the library in the Robertson House [main building at the Banbury Center, across the harbor from Cold Spring Harbor Laboratory] when Bourke had -- and -- but anyways, that letter from Lee, which I somehow saw, was used by Bernadine when she's -- you know, there was the patent thing.

Bob Cook-Deegan:
Right. And the allegations of conflict of interest.

James Watson:
I was really, you know -- all I didn't want is patents on nonsense DNA. You know, the cDNA was --

Francis Collins:

The ESTs, yeah.

James Watson:
You know, I wasn't trying to break the patent system at that time. You know, I wasn't. You know, there -- there hadn't been Myriad [patenting of *BRCA* genes], you know --

Bob Cook-Deegan:
Right.

James Watson:
A case where I felt the public was losing.

Francis Collins:
Yeah. Took 20 more years to break the patent system.

Bob Cook-Deegan:
Yeah.

[laughter]

James Watson:
But -- so I think --

Bob Cook-Deegan:
So Jim, basically, you've done -- sorry --

James Watson:
-- that Bernadine probably -- the letter from Hood gave her the ammunition. And I don't know who told me; all I know is I met with the attorney. And then, I had to hire an attorney.

Bob Cook-Deegan:
So you go from an office -- a coordination office -- to a National Center for Human Genome Research that is funding the beginnings of the Human Genome Project, starting to get maps --

James Watson:
Yeah.

Bob Cook-Deegan:
-- genetic linkage maps. Physical mapping effort is starting. Technologies for doing sequencing faster and faster.

James Watson:
Yeah. But I was trying to run this, you know, through advisory committees because I remember meeting Venter, and going to his lab, and liking him, and encouraging him to apply for money.

He was then turned down by the committee which, I think, was in sequence -- the committee was chaired by Joe Sambrook. And the money went instead to Lee Hood. And so, Venter didn't get any money from us; it was an incentive. But I would have given him the money.

Eric Green:
Was that when Craig was here in the intramural program?

Bob Cook-Deegan:
Yes.

James Watson:
Oh, yes.

Eric Green:
Okay. So he applied as an intramural scientist for --

Bob Cook-Deegan:
So -- yeah. So what happened is they did a study section. And it was a very odd arrangement, but they did a study section that, in the morning, reviewed a whole bunch of extramural grant applications.

Francis Collins:
[affirmative]

Bob Cook-Deegan:
And in the afternoon, they did a review of the intramural proposal --

Eric Green:
Which was one proposal.

Bob Cook-Deegan:
Which was one proposal that involved Tom Caskey and Craig and Steve Warren and a bunch of other people.

Eric Green:
But Craig was the only one in the intramural program at that time?

James Watson:
Right.

Bob Cook-Deegan:
But the money was going to be channeled through --

Eric Green:
Got it. Got it. And that didn't -- that review didn't go well.

James Watson:
Actually, you see --

Bob Cook-Deegan:
Did not -- to say the least. You could talk to Tom Caskey about that.

James Watson:
Yeah. But in the --

Bob Cook-Deegan:
He still remembers that review committee.

James Watson:
All the sequencing in the Venter lab was done by Dick McCombie.

Eric Green:
Right.

James Watson:
[affirmative]

Eric Green:
I remember.

Francis Collins:
Very well.

James Watson:
And who I hired afterwards.

Eric Green:
Right. At Cold Spring Harbor.

James Watson:
And so, Craig had good people working for him. He always did.

Bob Cook-Deegan:
[affirmative] So -- what happened?

James Watson:
Yeah. Anyways --

Bob Cook-Deegan:
They didn't fund Wally Gilbert.

James Watson:

You know, I wasn't --

Bob Cook-Deegan:
They funded John Sulston and Bob Waterson to start on the nematode. And they funded Lee. They didn't fund Wally. I can't remember all the results. And they did fund Fred Blattner to do E. coli.

Francis Collins:
[laughs] Which took a very long time, as we all know.

[laughter]

Bob Cook-Deegan:
So now we have a National Center for Human Genome Research. Jim has resigned. We have an interregnum. Bernadine Healy is the Director of NIH and is in charge of a very high-profile search to find someone to take the reins of this National Center for Human Genome Research, and enter Francis Collins. So tell us a little bit about the process --

James Watson:
A second --

Bob Cook-Deegan:
Yeah, sure.

James Watson:
There was then a temporary head.

Francis Collins:
Yes. Don't forget Michael Gottesman.

James Watson:
Yes.

Bob Cook-Deegan:
Thank you for doing that. Great. So, tell us about that.

Francis Collins:
Well, Michael would say he got a call from Bernadine the same day that Jim was being asked to leave, and basically called in and said, "You will do this." There was not a, "Are you interested? Are you willing?" It was, "You will do this." And Michael, being a good scientist and somebody who I guess thought this was good for the country and good for science, didn't object and took this on, hoping that he would have a short stay in that role. But he actually had about a year.

Eric Green:
Yeah. And his role up until that time was being an intramural scientist, and at that status in the immuno laboratory chief in the Cancer Institute.

Francis Collins:
Yeah, exactly.

Eric Green:
So, it's not that he had a major NIH-wide leadership role up until that point.

Francis Collins:
But a thoughtful, dedicated, wonderful human being, so.

Bob Cook-Deegan:
With fabulous political skills and a fantastic network --

Eric Green:
Yes.

Bob Cook-Deegan:
-- and highly respected by almost everybody --

Eric Green:
Correct.

Bob Cook-Deegan:
-- which was exactly what was needed.

Eric Green:
Yes, sir.

Francis Collins:
So I had been a fan from the beginning of the importance of doing the Genome Project, but did not in any way imagine being called upon to take on this kind of role. I was at that Reston Meeting; I remember it well. I was at a meeting here at NIH where Ruth Kirschstein stood up and said that this should all be in GM -- all the things we've just been talking about. I remember Jim standing up at that meeting and saying, "Everybody I've talked to at Cold Spring Harbor is opposed to the Genome Project. But I'm for it."

[laughter]

I remember that very clearly.

James Watson:
Yeah, sure.

[laughter]

Bob Cook-Deegan:
That was actually in this building on the top floor.

Francis Collins:
It was.

Bob Cook-Deegan:
On the sixth floor.

Francis Collins:
Right. Conference Room 10, probably. So, as the project began to have real opportunities for getting going, yeah, Michigan was one of the first centers to apply and get supported. And ours was much more a medical genetics focus.

James Watson:
Wasn't Tom Caskey the second?

Francis Collins:
Tom was one of those first six as well.

Eric Green:
Washington University.

Francis Collins:
Wash U was one. Boy, who were the other three? I couldn't, at this point, tell you.

Bob Cook-Deegan:
Stanford.

Francis Collins:
Stanford.

Bob Cook-Deegan:
UCSF, that then became Stanford.

Francis Collins:
[affirmative]

Bob Cook-Deegan:
And then, David Botstein had a center. Right?

Francis Collins:
Yeah. Okay, okay. So, this was exciting trying to set this up.

Bob Cook-Deegan:
I can't remember the others.

Francis Collins:
And this was at a point where I was also the principle investigator on a gene therapy program project. So, life was pretty busy. And I was a Hughes Investigator and had a fair amount of clinical and teaching responsibilities. But I was having a great time. And I'm very much amazed at Jim's leadership in recruiting talent into this area because, I mean, Jim, well, hasn't really mentioned this, but the Genome Project never would have succeeded without his skill in convincing the best and brightest that this was a project they just didn't want to miss. They had to be part of this, and pulling people like Lander into this, who might have done something totally different, as well as many others. And that was fun to see the way in which that community began to develop.

I was also a charter member of the advisory council to NHGRI -- then called NCHGR. So, I had the chance during those first couple year --

James Watson:
Did you really know what was up?

Francis Collins:
Yeah, I knew what was up and certainly participated in a lot of those discussions. Those were fascinating times. And, by the way, there was already, at that point, even before I got here a discussion about -- well, maybe there should be something intramural that had a focus on genomics, because you could look at intramural and say, "Boy, they're good at a lot of stuff," but other than Venter and his sequencing effort, not much you'd call genomics going on there. And that doesn't seem like a good thing in the long run.

James Watson:
The strength of NIH was never genetics. It was always biochemistry.

Francis Collins:
Exactly.

James Watson:
And they were very good.

Francis Collins:
They're very good at that, but they sort of weren't ready for this next generation of ideas. But I thought, okay, this is the way it's going to be. I will hope that my genome center at Michigan can remain competitive, recognizing this is not going to be easy, because Jim made it very clear, "We're going to start funding, but we're not guaranteeing that you're going to stay in the mix for 15 years."

And then, all of the sudden, there was this earthquake. And phones rang. And people said, "Watson has resigned." And we were all in deep gloom about -- my gosh, this is like a project

that's still a baby in the crib, and suddenly, Daddy has left. And who's going to take care of the baby? And a couple weeks later, it was Rick Klausner who called me, because Bernadine -- I didn't know Bernadine, and Bernadine didn't know me. And I guess she asked Rick to make the call because Rick and I were scientific colleagues.

James Watson:
He got along very well.

Francis Collins:
They got along well. And Rick called and said, "Hey, Bernadine asked me to call you. And there's a search getting ready for this and she wants you to apply. She thinks you would be appropriate for this." And I said, "Well, gosh, that's really flattering, but that's not my life plan. So maybe you better let Bernadine know that I'm probably not going to be a candidate."

And Rick called me another time or two and said, "Well, at least put your hat in, come down, do an interview. At least find out what the job's about. Let people talk to you." So, I really went through the motions on that and showed up on a very hot day in August of 1992 to be interviewed. And I think the search committee was chaired by Shirley Tilghman. And I had not prepared anything. I just sort of walked in wearing cowboy boots and carrying my guitar, because I had just been at a folk festival and I didn't want the guitar to sit in the car because it was too hot. So, I'm sure I made a really good impression. [laughs]

Bob Cook-Deegan:
At least you weren't on your motorcycle at that point?

Francis Collins:
Walking into Building One like some country yokel. But it was an interesting conversation. And it did intrigue me that this was shaping up to be a pretty interesting opportunity. But it still didn't feel right for me. I got shown around the lab space because I was, you know, running a lab that was very productive. I didn't want to give up being an active scientist. They showed me Craig Venter's lab space [laughs] because he might be involved --

Eric Green:
New lab space.

Francis Collins:
Brand new lab space -- but it just didn't feel right at all. Government employee, really? I don't think so. So, I actually did have some discussions about is it possible to do this and keep my lab and myself in Ann Arbor? Do what Jim did and try to stay at a distance. And they would have none of that.

James Watson:
Sure.

Francis Collins:
That model was no longer acceptable.

James Watson:
And of course you never had -- it'd probably not work.

Francis Collins:
Probably. Yeah, they were right. So ultimately, I did get offered the job in probably September/October. And I said no. It was not fitting with what I thought I really could do.

James Watson:
Did your salary go up or down?

Francis Collins:
You know, I don't remember. [laughs] I may be not even have been smart enough to ask the question. I think it was fairly sort of neutral in that regard --

James Watson:
Yeah.

Francis Collins:
-- as opposed to later on when it became very negative.

[laughter]

James Watson:
And Washington then wasn't hopelessly expensive.

Francis Collins:
Not hopelessly, but --

James Watson:
It was expensive.

Francis Collins:
Compared to Ann Arbor, it certainly --

James Watsons:
Yeah, yeah.

Francis Collins:
So I was actually -- speaking of personal issues -- in the midst of going through a divorce. And my kids had just reached the point of being just about launched. My youngest daughter was a senior in high school. So maybe it was sort of a moment of thinking about being more geographically portable. But again, scientifically, I just couldn't see walking away from what I had been doing. And we were in the throes of trying to actually find the Huntington's gene, which we found a couple months after that, and trying to find the breast cancer gene, which

Mark Skolnick beat Mary-Claire and me to a few months after that. So, I was intensely involved in other things, and I said no.

And the search got started again. And there was an effort to identify the candidates. Frank Ruddle as a possible choice; Mary-Claire emerged as a possible choice. And I came back -- I think it was for a study section, and Bernadine asked to see me. And I thought, "Oh boy, here comes the hard sell." And this must have been like late -- maybe November of '92. And yeah, she brought me in. And she had Lance Liotta in the office. Lance, who was the Director of Intramural, who was making all sorts of inappropriate comments about how great it would be to be at NIH, in which I had no real interest. I was there to say no again. But Bernadine kind of took over the conversation and she got me right in this vulnerable place. And she said, "I can tell I'm not getting through to you," she said. And she was right. She said, "I had this vision, Francis, that we're both somewhere in an old-age home. And you're walking down the hall with your walker. And I'm walking down the hall towards you with my walker. And we come up next to each other. And you turn to me and you say, 'Damn it, Bernie, I should have taken that job,'" which is the dumbest thing anybody ever said to me in a serious job interview, but it totally nailed what was bugging me -- that I was about to walk away from maybe the most significant scientific opportunity anybody of this era could dream of because it didn't happen to suit my timing. And it really shook me up. I mean, isn't that stupid? That's what it took. So, I went away and thought about it. And two days later, I called her and said, "Okay, I'll do it."

Bob Cook-Deegan:
So, she did have some of Lyndon Johnson's political skills?

Francis Collins:
Something, I don't know. Or maybe I was ready to give in and I just hadn't admitted it.

James Watson:
No. She could be charming.

Francis Collins:
She could be. She could also be really --

Bob Cook-Deegan:
She was generally charming.

Francis Collins:
-- difficult.

Bob Cook-Deegan:
Brilliant, brilliant --

James Watson:
No, but she didn't charm the people at Johns Hopkins. They couldn't stand her.

Francis Collins:

Oh. And she terrified her own staff. I mean, boy, once I got here and began to see what happens when there's a meeting in Building One, everybody comes out [laughs] looking devastated, white [laughs] tearing their hair out -- what they've been asked to do. So, there it was.

Bob Cook-Deegan:
Francis, what was your -- how important was constructing intramural research program? How was that involved in these negotiations over becoming director of this then-still Center for Human Genome Research?

Francis Collins:
Yeah. Again, the council had already made a conclusion that there ought to be something going on intramurally. And I felt like -- okay, that's something I could help with, because it was clearly going to have to be built by recruitment. There was virtually nobody on the campus other than a couple of very junior people like Dave Bodine that could be recruited into this. Otherwise, I'm going to have to convince other really good scientists -- had to come and work in this environment, which meant people were skeptical about. But I thought I could do that. And I thought, in the longer term, that's a contribution I could make. But I never had any misgivings about whether that was the main job.

Francis Collins:
The main job was to get the Genome Project to succeed in that rather arbitrary 15-year timetable that Jim made up at some point along the way, because it sounded like something you could sell to the Congress. Right? I mean, where did 15 years come from anyway?

James Watson:
Generally, you don't propose anything more than 10 years.

Francis Collins:
[laughs]

James Watson:
And I knew 20 would mean the project would be finished by people who didn't start it, and that it would be -- but I just didn't see it being done in 10 years.

Francis Collins:
That was good.

James Watson:
And -- but I didn't see the machines taking over.

Francis Collins:
[affirmative]

James Watson:

So it was -- the machines made 10 years possible.

Bob Cook-Deegan:
Well, and I think there was another element to that. And that was when the NRC Committee was meeting, and David Botstein was in charge of the subcommittee that was supposed to come up with budget numbers, where they did the famous go-around-the-table-and-vote. They'd gone around the table once. And they had ranges from 50 million, 100 million, and 200 million. Jim intervenes and says, "No, I want to propose 500 million a year because if I -- if 200 is the high one, everybody's going to go for the middle."

Francis Collins:
That's a very important principle.

Bob Cook-Deegan:
Right? So the budget had come out at 200 million a year and everybody had agreed to that. Well, how do you get to 3 billion from 200 million a year?

Eric Green:
Do the math.

Bob Cook-Deegan:
Fifteen years.

Francis Collins:
[laughs]

Bob Cook-Deegan:
So, that's part of the origin of the 15 years also.

James Watson:
It was -- but there wasn't much disagreement. I think if -- it didn't put much pressure on us to start with. You know, we have 15 years.

Eric Green:
Yeah.

James Watson:
And just thank God for those machines.

[laughter]

Francis Collins:
Yeah. That came along just in time.

Bob Cook-Deegan:

So, you step in, and what are the problems that are facing you as you're taking the reins of this National Center for Human Genome Research?

Francis Collins:
Well, there were lots of them. It still seemed like this project was barely beginning to get itself organized. And, I mean, it's only three years into a 15-year effort. And frankly, most of the centers hadn't really gotten started for that first year and a half. And it was clear that there were some that were starting to catch some real momentum; and it was already clear there were some that were going to be struggling. And so, part of what I would have to do is not only give money to people, but take it away, which was not going to be that much fun.

Fortunately, at that point, a new NIH director arrived on the scene. Just six months after I arrived, Harold Varmus arrived. Harold and I, for the first six months, lived in apartments in the old nurses' dorm right here on campus, a cockroach-infested facility. But it was great because we had many evenings after struggling with how to make things work in the government, which was foreign to both of us, and neither of us had ever really run anything very big. We would meet in Harold's apartment at 10:00 p.m. over a glass of wine and try to figure out what the hell we were doing and how to make the whole thing succeed. And that was really helpful. And he was enormously supportive in lots of things.

James Watson:
So, this was in the Clinton presidency.

Francis Collins:
By this time, Clinton had been elected. And Donna Shalala was the Secretary, who was enormously encouraging to both me and to Harold. So yeah, the environment for support of science was very, very good. And that helped a lot. And I did have good fortune by recruiting, not just one at a time, but sort of a whole cohort of really excellent extramural scientists to come and start this intramural program -- people like Bob Nussbaum, Eric Green, David Ledbetter. People that I always thought, "Boy, it'd be great to work with them." And they all made the same conclusions.

James Watson:
What happened to Klausner?

Francis Collins:
That's a long story. [laughs]

Bob Cook-Deegan:
Yeah. We don't want to get into that.

James Watson:
No, I know there was a --

Bob Cook-Deegan:
But yeah, yeah, yeah, we'll take that offline afterwards.

James Watson:
He went to Harvard.

Francis Collins:
He went to the Cancer Institute. Then he went to the Gates Foundation. He is now --

Bob Cook-Deegan:
Oh, Case Foundation, and then Gates.

Francis Collins:
And then Gates. Right. I forgot about Steve Case was in there, then Gates. He is now the Chief Medical Officer for Illumina. He's out there pushing DNA sequencing.

James Watson:
Oh, boy.

Francis Collins:
[laughs]

James Watson:
So he's on top.

Francis Collins:
He's doing well. [laughs] He's doing just fine.

Bob Cook-Deegan:
So, Francis, you've been involved at this point in very high-profile gene hunts.

Francis Collins:
[affirmative]

Bob Cook-Deegan:
A couple questions for you. One is, what's the first time you ever testified in Congress?

Francis Collins:
So, it was in front of Al Gore and a Senate panel about the Genome Project, other witnesses being Jim, Nancy Wexler --

James Watson:
This was the ethics --

Francis Collins:

This was the ethics thing. And the poor guy from DOE, Benjamin Barnhart, who was basically saying DOE didn't have a plan. And that didn't turn out so well. [laughs] You remember that? And Gore was very well-primed because I think somebody had helped him think about these issues. And that was my first appearance.

James Watson:
But the DOE decided to do education --

Francis Collins:
Yes.

James Watson:
-- whereas we were going to do ethics.

Francis Collins:
Yes.

James Watson:
And I went into -- when I was appointed -- into that press conference knowing I should say something about ethics because I was afraid of being attacked this way. So, the first thing I said is, "We're going to have an ethics panel and we're going to spend 3 percent of the money," because 1 percent sounded like a token.

Francis Collins:
[laughs]

James Watson:
And then, Gore said, "You're going to spend 5 percent." I remember sitting next to Nancy when he said that.

[laughter]

Francis Collins:
Yeah. That was a moment. [laughs]

James Watson:
And -- but --

Bob Cook-Deegan:
So, Jim, just to put that in context. So, you're talking about the press conference when you were announced as the head of the Office for Human Genome Research in September of '88. Is that -- that's what you're referring to there?

James Watson:
Yes.

Bob Cook-Deegan:
Okay.

James Watson:
Yeah. And that was --

Bob Cook-Deegan:
So, that's -- in many ways, that's the origin of what became known as the Ethical, Legal, and Social Implications research program.

Eric Green:
ELSI.

Francis Collins:
That was ELSI's start right there.

James Watson:
It was basically premature. Until you had the genome, there weren't that many ethical issues.

Bob Cook-Deegan:
So, I'm conflicted on this issue. But what do you guys have to say about that?

Francis Collins:
[laughs]

Eric Green:
Yeah, I bet you are.

[laughter]

James Watson:
No, because -- and now we have real ethical issues, but we don't -- we can't solve them. You know, beginning of life and end of life issues. Should you encourage life if someone will have no future? And then, how do you define -- how do you know someone will have no future? And these sort of things, but I think there's no point discussing them because it'll get nowhere. But --

Bob Cook-Deegan:
But back to the sense of having a program in this area. It's a truly distinctive feature of -- it's been in so-called "in the DNA" of this institute, from what became an institute, from the very beginning—from the press conference where it was announced.

James Watson:
No, but I think the ethical things were largely taken over by mediocre people.

Francis Collins:

I have a slightly more positive view, although I do think there were some of the ELSI activities that had very little long-term impact on anything. Certainly the more specific policy-focused efforts, like how do we begin to think about what is appropriate to be publicly disclosed and what's not is something we're still arguing about, of course. Things about, you know, if you're going to sequence the human genome, whose DNA should it be? And is that somebody whose identity should be known? Who's going to be the reference standard? Issues such as genetic discrimination, which became a personal passion of mine, because I was really worried quite worried if we didn't deal with that that the public would stay away from involvement and utilization of all of this science. And we had to have some pretty good, serious, legal sort of deliberations about how do you solve that; which ultimately, after 12 years of struggling with the Congress, resulted in GINA being passed. And I think while the ELSI program was not the only reason that succeeded, it provided a useful, scholarly foundation upon which you can build a case.

Bob Cook-Deegan:
So, Eric, how do you think of having an ELSI program being integrated into your institute?

Eric Green:
I think it's valuable. One of the things I would immediately say is you go talk to members of the general public. You go talk to a high school class. You go talk to a PTA or any of these public outreach efforts and you explain genomics, their questions inevitably are heavily enriched to ones related to ethical and societal issues.

And so, I think it's irresponsible not to then immediately say, "It's very important that we study these things because these are clearly concerns people have." One of the surprises I would certainly say I had when I became director was when somebody came and told me that our ELSI research program is the largest program in bioethics in the world in terms of --

Francis Collins:
In the history of the world.

Eric Green:
History of the world as a block of funding, which I admit, I hadn't realized. I mean, I knew it was distinct. I knew there weren't very many of them. I just didn't know it was the largest, because I feel like everything we do as an institute is relatively small because the size of our institute -- and it's only 5 percent. And so, with that comes a lot of responsibility in terms of trying to prioritize. I -- in the time since I've been director, I've tried to broaden the discussion around the broader societal issues, not exclusively focused on ethical, legal, and social. I also think the ELSI brand has accumulated some baggage. You can hear in some of Jim's comments the kind of baggage it's accumulated. So, part of the reason I even wanted to change the focus to a broader label was also to give us more flexibility to think about what are the societal issues we should be studying in thinking about genomic advances?

James Watson:
I think now I am much more libertarian than I was when I started the ELSI program.

Francis Collins:
[laughs]

James Watson:
And just find it so arbitrary as to what answer you come to. Yeah, I prefer no regulations and no one telling you what to do or not do would be healthier than our current one, which -- I saw the ethicists as people who fundamentally hated genetics. And so, they were really trying to block us. That's what I -- but I saw no alternatives, but at least when I started to have them. But then, it was that we're dealing with problems which don't have obvious answers or -- and so --

Bob Cook-Deegan:
Just to --

James Watson:
-- we were giving money so we could have discussions, but it wasn't going to change how humans behaved.

Bob Cook-Deegan:
Well, just one very practical thing. You alluded to it in passing. Francis, you might dilate on it a little bit is, if the sequencing effort had built on the resources that were available from the one individual from chromosome 19 studies that had been selected, the world would have been a rather different place because our reference sequence would have been for a person who could have been identified. And as I understand it, the reset button was pushed at one point precisely because somebody thought, "Oh, maybe it's not such a good idea." I don't know if that somebody was you or a group.

Francis Collins:
I was part of that.

James Watson:
But I think --

Bob Cook-Deegan:
So that seems like it's a very practical thing that changes because you're thinking about these issues. It may not be the research program per se. And it's not really regulation; it's a fateful choice that you make in light of having thought about something you might not have otherwise thought of.

Eric Green:
Stimulated the dialogue.

Francis Collins:
[affirmative]

James Watson:

But I think, you know, we don't spend lot of money talking what to do about medical records and how are they secure; and we were saying genetic data are more important. I don't think they are in a practical way, as to affecting whether they should have a job or something like this.

And I don't know so far of anyone who's yet been damaged by release of genetic knowledge. I mean, you can. But it seemed to be just minor problems compared to the very major problems of genetic disease, that's all I'm trying to say. And I think -- I wouldn't recommend you guys get rid of ELSI -- you'd just get into trouble -- but I'd give the program about 0.5 percent.

Eric Green:
[laughs]

James Watson:
That is, you know, because I'd have to compare the alternatives -- which ways you would use the money.

Eric Green:
Right.

Francis Collins:
Jim, it's very interesting because right now as we're starting the BRAIN initiative -- this ambitious effort, which many people are coming to the Genome Project, because it's a 12-year program to try to understand how the circuits in the brain work -- very challenging. And we're getting a lot of pressure. Well, you need to have an ethics program because this is going to result in the opportunity to manipulate the human brain.

James Watson:
The ethics program -- you know, we're not going to understand the brain in 12 years. I just --

Francis Collins:
Well, understand -- we have to decide what we mean by "understand." I think we can understand it better than we do now.

Bob Cook-Deegan:
That's safe.

[laughter]

Francis Collins:
We better.

James Watson:
But right now, we have not solved any big problem.

Eric Green:
And we need to do that.

James Watson:
That's all.

Bob Cook-Deegan:
So Francis, back to --

James Watson:
And it's very hard.

Bob Cook-Deegan:
You walked in the door, and you're trying to get the reins in [your hands]. Maybe just walk us through: what's going on with the genetics linkage map? What's going on with the physical map? Where are you in sequencing? Give us a segue into this move from laying the foundations for the ultimate goal: the reference sequence. This is happening on your watch. And also, you go from a center to an institute. So tell us a little bit about what's going on on your watch, the structural features of your institute.

Francis Collins:
So, it's fascinating. It's a bit chaotic. It's up and down. The interactions between the centers are not always as smooth as you would like. [laughs] The genetic linkage map is coming along using micro-satellite maps, which is finally sort of really beginning to produce reasonable quantities of such markers, so that people can start to do linkage much more efficiently. The physical maps are starting to take shape as well. BACs and YACs are making it possible to do things across long distances.

Sequencing is pretty much devoted to model organisms. The *E. coli* [sequencing] effort is taking forever. Yeast coming along, but *C. elegans* is really becoming the place where you could see "this is how to organize an effective program" between Sulston and Waterston. This becomes our model of what we hope ultimately could be scaled up, but not without a lot of very hard work -- and something that, in many ways, doesn't look like it will be very scalable to a genome the size of the human.

So, I had many anxious moments in that first five years of trying to figure out "how am I going to give the speech when we basically miss our deadline and we don't have the human genome sequence at the deadline that Jim had promised?" Fortunately, I never had to give that speech. Fortunately, things really began to connect.

But I depended a lot on these various -- some small, some large -- gatherings of advisors. And we -- the fact that we did this with what sounded rather Maoist -- a series of five-year plans -- was very valuable for this program. And of course, there was one in 1990, and then there was another one in 1993, shortly after I got there. And then, there's another in 1998; so, we kept refreshing [the five-year plans]. And those plans incorporated the best ideas of 200 or 300 people in various ways, in order to be sure we were on track.

You know, it's interesting. You talked about this was a top-down project; and of course, it did have to be in a certain way. But it was also bottom-up. I mean, we basically said: here are the big goals. But then we didn't tell Bob Waterston what particular strategy he should use --

James Watson:
No.

Francis Collins:
-- to achieve those goals. And ultimately, when we got to the point of being ready to really scale up human sequencing, it was those five centers that we referred to affectionately as the G5. Starting in 1998, every Friday morning, 11:00 a.m. -- I still, Fridays at 11:00 a.m., I have this anxious moment about, "Oh my God, am I ready for the G5 call?" Because I had to set the agenda; and you never quite knew, and some of those were pretty prickly at the beginning, before we finally really all gelled the whole thing as a team. But those five were very much bottom-up making this happen.

James Watson:
When did Venter appear at Cold Spring Harbor?

Francis Collins:
May of 1998.

James Watson:
'98.

Francis Collins:
Yes. And that was a month before I got married. [laughs] Yeah. And that was quite the experience, because he was going to appear at Cold Spring Harbor the next week. And he already had talked to Nick Wade and Nick Wade already had his story ready for the Sunday *New York Times*. I was on my way to California to talk at some meeting. And I was asked to meet Venter and some surprise person in the Red Carpet Lounge at Dulles Airport. I walk in and there's Venter and there's Michael Hunkapiller.

James Watson:
Oh.

Francis Collins:
And then, I know what's going on. And so, they sort of --

Bob Cook-Deegan:
Had you gotten wind of what became Celera by then at all?

Francis Collins:
We knew something was up because Venter's TIGR genome center, which was doing chromosome 16, had suddenly -- well, not suddenly -- over the previous year sort of seemed to

have slipped into the doldrums, whereas usually he was so aggressive and driving -- and just like it was coasting. And you had to think, something's going on here. [laughs] Craig's got another plan, but we're not --

James Watson:
When was TIGR founded?

Francis Collins:
Oh, gosh, '94, '95? Somewhere --

Bob Cook-Deegan:
I don't remember.

Francis Collins:
No. Maybe in '93. It was when Craig left NIH.

Bob Cook-Deegan:
It was when he left the intramural program.

James Watson:
And when was Human Genome signed?

Francis Collins:
Same time.

Bob Cook-Deegan:
Same time.

Francis Collins:
Yeah.

James Watson:
So, basically, Human Genome Sciences funded TIGR.

Bob Cook-Deegan:
So TIGR's formed from Human Genome Sciences --

Francis Collins:
Exactly. TIGR was their, sort of, action plan.

James Watson:
And that's where, through selling it at the right time, Bill Haseltine became rich.

Francis Collins:
He did. [laughs] He did quite well for himself. [laughs]

Bob Cook-Deegan:
Yeah. So, Craig was hired to do TIGR; and then Bill Haseltine was hired to direct Human Genome Sciences.

James Watson:
Human Genome Sciences.

Bob Cook-Deegan:
Right.

James Watson:
And Human Genome Sciences, they finally did produce some drug, I think.

Francis Collins:
Yeah. A drug, Benlysta for lupus, which has been moderately successful. I don't think anybody would say it's turned into a blockbuster home run. But it's been a drug.

James Watson:
But Bill certainly left Human Genome Sciences under a cloud, per se.

Francis Collins:
I think people felt, yeah, he was --

James Watson:
Because --

Francis Collins:
-- ready to move.

James Watson:
-- his daughter had built a really very nice sculpture on protein synthesis, which was at Human Genome Sciences.

Francis Collins:
Oh.

James Watson:
And suddenly, we were offered it at Cold Spring Harbor.

Francis Collins:
And that's the one that's up there on top of this hill?

James Watson:
Yes.

Eric Green:

By Koch? --

James Watson:
Yes.

Francis Collins:
That was made my Haseltine's daughter?

James Watson:
Yes.

Francis Collins:
I did not know that.

James Watson:
It's very good.

Francis Collins:
It is very good. I look at it every time I'm near --

Bob Cook-Deegan:
I didn't know that story.

Francis Collins:
[laughs]

Francis Collins:
And of course, his brother is, like, a big fixture at Disney. Did I ever tell you the story about calling his brother? This is a good story. [laughs]

Bob Cook-Deegan:
Go for it.

Francis Collins:
When we were getting ready -- this is after the genome of the human is done, and it's time to try to finish off the mouse.

James Watson:
Yeah.

Francis Collins:
Because everybody's clamoring, "Can we get the mouse? Can we get the mouse?" And we didn't have enough money. And I was tin-cupping all the institutes asking them to donate. And they were giving little bits and pieces. And I got some money out of Perlegen because they were feeling like they needed this, too. But it still wasn't enough. So I had this great idea. Okay.

What's the most famous mouse in the world? Well, it's Mickey Mouse, of course. So, maybe Disney would like to contribute --

James Watson:
Yeah.

Francis Collins:
-- so we could hurry up and sequence the genome of Mickey Mouse. So I called Eric Haseltine, who is Bill's brother, and made the pitch.

James Watson:
Oh.

Francis Collins:
And he said, "Well, I have to think about that and talk about it to the board." And he calls me back the next day and he said, "Well, I've discussed it. But I'm sorry to say we're not going to support this. Mickey Mouse is magic. He doesn't have a genome."

[laughter]

James Watson:
Well, that's a good story.

Francis Collins:
They thought it was going to ruin their brand. You know? Mickey with DNA? No, can't do that.

[laughter]

Bob Cook-Deegan:
That is a good story. So, back to you're trying to construct this. Tell us a little bit about the shift to sequencing, the Bermuda Principles, --

Francis Collins:
Yeah.

Bob Cook-Deegan:
-- the consolidation around a model of *C. elegans* as the way to do science. Right?

Francis Collins:
Yeah.

Bob Cook-Deegan:
So, tell us a little bit about your role as the NHGRI Director.

James Watson:
Weren't there two Bermuda meetings?

Francis Collins:
Oh, there were --

Bob Cook-Deegan:
Three.

Francis Collins:
-- three. At least three.

Eric Green:
Three.

Francis Collins:
Yeah, three.

James Watson:
Oh.

Francis Collins:
But 1996, sort of the signal moment of gathering together the sequencing centers to see where are we and what path are we on? And I still have my notes from that meeting --

Bob Cook-Deegan:
Which you kindly shared with us.

Francis Collins:
That's right. You have --

Bob Cook-Deegan:
They've come into the archives.

Francis Collins:
You have seen those.

James Watson:
That's the one where we said they did ask for place in front of the public.

Francis Collins:
Exactly. And so, there was a session -- in fact, it sort of came up twice. There was an initial session that John [Sulston] and Bob [Waterston] led. And there was a general sense that "this is probably the right thing to do," but we hadn't actually reached a conclusion. And then, we came back to it. At that point, by the way, Venter had left; because he was clearly one of those who

was not particularly positive about this Bermuda Rules proposal. He left early. We came back to it at the end and everybody agreed. Although most of the people in the room had no authority to agree to this -- representing countries whose intellectual property they had just given away. [laughs] But, oh well.

James Watson:
But it had a great effect.

Francis Collins:
It had exactly the right effect. And, you know, when everybody talks about the race for the human genome between Celera and the public project, it wasn't about the technology. It wasn't about, you know, who had which machines or which software, as much as people tried to make it that. It was about what is the model? Is this a public domain deposition of our shared inheritance? Or is this a commodity? I wish they had gotten that message a little more clearly as people began to argue about which model was right, because so much of the focus missed the point.

James Watson:
I mean, it was really there when Wally was going to form his company and own the genome.

Francis Collins:
Yeah.

James Watson:
And it was certainly there when Bourke was going to form a company and own the genome.

Francis Collins:
It was. And then, it was there again when Celera was going to do the same thing. Although I think they tried to mask the intentions in a fairly clever way, so that if you weren't paying attention, you might have thought, "Oh, they are going to give it away." No. [laughs] We all knew that, didn't we?

James Watson:
They're not going to give away their founder's sequence. [laughs]

Francis Collins:
Meanwhile, in that mix -- of course, we had that very awkward moment when DOE pretty much came that close to signing a memorandum of understanding with Celera on their chromosomes; you know, that they were going to make a partnership because they felt under pressure to work with the private sector. And I think, quite naively, thought that this memorandum of understanding had no consequences for Bermuda Rules; and it clearly did. And only at the very last minute did this get realized. And I and Waterston and Lander and Michael Morgan basically said, "You can't do this." And that was a very bad, awkward moment for Ari Patrinos, for everybody else involved at DOE who thought that they were kind of trying to do something to make peace, and realized that the terms of the peace agreement were not what anybody really would have wanted to live with.

Bob Cook-Deegan:
So, this is going on at more or less the same time as you're just now an institute. So, talk a little bit about the process of going from center to institute. What does this mean? Why does it matter?

Francis Collins:
[laughs] Well, frankly, the difference in terms of the mechanisms that an institute can use, compared to a center, are pretty small differences there. So, while I made the case the we needed to be a full-fledged institute in order to have the same capabilities as all the others, it was really, I think, more about recognition that this is here to stay; that this is not something that's maybe going to just be absorbed in some other way. That this is really serious. That NIH is making a long-term commitment.

And so I pushed -- you know, when I first agreed to take the job back in 1993, I wanted NCHGR to become an institute then. And Bernadine said she would support that, but it didn't fly. It was late in the process of NIH's reauthorization, which happened in 1993. And it was already pretty much a done deal, and nobody wanted to open it up again and do something that might be controversial. And frankly, the human genetics community was not supportive of it at that point. You said human geneticists always supported the Genome Project. Not all of them did. Some of them were threatened -- thought it was going to take money away from their R01s.

But every year that this would come up again, I would make the case. And it was Donna Shalala who really got that, supported that, saw that this was something that she wanted to take a role. And she had the authority. It did not require an act of Congress to elevate us to an institute. The Secretary could do it. And she --

Bob Cook-Deegan:
So who did figure out that you had to change the acronym order?

Francis Collins:
[laughs] That was not hard. Substitute “I” instead of “C” and then try to pronounce that. You don't want to go there.

Bob Cook-Deegan:
Right.

Francis Collins:
So, we had many other --

Bob Cook-Deegan:
But somebody's awake, you know? That's good.

Francis Collins:

Many other arguments about what the alternative should be. And it's not unprecedented. I mean, NHLBI -- NEI -- there's lots -- NCI -- lots of institutes where "I" is the last letter.

Bob Cook-Deegan:
Right.

Francis Collins:
So, why not NHGRI? Took us a while to say those letters without tangling our tongues up, but--

Bob Cook-Deegan
Stumbling, right.

James Watson:
How did Santa Cruz get started?

Francis Collins:
Oh, that's a good story.

Eric Green:
Lander.

Francis Collins:
Lander recognizing that, while we were winning the battle in terms of data production, we were not getting anywhere as far as data assembly, and that the gurus that were supposed to be helping us -- many of whom were at NCBI -- were working hard, but they were not really creative about solving the problem of this large-scale assembly. So, this was an opportunity that UC-Santa Cruz was just emerging with David Haussler, who clearly had both the smarts and the drive to make that happen. And with Jim Kent, his -- you remember Jim, who's this guy with hair out to here --

James Watson:
Oh, Jim.

Francis Collins:
-- and who had basically been a video game programmer. In his garage, kind of put together the algorithms that started to make the assembly work. And now, look at UC-Santa Cruz. I mean, they are the powerhouse of large-scale representations of genomes.

James Watson:
I mean, how much money did you give to Santa Cruz?

Francis Collins:
[laughs]

Eric Green:
Oh, a lot. I don't know the exact figure, but yeah.

James Watson:
I mean, is it, you know, more than 1 million --

Eric Green:
Yes.

James Watson:
-- let's say, up to 10?

Eric Green:
Yeah, probably in that range.

James Watson:
Yeah, okay.

Eric Green:
But Lander personally got Haussler engaged, correct?

Francis Collins:
And I -- and it was at Cold Spring Harbor, Jim. It was -- must have been 1999, Cold Spring Harbor meeting in May, where Haussler came. He had not been known by most people.

James Watson:
Yes.

Francis Collins:
And Eric had brought him there. And we had this long conversation out on the lawn about what needed to be done. You were around for that, too.

Eric Green:
I think I was.

Francis Collins:
And it was pretty compelling that this was a solution to a problem that we had only fairly recently began to appreciate could have ruined the entire promise of --

James Watson:
I assumed that Lander would do it, but he couldn't.

Francis Collins:
Couldn't do it himself. Didn't have --

James Watson:
No, no, no. And he didn't have anyone else there who could do it.

Francis Collins:
[affirmative]

Bob Cook-Deegan:
And so, one other thing that you haven't touched on quite yet, Francis, is this change of politics with the emergence of Celera. We've mentioned that Celera comes on the scene in May of 1998, but that changes the politics of how you're going to go about your job in two respects. One is you have to defend your project suddenly in Congress that July. And also, you now have a common enemy that unifies your troops. Can you do -- I don't want to do too much counter-factual what would have happened but for if there'd never been a Celera. But how do you balance thinking about the presence of a private sector, basically, a private sector competitor that enters your space?

Francis Collins:
That was tumultuous, to be sure. And, of course, Venter, not lacking in confidence, was certainly making it quite clear that, from perspective of anybody willing to listen to him, the public project should probably just step back. And, as he said, "You can do mouse. We'll take care of the human."

James Watson:
Yeah, and that was a very stupid statement.

[laughter]

And it really mobilized me, I'll tell you.

[laughter]

Francis Collins:
Well, right. So, this was the famous meeting at Cold Spring Harbor shortly after that, where I remember Jim coming up to me in the cafeteria and saying, "So, are you going to be Neville Chamberlain or Winston Churchill?"

[laughter]

James Watson:
No, I guess --

Francis Collins:
It's pretty clear what you meant.

James Watson:
Yes, that we had to -- we couldn't lose.

Francis Collins:
We could not lose. Yes.

James Watson:
That's all. We could not lose.

Francis Collins:
So, there was a lot of tumult in terms of, "Okay, should we stay the exact course that we are on," which was finish as you go, build the physical maps, then sequence those BACs [Bacterial Artifical Chromosome clones of DNA inserts] as you are sure that you have them in the right order. And then you've got the assembled sequence, and you don't have to go back and fill in many gaps later because you've already done that part.

Or is it time to say, "Our sequencing capacity has now started to really increase. Machines are coming on board that have high throughput. We're having trouble keeping up with the machine capacity with the BACs that have been mapped. Should we go into a different mode?" And that's the big debate that then raged in the course of the summer and the fall of '98, at one point resulting in a very angry email from John Sulston with -- the subject line of which was, "Friendly Fire" -- where he was very upset that the U.S. seemed to be deviating from this --

James Watson:
He wanted to go into the whole genome --

Francis Collins:
Yeah, instead of starting with a random-BAC strategy, which would keep the machines busy but sort of abandoned the process that particularly Sanger had been very much devoted to and were very well-prepared to do. That was a bad moment, that big uncertainty. We fixed it pretty quickly. I think, Jim, you got involved in helping a little bit to calm down the British emotion.

James Watson:
Yeah, Sulston has -- he's like a preacher. I mean, he's really --

Francis Collins:
[laughs] He got very righteous.

James Watson:
-- almost though, you know, he may have come out of a Methodist background, but, you know, there was a certain --

Francis Collins:
He was a Baptist at heart, yeah.

[laughter]

James Watson:
I know, but you don't know what it was, but he was so clearly wrong.

Francis Collins:
Yeah, he was in that situation, I remember. But boy, he was powerfully excited.

James Watson:
He was not a mathematician. He didn't understand it.

Francis Collins:
Yeah.

James Watson:
And so, he wanted to say with something that he can control.

Francis Collins:
And he felt he put a lot -- and frankly, there was a little bit of, "Hey, we did this part already, guys. You over there in the U.S., you didn't build your maps as nicely. Don't look to us now to say you have to change strategy because you're behind your schedule." But he was wrong. He was wrong.

Bob Cook-Deegan:
So, what does it feel like to manage this kind of army in rebellion against well-greased, well-oiled, well-funded machine?

Francis Collins:
It was a wild ride. But it was great fun.

James Watson:
The White House appearance was in the last year of Clinton's term.

Francis Collins:
Yep.

James Watson:
So, it would be in 2000 --

Francis Collins:
2000 -- June 26th.

James Watson:
-- that we all went to the White House.

Francis Collins:
We all did. You know, I remember a particular meeting in Houston, sort of -- February, 1999. We had had this discussion about, "Are we going to shift more into random-BAC strategy?" And I -- on the way out there, I had been looking at all the throughput numbers from what the centers could do. And at that point, we were still saying, "We're going to finish the genome in

2003." And looking at the way in which machine outputs had been going up like this and what you could do if you decided to really pull out all the stops, it looked to me like we could get it done in the spring of 2000. And I hadn't talked to Elke. And I hadn't talked to Mark. I just decided, "Okay, let's lay it out there."

And so, at the beginning of that meeting of the PIs, I basically laid it out. I still have the overhead -- because, of course, we used overheads in those days -- that went through the tabulation of how that could be possible. And there was a furious discussion at that point because the Genome Center Directors were really tired of having the plan changed almost every couple of months. Just when they thought they had their teams organized -- "We're going to do this" -- and now, all of the sudden, Collins is saying, "No, we're going to do that."

But ultimately, by the end of that two-day meeting, people said, "Okay. Let's pull out all the stops. Let's go." And it didn't hurt that Celera was, you know, breathing down our necks. This was, by now, February, '99. Craig was making all sorts of noises about how much he has done. And, of course, nobody could tell because none of the data was public, but it made you nervous. So February '99, it was just then 16 months later the draft was announced as being done. So, most of the genome got sequenced in that last 16 months. We were only 10 percent done in February of '99. Then, we had our Billion Base Pair Bash in November.

James Watson:
No, it was, you know, the -- the only thing that mattered were the machine progress then.

Francis Collins:
That's what made it possible. We had to do 1,000 base pairs a second, seven days a week, 24 hours a day, to get this done.

James Watson:
Yeah.

Francis Collins:
One thousand base pairs a second was so far out of range of the previous version of the machines.

James Watson:
Yeah, sure.

Francis Collins:
But this made it all possible.

Bob Cook-Deegan:
So Francis, to your knowledge, has an NIH institute director ever stood beside the President of the United States with a press conference that's going on in Downing Street and at the U.S. White House simultaneously?

Francis Collins:

Probably not. Probably not.

Bob Cook-Deegan:
So, tell us a little bit about that moment -- what that felt like.

Francis Collins:
Well, it was --

Bob Cook-Deegan:
What's going on up to that?

Francis Collins:
It was a little odd. I mean, of course, only a month before that was there an agreement about how to do this announcement so that there wasn't going to be competing claims from the public project and Celera about who had done it. I mean, it was pretty clear that they were moving along. Of course, they were using all of our data, plus adding their own data to it. So, if we had A, and they had generated B, they really had A plus B, so how could they be behind, right? And it was pretty clear by about that time, we would all be able to say, "We have 90 percent of the information. So, let's call that a draft."

But it was getting really nasty. There was all kinds of claims and counter-claims. And I will say, after one of those really difficult times, I went to Ruth Kirschstein, who at that point was [Acting NIH Director] -- because Harold had stepped down -- and said, "You know, Ruth, I think I want to try to broker a peace, but I can't do it myself. I just want you to know, I am going to ask Ari [spelled phonetically] to help with this," because Ari had said all along, "Hey, if you need a peacemaker, maybe I can be it."

James Watson:
You mean -- and that led to the White House meeting.

Francis Collins:
That did. So, Ari convened Craig and me in his basement over pizza and beer. And I felt very awkward about that because nobody knew that was happening, including my British colleagues. And I sort of felt like I'm negotiating for people without their knowledge. But it just seemed like we had to come up with something that got away from all the tawdry accusations about who was telling the truth.

Eric Green:
Did institute staff know at the time? Your senior institute staff?

Francis Collins:
No.

Eric Green:
It was just you alone.

Francis Collins:
The first meeting, I told them. And then, we met again the second time. And basically -- and to Craig's credit, he agreed that this was the best outcome as well. And I'm sure he didn't mind the idea of standing next to the President either. And so, then, there was this furious arrangement about the timing and when was the President going to be in town. And then, ultimately, there on June 26th, we all arrived.

And so, we all arrived in the Blue Room and stood around waiting. And the President shows up with his Diet Coke. And we've all gotten our instructions about who's supposed to stand where and how you're supposed to walk down the carpet to the East Room. And I did have an embarrassing moment there -- one of many in my career -- where the guy who was doing the stage managing said, "Now, you're going to walk on the left-hand of the President and Venter's going to walk on the right-hand." And we're in the Blue Room, so we have to walk out into the hallway. And I'm thinking, "Well, if I'm on the left, that means I need to be here. And the President will be next to me, so I better kind of go out there first." And they start playing "Hail to the Chief." So, I head out onto the red carpet. And Bill Clinton's arm is on my shoulder. And he's saying, "No, no, I go first."

[laughter]

Oops.

Bob Cook-Deegan:
He had a point.

[laughter]

Francis Collins:
I'm just trying to follow the directions. So, you know, as Sulston said in his book, "We were all phonies that day," because we didn't have a publication. We didn't have the usual scientific standard for having something that you could really look at and say, "Wow, look at this." That came, of course, in February of the next year. But it was the right thing to do, to get the word out there. And, my gosh, the way in which that electrified public imagination was far beyond anything I would have guessed.

Eric Green:
It also changed the topic.

Francis Collins:
Changed the topic. We're not doing a race anymore.

Eric Green:
Right, right.

Francis Collins:

Now we're going to figure out, what do we do with this information? We crossed a threshold into a really exciting place.

Bob Cook-Deegan:
So Francis, one of the other things -- so, you're finished -- in a way, you're not really finished, but you are -- have a lot of momentum to finish in 2000 -- two years later. And you celebrated that moment on April 14th of 2003.

Francis Collins:
Which happened to be my birthday, yeah [laughs]. But that was a pure coincidence. And of course, the other wonderful thing about April 2003 was this 50th Anniversary of the double helix. I mean, talk about having something in perfect poetic alignment to have those things spanning by exactly 50 years to the months just seemed --

James Watson:
No, that was --

Francis Collins:
-- ideal.

James Watson:
That was nice.

Francis Collins:
That was really nice.

Eric Green:
So, Bob, your question about sort of what's next, I think Francis mentioned two critical things that happened in April, 2003: completion of the Human Genome Project, celebration of the 50th Anniversary discovery of the double helical structure of DNA. But there was a third thing that happened on that day for the Institute, and that was publication of a new strategic plan, which followed in the footsteps of what Francis talked about earlier, this culture of always renewing your vision.

Bob Cook-Deegan:
Yeah.

Eric Green:
So, I think Francis should say some things about what led up to the end of the Genome Project. It wasn't as if we weren't thinking about what's next, because he had put in place a planning process that led to that 2003 strategic plan.

Francis Collins:
And that was a vigorous process, to be sure, extending over about 18 months. I think we had two major meetings, nine topic-specific workshops, input from all kinds of people with bright ideas,

and ultimately resulting in this piece in *Nature* that laid out what we hoped we could do in the next five years, pretty much all of which we did. And of course, a lot of that was, "Okay, let's learn about variation." So, HapMap, which I think became a very important next-step contribution which has opened up all kinds of windows into understanding genetics of common disease. Projects like ENCODE [the ENCyclopedia Of DNA Elements project].

James Watson:
They gave us GWAS.

Francis Collins:
Gave us GWAS, which has been, I think, actually undervalued for what it has told us about mechanism, but overvalued in terms of what it's told us about predictions because the things we have found have relatively weak contributions as far as risks. Things like ENCODE really -- an organized effort to bring together dozens of laboratories to understand what are the -- you know, what's the parts list of the genome and what do those parts do? How does the function work?

Eric Green:
And technology investment.

Francis Collins:
And technology investment, in a big way. And lots of other things. The Knockout Mouse Project to try to systematically --

James Watson:
Can you really compete with private investors?

Francis Collins:
In technology development?

James Watson:
Yeah.

Francis Collins:
You know, not at the sort of end point of getting something hardened and out there. But boy, at the front end of coming up with a new idea -- I mean, if you look at sequencing technology. The stuff that Jeff Schloss has made possible is one of the reasons why we have almost a $1,000 genome, because of all those academics and small companies that were boosted by NHGRI's support to take a risk they would otherwise not have taken.

Bob Cook-Deegan:
Well, so, just to --

James Watson:
I think that's worthwhile --

Francis Collins:

I think it is.

James Watson:
-- recording as a serious document.

Francis Collins:
It is really There was a nice *Nature* --

Eric Green:
Beautiful article in *Nature* this year that had a wonderful shout out about the Institute, saying that a major part of the credit for the rapid decline in DNA sequencing costs go to the grants program out of NHGRI.

Francis Collins:
Yeah, and documenting the reasons why they said that.

Eric Green:
Right.

Francis Collins:
Yeah.

Eric Green:
Yeah, so --

James Watson:
Even if it's been done already.

Eric Green:
Well, it's been done in a sort of a news article. We're in the process --

James Watson:
Yeah, that's not sufficient.

Eric Green:
No. Within the Institute, there is an effort to document exactly how it is that our grants program has led --

James Watson:
[unintelligible]

Eric Green:
One of the scholarly --

James Watson:
I think -- because Congress will be inherently against the idea of wanting it private.

Francis Collins:
Yeah, yeah.

James Watson:
And so, I'm just curious --

Francis Collins:
Yeah.

James Watson:
-- what the truth is.

Bob Cook-Deegan::
So, I was going to double click on that. Do you think that pyrosequencing or pH-sequencing or nanopore sequencing would have happened but for having an NHGRI program?

Francis Collins:
Maybe eventually, but not at this pace. We would have lost many years if it weren't for that source of support to have people pursue those ideas on a shoestring when they weren't at all sure they were going to work. And they would have had a hard time getting funds on this.

James Watson:
Where did Illumina's ideas come from? They were Solex… --

Eric Green:
The original Solexa, they came out of, I think, private money. But if you actually look at the current machines that Illumina sells, there's a number of technologies that were acquired and cobbled together to help refine the original technologies. So, I think NHGRI fingerprints are on the -- can be found in places on the current instrumentation.

James Watson:
Oh, I see.

Francis Collins:
Yeah, yeah. It's true.

Bob Cook-Deegan:
So, back to 2003, you've fulfilled your goal.

Francis Collins:
So, we have this grant and the next vision.

Bob Cook-Deegan:
You got a new plan.

Francis Collins:
And this means, then, setting up in a similar fashion, perhaps, to the Genome Project teams that can accomplish these next round of goals that are sort of big science and that are somewhat top-down, but you're encouraging all of the participants to come at this in the most creative way and invent new ideas and technologies as they go.

And it's wonderful to watch that emerge, whether it's ENCODE or the HapMap Project or Knockout Mice for every single genetic locus. All of those assemble together with some support and begin to go and take a lot of my time. And so, I've found the time I spent between 2003 and 2008 was not that different than what I had spent in the previous five years. A lot of it was being sort of a project manager for very large projects with excellent staff. And so much credit should be given to people like Mark Guyer and Jane Peterson and Jeff Schloss and Elaine --

James Watson:
Is Jane still --

Francis Collins:
Jane is now running the Keystone Meetings.

James Watson:
Keystone?

Eric Green:
She's Scientific Officer for the Keystone Symposium.

James Watson:
Okay.

Francis Collins:
Yeah. Just moved there a couple months ago.

James Watson:
How old is she, 65?

Francis Collins:
Great team to work with.

Eric Green:
Something like that.

Francis Collins:
Yeah, ballpark.

James Watson:
Oh, maybe more?

Eric Green:
No, not more. I don't think that was more.

Francis Collins:
So, that was great fun. But after a while, I kind of felt like, "I've done this. I've been doing this for 15 years. It's time to think about doing something else." But I didn't know what it was going to be. So, hence, May 2008, decided, "Okay, guys, three months more and I'm going to step away into the white space. And I don't know what that's going to look like. I want to write a book about personalized medicine. And I can't do that as a federal employee, at least not if I want to ever get a dime of royalties out of it because that would be a conflict of interest. So, if I want to write a book, I've got to quit my job." And I really wanted to write the book on how it's done.

Bob Cook-Deegan:
So, did the rules change between book one and book two?

Francis Collins:
Well see, book one was not about personalized medicine. Book one was about science in faith, which was not considered to be part of my official duties. So, I could write that book without it being a conflict.

James Watson:
Do you define personalized medicine as starting with your genome?

Francis Collins:
It's in there, but it's not all that's in there. It's genome, it's your environmental exposures, it's your lifestyle. It's the whole package.

James Watson:
Yeah. But the genome gives a reference.

Francis Collins:
A very critical one. Probably the most fundamental reference that I can imagine. Yeah, that's what --

James Watson:
But this is why I think -- I'll just argue. You got to get more genetics in the medical schools and not just in terms of research projects but real practical as part of medical practice.

Francis Collins:
[affirmative] I'm with you.

James Watson:
And --

Bob Cook-Deegan::

Well, so maybe both of you could actually comment on that, because you – you were at UNC and Michigan for part of your training. Eric, you're at one of the places that's one of the ground points of ground zero for medical genetics [Washington University in Saint Louis], and certainly the medical technologies in your career. So, maybe you guys could talk a little bit about medical education and what was unusual about your backgrounds that suited you to your later career compared to what you would have gotten if you'd been at other places.

Francis Collins:
Well, I think Eric and I probably caught the fever early of seeing how this fundamental science of genetics was the way that you were going to really understand answers to all these mysteries about disease. And how could you not get compelled by that? But most people don't catch that fever, and they get channeled into other more traditional ways of approaching medicine, or at least ways that are not tapping into this.

And medical education is pathetically slow in changing curricula and emphasis. And it's very frustrating. You know, back -- what? -- 15 years ago, I helped form this thing called the National Coalition for Health Professional Education in Genetics, NCHPEG. We were going to solve this problem, because it was so compelling and so much need was out there. And we couldn't get traction with any of the major physician societies. They just didn't see that this majored up on their list of things they needed to know more about. And that's still where we are. It's very troubling.

Eric Green:
I mean, these challenges, really are -- around genomics, are quite new. I mean, the story I like to tell is I graduated medical school and graduate school with my M.D.-PhD in 1987. And 1987 was when the editorial came out in the inaugural issue of the journal *Genomics* that told the story about how genomics, the word, was actually sort of created. And that was 1987. I mean, that's why when I think back on my medical school and graduate school, I never heard the word genomics once, nor should I, because it didn't really get put into existence until 1987.

So yeah, when I think back on what I learned in medical school was like a two-week elective in medical genetics. I mean, it was so minimal. Fast forward to today, and there are some examples of some medical schools that have infused more genomics and genetics in the curriculum. But there's just a few examples. And it's not nearly the extent that I think is needed.

Francis Collins:
What is needed is for genomics to emerge as being a central part of the need that a physician must have in order to take care of a patient. And I think most physicians aren't aware that that need has arisen yet, but it's really happening, particularly in the field of cancer. They're not going to be able to stay away from this space for much longer.

And then, there will be a deluge of requests for, "How do we learn about this?" and "Give me some decision tools," and everything that the average physician needs to become a genomic medicine practitioner. But until that sort of critical moment arises, people are too busy to spend their time learning something that they're not convinced is going to help them with the patient they're seeing right now.

Bob Cook-Deegan:
So, if I'm sensing a theme here, there may be a theme of "build it and they will come." And sensing where the puck is moving technologically, scientifically -- and is this a characterization of your jobs as the head of this part of NIH that one of the distinctive themes is you do things big and you do things that are technology-intensive and data-intensive --

Eric Green:
And heavily managed. Heavily managed.

Bob Cook-Deegan:
-- and tailor a fair amount of central management relative to most other --

Eric Green:
Right.

James Watson:
I'm thinking you got to, though, just get into the medical curriculum and practice more. And I think you only do it by offering them sort of $5 million each and they'll do it.

Francis Collins:
So, talk about your Mendelian Centers because that's kind of the model.

Eric Green:
As part of an example, that would be in the discovery. We have a program now to focus on the remaining 2,000 to 4,000 rare disorders where are thought a single gene is involved. And we have set up a series of centers -- three of them -- to focus on really industrializing the process of going from a remaining example of a disease for which we don't yet know the genomic basis to getting and sequencing patients, analyze the data, and quickly getting the information out.

That's more on the discovery side. I think on the more applied side, which I think is also what Jim is implying, we have set up also a series of exploratory centers to look at what is it like to take genome sequencing out for a test drive out in the public.

Francis Collins:
So, Congress -- you know, I spend a lot of time now as the NIH Director talking to Congress. In fact, I'm going to have to go in about five minutes to go downtown and talk to Congress. I've met probably 300 members of the current Congress in the current term one-on-one just to talk about medical research and the exciting ways that that's changing things.

James Watson:
Yeah.

Eric Green:
Oh, do you want to --

James Watson:
I think we're -- we've done our job.

Francis Collins:
[laughs] Jim is declaring --

Bob Cook-Deegan:
Yeah, yeah.

James Watson:
No, I'm not speaking to the public. I'm just giving my own -- because I was the big fighter of comprehensive cancer centers. That's why Ben [unintelligible] fired me in '74.

[laughter]

I said we didn't know enough to actually deliver any medicine on the basis. But I think we are reaching the point where we really can deliver something to the public. That's all.

Francis Collins:
And ironically, a lot of it's in cancer now, too, Jim, because that's maybe the place where we are most actionable. I mean, if I had cancer today, you think I don't want to get my tumor genome sequenced? Yeah, it's darn sure I do.

Francis Collins:
You know, I think medical research, whether it's genomics, whether it's heart disease research, whether it's Alzheimer's, is an incredibly compelling story. And it doesn't matter whether you're a Republican or a Democrat or a Libertarian or whatever, this is something that you have to care about. And so, I have no problems, I think, when I meet with a member, convincing them that this is one of the most critical things that a government can do is to support research. And it's not something that just the private sector alone can do. They get that, that this is an ecosystem where you need the basic and you need applied and you need all these partners to work together.

So, I don't have a problem convincing congressional leaders about the value. The problem right now is that we're at this gridlock of making any decisions about what's in the discretionary budget, which happens to include NIH and everything we're talking about. And until that gridlock gets resolved, we're stuck as an innocent bystander with gradual erosion of all of the capabilities that were built up over the doubling, and which are now many of them been lost over the last 12 years now, with more than 20 percent of our purchasing power going away. I don't think we lack for congressional enthusiasm; we just lack for congressional fiscal decision making.

Bob Cook-Deegan:
So, one other counterfactual that I just wanted to ask about is if -- I mean, so, the Human Genome Project got launched at a time when budgets were incrementally increasing, year by year. And would it even happen in the current environment? If the idea of the Human Genome Project came along in 2014, would something similar --

Francis Collins:
It would be a hard sell because of the fact that budgets everywhere are either frozen or going down, and argue for something new -- we're trying to do that with the BRAIN initiative. I don't know how it's going to go. I think it's a compelling scientific opportunity. But will it be possible in the face of declining support for everything in medical research because of this gridlock, I don't know.