

GENOME INTERVIEW TRANSCRIPTION: James Watson, 10/1/1990

SUBJECT: James Watson, October 1, 1990 at Hilton Head

INTERVIEWER: Robert Cook-Deegan

TAPE NOTES: Interview begins at start of tape side A.
Interview stops at about 2/3 through tape side A, and resumes 1/3 through tape side B.
Interview ends approx. 3/4 through tape side B.

MISC NOTES: Proper names, acronyms, and uncertain phrases are in parentheses, ending with a question mark.

Note to editor: numerous grammatical shifts and non sequiturs are included below. They are an accurate representation of the verbal interview.

*** START OF INTERVIEW

COOK-DEEGAN: OK, this is Hilton Head, the Hyatt Regency at Hilton Head, an interview with James Watson, director of the National Center for Human Genome Research, and it is October 1, 1990. Jim, we're doing this series of tapes, and I wanted to get a kind of global historical view from your perspective on the development of the genome project. I thought a good way to start doing that is to get your sense of what's the definition of the genome project, and how has that changed over 1985 to 1990.

WATSON: Well, I think the definitions always really stay pretty much the same, we're going to work out the DNA sequence. That was certainly the way.. I think I read my first presentation, I phoned Dulbecco in September of '85.. we should work out the.. and..

It was really at that time.. as stated.. it was sort of a.. the ultimate objective wasn't linked to medicine the way it is now, I think. It was just, "the time has come, let's just do it, and it will have medical implications", but I think it was probably.. I can't be sure, but I remember it as just.. we were going to sequence, and that was the word, whereas today we say "map". And we'll sequence what we can sequence.

COOK-DEEGAN: Was that your first contact with the genome project, was his presentation? That was the thing that ultimately resulted in his editorial, is that right?

WATSON: In Science, of 4 months later. He came to dedicate the center, and gave this speech, and at the time I wasn't very interested, I think because it didn't seem that real, it seemed too much to take on. And if you think back in '85, was before (PCR?), so it's certainly much easier now to imagine getting it accomplished in a decent way. And then the second time, then I was aware of (DeLici's?) meeting in..

COOK-DEEGAN: Santa Fe..

WATSON: Santa Fe, and then afterwards it was the Cold Spring Harbor meeting. Really it was DNA..

COOK-DEEGAN: The "Molecular Biology in Homo Sapiens" meeting?..

WATSON: No, it was before, it was the small (Banberg? Banbury?) meeting, and someone from Los Alamos came. It could have been (Greg? Gregg?), but more or less said, "DOE's good to do it", and I said, "well why DOE", it's intimately connected to NIH, and NIH had more expertise capable of actually supervising it and providing the structure. And, I don't remember whether I called Paul Berg or he called me, it was my impression that he called me, but I can't.. about having a session at the symposium.. meeting.

And then it was very much in the air, after the Santa Fe meeting, and it was seemingly going to be announced as a big DOE objective. And after Cold Spring Harbor there was first (Frederickson's?) meeting, and then the Woods Hole meeting, because I'm not sure who's idea it was to have the Committee on Life Sciences have the meeting, it wasn't mine, I know that. But I was invited, and I think it was at that Woods Hole meeting, that.. it seemed desirable to give the National Academy, actually, the report.

I forget who I was talking to, (Michael Rotunski? Watunski?) who was with the (McDonald?)

foundation, he was very interested in the human genome discussion, and had told me that the (McDonald?) foundation was interested in supporting at least these discussions. I raised the possibility of funds for that National Academy which would come from (McDonald?), I think that was the origin of how..

And I forget the, really the origin, (John Burris?) would probably know better, of how (Bruce?) was chosen as chairman of that committee, and its composition.

COOK-DEEGAN: As I recall, you gave a talk at the Howard Hughes Medical Institute meeting, where you said something about, "I'm in favor of the genome project 'til everyone else at Cold Spring Harbor's against it..

WATSON: Yes, I think I certainly would have said that. And I was certainly in favor of it, I guess once I began to think about it, and my chief fear was that.. that summer I went and talked to Charles DeLisi at DOE, and he was just a name, and I liked him, but I was left more worried than ever about DOE running it, because he was just so ignorant, really, of the issues, in terms of the technical difficulties, he was so proud that Los Alamos was going to get this rapid sequencing, and didn't I think realize the.. why the average person would think that's a far-out possibility that you (would ever pull about?).

And so the assignment of budget was worrisome, and when I first met David Smith he never said anything, but he seemed to be.. I think we gave him more power than he had.

And there was also the statement that bothered us, that DOE wasn't interested in model organisms, was only interested in naming the genome. That struck me as just from a scientific approach, was very short-sighted. Not only would it antagonize everyone else, but you might be taking on too much, and it would be better to, very very early on, get a program to do e. coli.

And.. I think it was probably at the Cold Spring Harbor meeting that I first heard Wally's idea of how it should be done, in one place. I think.. we were all worried about that concept, it was too soon to give anyone that amount of power, and it wasn't clear that he would have to have those sort of DNA (city?). I think that image struck me as a hard one to sell to anyone, and wouldn't work.

But even if .. if it turned out to be right, you wouldn't have to move in that direction for at least five years before you had some experience in sequencing DNA, whether there was a learning curve.. who should do it, whether it should be done by - (Bud Armson?) now uses the term "mercenaries" - or should be done by people who care about the sequences, and want to interpret them, or someone who just wants to do it correctly, and hand them off to someone else to interpret.

COOK-DEEGAN: You've talked a little bit about DOE policies and what you were worried about. What was your sense of what NIH was up to in those days?

WATSON: I guess I was horrified by that statement that came out that they were spending 300 million dollars, and effectively none was being spent. I was aware of the history of how that grant had been turned down, the Small Business grant, (collaborative?); and how that eventually led the collaborative putting all the money in a strictly.. I dislike the idea of collaborative controlling the tests, I just thought those reagents should be available, but one the other hand I was sympathetic that collaborative put the money in, it was just too bad that the public money hadn't gone in to ensure that this was in the public domain. It seemed to me quite important to get the concept through that the government was going to pay for the whole thing..

I thought it would be inevitable that other countries would join industry because I found the project so inherently scientifically exciting that I couldn't imagine that someone would let the Americans work out all the details of all the human chromosomes, when you got down to it. And that wasn't just solely because of possible patent, it just seemed to me scientifically, and that..

COOK-DEEGAN: Elaborate on that for a second, if you can kind of reconstruct, what was it that as you thought more about it, changed you from being an early skeptic to being..

WATSON: Well, I guess it was.. I just like to see the instruction book for a cell. So coli was to me certainly an achievable objective, that might come faster with the human program, in other words you would.. that developmental biology was moving so fast, even the developmental biologists felt that they didn't need the total set of instructions, that by the time we could get the instructions, they would probably want them.

So at the level of (c. elgin?) or drosophila the project is just actually coming at the right time scientifically, it's not coming too soon, that you get all this data that won't

be used, in fact I think it will let developmental biology move much faster because you will see all these components and know the actors in the whole thing.

I guess from my point of view I've always been a reductionist, it's the sort of ultimate reductionist, that if you knew the sequence, you would, at the level of e. coli essentially, know what's up. Major problems like how the brain functions, might just demand the prior acquisition of developmental biology. Having certainly the programs for the simpler organisms has drastically changed the way we thought about the human development.

So, well, someone could argue "well you're starting too soon", certainly.. but not in any sense five years too soon or ten years too soon. I think with.. initially my interests were, I saw it as simply a marvelous scientific objective. And now that I'm the.. connected to the government and connected to raising it, I see that in trying to raise money for.. the practical consequences of it are why we would get the money, not the sort of view that this time in science has come, that that was unlikely to get a responsive chord right now in money situations sometimes, it could sell it on his vision as the ultimate instruction books, but more on a necessary tool in understanding diseases that we might not be able to understand, so..

So, I guess I become more practical every year.

COOK-DEEGAN: What was your sense about why it happened in 19.. when Dulbecco more or less independently of Sinsheimer more or less independently of DeLisi.. given some vaguely similar ideas..

WATSON: I had written a manual report before this, in either '83 or '84, about the (gos prodis?) sequencing. I should go back, but it was before the discussion, and I was putting that up as, this was the reality, that there was no conceptual reason why it couldn't be done, we were moving to bigger viruses, and we were going to move to the point of the other, so..

I think there were maybe a couple of things which certainly created.. one was that, even if you'd done it in 1980, is that the computers were really coming in, into biology by 1980 in a big way. In '70 they weren't there. And, so one never really thought of the computers as a limiting factor, which might have before, I mean the computers were, their power was, each year they were getting cheaper, and the whole thing was getting better. It was clear that you couldn't handle this amount of information without it. So I think a reasonable is just the.. you know, enough is, the first sequences were in, people were storing them, comparisons were.. I don't know when "gen banks" started.

COOK-DEEGAN: 80.. early 80's, '81 maybe.

WATSON: Something like that, and.. I think if you just talked in terms of big biological objectives, it was really a reality. In my.. I discussed (a cross-gene?) sequencing, and recombinant DNA short course, and I say it's 5 or 10 hours a base pair. So I'm thinking in terms of how much it would cost, the money was.. you didn't think of money when you did the (SG40?) with five thousand, once you began to think in terms of bigger objectives, you had to think, well that is going to cost money, and at a certain point you clearly had to have a big program, it wasn't going to occur spontaneously. The inevitability of..

COOK-DEEGAN: What was your sense of what the major steps were, you talked about the creation of the NRC panel, what do you see as the major steps in launching the project?

WATSON: I think the National Academy report, and the visit of David (Waldermower?) and I to Congress in the spring of '87. I think that was probably the crucial, because that got this 18 million dollars into the budget, and with that money into the budget, then Jim could do something without diverting it away from general medical sciences. I think the amount that was put in was small enough to be a true add-on, for starting something. So, I think that was a crucial event.

It was about the same time that Bruce must have sent out the first RFA, some request for genome applications, so, and there was the (OP?) meeting when costs were discussed, and I guess that was August. (Paul Berg?) was there..

COOK-DEEGAN: June or August? Can't remember the date..

WATSON: Or July, but I think it was after the (Frederickson?) thing. I remember that Bruce was there. By that time the National Academy had begun its deliberations, and we were talking about a program led by the scientific community as distinct from led by the bureaucracy. I remember disagreeing with Bruce quite clearly on this matter, that there

had to be, because we were using this sort of (cyclotron?) and knowledge, because it was a big program, and had to be.. an active rather than a passive program, where we were responding to just the grants, you have to have your objectives and get it done.

And.. I certainly never thought of myself running it, and I think an obvious reason was the problems we were having with our son, which were enormously emotionally draining, and I was hardly able to function as director of the lab, so the thought of actually having.. because (Rufus?) had run away during the '86 symposium and we didn't know where he was, and it was, that symposium was pretty scary, I didn't go to most of it, because then, we found him. But that was.. certainly dominating our existence..

So it wasn't in fact until the actual Reston meeting, at the end of it Jim took some people aside and said "well who should run it", I think my name came up, certainly I was aware that there were some people, but until that meeting.. I thought that meeting was very important, I thought David (Baltimore?) did an extremely good job in running it, came off with the right sort of.. he ran it the way I could have never run it, I mean he really knows how to run a meeting pretty effectively.

So, I think it was the decision Jim (Weingarden?) made in making the Reston meeting going. I'd had one meeting with them with Brady, which I guess I was pushing it, but I'm not sure he hadn't already called the Reston meeting.. more or less in despair, get a real program going, we'll have no choice than to throw our support behind DOE, because we really want the program. And having the program was more important than giving to an NIH which didn't want it.

COOK-DEEGAN: You were here talking about the NRC deliberations toward the end there..

WATSON: They were really finished, I mean the report came out, it wasn't released until about April, but I think there were sort of versions of that report..

COOK-DEEGAN: Actually it was released in February..

WATSON: It was released in February, but there were versions of the report floating around, probably by November, because I know Bruce worked on it, the conclusions, it was effectively done by the end of the summer I think.

And.. if you see the committee itself.. it was probably (Dan Nathan's?) in his quiet way for it, and (Bob Steen? Bokstein?) obviously coming out for it, because he saw it was the way to get the genetic markers, I mean he was interested in the mapping. And the mapping was not as far collaborative.. one could see it as a.. there was certainly a lot of suspicion about whether the worldwide approach was available, trying to open up the human genetics to a larger number of people.

COOK-DEEGAN: What was the, what's your recollection about the final deliberations about that NRC recommendation about who should run it and all that, that's what I was actually alluding to..

WATSON: Well there were.. I think there wasn't much argument that it should be run by a scientist. There was more discussion about whether there should be a lead agency, I think those were the things which.. I forget how it came out, I think we more or less said we preferred NIH, but we didn't, it didn't come out I think as a very anti-DOE report, it was more or less a report for the program, and made some suggestions. I think we were more worried that it would be led by the bureaucracy, that was our fear that..

COOK-DEEGAN: What, on the NRC committee, what was your sense of, you said that for David it was kind of the genetics, the genetic markers that might have..

WATSON: Genetic markers and model organisms. Certainly the model organisms I think Bruce felt strongly, you can just ask him.. It was the genetic markers. Another decisive thing was Maynard coming and talking about (yaks? Y.A.K.S.?) (Yaks?) made the physical mapping seem, because.. whether the (constructs? cause models?) were really going to give you enough continuity to give you the physical maps, and..

There was talk about pulse-field maps, but except for Charlie, I think most people realized that was not going to be a winner. You had to get the DNA in your hand, in some clonable form, and I think it was the (yaks?) was a psychological thing, we weren't proposing something that could fail, I think that was the.. It wasn't the.. I think any discussion was to whether.. I think there were some unrealistic statements about the costs of sequencing given by Lee, or (Wall?) who said we could do it for a penny a base pair, but that didn't include the whole package, and we were certainly never governed by it.

I think we had (Elson Chen?) he came, and from him I think was.. and then.. it was about

only the cost of sequencing. I don't think, I think it was after the report was out, I think (Mark Garr? Mike Garr?) went and saw (Bart Burrell?) and tried to get from him how many people were actually used in a sequencing project and give it back that way to the clients. But I think we knew it hadn't improved very much and was in the five to ten dollars, but a ten-fold improvement in cost struck me as not very far-fetched.

I think that's finally how the cost came out, we thought we could go a factor of ten, and then if you took part of the learning curve, you were going to consume much of three billion, by the time you got them done.

COOK-DEEGAN: Jim, what's your sense, what's your changing perspective of shifting from being, making the transition to the new sets of activities you have to do, you have to talk to Congress now, you have to plan the operations of essentially a small agency. What's that entailed for you?

WATSON: Well, two positions is more than I can look forward to.. I see no way easily off of the limb. But as far as responsibilities, I'm doing just about what I expected. I never expected to provide scientific leadership, but merely identifying and encouraging people that I thought actually could do it, and trying to recruit people into the project, so that we could actually spend the money on people who could use it well. I guess that's been the.. and I think here it's been pretty satisfactory. The initial year or two was like anything, where the money went out just to the applications in hand, because the money had been voted, and you hadn't time to put anything together, but I think now..

*** INTERVIEW STOPS ON TAPE SIDE A, 2/3 through the side.
TURN TAPE OVER; INTERVIEW RESUMES ON TAPE SIDE B, 1/3 through the side.

WATSON: .. So it wasn't I think that we gave out bad grants, but as Maynard said, they're not getting the job done. So finally we're putting out money to get the job done.

COOK-DEEGAN: What's your sense about what job it is that Congress wants you to do, and that part of what kind of this dependence of science on the federal government?

WATSON: Oh.. I think Congress has bought the social view that the next major big events in medicine may come about through using the tools of genetics, and this program is part of that. Certainly the mental health institute, the emphasis is on, let's find the genes. I don't think anyone knows how hard it's going to be to find them, given diagnosis and all that. So, it's going to be a hard job, but I don't see any other way to do it. So, I think they just want us to.. do something if we can about alcoholism, or Alzheimer's, or schizophrenia, or juvenile diabetes, or any of the.. and identifying people who are at risk, so that hopefully the people can, you can respond in some way so that you're not trapped by your heredity, as much as if we don't find out about these diseases.

COOK-DEEGAN: That kind of brings us to the next, one of the major innovations at the national center, is this commitment to doing analysis of social impacts of the research that it supports. What was your, I mean as far as I can tell you're the person who made that choice, to kind of package that as far as a program..

WATSON: Well, I think I wanted to because I was really aware of the misuses of genetics in the 20's and 30's in the United States and of course the using of bad genetic reason for the genocide programs of the Nazis.

COOK-DEEGAN: (Bennow's?) book, or (Dan Keblis? Kevlis?) book, or?..

WATSON: Being director of post, I knew what was the past, so.. being director of an institute which some people would virtually like to expunge to the past. So I don't think it was in any sense, even as (Kevlis?) tries to point out, because I think you have to see what they were saying in terms of the generally accepted ideas of 1910 or 1920, that genetics fitted in very nicely in some of the preconceptions of people. But it was certainly bad reasoning, that if you weren't aware of the past, you could easily slip into some of the mistakes of the past.

And it's very important to get across, it's this concept of confidentiality. If there's anything someone wants to keep secret, it's his set of genetic constructions. You can't imagine a company wanting to reveal to everyone else, you know, your balance sheet. So, I just..

The concept that so much of our destinies is due to our genes is something that I think anyone trained in genetics just naturally assumes. But that's certainly not the way the average person has thought. And there's bound to be a change in the way even the average American with time probably things about himself. It won't happen now, it might take a hundred or two hundred years, but I think it's bound to come. Some of this will be hard

to accept for many people, and you don't want to push them into it. One the other hand, you don't want to not give them the advantages which can come from genetic counseling, or understanding actually what..

COOK-DEEGAN: In another area, what's your sense of.. I gather from the NRC committee's report that there was this kind of dream of a lead agency that had complete control, and obviously that hasn't happened. What's your sense of the kind of political compromise..

WATSON: I think it's working very well, and I think that's really because there's so much to do that you really don't have to compete on the same project. There isn't something that both people are racing to get. And the other is from the very start, it's been almost the same group of advisors from DOE as with NIH, so it's been the same set. So in a sense, you can say there's an advantage, that two (combined?) doesn't get as much as DOE will, and the programs aren't that different, and I think we're moving. So, I don't see that as a problem. It could have been, if.. conceivably, just in reference to, the fact that with DeLici, when he left, there was really no leadership for almost three years at DOE, it sort of created a vacuum by which, in a sense, the agenda was set by NIH, more so, in a way.

So by the size of our budget, and by the fact that that had no strong leadership for awhile, left us in effect acting as the lead agency. But I think just the fact that for the most part we know each other as friends, it's just two packets of government, we have one program, I think that's the way most people feel about it.

COOK-DEEGAN: What's your sense about, looking back, what was kind of the.. of the things that changed, you've described your own kind of transition from kind of skeptic to whatever, what's your sense of the politics of the genome project in biomedical research..

WATSON: Well I think we have to accomplish something, most people like.. even most, and scientists are sort of indifferent, they're not thinking about it, it really isn't that big, at 2% of the NIH budget, if you want to make something of it you can, but you don't have to. So most people's life goes on.

We have to be responsible for our program for actually finding the disease gene that might not have been found without.. I think that's the way we're going to.. or to begin to produce sequences for drosophila and yeast, then people will sort of begin to be dependent on our continued good success. Now we haven't given them much, and so.. yeah, it might turn out in sequencing the end of chromosome four, it will turn out to be necessary for finding Huntington's disease. Then it'll undoubtedly have an impact on people who say, "yeah, you weren't crazy to get into sequencing"; reduce the cost dollar, get a program so that you could even contemplate sequencing a region that long in order to identify all the potential genes which might be at the root of it.

I think it's going to be.. the real test case might turn out to be Alzheimer's, because its economic consequences are so much greater, that.. individual congressmen can worry about Huntington's because it is such an awful disease, and (Nancy's?) been very effective in getting.. but it doesn't affect most people's lives the way.. if we could come up with a way of identifying people at risk through alcohol. Once you had done that no one would ever question that what you have done has been very cost-effective.

So, I'm thinking in terms of trying to help accomplish something with the other instances, which wouldn't have happened without it, and which would be enormously cost-effective, and the factors are cost-effective.

COOK-DEEGAN: One thing that strikes me, and that must have affected your own life, is the genome project, you've never really been out of the fishbowl, but certainly the genome project came along and threw you back into the fishbowl and put you in the spotlight in a way that you hadn't been for a while. What's your.. it hasn't always been positive..

WATSON: No, that's not a very.. yeah, for the first time in my life, I really.. want vacations, or just want to get away from people, because I don't like.. for the most part, public figure just means responsibility, it doesn't.. but, as long as my reputation isn't destroyed by mistakes or something, they probably can't attack it.. I could probably bring something to the program that no one else could I guess, at this stage. But, it's no fun seeing your aged face in a photograph!

COOK-DEEGAN: The cover of New Republic magazine..

WATSON: Well, that was initially upsetting, but I couldn't care less that.. because I've always had people disapproved of what I've done. If you don't have people who are against you, it probably means you're not trying to do something really useful, just because of the way society operates. If you're upsetting something, some people will prefer that

nothing new happens.. There's always been a lot of people who did not look forward to my involvement in something. I think it's harder for my wife and children, you know, being married to a public figure has no advantages whatsoever. You're just at the mercy of other people, you don't have the freedom, you're responsibility is to the public, not to your family, so they don't get much out of it. You seldom if ever read of any politician's family saying how nice it was to be part of this world.

COOK-DEEGAN: What's your sense of the degree to which your reputation has now hinged on the success of the genome project?

WATSON: Not very much.. I think I've done enough, I don't have to do any more. It's just a burden. You know, people like (Poffberg?) or (Dan Nathan?), they're not putting out like I am! (laughs). You can always think of reasons.. I seem to have more.. I've got greater burdens. You know, you can get fame with it, Life puts me on there, and things like that..

COOK-DEEGAN: You probably would have been in there without the genome project..

WATSON: Yeah. So I guess that's what, it really doesn't matter that much.. unless of course, the thing's deferred..

COOK-DEEGAN: Do you think it will be?

WATSON: No, I don't think there's any chance of that. I mean, it could be slowed down because we don't have the money, but, even at this meeting.. Sequencing's going to work, it's going to have ups and downs, how fast we're going, but it's going to work. So it wasn't a very chancy thing. But I think that's true of most things that succeed, that.. I was impressed with that when I worked on the DNA structure. We thought, you know, it wasn't a far-out objective. So, I think that most good people don't work on far-out things. Now you could say, the Hubble telescope!

COOK-DEEGAN: Well, Hubble isn't so far out, it just needs to be tested a little more, right..

WATSON: Yeah, I mean.. sitting out there in space, you can't correct it. We make a bad decision.. you know, you could create a DNA (city?) and put it in the wrong hands, but we're being very cautious, and we're not trying to give any one approach so much money, that it's more or less spreading our bets. Which is I think the way to proceed.

I think the.. the major dilemma of running projects, of running anything these days, is that everyone's individual lives have become more difficult, just because we expect more from life, we sort of need more money to live like everyone else, but that means we have to work probably harder than we should, such as, you know, families have to have two jobs. It's a way of life which I think is actually very hard, and it's leaving less and less time for people to worry about anything other than themselves. I'm sure that's part of, there's no..

As far as I can tell there's no scientific establishment. People actually think they control things. Or, you know, from the sense that, if they want something done, it'll get done. Like, (Bronk?), or (Robbie?), or the groups when I was younger. So, you see less evidence of leadership, but I think more people find it very hard to find the time, or just the energy to do it. Because the fast pace of everything means.. You know, once, if you were a Harvard professor, you had it the rest of your life. You'd go to the cape for the summer. But now, you have to get grants, and if you don't get grants, your reputation is, you're humiliated, and so even the people at the top I think are much less stable than they were, much more instability.

And.. the whole attitude toward government officials, conflict of interest and everything, makes it harder for anyone to actually want to come in and be part of the system. I'm really, this is made possible because at Cold Spring Harbor they take care of me enough so that I can do that, but most people aren't in that.. (Lee Hood?) wanted to run it and still be at Cal Tech, Cal Tech couldn't take care of him. So it's just a, slightly a fluke, that they take me.. But it should be done more, something should be done to get people down here worrying about..

COOK-DEEGAN: Have I forgotten to ask you any questions that I should ask you here?

WATSON: No, I think I've, I'm talked out.

COOK-DEEGAN: Me too..

*** END OF INTERVIEW.