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Elana: Ok, so the information that I am about to give you and your response will now be recorded. My name is Elana Berger and I am a student at Duke University. I am in a course on the history of genomics that includes oral history. One goal is to produce a written transcript of interviews with important figures in genomics. Some of the interviews may be archived or made public through a website. I selected you as the person I would like to interview. The interview should last about 45 minutes. Your participation in this interview is strictly voluntary, and you may withdraw at any time. You do not have to answer every question asked. The information that you provide will be “on the record” and may be attributed to you. This interview is being recorded and I will take written notes during the interview. The interviews that are posted publicly will be archived as a history resource. If you prefer that the interview be used only for the course and not made public, please indicate this. One risk of this study is that you may disclose information that later could be requested for legal proceedings. Or you may say something that embarrasses you or offends someone else when they read it on a public website. The benefit of participating in this study is ensuring that your side of the story is properly portrayed in the history of genomics. Dr. Branscomb, do you agree to the interview?

Dr. Branscomb: Yes I do.

Elana: Ok, thank you. And thank you again for doing this.

Dr. Branscomb: Elana, I need to, to clarify a mistake in understanding you have about my position. I have since, since September, Lawrence Livermore National Laboratory decided to not have a separate biosciences directorate and to merge biosciences with another larger directorate called Chemistry and Material Sciences. So, there is no longer a Biosciences directorate and I am no longer an A. D. (Assistant Director) at Lawrence Livermore National Laboratory.

Elana: Ok, so that was very recently?

Dr. Branscomb: Well it was mid-September, yeah. I didn’t realize, when I saw your list of questions and that you were referring to me in that position, I’m sorry I didn’t tell you, that I didn’t get that information to you before.

Elana: Oh, that’s ok. I guess that’s the most update information I saw.

Dr. Branscomb: Yeah.

Elana: Ok, so what did you say your current position is again?
Dr. Branscomb: Well, I’m science advisor to the Associate Director for Chemistry and Materials and Life Sciences, the new directorate.

Elana: Ok, so the first question was about how you got that position as Associate Director of Biosciences. So do you still want to touch on that even though you might not have that position anymore?

Dr. Branscomb: Well…

Elana: Or you want to talk about your current position?

Dr. Branscomb: Well no, I mean, let me just make a remark about that, my personal history with respect to the Genome Project, both my holding the position while I held it, of Associate Director here, and the prior position of being the founding director for the Joint Genome Institute. The truth about that, as I see it, sounds like false modesty, so I want to disclaim that it is, just to protest that it’s not. But, in both cases the… you phrase the question as how did you end up, and that’s kind of the right way to phrase it. I ended up in those positions, in some sense, mostly by a very accidental process that was not, in some sense, qualitatively different from a famous Peter Sellers movie called Being There.

Elana: Ok.

Dr. Branscomb: And it was…it was just that I, for some reason, was in a position where a leader was needed, and I was willing to do it and in both of these cases, I didn’t have the qualifications that you would normally expect for somebody holding those positions. So, there wasn’t a kind of a rational path, an explicable or explainable path, for my doing those jobs. That always amused me, but it’s the case that I was not sure this would happen, any of this stuff would happen, including my change from my formal education as a theoretical physicist to doing biology, which, the actual change took place without my committing to it, I just thought I was doing something else for awhile. So, at any rate, there nothing about my career in biology that makes very much rational sense or that I would advise anybody else to follow.

Elana: Ok, fair enough. So, I guess going on to the next question, given that you have been involved with the Department of Energy (DOE) for many years, while you have been working at Livermore Laboratory, and I know that you were at Livermore when the Human Genome Project first started going…

Dr. Branscomb: Yes.

Elana: How do you feel about the DOE’s initial involvement in the Human Genome Project?

Dr. Branscomb: Well, I think the Human Genome Project, or the huge effort that got started under that flag, as Watson and others understood from the very first moment was really the
Genome Project and not the Human Genome Project in any particular way. But, that was an extremely good thing to do, an extremely important thing to do, an extremely efficient way for the government to spend money in support of the biological sciences by some huge factor of greater impact and greater efficiency than had it not been done. As you undoubtedly know, it has been well-documented, the wise men of the time within biology, primarily within the NIH apparatus, more or less agreed, when the idea was first being floated, that this was a very stupid thing and shouldn’t be done and it was somewhere between evil and corrupt and insane. And, so the fact that the project got started was due to Charles DeLisi, who was coming from an agency that didn’t have a real mandate in biology that was very compelling or very much recognized as a solid mandate, and somehow by a lot of work and smartness about how to do this sort of thing, he lined up the political ducks so that he was able to, in spite of the prevailing opinion from the NIH wise, to launch an initiative.

Elana: Right.

Dr. Branscomb: And in Jim Watson’s telling of these events which I have heard him do in public and more than once, this was a disaster. DOE was the least qualified agency on the planet to manage such a project for all sorts of reasons, and I don’t particularly disagree with what Watson has said about those reasons. But, again paraphrasing him, so we tried to stop it, we didn’t have the political power to stop it, so we co-opted it. And by we, he means the NIH-based biological establishment in the US. And indeed my view of the history is that is what happened and that it was a very good thing all around. DOE could not have, in any sense, carried this project by itself and it played the role, in some sense, of forcing the NIH to take the project on. And then, that precipitated a lot of other things, including other national efforts to contribute, of course, of which overwhelmingly the most important single one was the Wellcome Trust effort in Great Britain. So, the major thing that the DOE did for the HGP was a kind of, in some sense, unjustified forcing of the hand of history. They then, subsequently, the role that the DOE played was, I think, significant but not quite in the way that the DOE wished it to be. That is, it wasn’t as if the National Lab-based efforts played a particularly critical or important role. In the end, the DOE contributed just about 10% of the total. And only through a very aggressive reorganization in the last few years to try to have the DOE contribution be significant, and it was that sort of last minute effort which caused the relevant manager at DOE, a guy named Ari Patrinos, to push his previous investments, which were at three separate laboratories, into a single effort, that was the Joint Genome Institute, to essentially force that to happen in order for the DOE to be doing something at all that would really count at all in the end of days. However, what I think the major contribution of the DOE was to the Genome Project, apart from just forcing it to come into existence, was its contribution to various technology improvements that were critical to the ultimate success. And, there is a substantial list which we could come with, and I think they did play an important role there, although again, almost all of those, or essentially all of those, substantial technology advancements were results of research not done at the DOE national labs, but the DOE funded labs at universities in various places. So, it’s a mixed and complicated picture…
Elana: Yes, of course. So, you touched on this a little already, but maybe you could explain a little more how you felt about the DOE/NIH collaboration. Do you feel it was a successful collaboration, is there anything else you would like to say about that?

Dr. Branscomb: Well, it was successful in the fundamental sense that it needed to be. That is that, they needed to be working together, or in some sense, appearing to work together, in order for the political support, that’s my view at any rate, for the political support for the project to continue. And, you know, in the end, it achieved the outcome. In terms of the total contribution to actually producing the sequence, you could have subtracted the DOE’s 10% entirely and only been delayed a little bit.

It was, in general, a highly conflictual and problematic interaction and not exactly a collaboration that was worthy of the word. But nonetheless, the people involved, Francis Collins and Ari Patrinos, and others, and the Wellcome Trust managers, found a way to keep themselves together, and through their keeping themselves together, to be the force that kept the worldwide effort together. And, this was, in some sense, largely through the contribution of the Wellcome Trust, as organizers of the worldwide effort, to convene and manage the so-called Bermuda Meetings that were held. And it was their moral source that kept forcing the discipline of prompt public release of data and to force continuing improvements in the standards and some degree of accountability for costs and so on. But, especially the public release of data, basically you couldn’t be a member of the community and be invited to the early meetings if you were not releasing. And this got to be extremely emotional and contentious and problematic for some of the nations involved. But, holding that together was very important and in the end, the DOE-NIH relationship, and in particular the relationship between Francis Collins and Ari Patrinos, was essential to managing the highly charged and problematic conflict with Celera and Craig Venter.

Elana: Right.

Dr. Branscomb: But that again was much more of a two or three person personal issue, rather than an institutional issue. It wasn’t so much DOE and NIH collaborating as much as it was Ari and Francis, and then finally with Craig in the room, when that was the important issue, working things out, in Ari’s basement having pizza.

Elana: Right, the “pizza diplomacy.”

Branscomb: Yes, as it was famously romanticized.

Elana: Right. Ok, and again, this is something you also began to touch on already, but this popular view of the Human Genome Project as a “mindless sequencing operation” at the beginning by many prominent scientists…

Branscomb: Yes, many of the most eminent scientists scorned the idea – often in the most imperious, emotional, and intemperate terms – yet they are all now amnesic on the point – whilst they greedily consume genome data.
Elana: Yes, so why do you think so many people reacted this way?

Branscomb: Well, Elana, I think that it’s an obvious fact that the proposal was upsetting to established scientists for a host of reasons having to do with a very strongly and passionately and almost uniformly held belief, I want to call it a religious belief, as to how science should be done. It should be done as a small step by small step of going from what you already know for sure, or know with high confidence, advancing some hypothesis that is clearly justified by the established evidence and then working on that in a very focused and confined way. The Genome Project has violated that and that’s what a lot of people complained about and reviled it specifically for these reasons, that it was a moral corruption of the process of science. Instead of advancing hypotheses and testing them, you just went out and gathered data blindly.

There is nothing that guarantees, even to this day, in most contexts, having an RO1 grant rejected, more than that it can be called a fishing expedition. And the Human Genome Project was the fishing expedition beyond all fishing expeditions. The only hypothesis being tested was that, boy, will we discover a whole lot of wonderful science if we have the sequence of the human genome in our hands. And, it has all sorts of problematic elements. It violates the hypothesis of testing morality, it violates the territorial control of individual problems that scientists have customarily expected and enjoyed. It says that anybody on the planet sitting at a computer can start working on your genes, or your gene family, or your pathway or something, because the sequences are all out there. Individual established scientists lose control, in some sense. And there has been, subsequently, a huge amount of that. That is partly what has made the science now so exciting and rich. There is much freer access for going after scientific questions.

Moreover, most of the hypotheses that are now driving scientific research would never have been guessed in advance until you had the sequence in your hands. Quite a few scientists have celebrated the fact that, when they finally got the sequence of their organism, their microbe or whatever, that they discovered all sorts of things about the microbe that they thought were absolutely not true. But there it was; there were the genes for it. And when they went back and tested, sure enough, the organism had the properties that the genomes implied they did. But all of this, I think, is and remains, for many scientists, a truly disturbing operation.

So, the idea that it was mindless was kind of just one way to attack it. All very large data-gathering projects have a tremendous mindless aspect and this was, at the time, thought to be huge. And indeed, at the time that it was being considered it looked like it was going to be 20 years and more than 3 billion dollars. It was going to be a hugely, in a certain sense, hugely expensive, not compared with the total budget of course at all, but nonetheless as a single effort, and that it was going to take a long time, and that it would be of uncertain quality, and on and on. But, so much was this, in my mind, kind of an arrogance of what an operation like this implied, an arrogant demeaning of it, that it was suggested in the early days that prisoners could do it, or something like that. What in the end I think turned out, is that it turned out to be far from mindless, but it is an industrial operation. And so, it is very much unlike research; the big sequencing houses are very much like industrial assembly lines. They operated on the same principles and have the same style and personality on the large part. They have purified themselves of research people because that just gets in the way of high-quality, highly-efficient,
cost-competitive operations. But, what it produces is exquisitely beautiful, and important, and exciting, and unexpected, surprising science that puts a rocket engine under discovery.

**Elana:** Right, it’s just much less personal than what the scientists might have been used to.

**Dr. Branscomb:** Yes, and at one point, in the early days, when we were just sequencing away by obligation and by necessity, we were paying no attention to what data we were putting into the database every night. And, I got a call from a soft-spoken man who said, “Hello, my name is Tom Maniatis and I’m from Harvard,” and I was talking to somebody else and I put my hand over the receiver, and I said, “There is somebody here who says he’s Tom from Harvard.” And then I realized that it was the Maniatis from Harvard. And it turns out that we had just put into the database a bunch of sequence on some genes that he had been working on for a long time, some really important genes expressed in neurons, and it was very exciting. He started describing to me that we had a gap in our sequence, and he asked me very modestly if we could possibly try to close this gap. And, I almost burst into tears because it was just such a wonderful thing to be able to contribute to discoveries like that in such an easy way, in some sense. And I said, “of course, and would you like us sequence the corresponding parts of the mouse genome?” And he said, “of course.” And, so, I said, “well, here is our price, our price is you come and give us a lecture on your science,” and he did.

**Elana:** That’s great.

**Dr. Branscomb:** And it was this sort of thing that happened over and over again in various ways that, in some ways, showed how wonderfully scientific and effective a mindless operation like this can be. And it is the whole history of expression arrays and other technology advances like that has had this same character. That if you get very efficient and high-quality in gathering large amounts of data, if you do it fast and cheaply, the science explodes, and largely, in completely unpredictable ways. So, you do expression arrays, and people do this and it is now a feeding frenzy, you do an expression array and you discover genes that are involved in some process that you would have never guessed they were. Mindless indeed. This is, in some sense, what we need to do, in order to build the foundations of our science, is to do a lot of wonderful mindlessness.

**Elana:** Yeah, that’s great. Ok, so a slightly different topic, but related, looking back on the whole sequencing operation, what is your opinion of the clone-by-clone shotgun method used by Livermore and the Joint Genome Institute for physical maps of different chromosomes like 19 and 5? How do you compare that to the whole genome shotgun method?

**Dr. Branscomb:** Ok, first of all, the clone-by-clone approach was used by the public effort for the whole genome.

**Elana:** Right.
Dr. Branscomb: We used it for our 3 chromosomes, our little 10% of the genome, but it was the foundation of the public effort.

Elana: Of course.

Dr. Branscomb: In my view, it was absolutely essential that we proceed by a clone-by-clone approach given the limitations of our technology at the time. And in fact, the clone-by-clone approach that we were using all those years, that was cosmid-based clones, turned out to be essentially, or almost, useless. The clones are just not long enough and are in other ways problematic as to what’s clonable and what’s not and so on. The genome actually came together by having much of the cosmid-based sequencing replaced by BAC sequencing. So, I think it would have been mad, in my view, in the beginning, to have proceeded on a whole genome shotgun basis. When we started out, a read of 300 bases that was at all acceptable quality was about the standard. And many of the reads, because we were using slab gel machines, were wrong because one lane was walking into its neighbors and so on. The data was really very terrible and would never have assembled. We had to go to larger clones for it to work, we had to get up to much longer and much higher-quality read lengths, which none of us believed was going to happen, but it steadily happened. And, to develop other refinements of the technique, such as the paired-end sequencing issue, which was absolutely critical; we didn’t have that in the beginning, and so on. Everything that made it possible, we didn’t have when we started out, and if we had stayed where we started out, it never would have worked, without a doubt, this wouldn’t have gone together.

So, now, given modern technology, it then makes sense to go over to whole genome shotgun, sometimes augmented by a certain amount of paired-end clone-based sequence. I think in most cases its proving worthwhile to mix these strategies. So, the relative role of these two contending ideas about how to go, is basically a historical developmental issue, and a technology-dependent issue, and whether you can get away with whole genome rather than needing to painfully map clones first and then put them together. It depends a lot on the level of technology that is underlying it. It wouldn’t have, in my view, made sense, to do whole genome shotgun up until the time that Craig and his company first tried it. But, I think the resistance to it that the public effort showed, again on sort of moral grounds, was inappropriate, in my view.

Elana: Yes, ok.

Dr. Branscomb: Making it work and showing it could work, and showing what its limitations were, was a huge contribution which, in my view, has gone unacknowledged.

Elana: But, I guess there was no way to know that it (whole-genome shotgun) could work when you first started doing the clone-by-clone method.

Dr. Branscomb: Well, I think there was every reason, and in my view a justified reason, for being certain it would not. But, you know, it turns out, that the difficulty of assembling sequence reads into anything, into anything approaching significant pieces of a genome, is extremely sensitive to sequence aspects that differ between genomes. Approaches that work perfectly fine
with one genome fail significantly with another if the repeat structure is more problematic in one than the other. And the degree to which the repeat structure is problematic differs greatly between genomes and the degree to which all the DNA is or is not clonable in the sequencing vectors that you are using differs. And, there have been some big surprises of people, including at the JGI (Joint Genome Institute) and other places, of trying to sequence genomes and finding, holy mackerel, this is a genome that is really tough and is not going together. Therefore, what strategy is the right strategy is really not something that you can necessarily guess precisely in advance and it does depend on the agonizing, biological, idiosyncratic weirdness of one genome versus another.

**Elana:** Right. So, my next question, looking into the future implications of this project, I know you told me before that you are very interested in the ethical and social implications of the Human Genome Project and the medical applications. I happened to find a quote of yours in an article in *The Scientist* from 2000, in which you discussed how, at that point, we still did not know the “real repertoire of genetic variants,” and that it was hard to correlate our phenotype and genotype at that time. But, you seemed to be optimistic that soon we would get there and that this would become a “hotly contested issue.” So, I’m just wondering, since you said that in 2000, how far do you think the field has come? Do you think we still have a long way to go?

**Dr. Branscomb:** Well…

**Elana:** It’s sort of a loaded question.

**Dr. Branscomb:** Well, yes. So, by the way, your way of phrasing that makes me feel uncomfortable because it makes me sound like a socially responsible person, which I’m not. But, I find the implications of the project in these regards interesting and I think it is going to be quite significant and quite problematic. One aspect, is this one that you have pulled this quote out about, is the ability to genotype an individual, which is really what is at issue here. To answer, in some sense, when I’m born, to say, Elbert, here is what you were dealt in terms of the standard options available in the human population for each of the genes in your genome. Here is what you got from your father, here is what you got from your mother, and here is your whole kit. For gene number 274, you got this standard variant from your mother and this other standard variant from your father. And then there are a few novel bits that just arose that aren’t in your recent genomic history that aren’t spread across the whole population.

But basically, to characterize my genetic individuality as a particular choice out of the whole popular repertoire of alternatives, the allelic variants of all the genes that make up the human genome. And the ability to do that was clearly coming down the road, and is now very much advanced beyond where it was in 2000, due to the investments of the NIH specifically to empower that capability. And, the subsequent ability to increasingly correlate the answer to the question, “which genomes did you get, Elbert?,” with the implications, what are the consequences of having been dealt that hand. That’s of course slower to come along, but will come along. It depends on the ability to get the detailed data, but increasingly, and in a way that will accelerate, the ability to characterize individual genotypes and to then predict what that genotype means will get stronger and stronger. And therein lies, in my view, the huge payoff.
and the huge dark side, in some sense, not just of the Human Genome Project, but of what the Human Genome Project is a milestone in, or a piece of, or a facilitator of, and that is just figuring out how life works. We are, in some sense, closing in on that great mystery; how does it work? We are, in some sense, and the Human Genome Project is a great part of getting us there, we are now suddenly in the room where all the secrets are and we’ve got the lights on and we are opening all the doors and shouting in delirium about what we find.

And we still don’t know what it means and how we put it all together, but at last we are, in some sense, on the playing field with life itself. We are looking at its real machinery and we are taking it on in its terms. And so, as part of that, two major capabilities are going to be put in our hands. One of them will be this one that what I was referring to here, which is to know a person’s genotype at birth or whenever, and then with increasing strength to predict what implications that has or doesn’t have for that person’s fate or his properties or her properties in all ways. One might be waggish and say, and I think with some justification based on certain studies that have been done, for example, on identical twins separated at birth or raised apart, that you would be able to say well, at my birth the genomic physician would say, “Well Mrs. Branscomb, I’m sorry to have to tell you that your son is going to be a clueless science nerd and have no taste in ties. I’ve seen this in genomes before.” And stuff like that. All sorts of things that you would think have nothing to do with the particular genes you get. But in addition, all sorts of other things having to do with what people ordinarily associated with genetic influence, and that is disease susceptibility or health prognosis and so on. And I think this ability to know this kind of stuff is going to be extremely and almost surprisingly problematic. I’d like to tell a little story if I can to illustrate this.

Elana: Sure.

Dr. Branscomb: There is a hematologist, I think still at the University of Washington, named George Stamatoyannopoulos who, quite a large numbers of years ago, 25 or something like that, developed an assay for Beta Thalassemia. As you can tell from his name, he is Greek, and from the name of the disease it is a genetic disease that is common in that part of the country, or in that part of the world, and it has very serious health consequences. So, he developed a non-DNA-based, a protein-based assay, so that he could identify carriers. And, armed with this nice discovery, he went off to his native land to go into the areas, rural areas most notably, that had a high incidence of Beta Thalassemia, to bring them the help that could come from identifying carriers. And as he described it, I think to quite a few people, but on one occasion to me, he barely escaped with his life.

Elana: Wow.

Dr. Branscomb: The reason is, he was telling people a fact they could not socially metabolize, that they could not socially manage. He was stigmatizing young daughters and young sons and making them unmarriageable.

Elana: Oh, ok.
**Dr. Branscomb**: And it illustrates a rather deep, a point that I think at any rate is rather deep, and rather broad and is typical and is just true of us, life is manageable based on our being ignorant, not being able to know a whole bunch of stuff. For example, if it were very easy to determine all of my disease predispositions, what’s likely to happen to me here in all these ways, or of my son when my son is born, is it really something that I want to do, to know that? If in some magical way I could predict his fate into the future…

**Elana**: Right, do you want do know?

**Dr. Branscomb**: And our ability to do this will increasingly approach magic here, I think. But if we could magically know it, that would be a curse, I think, as much as a blessing and would be very problematic. Suppose a lady and I are considering marriage, and I say, “Well what’s your genotype? Will you please submit your genotype to my genomic counselor and I’ll do the same.” If there’s only a few serious diseases that can show up in that kind of test, then that makes sense in a way that it does not make sense, I think, when we could know an awful lot. And I think this is problematic even in the cases when we can do something about it, and that of course is the other side that for much of this information, there is nothing to be done. It’s just, well Elbert, you have a four-fold increased probability of having a neurodegenerative disease when you reach age 50, and you can’t do anything about it. And what a nice thing to discover. And, how can I live with that? Moreover, how can I even live with knowing that I could find out that I decided not to find out? Not that I couldn’t, it’s just, I think it’s quite problematic and across the whole population, it would be, I think, very problematic. But even when we can do things about it, the idea of going in and trying to fix maybe several tens of different things that we would desire to fix when we had a newborn and we knew all about the genome, is I think, in a certain sense, kind of the end of the Hippocratic romance, that every time we could do something to improve health, we must do it.

**Elana**: Right, and then where do you draw the line? What do you do, what do you not do?

**Dr. Branscomb**: Yes, and we go, in this case, way beyond. The line cannot stay with the understanding that we will be gaining, I think. We will be driven into kind of a mad endgame. And also it will almost certainly be again a situation in which the very wealthy will afford very much more in the way of interventions of this kind than the less favored and so on. And it’s really problematic, I think. So, that’s one aspect of what’s, in my view, the kind of Faustian Bargain aspect of the Genome Project or the whole historical development of which it is a part. The other is related, but it has to do with our mastery of genomes and our ability to produce them. We have gone from being genome readers to being genome writers, as it is famously being put now. As was illustrated in 2003, I think it was, by the De Novo synthesis, chemical synthesis of the genome for the virus… what was the virus? I’ll think of it in a minute.

**Elana**: That’s ok

**Dr. Branscomb**: Elana, help me, what is the paralysis that was…? Polio.
Elana: Oh, ok.

Dr. Branscomb: The polio virus was synthesized from scratch just by looking it up on a computer, you know, downloading it from the database, here is the sequence of 5 and a half thousand bases, or whatever it was, for this particular virus, ok, so let’s start making the pieces and putting them together. And it worked. Of course, it’s just in the sequence, and when the molecules were built and stuffed into cells that were susceptible to them, out came perfectly real, perfectly natural polio viruses with their full capsids and everything, and there you go. And so there is now something of an industry that’s exploding, using for research purposes, the ability to synthesize genomes, to synthesize significant pieces of DNA that can function then biologically. So you can study, as George Church is doing a lot of, modifying the genome of E. coli, and others are involved in synthetic biology or doing things like this.

We have made a transition into a time of our history where we have mastery over a property of matter, that DNA embodies, that is like in consequence, and in some sense, the mastery, the very problematic mastery that we gained once it was understood what $e=mc^2$ meant, on the one hand, and what the so-called nuclear-specific energy binding curve, meant on the other. That is, it meant that if you could blast a very heavy nucleus, like plutonium, with alpha particles and make it fall apart, you got a huge amount of energy out. And moreover, if you could find a way to blast very light nuclei, like hydrogen, together at very high energies and force them to fuse into helium, you would get a huge amount of energy out of so-called hydrogen bombs, right? And when that property of matter was discovered, we were suddenly living in an extremely problematic and dangerous world, very different qualitatively than the one we were living in before it was discovered. Although, of course, the property of matter was always there. In this case, when we are discovering the property of matter that is represented in that de novo synthesis of that polio genome, that all you have to do is put together, in a certain order, four simple molecules that you could get for a few bucks from a supplier off the web. And just put it together, and I’m waving my hand now because it’s not quite this simple of course, and in some cases it’s a good deal more tricky, and you can’t just use the molecules to make a real virus, much less a real organism that tries to live autonomously. But nonetheless, when we have discovered that property of matter, that certain sequences of these four simple molecules act as a catalyst to cause the condensation reaction that gives rise to a real biological entity, that could have huge terrible consequences. That’s all it is, it’s just in the sequence of this molecule, and if you put it into the right chemical context, and it just causes the biology to happen.

Elana: Yeah.

Dr. Branscomb: It catalyzes it, literally, in a thermodynamic sense of catalysis, it catalyzes the condensation of the real viruses and so on. Then, we have brought ourselves a world that is, I think, immeasurably problematic, and in a way which makes the difficulties that come from the discovery of nuclear energy and the ability to make bombs based on it, pale by comparison, I think. Primarily because, the exploitation of the first of these great discoveries, the practical exploitation of it, is extremely hard and complicated and expensive and tricky. The exploitation of the second, the DNA-based discovery, is not. It is something you can do in your garage with a modest amount of training, for a few bucks. As Drew Endy from MIT says, you know, now, at
current cost, we can make a virus for the price of a small, used Volkswagen. And moreover, our ability to synthesize DNA stands, I think, roughly where manned-flight stood at Kitty Hawk. We are just flying a few feet off the ground for a hundred yards. And, in a very few years, we will be flying at high altitude, at high speeds, and it will be extremely different. We will be able to produce genomes of bacterial size or larger, you know, for pennies. It’s just going to get very wild, very fast. And you know, with a genome in your hands, you can do incredible things. So I think it’s there that the ability to sequence opens the door to. The ability to sequence fast and cheaply, by about four-logs compared to where we were when the genome project was being contemplated, that and its derivative consequences are really important, and really qualitatively deep, and in many respects, a highly problematic matter. So, that’s it.

Elana: Yeah, well, that’s probably, I would say, a good way to wrap up the interview. I mean, if there is anything else you feel you haven’t said that you would like to say, anything else that you want to discuss.

Dr. Branscomb: No…

Elana: No, you got a lot out.

Dr. Branscomb: Just a personal remark that it was, for me, a tremendous piece of inexplicable good fortune that I happened to, in fact, be there when the Genome Project was casting about for somebody to put on a hat and say, “I’m a genomicist,” and so that I could play in this history. I just found it wonderful and lovely, and I feel extremely grateful for the odd quirk of history that let me do that. So, that’s all.

Elana: That’s great. Well, thank you so much for this again. It’s very appreciated.

Dr. Branscomb: You’re welcome, my pleasure. Good luck with your project.

Elana: Oh, thank you.

Dr. Branscomb: Bye bye.

Elana: Ok, bye.