

**Protocol 1277 Informed consent statement for Oral
History
Interview**

(This form can be sent in advance and signed or read into the tape at the beginning of the interview.)

The interview will be recorded, and I will use the audio file to make a transcript. The transcript will be shared with you, with an opportunity to correct it. The attached form indicates options for making the final edited transcript available.

My name is _____ 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. The conditions for making the transcripts public (the audio tapes will not be public) are indicated in the accompanying form, and you can choose any of those options, or write in your own conditions.

I selected you as the person I would like to interview. The interview should last 30-45 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 choose to share publicly will be “on the record” and may be attributed to you, unless use is restricted the conditions you specify on the form.

This interview is being recorded and I may take 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 on the form.

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.

Signed:  _____ Date: October 26, 2012

Person interviewed: Harry Ostrer Student Interviewer Alex Bennett
(Print clearly) (Print clearly)

Use of archived final transcript

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The form below provides you with different options for how, when, and with whom your interview materials will be shared.

(A) I place **no restrictions** on my interview materials.

OR

(B) My interview materials may be reviewed, used, and quoted by students and researchers affiliated with Duke University; *and in addition* (check all that apply):

Researchers unaffiliated with the Center for Public Genomics may **read** the interview transcript and any related documents only after obtaining my permission.

Researchers unaffiliated with the Center for Public Genomics may **quote** from the interview only after obtaining my permission.

Researchers unaffiliated with the Center for Public Genomics **DO NOT HAVE** my permission to **read or quote** from the interview.

Posting interview materials to public digital archives: In spite of any restrictions listed above, I give permission for my interview materials to be made publicly available on the Internet by deposit in an institutionally affiliated archive:

1 year from the date of this form

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Other: _____ (please specify a date or condition)

Signature: _____



Date: October 26, 2012

Interview with Harry Ostrer
Conducted by Alex Bennett
A Social and Political History of Genomics
26 October 2012

Harry Ostrer (HO): My trip to Austin got cancelled because of the storm, and so I am still in New York, and I'm in my office at Einstein now.

Alex Bennett (AB): Okay.

HO: And we actually came through the storm here pretty well.

AB: Oh wow, that's lucky.

HO: Yeah, no, we're very lucky close to home and at work. My former institution, NYU Medical Center, was completely devastated by the storm. I was just talking to some of my colleagues on the phone, and it is really bad there. It sounds like they're going to be out of commission there for weeks, if not months.

AB: Yeah, I have some family up in New York, and they said that everything is under water, and it's completely devastated.

HO: It really depends how close you were to the water.

AB: Yeah. Okay, so you did send back the informed consent, so just to check, do you have any specific restrictions you want placed on this interview?

HO: No. If something comes up, and I feel uncomfortable, I'll tell you.

AB: Okay.

HO: Yeah, I think it should be a pretty open interview. And you know, a lot of stuff that we're going to talk about is going to be public information anyway.

AB: Yeah, of course.

HO: Are you taking classes with Bob Cook-Deegan?

AB: Yeah, I am.

HO: He's a really good guy. I like him a lot.

AB: Yeah, it's a really interesting class. We discussed everything from the inception of the Human Genome Project up to today and what's going on in genomics.

HO: Excellent. And do you know what direction you're headed? You see now, I'm turning the tables on you, and I'm interviewing you. [Laughter]

AB: [Laughter] I'm thinking of majoring in biology, and we offer a certificate in genomics. It's in between a major and a minor. So, I'm thinking about doing something in that direction. But I mean, it's first semester, so everyone says it'll change...

HO: Understood. Understood.

AB: Yeah. Okay, and if you don't feel like answering any of the questions, or you don't want to answer them, or they're uncomfortable or if you run out of time, just let me know, and I just appreciate any time you can give or anything you can answer.

HO: Okay, fine.

AB: So, do you want to start by just describing how the conflict started with Myriad Genetics? You were still working at NYU at that point?

HO: I was still working at NYU at the time, and I was approached by Chris Hampton and Tania Simoncelli from the American Civil Liberties Union, and they said, "We're thinking about initiating this law suit. What do you think?" And we talked a lot about the gene patenting and its influence, and we had talked about the fact that I had received the so-called threatening letter from Myriad Genetics, and I never did anything about it. But, it was clear that we wouldn't be able to do genetic testing for *BRCA1* and *2*, that Myriad was going to be the sole source provider, and that we would need to look over our shoulders if we did breast cancer research. But, Myriad is not the only laboratory diagnostics company to enforce gene patents. Gen5 has done that. AESKU Diagnostics has done that. And, it does have an overall chilling effect in the field of genetic testing. It came as a bit of a surprise, because of when genes were first being cloned in the – let's say '80s and early '90s – the argument was made, "Well this is all going to be for the therapeutics so the models we're making would be competent drugs like growth hormone and insulin, and the argument was that the diagnostic market wouldn't be large enough to warrant enforcing patents for genes, and Myriad clearly broke the mold on that, but again, they're not the only ones here. It really dictated a lot, in terms of what's done with genetic diagnostics. Now obviously, if we end up having a favorable ruling from the Supreme Court in the Myriad case, it will be applicable only to the *BRCA1* and *2* genes, and those will still be one – 5,000 gene patents, many of which are being enforced and many for import condition. There are friends who filed briefs who said, "Well our disease, our gene of interest, is patented as well." And, it limits what's being done with regard to genetic testing, genetic screening, and so forth. Most notable in that regard, you might look at the amicus brief from the Claire Altman Heine, H-E-I-N-E, Foundation. Which is great, we've worked with pretty well, and they've come with research and testing for spinal muscular atrophy, which is

thought to be the second-most common recessive disorder, after cystic fibrosis, of which most are Caucasians. But, the gene is patented, and there are a limited number of licenses which makes – yeah, which limits the option for genetic testing. And I’m giving for instance a condition for which I believe that universal carrier testing should be available, but it’s not because it’s not affordable. We, for instance, not the cure, can’t readily offer a low-cost solution. But then, “Okay, great, now we’re going to start doing SMA testing, and we’ll make it available to all the people in the Bronx.”

AB: Okay.

HO: Okay, I took you – fast-forwarded through the lawsuit.

AB: [Laughing] That’s fine.

HO: But really, it started with a couple of people from the ACLU. Not surprisingly, people refer to them as the ACLU’s bosses. I would argue that the plaintiff’s bosses at the UCLU are our attorney. Excuse me for one second [...]

Yeah, so all of the plaintiffs had a hand in shaping the lawsuit. All the plaintiffs were voluntary plaintiffs. We didn’t have to say, “Yes.” And certainly many of us discussed, “Is this a wise or foolhardy thing to do?” And, I certainly discussed it with many of the other plaintiffs. I certainly discussed it with many of those the most near and dear to me. And, I certainly discussed it with lawyers as well, with regard to what the plan – course of action – was in the lawsuit. So there we are. The only plaintiffs who actually received the so-called threatening letters from Myriad were [Arupa] Ganguly and me, and being the pack rat that I am, I saved my letters. But, it took some work because I had to go through years of files in order to find the letters, and I did, and it’s obviously proved invaluable in the lawsuit.

Whether the Circuit Court would have decided that we had a standing, who knows, but the base for standing now is based on the fact that I have an actionable claim based on having gotten a threatening letter from Myriad. And in my deposition, I argued that I was ready, willing, and able down at NYU to do *BRCA1* and *2* testing, and that’s no joke. That is completely serious, and I’m not content by saying more than ever that, it is important for patients’ decisions to have second opinion options because Myriad has their own way of doing things. Their laboratory is very good. I don’t think that they’re a crass operation, but there are things that they don’t do that frankly could be done, and most notable, I think that the way they call variant as deleterious, potentially it could be erroneous, and potentially we’ve told thousands of people that they were not at risk for breast cancer, when in fact they might have been. And, that was nearby. I could foresee a future class action lawsuit against Myriad saying, from breast cancer survivors, saying, “You misled us with regard to the genetic information you provided.”

AB: So when ACLU approached you, they also approached others, but you were determined to be the only plaintiff that had a standing, correct?

HO: That's correct. Right, so if you look at the list of plaintiffs, there are many, including some large professional societies. If the case is – the case was originally called the Association of Molecular Pathology v. The Patent and Trademark Office. The Patent and Trademark Office was dropped. The defendant is now called AMP v. Myriad, and AMP is an association of tens of thousands of pathologists who do molecular tests of one sort or another.

AB: Okay.

HO: About that, they were held not to have standing, and basically, Judge Lourie saw this as economic opportunism with others trying to poach on Myriad's hard-won intellectual property.

AB: Was it stressful at all to be determined the sole plaintiff of this case?

HO: [Laughter] Not particularly. It sort of amazes people when I tell them that. It's not something I go and advertise, but sometimes I feel the need to disclose it. And it was really quite funny because my wife, my daughter, and a friend went to the hearing before the Appellate Court in July. The second time where the Appellate Court and then the ACLU staff had a reception afterwards, and so we went. And Daniel Kaplan, who is a historian of science now at Yale, is writing a book about the case. And the lead attorney at ACLU introduced us, and Dan's parting words to me were, "Stay well." But so far, so good.

AB: [Laughter] That's good. So I saw that Myriad claimed that when you changed your employment from NYU that your standing should be nullified. How was that resolved, or did the Court even take that into account?

HO: The Court denies – the Appellate Court denies their petition on that.

AB: Okay, so they just let that go?

HO: Then, Myriad had some claims that were false, about whether I had my petition, excuse me, my position, at Montefiore. Then Montefiore promptly updated their website to point out, I really did have my position there, the Court didn't buy the argument that their complaint was really with NYU and not with me.

AB: Okay. So has the litigation changed what you're researching, or has your research mostly stayed the same and you're still fighting to be able to look at the *BRCA1* gene?

HO: It has stayed the same, but I think that now, given where genomic medicine has gone, we know of many risk genes for breast cancer. There are new ones that are

being reported all the time, and they're from the point of view of patient care. It will be useful to have just one panel to do whole genome or whole exome sequencing or some sort of sequence-based approach where we could cast all of these known genes at one time and report on the risk. That's a challenge. It's really leading to piecemeal care.

We and others are sequencing genes from women at high risk, and I have to say that it's a part of our criteria, for instance, in our hybrid study, which we're just about to watch on a national basis with recruitment, will be the people of *BRCA1* and *2* negative. And so I could foresee that if the patients are nullified, and we or others make significant discoveries that have commercial possibilities, that Myriad could make a claim for patent infringement there because these discoveries were possible, only on the basis of knowing people's *BRCA1* and *2* status.

Now, all that said, it has become the official policy of the US government not to patent genes, and it's really having a very ground-shifting effect within the field of intellectual property law. So for instance, we do file patents for other things, and we're on the verge of filing a patent now for a method of assessing the effective genetic variants, not the DNA level that is approaching level, and Johnny, who was my research associate, and I got into a debate with our now patent attorney about "Is *Myriad* going to impact this? Is *Prometheus*, the antecedent case to *Myriad*, going to influence this?" And the issue is that we don't really know.

I think with *Myriad*, the genetic lawsuit forced the national administration to take notice of our gene patenting and to really do a 180-degree intellectual flip about this. You know, rather than having gene patenting be pro-competitive, in fact it was anti-competitive. There's much debate on what sort of patents really promote economic development and others with real intention to inhibit that.

AB: So where would you draw the line of what should be patentable in DNA, like, can you patent specific sequences of DNA or only altered DNA or cDNA?

HO: It's now – someone's at the door again...

AB: Okay, no problem.

HO: I'll be right back.

AB: No problem.

HO: [...]

Yeah, I don't like any of the idea of gene patenting because I think that it is an invention of nature and not an invention of people, so I would really draw the line. You know, I think that *Myriad* went way over the line at what they did. I'm saying literally they have probably the best patent attorneys that their money could buy.

And so, you know, they tried to patent everything that they could think of with regard to the genes and their applications and probes and primers and 15-mers and mutations and drug discovery. So there are multiple patents there. We are only challenging some of them. I think the expectation in challenging these will really strike at the heart of the implications for genetic testing.

AB: So going along with the Myriad case, what are your feelings on privatization of genetic research and just scientific research as a whole?

HO: I think there's certainly a place for private research as well as publicly funded research. A fair amount of work that I've done, for instance, has been sponsored by private funders and not by government funders. I think their support in that regard is essential. I think that the high-tech industry has many impressive clients under its belt. I think that some of the most exciting commercial development, excuse me, technology development, such as next generation sequencing, as recombinant and antibody pharmaceuticals were done in the private domain. I think that it's a very important sphere for providing progress and economic competitiveness.

I may differ from some of the other plaintiffs in that regard. I suspect that the other geneticist plaintiffs probably have a point of view that is similar to mine. I know, for instance, what David Ledbetter's point of view is because he's talked about it publicly. And you can see him, for instance, at the ASHG discussion from last year about gene patenting, talking about his point of view. I think it's similar to mine. He argues, for instance, that if we make a significant discovery on the academic front, and we patent it, and we want to promote competitiveness, well, we shouldn't have a single licensing agreement, which is what Utah did with Myriad. That, it would provoke competitiveness if we had a more open licensing agreement approach.

AB: Okay.

HO: I think that some of the counselors or patient plaintiffs in the lawsuit may have a different point of view.

AB: So when you're talking about your own research and looking at the breast cancer genes, do you think that when patients get predictive genetic testing done, that they understand their results or that they're interpreting them correctly?

HO: Yeah. I think that, for the most part, that we do. For the most part, we do pre-genetic test counseling to tell patients what they can expect with regard to their results, so it doesn't come as a surprise to them if they hear it's positive or negative, and this is what the options might be. But to their credit, Myriad, unlike some other commercial test providers, have been strong applicants [advocates?] for pre- and post-test genetic counseling, so they want patients to understand. I think they use pretty good material, educational materials. Obviously, they're not the only materials in the field. Now, with all the new risk genes that are being identified, I don't think we really know how to counsel patients post-test because there's a

whole new domain for it. It's going to become a whole new area of investigation and whether the *BRCA1* or *2* rules apply will remain to be seen.

AB: What do you think are the risks of predictive genetic testing and letting people know whether they're more inclined towards a certain disease?

HO: I think that we all have something, and obviously, I'm a medical geneticist, so I think knowing is useful and important. In terms of the dark side of genetic testing, some people, in fact, may not be prepared. Let me contrast two different experiences for you in that regard. For instance, in the case of high-risk breast cancer testing of *BRCA1* and *2*, I think that a very significant number of our patients who come from high-risk families, but are not affected with breast cancer, assume that they have the gene. Then they assume the likelihood of their getting the gene was 100%, which it obviously isn't, since it's [not?] the dominant condition. So they experience a sense of relief when they learn that they don't have the gene.

Now, there are some thorny situations there with regard to survivor's guilt. There are situations that involve identical twins. My daughter, for instance, who is now a junior in college, is taking a bioethics course, and she worked on a case that we've seen at NYU: identical twins where one had breast cancer. They came from a high-risk family, and she told her genetic counselor she wasn't planning to tell her sister. And the genetic counselor said, "How many times a day do you talk to your sister?"

"About 4 or 5."

So the counselor said, "How can it be you're just not going to tell her that you have genetic testing?"

And, as the woman relented and agreed that her sister should come and participate in the genetic counseling discussion.

There are funny situations like that that arise, and on a grander scale of course, once someone learns that they have a particular genetic risk, it may be applicable to other family members.

But the contrasting situation is that, in that instance, occurs with our patients with high-risk cardiac at Montefiore, especially the ones that come from the certain cardiac death families, from fatal arrhythmias. So my colleague here, Siobhan Dolan, surveyed a bunch of these people. And that is so horrible to contemplate, "I'm going to die suddenly from a fatal arrhythmia," that those people assume, "Well, I don't have the gene." And when they learn that they do, they are shocked. People then expected that was what would happen with *BRCA1* and *2*. I would argue, for the most part, it didn't, but with fatal arrhythmias, it does. So learning genetic information, despite pre-test genetic counseling, can be truly shocking to people.

And then, as we dig in more with some of these genes, one factor has more than one effect. It may point you – you may have a mutation of a gene that puts you at increased risk of breast cancer, but it may put you at increased risk for other cancers as well. It may put you at increased risk for other diseases. Another example in that regard, for instance, is genetic testing for the P53 gene, which increases the risk, not only for breast cancer, but for many other cancers. And, those are people who really tend to die young from cancer, and we don't necessarily have the quick screening strategies for how to treat those people.

AB: Do you do any of the genetic counseling or sit in on any of the counseling, or are you more behind the scenes?

HO: You're asking questions about genetic counseling?

AB: Yeah, have you ever sat in on the counseling, or do you do any of the counseling?

HO: No, no, no, of course, I [don't?] counsel people myself.

AB: Okay.

HO: I've sat in with my genetic counselors. For the most part, I don't because they're highly qualified professionals who do an excellent job providing this information.

AB: Yeah. So unless you've anything else you want to comment on with *Myriad* or anything in this regard, I just had a few questions about your work on the Jewish Diaspora populations.

HO: I think that *Myriad*, if it is successful in the Supreme Court, will be a game-changing case. I think that if it's not, then it will be just a historical wrinkle. So we're sitting on the edge of our seats now, waiting to see whether the Supreme Court will grant cert for a second time. Our attorneys think the likelihood will be that it's on the order of 50%, whereas for a general appeal to the Supreme Court, I think the likelihood of their granting cert is on the order of like 6% [60?]. So, it's pretty good. It sounds like we could be going to the Supreme Court.

The Appellate Court judges really thumb their noses at the Supreme Court. The Court has asked them to re-rule on *Myriad* and *Prometheus*. It was a majority of the appellate, the three-judge panel of the Appellate Court, that was, they think that *Prometheus* applies, and then they went back and rescheduled the argument that they had made the first time. I can imagine the Supreme Court being annoyed with that and saying, "Okay, well we're going to grab matters into our own hands." And in *Prometheus*, it was a unanimous ruling. The opinion was written by Stephen Breyer, and they were quite emphatic that natural processes should not be patentable – for instance, that it was like $E=MC^2$. It is reasonably likely that they will hear the case, that they will cite their own ruling and *Prometheus* and will say, "Well, DNA is like $E=MC^2$," but all remains to be seen.

AB: Yeah.

HO: And I guess if it does go to the Supreme Court, that probably, Kagan would recuse herself from it.

AB: Okay. So, I was just doing research on you and saw that you worked with the genetics of the Jewish Diaspora populations. I was just wondering what led you to studying that.

HO: Oh, it's something I've been interested in for a very long time. Since I was a medical student and my introduction into medical genetics was with the stab at creating a genetic screening program here in the Bronx, as a matter of fact, or the Ashkenazi Jewish community, to identify people who were carriers for Tay-Sachs disease. It led me to wonder about my own Jewishness, as well as to wonder about the genetic history of the Jewish Diaspora population, so now we know. And the work was independently confirmed by the Skorecki [sp?] group in Haifa and actually called Skorecki. My great competitor and great friend and I just wrote a review article that was published two weeks ago in Human Genetics.

It's really interesting because I was arguing that Jewish population genetics is really a micro continent to world population genetics. And what we see across all human populations can be seen in the 16 different Jewish populations that we've studied or 17 Jewish populations we've studied. We made some various interests now. There are new questions that we would like to pursue, but that's another thing related to genetic medicine among Jews. And Jews, Ashkenazi Jews in particular, are America's largest genetic isolates, the degree of relatedness between any two Ashkenazi Jews, we found, is what one would observe for fourth to fifth cousins. It potentially makes the process of genetic discovery more efficient among Ashkenazi Jews than it is, for instance, in the European-American population. So you have an investigator at Duke, David Goldstein, who has dabbled in Jewish population genetics at various times and was one of the players in the identification of the so-called, the Cohanim modal haplotype the preceding Y chromosome.

AB: Wow. So can you tell me just a little bit about the HapMap project that you worked on?

HO: We recruited people from 17 different Jewish populations in the United States, Europe, and Israel that all came from these different Diaspora groups. We required that people consent to participating in the project. We required that all four of their grandparents came from the same Diasporic community, and we ran DNA chips half female traits version six microarrays on them, which gave us about a million data points to study. And then we did a variety of different analyses that would give the relatedness of people within a population – were they actually a distinctive population group, and the answer is, in almost every case, they were. A couple of exceptions to that are Greek and Turkish Jews are pretty much identical. Moroccan

and Algerian Jews are pretty much identical. Not surprising that they were near one another, had similar population histories. We defined the degree of relatedness within and between populations. So I mentioned that any two Ashkenazi Jews that are related to each other is what one would have said for fourth to fifth cousins. For Israeli Jews, it's third cousins. For Libyan Jews, it's sixth cousins once removed.

We looked at the ancestry of these various groups and mostly middle-eastern to middle-eastern Jews, hybrid middle-eastern and European-to-European Jews, hybrid European and middle-eastern and North-African-to-North-African Jews. We published a paper two months ago about the nature of North-African Jewish Diaspora and despite their North-African ancestries, they are not closely related to the current North-African non-Jewish population. You know, there really was this divide that occurred a long time ago. It's not surprising. Jews in North Africa live very separate lives under Islam.

AB: Well, those are all my questions, unless you have something you want to add?

HO: I don't think so. If anything else comes up, shoot me an email.

AB: Definitely. Thank you so much for taking the time to do this.

HO: Okay, you're very welcome.

AB: Thanks.

HO: Bye-bye.

AB: Bye.