GENETICS & PUBLIC POLICY CENTER

"WHO OWNS YOUR GENES? INTELLECTUAL PROPERTY AND THE HUMAN GENOME"

WELCOME:
KATHY HUDSON,
DIRECTOR, GENETICS & PUBLIC POLICY CENTER,
JOHNS HOPKINS UNIVERSITY

PANELISTS:
ROBERT COOK-DEEGAN,
DIRECTOR, CENTER FOR GENOME ETHICS, LAW & POLICY,
INSTITUTE FOR GENOME SCIENCES & POLICY, DUKE UNIVERSITY

F. SCOTT KIEFF,
PROFESSOR OF LAW, WASHINGTON UNIVERSITY, ST. LOUIS;
FELLOW, HOOVER INSTITUTE, STANFORD UNIVERSITY

STEVE HARO, SENIOR ADVISOR & COMMUNICATIONS DIRECTOR,
OFFICE OF U.S. REPRESENTATIVE XAVIER BECERRA (D–CA)

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(*edited for clarity)*

KATHY HUDSON: We're going to go ahead and get started. I'm sorry for the delay in getting under way, but I understand and can hear that there's quite a storm going on outside, so we'll probably have some wet folks dribbling in.

I want to welcome you to this seminar on "Who Owns Your Genes? Intellectual Property and the Human Genome." My name is Kathy Hudson. I'm the director of the Genetics & Public Policy Center and our mission is to create tools for policymakers and the public to better understand and respond to challenges and opportunities arising from advances in human genetics. We sponsored this program, Genetics Perspectives on Policy Seminars, to explore areas that are not central to our own work and to identify issues that we might work on in the future.

We have four panel presentations today and we're going to have each of them speak sequentially, and then we'll have an opportunity for questions and answers and comments from you all. And so I will introduce them in the order in which they will speak. Our first speaker is Bob Cook-Deegan, and I want to thank Bob for co-organizing today's seminar with us. Bob is the director of the Duke Institute for Genomic Sciences & Policy Center for Genome Ethics, Law and Policy. That's a very long name. He chairs the Royalty Fund Advisory Committee for the Alzheimer's Association and is secretary and trustee of the Foundation for Genetic Medicine. Before he went to Duke, he spent many, many years in Washington in various important roles at the Institute of Medicine. He was the acting executive director of the Biomedical Ethics Advisory Committee that some of you will know who are familiar with the history of ethics. He was at the Congressional Office of Technology Assessment before its sad demise, and his Bachelor's degree is from Harvard and his Medical degree is from the University of Colorado. And he will sort of lay the groundwork for us and get us all up to speed before the other panelists.

Our second panelist is Scott Kieff. He is a research fellow at the Hoover Institute at Stanford University and a law professor at Washington University in St. Louis. So that involves a lot of commuting? (chuckles) He teaches contracts, patents and the interface between contracts and intellectual property and biotechnology. He formerly was an assistant professor at the University of Chicago and the Northwestern University School of Law. Before that, he practiced law as a trial and intellectual property lawyer, and his undergraduate degree is from MIT in molecular biology and microeconomics – all things small – and he later graduated from the University of Pennsylvania Law School.

He will be followed by Barbara Caulfield, who is the executive vice president and general counsel for Affymetrix Corporation. It's a science and technology instruments firm in Santa Clara, California. Before joining Affy in 2001, she was a partner at the law firm of Latham & Watkins and Orrick, Herrington & Sutcliffe. That's why I didn't go into law – all those names. She represented a wide range of companies including Microsoft, Hoffman-La Roche and Apple. Before that, she was a United States District

Judge for the Northern District of California and before that was in academia – a professor of law at the University of California, Hastings, and before that a trial lawyer. Her Bachelor's degree and law degree are from Northwestern University.

And finally, we will have Steve Haro, who is the senior advisor for Congressman Becerra who is from the Los Angeles District. He plays a critical role in advising the congressman on major policy issues as well as serving as his spokesperson for the media and to constituents. He has served as the congressman's press director and legislative director as well as the Colorado communications director for John Kerry in his presidential campaign. He, before that, worked for a public affairs firm in Los Angeles. He received his Bachelor's degree in political science with a communications minor from Loyola and also a Master's degree from there as well.

So we have an outstanding group of speakers. I think their presentations will be provocative and I hope that you find it interesting and engage with us in questions and discussion afterwards. Bob.

ROBERT COOK-DEGAN: So let me, on behalf of all the speakers, thank Kathy for organizing this and serving a function of pulling groups like this together. Thank you all for coming in from the bad weather outside, and I also wanted to extend a thanks for the people doing stuff in the background, Rick Borchelt and Shawna Williams. Thank you all for organizing this.

So I'm going to start at a very basic level. I'm going to assume that there's not a lot of detailed knowledge in the audience, although some of you probably do have a lot of it. I do want to start the discussion from a fairly straight forward base of why are we meeting here today and what's this all about. So I'm going to go through a few slides and then I'm going to show you some data about what's been going on in the real world, in different parts of the world.

But the first thing is, what's a patent? A patent is something that a national government gives as a right – it's not a human right, it's a commercial right – to block other people from making, using or selling something that somebody has invented. And there are these criteria of something needs to be new, it needs to be useful, and it needs to be something that isn't just something that Joe Schmo on the street would have discovered. There has to be something that's kind of cool and new and different about the thing that they've discovered in order to be able to get this government right. And you get a right to exclude other people from making, using or selling your things by using the national court system as the enforcement mechanism. So that's basically the package that a patent is, and what you have to do in order to get a patent is you have explain how you made your thing in enough detail that somebody else can make your thing. So you're getting the right to exclude them from doing that, but you also have to give them enough information that they could do it if they wanted to. That's kind of the tit for tat.

Patent, as a word, means open. So the original idea was in return for getting this right, you also have to disclose all sorts of information. It's an alternative to keeping

things secret. So that's why many governments all over the world have adopted patents as a tool for stimulating innovation.

So here are some basic numbers that are going to be surrounding us as we have these discussions today, and they're a little complicated. For those of you who want to actually trace these back to the sources, all of the slides that have data on them have sources associated with them, so we'll make those available, but here are some basic numbers. There are about 44,000 DNA patents that have been issued by the U.S. government, and a DNA patent here is defined as one that mentions something about DNA or RNA in its claims. The claims are the part of a patent that actually stakes the territory and says this is what I've invented. So a DNA patent is one that says something about DNA. A subclass of that is a sequence-based patent, and most of our discussion today would fall into that category, but not all of the examples that I'm going to go through. There are no precise counts, but there are probably something on the order of 16,000 of those. About 15,000 of those are in the U.S., and of those sequence-based patents, probably roughly on the order of 3,000 are gene patents. A gene patent is something that's basically encoding a protein in humans – that's the pink thing in the middle there. We don't have very precise estimates of any of these things, but to one significant figure, these are the right numbers.

This is true in the United States, it is not true abroad and I'll show you a slide in a minute. This is the time pattern of the issuing of those 44,000 DNA patents in the United States, and what you'll see is, there wasn't a whole lot of patenting activity. There were a few DNA patents, believe it or not, before Cohen and Boyer – Cohen and Boyer happened right here in 1980 – but the DNA patenting business didn't get really big until the 1990s. Remember the Human Genome Project started on a big scale sometime around 1990, although it kind of was gathering momentum in the second half of the 1980s. Gene patenting and DNA patenting went exponential from '94 to about 1999, and then it started going up and down, and in fact, for four years in a row, we saw declines from – this is 2001-2002, and then it dropped for these four years in a row. We thought it was going to keep going, we thought oh maybe we've hit saturation, but lo and behold in 2006 we were back up to the 2004 level plus a little bit. That last number is 2007. That's only through March, so we don't know what the numbers are going to look like.

So this is a little bit of the map of the territory. Now these are not sequence-based patents, and these are patents that have been granted in only one jurisdiction, which is the United States. This is a graph taken from a group that did a study for the European Commission that shows how starkly different the patterns are between the United States. So this big black mountain is the number of sequence-based patents. So of those 16,000 sequence-based patents, this is what has been issued in the United States. Red is what's going on in Europe and blue is what's happening in Japan, and the thing to notice here is the United States relative to both of the other major economic jurisdictions where patents matter a lot in this business – the U.S. has a whole lot more intellectual property than its two rival jurisdictions.

So that's the backdrop for our discussion. Summary of that is there's a massive social experiment going on with lots of stuff being covered by DNA patents and sequence-based patents in the United States and other places not being so friendly to gene-based patents, and these are natural experiments that are going on in real time, the results of which we will not know because the litigation cycle in this business is about 20 years. So if the patent stuff started happening in the mid-1990s, we're going to start seeing the story playing out over the next decade, and it will be carrying forward for the next two or three decades. So it's a social experiment, but we aren't going to know what the outcome is because we're going to be part of that outcome – we'll be living through it.

Now this is a complex slide that shows you a bunch of technologies that I think anybody who does molecular biology in the room would agree – everything on this slide is something that they've done or they know about in a lab. These are all very important technologies. The thing to notice about them is some of them are patented, some of them are not patented. Some of them are patented in the private sector, that is, by companies. Some of them are patented by universities and licensed to the private sector. The things in yellow are not patented at all, the things in blue are patented by universities, and the things in red are patented by companies. And this is a confusing slide because it's a confusing world.

So a few things to say about that: it seems like it should make sense that in fact, if something is patented and if the theory works, what you get a as a right is to block other people from making, using or selling your invention. That's what the patent gives you. Why does it give you that? Because it gives them an incentive to pay you or get your permission to use the thing that you've invented. So there is an anomaly here and that is if you have a patent, it's only valuable if other people use it and if other people pay for it. So there's this funny dynamic that goes on, and it's not a simple picture. So what we're looking at here are three incredibly important technologies in the early history of recombinant DNA or molecular biology. Everybody would agree these are seminal technologies. All three of them could have been patented. Only one of them was; it was patented by a private company, and this is actually a graph that somebody in the audience, Joe Fore, constructed about two years when he was a junior undergraduate. And this is basically a rough indicator of people using this technology and publishing about it in the scientific literature. So these are citations to the seminal paper for polymerase chain reaction or to this incredibly wonderful cloning vector, pBR322, that was invented by Bolivar and Rodriguez – that's what the B and the R stands for – at the University of California, San Francisco, and then a seminal technology for DNA sequencing that was invented by Alan Maxim and Walter Gilbert at Harvard.

The thing to notice here is you can't really tell the difference too much in the adoption of these technologies. So if your theory is if something's patented, nobody gets to use it – wrong. In fact, there are some stories behind this graph for polymerase chain reaction, which was discovered at Cetus, sold to Hoffman-La Roche, and Hoffman-La Roche has made something on the order of about $2 billion off of this invention. Cetus sold it for $300 million dollars about three or four years into this cycle, or actually more

than that – more like six or seven years into the cycle. But there is not a simple picture here and we have two technologies that are unpatented, one that is patented, and yet the graphs of adoption look pretty similar.

So why are we here today? Well we're here today because there have been some controversies connected to gene patenting, and so I've done the infamous patents on the left – they're in yellow, so they're the thumbs down, and the thumbs up patents on the right side in green are things that most folks would agree are success stories of gene patenting or DNA patenting. So on the left side, we have things that were patented, but the thing I want to point out is BRCA1 and 2. These are the breast cancer predisposition genes that were discovered by the University of Utah, NIH and Myriad Genetics and have, for the most part, all the licenses for those patents have been consolidated at Myriad Genetics in Utah. Canavan's Disease was a rare disorder that was a poster child for how not to license a DNA diagnostic for several years until it was settled out of court. Athena Diagnostics is another thing that is coming up where the model there is largely university-based. Intellectual property is being exclusively licensed to a single purveyor of genetic tests and it's causing some controversies There was also a controversy about access to research tools that was probably best embodied by two very famous cases that involved DuPont and Harvard and other academic institutions. These are seminal technologies for mouse transgenics that caused a lot of controversy for about three or four years until a settlement was reached between NIH and the company.

So these are controversies on the left side. On the right side, we have a bunch of things that, for the most part, were licensed – they're regarded as success stories. We have products on the market for stimulating the growth of red blood cells, erythropoietin, insulin, clotting factors, immune modulators – lots of, basically, protein drugs based on gene patents that have been brought onto the market using the classic blockbuster pharmaceutical model of you patent the thing, and the thing in this case is the gene that allows you to produce the protein. And that has been the economics of Genentech and Amgen for a large fraction of their products that rose them out of the ranks of baby biotechs into the ranks of baby pharmaceutical firms during the 1980s through the early 2000s, and they're still going gangbusters. Cohen-Boyer was a seminal technology; there is no more seminal technology in molecular biology than recombinant DNA. It was embodied in three patents that were very sophisticated. There was a very sophisticated licensing scheme that was essentially created by Stanford University, Niels Reimers – brilliant job of licensing. This technology got out, was very widely used, generated about a quarter of a billion dollars in revenue for Stanford and the University of California, and probably had zero impact on end prices of products that came out of recombinant DNA. So a lot of products – some hundred products or so – have come out of recombinant DNA. They made most of their money by getting one or two percent of the revenue from producing those products using recombinant DNA.

What is the patent system doing? I would argue that it's doing three things that I think will come up in the discussion to follow. Sometimes it is rewarding the inventor for having done something valuable for the world, and I think that's the story of Cohen and Boyer. That work was done at Stanford and the University of California. Who made

the money? University of California and Stanford created the conditions where these discoveries happened. They got a quarter of a billion dollars in return for that. They didn't really obstruct the research process.

In other cases, the patent system is inducing investment in new companies. So the story of Myriad is that they were able to attract new capital in order to pursue products as a biotech firm in part because of the prospect of patents. So it's inducing investment and, of course, Incyte and Human Genome Sciences were companies that in the early 1990s went whole hog into basically sequencing human genes in order to turn them into products like erythropoietin or insulin or tissue plasminogin activator. That was their idea. They were able to attract that capital because of the prospect of patents, and those companies probably wouldn't have existed to compete with the publicly funded Human Genome Project if there hadn't been a patent system. Is that a good thing or a bad thing? That depends on who you talk to, and you're going to hear both sides of that story today.

And then finally, there's another thing that the patent system does in the drug business big-time. The main problem that it solves is the problem with free riders. And what do I mean by that? I mean that if you're developing a product that requires a substantial amount of investment -- so, for example, you discover something and it may be really useful, but before you can put it on the market, you have to prove that it's safe and effective, and you're going to have to spend several million dollars – maybe $100 million, maybe $200 million – proving that it's safe and effective. The system of innovation will not work if we're relying on private capital markets, if, as soon as you put your thing on the market, somebody can make your product, they don't have to pay you anything. So that's the problem that the patent system is doing – that's the problem that the patent system is solving when you're developing a pharmaceutical product, and that is the model that the court systems all over the world basically said that's what gene patents are like. These are just kind of fancy drugs. Erythropoietin is just a fancy version of Viagra, right? And that was kind of the equation that's the intellectual foundation for most gene patents.

I'm going to finish with an empirical study that's been done by some of our colleagues at the University of Alberta that is looking at one particular controversy that probably is the largest and most important of – and it probably explains why most of you are here today, whether consciously or not, and that is the breast cancer controversy that began with Myriad Genetics. And this is a recording of articles published in the lay literature, so this is newspapers and news weeklies like Time, U.S. News and their foreign equivalents, all in English language – that's why you don't have the other countries. This is Australia, Canada, UK and the U.S. And what you see is this incredibly striking feature which is that in particular in Australia and Canada, there was a lot of negative coverage and a little bit of neutral coverage, almost no positive coverage. In the United States there at least was some positive coverage of the BRCA story, but most of it, even in the United States, which is the home to the company where this was happening and the market where the business strategy of Myriad was most successful, it was still probably three-to-one negative or neutral to the positive stories in the literature. That's you guys. That's those of you who do this for a living, and I think, in fact, it was

probably this coverage that drives the policy apparatus much more than what was actually happening in the slides that I showed earlier which is what's happening in the patent world, because people don't generally pay attention to the patent world until they read about it in the newspapers. So you guys are the vectors driving this story, and probably driving the policy apparatus much more than the practices of the patent office and the practices of the businesses. And I'll stop there and open it up to the other speakers. Thank you. (Applause.)

MR. KIEFF: Thanks a lot, Bob. That was really very helpful, and thank you everybody for coming. I understand that my job here is to be a bit of a troublemaker, and so I am supposed to give a presentation that will respond to that press and respond to what some of my colleagues are going to talk about. I guess it's a little weird to respond before they've had a chance to talk, so I hope that I am addressing the issues they will raise. And the point, you know, the bottom line takeaway -- I'm a professor, right? So there's a very good chance you guys will all be asleep in like 17 seconds, so the bottom line point here is that biotech patents, gene patents, I think are great. And I think they're great, not just for everybody -- I think they're especially great for the little guys, and here's why.

Let's just talk a little bit about how I think – my colleagues and I think – about these issues. We approach this from a field called new institutional economics. So this is a field of economists who, instead of thinking about how capital makes a difference or how resources make a difference or how technology makes a difference, we think about how institutions make a difference, and by institutions, we mean the set of human-imposed constraints, laws, rules, norms, and their enforcement characteristics. And this is a body of work – the old institutional economics folks were people who kind of noticed that law matters and then new institutional economics folks are folks who try to figure out how it matters. What are the reasons why you want a law that says don't go above 55, and what are the reasons why you might want a law that says don't go too fast? Those are different laws, different details, designed to basically achieve the same thing, and there's a whole body of political economists and social scientists who study this, the new intuitionalism, and you know, there was a Nobel Prize given recently in the field – '93 prize to Doug North and Bob Fogel. Doug is my senior colleague at Washington University in St. Louis and my senior colleague at Hoover, and it's important to remember – I don't think anybody would call Doug a Republican. I don't think he's ever voted Republican.

So the idea is that to think about these issues is to say to ourselves let's just compare different institutions, because we're going to recognize that they all are fraught with problems. And we have choices to make, because after all, who makes laws? We do. So we ought to be asking ourselves which laws do we want, and which set of problems do we want to solve, and which set of problems do we want to just say, actually, we can handle those – we can handle those problems because they are better than their solutions.

We've got a team at Hoover working on commercializing innovation, and our team is looking in a variety of fields in law and economics like intellectual property, like patents, but also at economic development, and we look in the public sector and private sector and we do a variety of approaches. We collaborate with people like you, we collaborate with other academics, we do dispute resolution, we do consulting, too. And so we're always available online and the slides will be available online, so you don't have to take too careful notes, and this recording will be available online. So, I'll just go quickly here and invite you to contact us if you have any questions. In fact, we have a media fellows program at Hoover. A lot of folks in the media like to come and spend time and talk about ideas. We love to talk about ideas.

Why is the United States so rich? I think it's a simple answer. We have property rights and intangibles. We're all the way over on the side of this graph, so the only countries that further over than us are countries that have a lot of capital and not a lot of capita. Like Qatar, right? They got oil but no people. But if you're like a normal country with a lot of people and money, we're the place to be. Why is that? I think it's because we have property rights. How do property rights matter? You read a lot of people who talk about land and how oh, someone's going to take my house -- that stuff matters, but modern economic growth is about intangible assets. It's about intellectual property, it's about contracts and it's about finance or capital. And this is not about protecting the wealthy. This is about helping the poor get wealthy. This is about lifting people up.

The U.S. financial system – it's massive. And again, why is that? It's because we've got property rights. We're all the way over on the side. Hong Kong is further over than we are. Again, it's because it's a city that's a capital market. But if you're a country with a lot of people and a lot of space, we're where it's at. Why? Let's just look at the example of banking. Let's take something other than intellectual property. You're not going to deposit your money in a bank unless you think you can get it back. The bank's not going to loan you money unless they think they can get it back. The minority shareholders aren't going to invest in the company unless they think the insiders who control the company can't take the money they've invested, and the bank's not going to park itself in your country unless it thinks the government isn't going to take over the bank after the bank's set up.

Let's look at Mexico. One of my colleagues studies Mexico – Steve Haber – he's an economic historian. He notices, in fact, you've got no property rights in every one of these areas, and what do you have in Mexico? Almost no banking system. Last year around 18,000 home mortgages in Mexico -- that's like Santa Clara County. Mexico is a big place, and if you want a home and you don't have like $1 million to buy it and you want to borrow that money, you can't. It's not easy to enter the market for home ownership because people can't loan, because there are no banks. So property rights make the system work, and they make the system work not for the people with the money – those guys can buy their houses anyway; it's for the people who need to borrow the money.

The U.S. IP system is massive. IP companies: big part of our economy, largest sector. IP is about $5 trillion; it's about half of our GDP and it's more than anybody else. All right, so let's ask ourselves, why IP? Justice Robin Jacob, he's a famous judge in England who specializes in IP, he has got a wonderful sense of humor, and he writes about the Connecticut Yankee who goes to King Arthur's court, and the very first thing he does is write a patent system so that his country can go forward. So the argument is you need patents to go forward.

But Justice Jacob is a bit of a troublemaker too, and he says, so wait a minute; do we really think that IP is so good, or – calling it intellectual is really misleading, he says; it's like a squirrel is a rat with good PR. This is really a law with private monopolies. So, hey, good point. So let's ask ourselves, what is IP really about?

Now, Bob I think talked about a number of reasons and I think Bob is basically right. That is how most folks think about it. They do increase innovation, but they are not just incentives to invent; they are not just about getting Isabelle the inventor to make her next invention – much more so than that. Patents are about getting inventions put to use after they have been made. Getting inventions put to use requires coordination, complex coordination among a lot of different folks: inventors, venture capitalists, managers, laborers, factory workers, skilled laborers, other technologists, and getting all of those people to dance with each other is what the right to exclude is all about.

So getting all of these people to talk gets the invention deployed. It's like the D of the R&D. And if that happens, that means that new players can compete in the industry. And what does that mean? That means that patents are actually anti-monopoly weapons. They are the vital slingshot that David uses to take down Goliath.

And it turns out that Giles Rich, the guy who wrote our patent system and the guy who was a famous judge in D.C. on the court of appeals interpreting the statute, he told us in the 1940s in all of his writing that he wrote the system not to help inventors invent, but to help us get access to inventions after they have been made.

Look at biotechnology. Before 1980, U.S., Europe, and Japan all had no patents in basic biotech. After 1980, the reason we have patents in biotechs and they don't is because we allow them and they don't. We changed our law to allow patents. All right, and what result? Only in the United States and only after 1980 do you see a massive increase in the number of new drugs and new devices actually brought to market. In fact, you also see a massive number of small and medium-size biotech companies. So the presence of patents in biotech is correlated with a drastic increase in access and a drastic increase in competition.

You see, people like to talk about norm communities like open source or open science, and there are a lot of benefits to those communities. After all, if we're talking about coordination, any type of centralization can coordinate. And in fact, there are some advantages to informal communities like the Hasidic diamond merchants or like a church, or like a group of Arabs who only trade with each other and don't trade with outsiders.

There are a lot of benefits, and lots of our societies around the world rely on norms to enforce our promises. And in fact, it can be very inexpensive to get that kind of enforcement and very effective with that kind of enforcement.

But like everything in life, there is no free lunch. There are costs to relying on norm communities. First of all, what allows somebody like Linus Torvalds to control Linux is that he is famous. That attribute turns out to be an attribute that is much more difficult, much more clumsy for human beings to negotiate over than an attribute like property. You see, I can sublicense a patent; how do I sublicense Linus's fame? And how do I merge the chief rabbi with the pope, right? It's very hard to merge and divide and bundle and trade the assets that lead norm communities, and it's very easy to do that with property rights.

In fact, norm communities rely on homogeneity, lack of diversity and exclusion. And so if you're in favor of decreasing diversity, you're in favor of norm communities. But if you're in favor of increasing diversity and increasing trade, you like property rights because property rights allow people who are different from each other to trade and enforce. Norm communities only get enforcement if everybody is the same and goes to the same priest or the same rabbi to enforce.

In fact, empirical research shows that Linux and other open-source projects and software end up being controlled by a very, very small number of people. And let's remember that the software industry in the United States had no patents in the '70s and '80s and ended up with, what: Microsoft, a single large player. So remember, the absence of patents and software was correlated with a single large player, and the presence of patents in biotechnology was correlated with a massive increase in competition and a massive increase of access.

In fact, today, IBM says, let's give away patents for free because we want free access to software. But if property rights lead to coordinated development, that means avoiding property rights leads to uncoordinated development. So if you have uncoordinated software development, that means, well, an increase of demand for consulting services. Guess who sells consulting services today. That is, IBM sold their hardware division, Lenovo, to the Chinese, and they now sell consulting services. They want uncoordinated development because that increases demand for the things they sell, not because it's good for the public – it may be or it may not be – but because it's good for their bottom line.

Same with biotech. Merck said, oh, we want open science in the genome project. Washington University – we were one of the three world centers for the human genome project. Merck gave us a lot of money at Wash U. – said, sequence the genome but only if you promise not to patent it. And Merck said, this is an example of a biotech company being against patents on its own assets. But wait a minute; the basic technologies that would have been patented would have been technologies that Merck would have had to pay for.

So this is big pharma simply saying no patents on the things we buy, but of course we love patents on the things we sell. And you will hear everybody make that argument: upstream patents are bad; downstream patents are good. To me, that is just narcissism; that is just, the things I buy should be free and the things I sell should be expensive.

So, in fact, for people who want to study property rights in the genome project, we put together a conference at Washington University and generated a book, and we asked everybody, what are the real issues. Rebecca Eisenberg, Arty Rei (ph), Michael Heller, and some other really serious people asked some important questions. And they said, look, maybe before 1980, we discouraged property rights in science, and after 1980, patents are increasing property rights in science. And these patents, they said, are going to block downstream research. They are going to lead to so-called transaction costs. It's going to be hard to get deals done.

But wait a minute; first of all, genes patents don't cover your genes or mine because the touchtone of patentability is novelty. Your genes, my genes, they are not new; they exist already. The patents in this area cover these isolated or purified versions of the genes. And while some people will tell you that is kind of like covering the gene, anytime someone tells you kind of like, that is when you check your wallet because that is like the street magician who waves his hands, right. Kind of like is a synonym for, I really don't want to explain why.

In fact, before 1980, the norms in academic science did not discourage property; the law did not allow for patents, but basic academic science has lots of property rights. It's kudos, it's fame, it's promotions, it's professorships, it's publications, it's grants, it's peer review. And the problem is the transaction costs that economists study that make it so hard to transact over patents are the same transaction costs you have when you try to transact over promotions or tenure or professorships, and economics has shown that making a market thicker decreases those costs.

So adding patents to the market for basic academic science turns it from a market for kudos into a market for kudos plus cash. It adds diversity to the market and it adds wealth to market. Are there transaction costs in that market? Yeah, sure, of course, but they are fewer and less serious than they are in the other market.

In fact, we saw again that 1980 increased access, and we see that in fact, number one, patentees share a lot of those transaction costs. And Bob Cook-Deegan and I and some others have looked at the empirical studies of sharing data among scientists. And we find that there are a number of statistically significant factors for data sharing. Are you black? Are you a female? Are you at a lower-rank school? That turns out to be statistically significant.

But you know what is not statistically significant? Do you have a patent or does the other guy have a patent? In fact, patents are not at all correlated with blocking transmission of academic science, and patents turn out to be a big part of the business models that property owners use to decrease transaction costs for users, by, for example,

providing a reagent freezer program where the basic scientist goes to the freezer, takes out a reagent, and then the company that provides the reagent just direct bills the lab. It's like going to a Coke machine but you don't even need the cash for the Coke machine. You just go to the freezer, you take your reagent, and somebody re-supplies the reagent and bills your lab for the reagents you used. Those business models depend on patents, and in that way, patents are helping science not hurting science.

People will talk about the so-called anti-commons problem. What if there are, like, lots and lots of IP rights covering a single good or service? In fact, look at DNA-on-a-chip technologies. There are lots of diseases where the patient populations need to be segmented. And there is a real fear that if we treat with a wrong treatment, we will be killing people or not helping people. And so the fear here is that those wanting to go into these businesses suffer and those who would be treated by these businesses suffer, and these businesses can't get done if they are going to infringe 10,000 patents. That is the argument.

But wait a minute; I think that argument goes way too far. First of all, the original work on the so-called anti-commons story was work that basically said in the post-socialist economy, after the Soviet Union collapsed, why were there so many vendors standing out in the cold freezing and not using the empty store fronts they were standing in front of? Why didn't they just get the requisite licenses from the bureaucrats to use the storefronts?

And Michael Heller found that the reason they didn't get those licenses to use the store fronts, why they didn't come in from the cold, is that there were so many bureaucrats they had to talk to to get permission that it was just like, hey; forget it, man; I would just as soon stay out in the cold and build a little kiosk. I think Michael was basically right, but I think his explanation was wrong. It's not the number of permissions that matter; it's the nature of the people you go to for permission.

So if I say to a bureaucrat, hey, look; you know, I really would like to pay for permission; how about just some money. What is the bureaucrat going to say – shh, right? They can't openly negotiate, because if I trade money with a bureaucrat for permission, that is a bribe, that is extortion, that is illegal. You can't do that. The patents are totally different. Patentees are out there saying, please buy my patent license; please trade with me. In fact, go to www.uspto.gov for free and you can find my name, address, and phone number; contact me if you want my patent license. Patentees are totally different from bureaucrats.

It's also the nature of the permission you get. When a bureaucrat gives you permission, she can change her mind. When a patentee gives you a license, every court will enforce that license, and they'll it enforce it not just against that patentee, but they will enforce it against everyone else who takes a share in that patent.

And so it's the nature of the bureaucratic permission and the nature of the bureaucrat that was causing the anti-comments problem. That is why there is no anti-

comments problem with patents. In fact, if there were, you wouldn't be able to go on the Internet and buy a laptop computer with one click or a thousand dollars. You would need to hire 10,000 IP lawyers to negotiate 10,000 licenses, and you would pay millions and millions of dollars.

You can buy a laptop for one click on the Internet without hiring a lawyer precisely because good businesswomen and good businessmen and good lawyers have figured out ways to structure deals to make it easy for us to get access. In fact, our team put together a paper that shows how you actually can get deals done in the face of even the DNA-on-a-chip business, and it's really a story of coordination and self restraint. That little kitty cat will be safe; those dogs won't attack. And we talk more about that for those of you who want to look at these deal structures. But like Ulysses tied himself to the mast so that they didn't crash on the rocks, you can structure deals to get coordination done by using a little bit of self-restraint.

People today in the U.N. talk about patents killing in Africa. People are dying of AIDS and malaria and drug patents are the reason. Okay, that is a tall order, but is that really right? In the World Health Organization, the World Intellectual Property Organization, we want everybody to say more compulsory licensing in order to save people in Africa. All right, wait a minute.

First of all, over 95 percent of the drugs on the World Health Organization's central medicine lists, are off patent – they are not even patented. Number two, when we give away free-patented drugs to Africa, what happens? A lot of times they just throw them away because no one gets paid for distributing them, or they resell them on the black market in Tokyo, New York, Hong Kong, because that is where people will pay a lot more for those drugs than the poor people of Africa.

And there are a lot of people in Africa dying from a lot of things other than drugs – they are getting shot, they are blowing up, they don't have food, they don't have water, they don't have basic healthcare. These are serious problems. Human beings are dying and we are counting number of angels on the head of a pin about whether this particular drug patent is the problem. We have real problems here; let's pay attention to them.

In fact, in Uganda, the director general of public health is saying – in fact, he wrote an op-ed just about a month ago saying this – wait a minute, I don't want to treat people for malaria; I want to get rid of malaria. Give me some more DDT so I can kill mosquitoes because mosquitoes are causing malaria. That is much better for me than treating people for malaria.

And who is behind all of these initiatives? Argentina, Brazil, and India: countries that basically have some biodiversity and they want a better share of the patents. And I would say, give them that share; that is what property rights and contracts are all about, but not patents. And by the way, these are the countries with manufacturing systems that would have to pay patent licenses, and so they are just arguing something that will help them, but they are doing it in the name of helping Africa.

Now, I'm not a geography specialist, but I'm pretty sure Argentina, Brazil, and India are not actually in Africa. Now, if you look, it turns out – I'm pretty sure Botswana, Malawi, they are in Africa, and what do they want? They want patents and they want property rights, and they want contracts. My colleague of Washington University, Peter Mutharika, his brother is the president of Malawi, and Peter goes back half a year every year to work with them on law reform to help build the economy.

And, again, you see, why do they want this? Because strengthening law, strengthening property rights is the way you get people at the grassroots level to get deals done. That is the way you get those drugs distributed, by making distribution systems viable. And there are all sorts of really wonderful things people are doing – the Gates Foundation, Paul Farmer at Harvard, Bono – people are working really hard to improve access for drugs. We should continue those efforts, but it's not clear that patents are the problem.

In fact, there is only one natural resource that is uniformly distributed wherever there are human beings, and you know what it is: brainpower, intellectual capital. Intellectual property is about making the most out of that capital.

Now, patents won't immediately cause those countries to make the next blockbuster drug, but those countries can make an immense amount of money without inventing the next blockbuster drug. Let's remember that most of the world of music that is popular in U.S. and Europe is music that is heavily influenced by African rhythm. All of that is intellectual property. That is a massive amount of money that could be flowing back to Africa.

And I'm not making that stuff up. Just last month, Starbucks and Ethiopia struck a deal on licensing terms for coffee, and let's remember that Anheuser-Busch is still in a battle with the Czech Budvar company over the trademark for Budweiser. So there are lots of ways the United States in fact could be infringing other people's IP, and respecting IP is the way to lift people up. Thanks. (Applause.)

BARBARA CAULFIELD: Basically the position I'm going to take today is that there ought to be a balance in the patent law between laws of nature or natural phenomena, or inventions that people make. It's just that simple. It's not about the economics; it's about whether somebody really invents or discovers something. And let me go through some examples.

First of all, we should go back to the basic principles of the patent system, which states that whoever invents or discovers any new or useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof may obtain a patent, and that is 35 USC section 101. That is the basic patent law. You have to discover and invent something.

Now, there was a case called Diamond v. Diehr – in 1981, Supreme Court of the United States, that said excluded from such patent protection are laws of nature, natural phenomena, and abstract ideas. Now, why? Because as a matter of public policy, that is what everybody owns.

And just to give you a couple of examples of that, for those of us who may remember the periodic table – remember, iron, gold, all of the things that are in there – is when iron is isolated from the environment, is that an invention or a discovery and can you patent iron so that every time somebody erects a skyscraper you've got to pay them a percentage because they happen to use iron in some of the composition of that? Answer to that is no. Another example: what about $E=mc^2$? Can you patent that? That is a relationship; it's a natural phenomenon. There are a lot of good things that have come from that. Can you patent that? The answer is no.

Well, let's roll up to modern times now and talk about DNA. And I think it was interesting that the BRCA patent comes up because I think it's a really good idea to take a look at what the BRCA patent says and then I'll try to relate it to this idea of balance between natural phenomena and discovery and invention. The BRCA patent, which has received press because it was an early DNA patent, it has had a profound effect on the market. The number of the patent – because it's always good to look at it – is 5747282; it's like a telephone number, you can get it from the government.

The patent asserts ownership over DNA that codes for a polypeptide. Claim one of the patent says "an isolated DNA coding for a BRCA1 polypeptide, said polypeptide having the amino acid sequence set forth in the registry." Okay, so what do you have there? You have an isolated DNA, a piece of the human genome, that codes for a particular polypeptide and has a natural occurring amino acid sequence. Now, that's the patent. Now, what does that mean? If you own that piece, you own that piece of the human genome. That's what that patent says as it was granted by the U.S. Patent Office.

And that's why it's been a cause celebre, because people say, is that balanced, should you own a piece of the human genome, even though you isolated – no doubt you isolated it -- but everything that we have discovered, every discovery of natural phenomena always starts with some brilliant person isolating the natural phenomenon. What is the role of blood in the human body? What is the role of a number of things that you can think about? And can you patent the natural phenomena? Can you patent a natural relationship that occurs in human nature, that occurs in the body? And the answer to that is no, under the patent law itself.

That's what this argument is about. Now, what can you patent? If you can patent the DNA sequence and say, look, I isolated it, I own it, and that means I own every test, every drug, every thing that uses that part of the human genome or comes from that discovery, then the patent owner owns it. And that is not balanced. What can you own? If you isolate the DNA sequence, then you can own the test that finds that sequence. You don't own all the tests; you only own the test that you invented. If you isolate – if you develop a test that goes with a drug that treats that condition, for example, breast cancer,

let's say there's a test and a drug that go together, you can own the relationship between those two and you can own those two. But you can't own the DNA itself.

Now, there's another reason why you can't own a natural phenomenon. How do people innovate if somebody owns the basics? If somebody owns all of iron, every use of iron, every test for iron, how do you innovate off of that? You can own a new alloy that you develop, because it's not naturally occurring; you change it. You make it something different than occurs in nature. Well, then you own that. And people have to pay you for that innovation. But to own the human genome, which has been around since there was the first ancestor any of us have ever had, whether you own one piece of it or all of it is not what the law was meant to protect.

And this is not just the U.S. Japan has the same law; India has the same law. This is an international principle and proposition. And that's what this challenge is about. It's not disrespecting patents or disrespecting innovation. It's saying let's put the ownership where the innovation is really going to occur, which is at the test, which is at the drug, which is at – let's change the DNA. If you could make a new DNA like we've made new small molecules and re-inject them into the person to help to correct something, if you've reinvented the DNA or changed its biochemistry and reinserted in a person, you can own that. But to own the basic piece, the basic DNA, is not right. It violates first principles of constitutional law and of patent law. And that's what this is about.

Now, the reason why this issue has become, again, cause celebre, and this goes to the point about what are we all going to do about this is –there was a case called Lab Corp recently in United States Supreme Court and three of the justices said that you cannot own and patent a natural relationship occurring in human beings. You can't do it.

Now, let's talk about the practical effect of this, because I think it's fair to look at that. The BRCA1 patent, if nobody else can write a test that tests for the relationship between that particular piece of DNA and breast cancer – and remember I read what the patent covered – if you can't write a test for that, then how do you get a second opinion on whether that test really covers the right thing? And one of the important things about human health I think that's different about all these other patents that have been discussed is that human health requires a second look, a look at the mutations, a look at what another doctor says or another testing lab says about how that test turns out. And you can't do that if somebody owns the DNA and enforces it.

Now, people will say, well, you know, people have been a little lax in enforcing their patent rights. Well, those kind of gentlepeople agreements fall apart very, very quickly when there's money involved. And that is what we would like to avoid by just going back to first principles and saying you can't own a gene, you can't own a naturally occurring sequence in the gene, but you can own the test, you can own the drug, you can own a change in the gene, and that is what the patent ownership is about. And I think it's not exactly accurate to say if you're against gene patents, you're against patents. That's

not true. That is not true because there are many, many people that have innovated around tests or around biochemistry and they're in favor of patents. It's just the balance.

Under-protection of natural phenomena – all that does is make one patent be the only answer to a very important health issue like breast cancer. And that can't be the case because medicine is set up differently than that; scientific discovery is set up differently than that. And let's face it, international competition is set up differently than that. If we have all of this rubric around DNA patents in the U.S., then the really good research is going to be done in places where they have more open ability to innovate at the test level, and where different doctors can order different kinds of tests.

Let's talk about one other thing, which is the basic science and these patents. It used to be – and we probably even all remember that who are in this room – that we really believed that one gene determined that this kind of disease might happen to somebody and boy have we learned a lot since that. Everything that we know about now, except for very rare diseases and that's why they're rare, is a multi-gene approach.

And so if somebody owns one gene of a 20 multi-gene test, is that really ownership of that test? Because if you own that one piece of the natural phenomena but it doesn't turn out to be the determining factor in predicting a particular disease, how are we going to sort that out other than through litigation? Whereas, if we'd stayed close to first principle, then the person that makes the next test with the 20 genes, they own that test and the person owns the one-gene test and somebody in the middle owns the five-gene test. And it's a race for the most efficient, best, highest quality, most published test, that's where the money is going to be made; that's where the innovation is going to occur. So the basics of what we're learning about the genome also supports this basic principle that you shouldn't own the baseline natural phenomenon, but you should own the test for it, the drug for it, the re-injection of it.

The other point is we've now got a new development that's just been published called copy number effect, which is that it's not just whether you have a gene or 10 genes or five genes that affect a disease. It matters how many copies of the gene that you have in your human genome, your particular human genome. So if somebody has one copy of a particular set of five genes and somebody else has two, it may make the difference between a propensity or susceptibility or not. Now, if somebody owns the DNA or the five pieces of DNA, how do you talk about copy number? How do you say, oh, but that ownership of that really isn't what determinative; it's how many copies of a particular gene you have. Whereas if you leave the ownership at the test level, then somebody who's testing for copy number is different for somebody who's just testing for BRCA1.

I argue for this basic principle because I come from a legal background, but also because I think the people that are missing in a lot of these discussions are the patients. They want more tests. They don't want just one DNA determinative test, because let's face it, it's better if more companies do it, if more doctors read it, and more people criticize the test. Thank you. (Applause.)

STEVE HARO: Can everyone hear me okay? Tall guy, short podium, doesn't necessarily make for good acoustics. Before I forget, please somebody write down "isolated and purified" and make sure you formulate your question for this table, because there are plenty of good comments that can be made about it that won't be taking any money from your wallet. (Laughter.)

Normally, I'd spend the opening minutes of a discussion like this thanking people, and in the interest of time, because I know that my friends here at this table and everyone else are interested in getting to your questions, can I just say one thank you – and that covers everybody, you, them, the organizers, is that fair? Cool.

Simply put, the practice of gene patenting is wrong, ill-conceived and stunts scientific advancement. And it's for this reason that in early February, my boss, the assistant to the speaker of the House, Congressman Xavier Becerra and Congressman Dave Weldon of Florida introduced HR-977, the Genomic Research and Accessibility Act, which we believe is the absolute right policy to address this pressing issue. The bill is straightforward: it ends gene patenting; it gives guidance to the United States Patent and Trademark Office on what is not patentable – in this case, genetic material. It's not retroactive; it does not rescind the patents already issued. Given that Congress has defined the scope of protected status to be 20 years from the point that the patent application was filed, if we enact this bill into law quickly, we will reach a balance in less than two decades: a patent-free genome that does not hinder scientific research, business enterprise, or human morality.

Fault should not be laid upon the Patent and Trademark Office for granting gene patents. These days, I'm sure it would not surprise anyone that innovative technology often outpaces innovative policies. It is doubtful that the PTO, or anyone else for that matter, had the technical expertise to fully understand the implications of gene patenting when they granted the first gene patents about 12 to 15 years ago. Those first patents set the precedent; the precedent created a practice and the practice has now proliferated. This would not be the first time in our nation's history where government has had to play catch up in order to properly understand technological innovation. And it certainly won't be the last.

I'm sure you'll agree when I say that precedent does not and should not simply guarantee continued practice. Indeed, Congress has a constitutional right to proliferate and reward the advancement of innovation, but it also has the responsibility to intervene should that advancement be misdirected or incorrect. Article 1, Section 8 of the Constitution states that we must promote the progress of science and useful arts by securing for limited times to authors and inventors the exclusive rights to their respective writings and discoveries. But implicit in those words is the power of discretion. Congress is charged to offer guidance on what exactly merits an exclusive right.

The human genome was not created by man, but instead is the very blueprint that creates man. The genome and the approximately 35,000 genes it encompasses has existed for millions of years, pre-dating the human species. And suffice to say, it will

certainly post-date us as well. If you agree that genes have existed beyond the full grasp of human knowledge and indeed before the dawn of humankind, then you must conclude that they're a product of nature and thus not patentable. Patenting the gene for breast cancer or any other gene is the analogous equivalent to patenting air, water, birds, or diamonds. We've overstepped our bounds; we've made a regulatory mistake.

Fortunately, we have the power to end the practice expeditiously and for the benefit of all. HR-977 will allow all doctors and researchers to have access to the genetic sequence which, as I'm sure all of you know, consists of the chemical letters, A, which stands for adenine, T, which stands for thymine, C, cytosine, and G, guanine. Just as we would never allow a patent on the common linguistic alphabet that would permit the patent holder to charge people a royalty every time they spoke, we should not allow a patent on the genetic alphabet that compromises our common genome.

The bill's current status finds it awaiting action in the courts, the Internet, and the intellectual property subcommittee on the House Committee on the Judiciary. We're also trying to find a senator to take up the pending legislation over on the other side of the Capitol. Believe me when I tell you that the will of the people can and does dictate the direction of policy. So if you believe this to be a good bill, then we need your help. You need to tell your representative or senator to support this effort and you need to tell them quickly. One-fifth of the genome is patented; 20 percent of everything that makes up you, me, my friends on this stage is owned by somebody else.

Enacting HR-977 does not hamper innovation. In fact, it encourages it. Medical innovation and economic advancement will occur if the study of genes is allowed to happen unabated. Incredible manifestations of intellectual property will result: medicines, processes, machines, most deserving of recognition, some potentially life-saving, and all deserving of a patent. Thank you for indulgence. I look forward to your questions. (Applause.)

MS. HUDSON: Thank you all very much. We have two microphones, one set up there and one set up here. And so for those of you who have a question or a comment, please come up to a microphone and if you'd please state your name – we're videotaping today for a webcast later on our Web site, www.dnapolicy.org. Also please state the organization that you're with.

And I'm going to start out with a question that has sort of been on my mind since I first encountered gene patents in the early '90s when I was working at the Department of Health and Human Services and I went to work one day for the assistant secretary for Health and the first thing that happened to me that day was the secretary, Lou Sullivan, calling down and saying, what the hell is going on at NIH, and the front page of the *Washington Post* that day reported on a large number of patent applications that had been submitted to the U.S. Patent Office by the NIH for small nucleotide sequences of unknown functions, so-called express sequence tags. They were just little snippets of DNA. Nobody really knew what they did, but they were really cool and, by golly, NIH

was going to patent them. And nobody bothered to tell the secretary which was bad; there was a moral there: tell your boss. (Laughter.)

But my question is, so we sort of resolved that issue over time by whittling down what is useful in a patent, a DNA patent, but a lot of the comments today have focused specifically on the BRCA1 and BRCA2 patents and Myriad being the patent holder and in that case, they have not licensed rights to use that invention to anybody. And so my question is how much of the harms in terms of test quality, in terms of innovation, in terms of prevention to advancement and research is because of the patent, or because of the license? And Barbara, I'm going to direct that to you to get us started.

CAULFIELD: Well, I think it's both really. I don't mean to dodge the question, but I really think it's both. If you own the patent and you license it for free, then there's no block at all to developing any number of tests. If you own the patent and you selectively license it, which you have an absolute right to do – I'm going to give a license to A but not to B – you are in control because that's what the patent gives you a right to do, so you can pick the people that you choose to give a license to. The ownership of the patent sets up as the arbiter of who does science on that piece of DNA, that person who owns the patent. And not everybody gives a license to all comers. So it's not just a cost issue, there is very often a selection issue involved: do I like your methods, do I like who you are, will I cooperate with you? And so I think it's both. The patent gives those kinds of rights and that's what I think part of the problem, because natural phenomena should not be owned by anybody because the innovation should be at the test level. The innovation should be at the discovery level, at the drug development level, and at the combination, the diagnostic combination of drugs and tests.

HARO: I'm going to apply the Wolf Blitzer use of discussion with a show of hands. How many people have $3,000 in their pocket right now? Raise your hand. (Laughter.)

HUDSON: You'll be mugged when you leave. (Laughter.)

HARO: You're a lucky woman. That's how much it costs to get a breast cancer test. Myriad Genetics licensed BRCA1, BRCA2, and they closed the door to all research on it. If you want to get a breast cancer test, it goes through Utah, which is where Myriad's located. Their scientists read it; their scientists give you their analysis back. And it will you cost you $3,000. That's not treatment; that's just to find out if you are predisposed to breast cancer. So you're basically paying 3,000 bucks to hope for a "no" answer. That's not fair. And if anyone thinks that that's the free market working its will to allow for personalized medicine to proliferate, you're probably wrong.

COOK-DEEGAN: So I think, Kathy, you can't completely separate licensing from patenting because if you don't have the patents, the licensing is completely different. And it is an exclusive right, so that is what a patent is. It does give you the right to block somebody else from making, using, or selling your invention. That doesn't say it's the end of the story. So the BRCA story, let's say, for example, this is the same

invention, this is your poster child not only of what's gone on in the United States, but, in fact, the United States is the only place where it has played out as a patent story. It's the only place where the patent has done the work that we expect it to do because we don't have strong patents in Europe. We have patents in Canada, but all the provinces except Quebec are ignoring them.

So it's a very strange story and it tells us two things. One, it does tell us that patents are not the whole story, that if you have a health system that pushes back against it, the health system probably will win. But in the U.S. system, we don't have anything that can push back. So the patent story really does explain a lot of what happened in the United States, but it actually explains very little of what has happened in the rest of the world. So it's a complicated world. But at the same time, Myriad wouldn't have existed but for the prospect of patents in the first place. Is that a good thing or a bad thing?

Well, you know what, that actually depends on who you ask. If you ask the folks who have invested in Myriad, that's a good thing. Those press accounts, the negative stuff, is mainly about ownership of the right to get testing, along the lines of what Mr. Haro was just alluding to. That is what the negative stuff is about, is about limiting access.

Now, can we say anything about the pricing? What we can say is that, in fact, there is a bit of a patent premium that Myriad gets. But colon cancer testing also costs about $2,500; there is no dominant patent position on colon cancer testing. So inherently it is expensive to do these tests. There is a patent premium on top of that in the case of breast cancer testing. That's probably on the range of 30 to 50 percent. That's a very loose figure, don't quote me on that, even though I'm in the National Press Club. (Laughter.)

But it's not a huge premium. It is not the premium that you would see in a drug; a blockbuster drug is usually 10X, 20X production costs. This tells you it's probably on the order of 30 or 40 or 50 percent of production costs for this particular test. So it's a complicated question.

HARO: But, Dr. Cook-Deegan, real quick, wouldn't you agree that if there were more folks, more scientists, more labs, more companies who had the ability to do research on BRCA1, BRCA2, colon cancer and whatnot and other diseases, they could bring down the cost of that genetic test? Because in the end, genetic tests aren't as expensive as I think people want to make them out to be.

COOK-DEEGAN: Yeah, I think it's right to say that there has been something of a chilling effect. Let me say one thing -- and I'm in this very strange position of defending Myriad, which is kind of a strange position for me to find myself in. But in fact, they have not ever asserted their patents against basic research. The place where there is dispute is against the diagnostic service. And there's a wobble zone when you're introducing a new genetic test into practice where it's kind of quasi-academic and the institutions that you would have to enforce a patent, again, would be half commercial

enterprises and half academic enterprises. There, there has been a fight. And there it's very clear that there has been an impact of the patent on basic research itself and even on the testing methods themselves, including the rearrangement methods, for example.

There was research that went on in the United States and a lot of it went on in Europe, because remember there were no patents on BRCA in Europe during this period, and the ones that exist now are quite narrow – it's only one. So it's a mixed story. It's more complicated, I think. I do think there was a chilling effect. And I think the chilling effect could have been solved if Myriad had ever done what Red Hat does for software, which is saying our policy is we will not sue if what you're doing is research, and here's how we define research. That could have been done; it was not done. And maybe some of the controversy would have gone away if that had been done.

HUDSON: Quickly and then we're going to go to the floor.

KIEFF: Sure. I think the details matter in all of these things. We were read the claim in the Myriad case and we were told that the sequence was a part of the claim. So that's like several thousand units long. Well, the name of the game in patent law is the claim. So if you change one of those units, you're not in the claim, you don't infringe. It is absolutely untrue to say that – what was it? – 20 percent of our genes are owned. There is nothing in your body or mine that is owned by anybody else. It ain't true. The patents on these things are only on the versions of these things that are sitting in a lab somewhere. They're not on the versions that are in you or in me. The claims don't cover those versions. That's really important.

$E=mc^2$, yeah, not patentable. The method of using $E=mc^2$ to convert energy into mass, we got a patent on that for Leo Szilard at Columbia University and in fact that was a very interesting industry. Isolated strawberry flavoring, isolated adrenaline, isolated insulin – all of those things actually are patented, were patented, and led to very successful industries. And by the way, I can buy strawberry yogurt; it ain't that expensive today and it wasn't that expensive yesterday either.

Society has figured out ways. You heard the math: $2,500 where no patents, $3,000 where there are patents. What's the marginal difference and who's really making the money? Is the patentee to blame or is the cost of healthcare to blame or is it the scientist? Or is this stuff just expensive?

CAULFIELD: Let me just respond to a little bit on a scientific basis. It's not my particular BRCA1 that's ever owned, but when you own the BRCA1 that shows the polynucleotide sequence and nobody else can test whether I have it or not, it doesn't matter whether they own my human genome. Nobody else can do the test to give me the information. That's the problem. You have to isolate something to create a test to look at it. So that is true: Nobody can own Barbara Caulfield's DNA. I mean, maybe they can, but they haven't tried yet.

It's the fact that you can isolate a particular formula of a human genome, and when you do that and you own a patent on it, then nobody else can run this test the way this claim is written. And the other part of it that goes back to my principle -- and I think this is important to go back to -- in order to own something, you need to transform it in some way in order to discover it or invent it. I mean, that's what I think the law means. That's why you can't own natural phenomena. And you don't transform anything when you simply isolate something that occurs naturally in nature. And that principle is going to be tested out in the Supreme Court of the United States very soon, I think, within the next two years and we'll have a legal answer to that. But that is what I think is happening, and I'm just offering a clarification of what my position is on this and why I believe it.

Q: Jon Rockoff from the *Baltimore Sun.* I'm just having trouble getting my head around how abstract this discussion is. In terms of gene patents, are there any specific harms beyond the cost of the BRCA test, for example, or Myriad's monopoly status that you can point to? For example, are there concrete harms in terms of the quality of the testing or anything like that?

CAULFIELD: Well, what is concrete? Can I prove statistically that people have stopped looking at certain genes because they're owned by other people? No, I can't, because the kind of research that you'd have to do to do that is very – what do you think, and if somebody is actually doing research on a gene that's owned by somebody else, are they going to admit in a public forum is another question. So you wonder whether you're getting accurate data on some of these things. So I can't say that.

But let me just give you some thoughts about the principles of this. If there is only one test and it's done in one lab – let's just put cost aside for a minute, there's only one test and it's done in one lab and that's what gene ownership means you can do, then how do you ever double check what that lab is doing? How does somebody ever run a parallel set of tests? What about mutations? I mean, this particular DNA coding for this particular sequence is not the end of the story. We know that now from the other research that's done. So the argument isn't abstract; it's based on scientific principles. Wouldn't it be better to have five labs running parallel tests in blind studies to say, 'what is the accuracy of the test?' 'What is the accuracy for outcome? I mean, is Myriad studying outcome the way hospitals do for certain interventions for chemotherapy?'

KIEFF: Yeah, there have been, actually. Bob and I and some others had a paper in *Nature Biotechnology* last year that collects all of the studies done by a lot of people that are really interesting. They show that for data sharing and material sharing among academic scientists, the fear that scientists aren't doing these research experiments -- turns out the predictive variables are race, gender, and the brand name of the academic institution -- all those kudos and informal property rights that human beings fetishize. And it turns out the one that is statistically insignificant for whether there's a share is whether the technology was patented, except it's statistically very significant in that it's closely correlated with all of those industries where we have these very well-developed

freezer programs and distribution programs to make reagents available at surprisingly low costs for academic scientists and slightly higher costs for commercial scientists.

So there's an immense amount of data. And the data is clear. The data shows patents don't block research. What blocks research are all the other human elements like gender bias and race bias and snob bias and things like that. And economists have taught us that the way you solve that problem is you open up the market by adding more property rights that people can trade so that they can trade outside of the academy with Wall Street, so they can start a company if somebody won't promote them.

HARO: In August of 2006, the National Science Foundation put a paper out on this issue, which – let's be perfectly honest, biotech is in its infancy. There are really only a few handfuls worth of biotechnology innovations that you can point to over the course of its history thus far. And the promise of biotech is still – we've got a long way to go.

But going back to August 2006, the National Science Foundation said that gene patents at current were not hampering research, but they will. And here's an example of how they can and this has already happened. Let's say I have a certain disease and a certain company has a drug to treat that disease, but the drug only works in about 60 percent of the folks who have it. Company A, who creates that drug, finds the genetic marker to determine who those 40 percent are that the drug it won't work for and they patent it. Well, under U.S. law, if you get a patent, you don't have to do anything with it. It's different in the EU; you actually have to make a utility out of your patent. In the U.S., you could just sit on it for 20 years.

So going back to this company's example, I have a drug, it treats a disease, it only works in 60 percent of patients, and I have isolated the genetic marker to determine how it doesn't work in 40 percent of those patients. What do I do with the patent? Nothing. Because I want those 40 percent to buy my drug. And then they spend the money and through trial and error determine it doesn't work for them, but they've still spent the hundreds of dollars on the medicine and I just helped my bottom line. That's a problem and a potentially harmful one. That's why – unfortunately, this is abstract, and I wish there were a lot more concrete examples like Myriad, like the Canavan's example, but the potential problems that exist are much more downstream. So why not nip it in the bud before we reach that point?

HUDSON: We've got a question over here.

Q: My name is Margaret Woodbury and when I was working as an editor with Time, Inc., I went looking for something to show my readers how Myriad or any gene patent might stifle their lives. And what I found was a concrete and understandably not abstract example, I feel, and I'd like you to all to respond to this. I called Myriad and there's a test called preimplantation genetic diagnosis. Now, imagine you have a mother, a grandmother, a great-grandmother, all who have increased your risk of cancer up to 80 percent possibly. Myriad refused -- they don't do pre-implantation genetic diagnosis and

they were refusing to let the leading center for preimplantation diagnosis run this on women who had requested this. So I think that's pretty darn concrete. And I think that I called Myriad and I asked them about this and I said to Myriad, what do you have to say to my readers that – what would you possibly say to them if you wanted this test? And they had no answer. They sort of spiffed and spaffed and finally I hear later that they have licensed it – and this goes to Dr. Caulfield's remark and I haven't kept up on this, but to a few providers and some of the infertility clinics, most of them in New York, don't provide it because of this issue, as my understanding. So if you could speak to that.

HUDSON: Actually, can I respond real quickly? There's a number of different kinds of preimplantation genetic diagnosis, but the kind for single gene diagnosis is done by only really three primary centers in the United States and all three of them have gotten licenses from Myriad to do preimplantation genetic diagnosis, presumably because Myriad can't do that diagnosis on a blastomere from an embryo itself and so they've licensed that technology. Of course, that's raised its own set of controversies about should you really be selecting embryos based on a risk that they may one day get breast cancer. But that's another discussion for another day. Paul, did you have a question?

Q: I'm Paul Billings, I'm with Lab Corp and the University of California. So I also find it a little odd to be in the position of defending Myriad at this point, but I think one ought to say that Myriad is a very high quality sequencing lab, that they are licensed to provide services, that they're inspected, that they do proficiency tests, and that I don't think there's any evidence that they're an any better or worse lab than many of the other ones who are providing clinical services in the United States.

HUDSON: Thank you.

KIEFF: The argument for so-called patent suppression, or that patentees are going to make their living by stopping people from using a technology, is an argument that probably has some correlation to truth to some degree. But you then have to balance the likelihood and severity of that harm against the likelihood and severity of the harm of a rule that allows me, anytime you're not giving me permission, to go to a court or a government and say, 'she's not giving me permission – you ought to give me a special exemption' -- think about the incentives. If I have to reach an agreement with you, when we talk, boy am I going to be friendly. I'm going to try to figure out all the things you care about and I'm going to try to express to you the things I care about. But if the rule is that these folks will intervene whenever we don't reach an agreement, when you and I meet I'm going to poke you in the eyes and step on your toes like the Three Stooges and call you names so that I can say, you see, government, we're not getting along, you need to step in and give me an exemption and set a price. Then if they set a price that's too high, then I'll serve you coffee and tea and be your friend. I get two bites at the apple if the government will step in anytime a deal doesn't get reached. I only get one bite at the apple if I know I have to negotiate with you, and that provides an incentive for me to reach a deal with you.

And how do patentees reach those deals? They charge people more who can pay more and less who can pay less. There is lots of discrimination that we don't like in this country, but there's one form of discrimination we love, and that's price discrimination. I flew here on an airplane and I'm going to fly back on an airplane and there was nobody on those planes who paid the exact same price I paid for my ticket, but social unrest didn't result. I didn't look at the person next to me with envy or pride that I had gotten a better deal or they had gotten a better deal. Price discrimination works very, very well and property owners make a living by giving away free stuff to the folks who can't pay and expensive stuff to the folks who can pay. And it's in their self interest to do that, because what every patentee wants, especially in biotech, is a large number of users, because that generates data for them about which classes of users are likely to want to pay for their technologies and how. And that data is worth far more to them than the few pennies they could elicit by holding out for an extra better deal.

HUDSON: So we're going to take a question here and a question here. If we can make our responses fairly brief, we've run a little bit over and I sense that we're nearing agreement here in the room, so – (laughter).

HARO: The issue is solved.

Q: We're very close, yeah. I'm Mike Watson with the American College of Medical Genetics and an adjunct professor at Washington University in St. Louis of pediatrics and genetics. I want to come back to the healthcare side of this. I pretty much accept that most of the literature doesn't show that research has been impaired by gene patents, but I think clinical investigation has been somewhat impaired. And there's this balance between regulation and legislation that occurred with the Gansky Amendments back in the mid-90s sometime, that basically banned or exempted medical procedures from patenting based on a surgical incision in the eye that somebody patented – because of the sort semi-circular nature of the cut made, it healed better. And I very much think that our genetic technologies are becoming so analytically simple that the interpretation of what that result means is going to be the medical procedure of the day and of the future, so I'm wondering what are your views on really medical procedures having been exempted, whether that was an appropriate legislative activity – I think it was because of the nature of the case on which it was based – and then to the extent to which that might extend to genetic testing.

CAULFIELD: Well, I agree because the concept of – and it kind of goes with natural phenomena, the principles are the same – the medical procedure is something that all of the doctors share as a way of approaching an issue. However, it's not how you make the incision, but if you invent a good scalpel that can do it better than anybody else or has particular properties, then you can patent the scalpel. But you can't patent the fact that you open the eye and make an incision in a certain way. So I think that that was the right way to approach, for public policy, the delivery of health care.

And I think what we're talking about here is not the same principle, but it's the idea that the test should be read by a doctor who decides what the diagnostic approach is.

And the more tests for DNA and signatures and related diseases you have, the more the medical profession can do the work that they do the best, which is take care of the diagnostic part or do the intervention part. And so the healthcare principle is the same and I do support and I did support that medical procedures should not be owned.

HUDSON: Thanks, Mike.

Q: Hi, I'm Kurt Calia. I'm a partner at the law firm of Covington & Burling here in Washington and I focus on patent prosecution, but largely patent litigation, so I bring my bias with me, in the interest of full disclosure. I'd be curious to get the reactions of the panelists to the concept of a patent pools for gene sequence patents, especially in light of the fact that they're already out there. And it seems to me that at least it has the prospect of providing some compensation to people that have invested in research to identify sequences, particularly sequences that encode some proteins of interest, on the one hand, but making sure that there's access to people for basic research and otherwise, on the other hand, much like is done in the copyright context with the copyright collectives like ASCAP and BMI.

HUDSON: Thanks. So why don't we go quickly down the table and get quick reactions to the concept of – not only the concept of gene patent pooling, but also the probability or likelihood, and then we'll wrap up.

HARO: A patent pool technically already exists; it's called GenBank. And it's owned by the NIH; it's run by the Human Genome Project, and it's open access for all. You want a patent pool, fine. You should first ban the prospective patenting of genes. So much of our discussion is, okay, what do we now that the genes have happened, we just kind of accept it as common practice, that we're really getting away from the very formative question that we should be discussing in the first place, which is whether or not we should have allowed it to happen in the first place. And we shouldn't have.

So first you pass my boss's bill, immediately stop the patenting of genes. Then you now have – you probably have about 16 to 17 years while these patents are still alive, essentially, because you have 20 years from the point of your application to which you own the patent. Put those in a gene pool and then you're fine.

CAULFIELD: Yeah, I think the pool idea is very appropriate. It's certainly what's happened before. And I think there's a couple of practical questions: who starts it? And I think the answer to that is obviously the National Institute of Health, major universities who own a lot of these gene patents, and if the public sector, if you will, got together and started the gene pool, then it would have enough girth and breadth to be of interest. The next question is how do people get paid out of it? And I think there are two fundamental concepts that I'd like to put out there. One is if you're doing basic research, dipping into the pool is free. If you have a test or you commercialize something, then you pay X percent, all are welcome, and everybody pays the same. That's what I think would make a pool work.

But the real interesting part of it is how are we going to get the University of California, Stanford, the NIH, everybody that's got those patents, how do we interest them in this? And I think if research is free for all institutions, commercial, profit, non-for-profit, doesn't matter -- if you're doing basic research, you get to dip in the pool free. But the day you have a test and it shows up out of the pool, then you pay X percent, let's just say 1 percent per test, that's it. You don't pay five times to five different people because they own five of the 20 genes that you're testing for. You pay one time and you pay 1 percent. And then you get equality for developing new tests; you get a 1 percent gate fee which should hopefully pay for the cost of running it. And I'm just hoping some day somebody starts a pool because I think it's a very good answer to a lot of these issues.

KIEFF: Patents on basic technologies block those technologies from getting used. That's why we don't have the airplane, the telephone, the TV, the Internet, any of these technologies, all of which were heavily patented, all of which were broadly distributed at prices that were totally reasonable, and all of which are very accessible to all of us. Same in health care, whether it's basic research, applied research, upstream or downstream. I can't be upstream of you unless you're downstream of me and vice versa. We will figure out how to get deals done.

One of the ways we'll structure a deal, if it works for us, is we will create a pool, so I'm in favor of people having the option to do that. But if it doesn't work for us, we shouldn't be required to do it. One click on the Internet, less than a thousand dollars, great laptop computers, don't have to hire a lawyer to get them. If it were the case that you needed to negotiate and negotiations broke down, then you wouldn't be able to get a laptop on the Internet one click, a thousand bucks. That is a bundle for several thousand IP licenses. It works for hardware; it works for software; it works for biotech; it works in all areas of technology. I don't work for a company that makes more money if gene patents aren't patentable. I argue in favor of patents for companies like Affymetrix who provide wonderful innovations in the field of gene chip. And I think they do great stuff and their patents are great and should be respected. But I think everybody else's patent should be respected too.

COOK-DEEGAN: So I think the theoretical reason for patent pooling is almost – I can't imagine a case that is better than gene patents where the theoretical reasons that you might create a pool would exist. It's an idea that has been out there for about a decade. I think the reason we haven't seen them materialize yet is we haven't encountered a problem where the pool is the solution, that is severe enough to force all of the players to the table. And this is a disparate group of players. It's universities, it's baby biotechs, it's big pharma usually in the mix. So that is a harder kind of a pool than the DVD groups faced – they were basically in the same lines of business.

One final observation: For those of you who are reporters and really do go out and cover these stories, a lot of the questions that have come up in the last round are actually not about intellectual property, but they are about how intellectual property

interacts with other areas of policy. So the question about BRCA testing, for example, was about what kind of testing situation would you allow something to happen.

One of the things we are noticing in our research is in fact this is becoming an extremely common story. The reason that Apolipoprotein E was exclusively licensed was not because of monetary considerations initially; it was because there was a standard of care that you shouldn't be allowed to do Apo E testing unless the person you were testing had a diagnosis of dementia, and the way to find that out was to have a letter from a doctor saying this person has dementia and therefore it's okay to test them. And that is why there was an exclusive license.

The reason – one of the big reasons that the WARF patents on stem cells were licensed the way they were, were promises that WARF made to state legislators about the use of their cells down the road. So this is a place where, if you guys are covering stories where intellectual property is part of the story, it's not always going to be about money changing hands; it may also be about how the exclusive rights get connected to other domains or policy, and you may have to ask a question or two about, well, is there a patent there or why are you doing things that way that you aren't going to know what the story is unless you ask that question of why and how it links to intellectual property.

HUDSON: Thank you. In closing, I want to thank Rick Borchelt and Shawna Williams from my communications department who worked hard to put this event together. I want to thank Bob for helping co-organizing it today. I want to thank the entire panel for a thought-provoking and interesting discussion. And I thank you all for coming, and have a good day.

(Applause.)

(END)