Genetic Technologies and Intellectual Property Issues

Lawrence Sung, Ph.D., J.D.
Assistant Professor of Law, University of Maryland School of Law

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DR. McCABE: Our last speaker in this group before the roundtable this afternoon is Dr. Lawrence Sung. His topic is genetic technologies and intellectual property issues. Dr. Sung is Assistant Professor of Law at the University of Maryland School of Law.

DR. SUNG: Good afternoon. I wanted to thank the Committee for having the opportunity here to come and address you today on the intersection between intellectual property rights and genetic technologies. I realize that you've had a very long day. You've heard a wealth of information in some ways. There's some information overload as a result of it, and I know we're drawing to a close, so I want to take somewhat of a more modest approach with regard to some of the intellectual property protection issues, really to set the stage for you, introduce the cast of characters, and tell you a little bit about the story. But understand that the story, certainly in large part, has not yet been written, and the parts that have been written are very likely to be rewritten as a result of what happens through their application to genetic technologies.

I've been asked to talk a little bit about intellectual property generally and then to focus on specific issues with regard to patent rights and to tell you a little bit more about what it means to obtain patent rights, particularly in biotechnology and some of the genetic arts; and then lastly, to conclude with some of the rising concerns that we see at this point in time and those that are on the horizon.

Now, I understand that there are a variety of individuals here with disparate expertise in intellectual property issues. For those that are more sophisticated, I do beg your indulgence somewhat, that there are certain portions that will be somewhat oversimplified to get through our presentation today. Understand that intellectual property protection is a general matter, especially today is highly controversial. As a result of that, like any good attorney, I'm going to start with a disclaimer. I'm here neither to advocate a particular position for open access or exclusivity along those lines, but to give you as much of a balanced approach as possible, recognizing that with a balanced approach, like any good compromise, no one will really leave happy. I just recently finished grading law school exams, so I'm pretty steeled for that reaction generally.

(Laughter.)

DR. SUNG: What is intellectual property? It's designed to look at ingenuity and creativity and to place some type of value on that. The value that's placed through the legal component is really to look at a grant of exclusivity as a result of intellectual property. The subject matter that is embodied within that can be fairly loose, and there are a variety of different types of legal protections that are involved. We can look at patents, copyrights, trademarks, trade secrets, rights of publicity, and a whole host of smaller categories of intellectual property protection. Again, we'll probably focus most on patents today, but understand that there are a variety of mechanisms that exist for covering various types of subject matter.

Now, how is this different from real property census? Well, there's an exclusivity aspect to it in terms of the ability to use intellectual property. So if we look at a house or a car, for example, if I were to take a real property concern like my car, if I loan it to you, I can't use it myself, nor can anyone else use it because you are in the driver's seat. You're out there, you're using it to the exclusion of others.

Intellectual property doesn't necessarily have that same constraint when it comes to the real property considerations because I can license my intellectual property repeatedly in a non-exclusive fashion to a variety of individuals, and indeed I may still be able to use it as a result of the negotiations that are involved with that. So that's how, on a fundamental level, it differs from the intellectual property standpoint.

Limitations to intellectual property are defined in the law. There are territorial restrictions to it, there are temporal restrictions to it. Each national jurisdiction has their own intellectual property law. So obtaining a U.S. patent, for example, does have no effect extra-territorially from the United States other than to seek corresponding protection in each of the individual nationalities. In addition, based on the way our laws have been framed, there is a temporal limitation. This is only for a temporary period of time. For patents it is a 20-year period from the day you file your patent application. In copyrights, that term seems to be extending every day. However, it is still somewhat limited, at least one day less than perpetuity.

The value of intellectual property, because it has a property characteristic, is fungible to an extent. You can buy and sell this. It can be somewhat of a commodity item. But I think as we go through our discussion today, you'll realize that there aren't that many comparables with regard to a lot of the technology that's involved. So valuation itself can be difficult, but it is fairly straightforward to assign a value for intellectual property generally.

Now, what do we do in terms of patent rights? Well, patent rights specifically, there are a variety of different rationales for why we have patent rights in the first place. Let me start off by saying it's based on the Constitution, so it's a legal doctrine. It is fairly entrenched. We look at, again, according inventors particularly rights to their ingenuity, their ability to bring this forward to us. But what are some of the underlying rationales for why that mechanism is in place?

We look at this and we say to ourselves, number one, by having you come and seek patent protection from the U.S. Patent Office, it requires you to disclose your information to the public. Otherwise, you could simply have maintained it as a trade secret. You might just not have told anybody about it and just practiced it along those lines. But here we have you coming to a centralized repository and making a dedication of information.

Now understand, in response to that the government, under certain circumstances, will give you that exclusivity for a limited period of time, which allows you to really adopt what's known in the economic area as a first mover advantage. You really are the first on the scene. It gives you a period of exclusivity to really develop it if you so want. You can also transfer it to others to have that exploitation occur.

But if we get to the original question about exclusivity, why do we like exclusivity? Well, there's certainly a theory behind this from an economic basis known as the public goods problem, just a highfalutin way of really talking about what I would characterize as the common household kitchen problem. If you've ever lived in a group house and you've ever walked downstairs in the middle of the night and looked at the kitchen sink, it's full of dirty dishes. What are you motivated to do at that particular point in time? Well, the economist would typically say that unless you had some sense of proprietariness to washing the dishes and having been able to reap the benefits of that by having clean dishes, you're less likely to wash dishes just for the entire house. Everyone gets to use it. You're much less motivated to go out and move things forward.

So that public goods issue is the reason that exclusivity is touted as being an important consideration. We've talked about information disclosure and an incentive to then innovate or to move forward because

we've overcome the public goods issue. Well, what does innovation really mean through that incentive? Number one, you can reward inventors. You can say to them, "We're going to give you something as a result of your decision to disclose this to the public."

But more importantly, innovation is also achieved because we avoid what someone raised earlier as a potential cumulative problem, because if I know that someone else has worked on what I thought I want to work on, I'm more inclined to say, well, if they have exclusive rights to it and I'm not denied the ability to obtain exclusive rights, I'm going to do something different. I'm either going to design around it or I'm going to take a separate path that adds to the overall social wealth, because again, the disclosure adds to the information that is in the public domain, and I want to distinguish the public domain from necessarily what you can do at a particular time versus what the public is now aware of.

So disclosure is definitely an important characteristic to this. It contributes to the innovation that's involved. Arguably, there are some anachronistic characteristics. Certainly, 100 years ago, the U.S. Patent Office was a great centralized repository for scientific knowledge. If you wanted to find out what was cutting-edge technology at the time, you could easily go to the government institution, look through their files and say ah-ha, I understand what is really at the forefront of technology.

Nowadays, with the Internet, with a variety of other organizations and publications, it's somewhat anachronistic in that sense, but it still does have some continuing value along those lines. More importantly, the investment potential. As we get into our discussion about biotechnology, we recognize that there are differences among industries about how the industry sectors result from investment purposes and commercial considerations. In the biotechnology area, as you've certainly heard, the length of time between commercial development from an idea tends to be far greater on a time horizon than any other technology. So investment in this sector tends to be focused much more on intellectual property as opposed to a proven product or a commercially marketable product at that point in time. So again, there are some differences in sectors as we talk about patent rights generally.

The U.S. Patent and Trademark Office has its supporters, has its detractors, and the patent system in general in the United States, similarly you can find support either for or against it. An example of this is we'll go through some of the actual requirements for patentability to sort of lead you off with a sense of the frustration that can be involved. If you imagine yourself at the airport baggage claim counter, you're sitting there waiting for your bags to come off the conveyor belt and you're still wondering just all of these different questions that you have in your mind. Why isn't it that they go in in a particular order and come out in a particular order? Why is it that if I paid for this particular fare ticket, there isn't any priority basis? There really is no rhyme or reason similarly between your baggage claim experience and the U.S. Patent Office in this regard.
(Laughter.)

DR. SUNG: Things also get lost, one of the more important considerations.

Laughter.)

DR. SUNG: And this is, again, not an opportunity to bash the Patent Office. I think it has an almost insurmountable job as a result of it. But we've made a policy decision within United States taxpayer policy to not fund the U.S. Patent Office so that it does the most accurate, comprehensive job possible. We ask it to do a certain job within certain limitations, and that is following these particular guidelines with, again, limited resources. It sometimes shocks individuals to know that the average patent application is probably vested with about 30 hours of an examiner's time, regardless of technology. So

you can well imagine that there are ones where you can barely scratch the surface of even understanding what's gone on within that period of time.

Again, they labor under quite difficult conditions there. So we see some results as a result of that, but there really is only so much that they can do in this regard.

Now, what are some of the requirements? One is that a patent right is only accorded to an inventor. It is not a matter of attribution, it's not a matter of credit. It's a matter of a legal definition as to who conceived and reduced a practice, a particular product or method? The conception is that eureka moment, that you can think of the reduction to practice as really being able to implement it in your mind and being able to describe it to someone in a manner that they too can ultimately go forth and use it, and that can occur one of two ways. Either you describe it in a publication, such as a patent application, or you can actually build a prototype or a model along those lines.

Inventorship is not coincident with ownership, at least at a practical level. Inventorship is the first supporting premise of ownership, but understand that in reality and in practice much of what is done in the patent area for inventorship purposes is automatically assigned to an employer, for example, through an employment contract or an employment policy. So there isn't this arms-length negotiation or transaction that occurs between an inventor and many owners as a result of that. Institutions may be owners in the United States, but they may not be inventors. It is unlike some other countries where actual institutions can be the inventor.

Conditions for patentability include that it has to be of the appropriate subject matter, that it has to be useful in some regard -- and we'll speak a little bit about that -- it has to be new or novel, and more beyond that it has to be non-obvious. The non-obviousness component is a little bit vague and ambiguous. But what it really goes to is that not only must you come to us with something that is different from anything we've ever seen before, but it needs to be so different that no one else would have thought to have done it, and that is an incremental step beyond simply bringing us something that's new.

More importantly, the disclosure requirements are important here, because again this is the quid pro quo. We are willing to give you a temporary right of exclusivity, but only if you teach us about your invention in a sufficient manner that others may be able to benefit from it. So again, we don't get into this cumulative problem where people have to read your patent and somehow figure it out and waste time doing so. We want everybody in the public to be vested so that they may stand on your shoulders and go beyond that point in time.

Now, in the biotechnology realm, why is this so difficult? Well, there are a number of different reasons for that. One is that we are dealing with natural subject matter, and there is an inherent consideration that people have in this. How can someone patent what is otherwise found in nature? Well, from a very strict legal perspective, that's really not what's happening, although no one ever likes to explain it that way because you don't get many takers. But essentially, what someone is saying is from a gene standpoint, I can patent an isolated, purified nucleic acid because it doesn't exist that way in nature. It has a natural component to it, but what I'm actually claiming isn't what is in all of us the same way.

Another limitation to it is that patents, as well as other forms of intellectual property, are not really designed to protect information. So if I tell you about something through my patent, others should be able to use that information to the extent they are not somehow using the same product that you've claimed or the methodology that you've claimed. The difficulty in the biotechnology area is that distinction is blurred and in some senses can be co-extensive with one another.

For instance, if I have an isolated nucleic acid of a particular sequence, what's the difference really between the information and the actual structure that's involved? If I somehow use that information, am I also concurrently using the structure? And in some cases, the answer to that might be yes. So the dichotomy that sometimes exists between the two may not exist in this circumstance.

The next indication is what I call de facto industry standard. We are not dealing with a technology that allows you to adopt a different approach. Going from VHS to Betamax is an example of an industry standard design-around. The folks that were working in the VHS standard said, no, we're not getting the operating procedures that we'd like to using the Betamax format. Let's use another one. In fact, that became more successful to the demise of Betamax.

However, in this area, it's not as if we're going to wake up tomorrow and say forget DNA. I don't want anything to do with it. I'm going to try to develop things based on another design. There is much more of a cause and effect linear situation that we have here. So that is yet another distinction between this area of technology and others.

Now, doctrinal meta-stability, again another fancy term which essentially says that in this area I think that observation leads us to believe that there are certain rules and guidelines about science in general. The difference is that in certain other industries you may be able to climb the highest mountain, and then once you summit it look down and have a worldview. You may be able to say this is what we know now.

But I think in the biotechnology genetic area, a more apt sense of the landscape is that you go to the top of the mountain and you look, and all of a sudden there are 100 other mountains. There's a lot of uncharted territory that you may not even begun to have seen until you've gotten to that point and expended that amount of effort, and that may in turn change your own worldview about your mountain. Maybe it's no longer the highest one because you've seen yet another one that's higher. So there's a lot of change that can occur in this area. There's a lot of revisiting of old notions about science in this sense.

The last area is what I call an art maturity compression. What we have in this circumstance is that legal doctrine is being formed today based on case law that's being decided on technology in genomics and in biotechnology that is sometimes 20 years old. The period of time that it can sometimes take between filing a patent application to obtaining the patent can be 10 years. The period that it would take from that point forward to enter into litigation can be another 10 years. As a result of that, you look at what the courts are resolving at this point in time. It's not necessarily instructive because it's based on the facts and the law as they are applied to a scenario that had existed that's now obsolete.

So how much guidance do we really have from the judiciary in this regard? The difficulty, because of the way our patent system is set up, is the indication from the patent office is not the final say. If it were, I think it would be a lot easier to navigate around patent rights. But you really don't know the scope and extent of a patent right until the courts have had an opportunity to pass on it, and not just the trial court level but the appellate court, and perhaps all the way up to the Supreme Court, before really understanding what the overall scope of this will be.

But the reason that we allow this to occur is, again, it's not worth spending the money at an earlier time point because there are so many applications that are submitted, some for which will never reach any type of commercial maturity whatsoever. So rather than expend money up front for a more accurate, comprehensive examination, we allow certain patents to issue knowing that they may be on the verge of invalidity, but at the same time we'd rather have interested private parties resolve the issue for the public because they are the most self-interested but also in the most financially capable position to do that.

Again, that is inherently a difficult standard, because at what point in time are you comfortable knowing what the true scope of a patent right is? Until the very end, you really don't, and that's very difficult.

But predictability and probability in science changes quite dramatically. I mean, certainly we can look at the rapid advance of sciences, and if we're talking about a 10- to 20-year time frame, what is predictable at some later point certainly may not have been predictable much earlier.

The other issue that comes into play here is that there are routine methods of manufacture that can occur in biotechnology that still lend themselves to producing new and non-obvious products. So, for example, after we go through and discover technologies that would be useful in sequencing, in proteomics, in bioinformatics, we may be able to take those same standard protocols and methodologies and go into the vast array of information that still hasn't been touched and ultimately generate some type of data and develop that into a product or a method and obtain a patent to it.

That's very unsettling for most because they would say, well, what you've done is essentially applied routine methodologies to come up with something. Why should we accord an exclusive right as a result of that? There are specific circumstances where that does apply, but that is one of the areas that causes a great deal of consternation with regard to the scientific community.

How does this also work? Assuming that we are able to get patent protection, we dispense with the issue that is natural subject matter of some sort. We talk about its utility, having some practical application. These days, the patent office requires something that is of substantial, specific, and credible utility. As Dr. Collins had mentioned, we're beyond talking about gene fragments and gene patterns and ESTs and SNPs. There are a host of other newly-developed technologies that have emerged from that which require that same consideration.

But once you get the patent right, there is something else to be aware of. It is not as simple a proposition as you might think, because there is a dominant/subservient relationship between patents. I may be able to get patent protection, but yet that doesn't necessarily give me the right to use what I've patented, and that's quite surprising for most people because you feel like if you've purchased the property, if you've invested in it, you've gotten it, it's yours, and you get to do what you would like. However, the way the patent system works, it's entirely possible for your patent rights to be dependent on permission by another to use their technology, because there may be some interrelationship between the two.

As a result of that, you have a large thicket or web of patent rights, and sometimes it's very difficult to distinguish whether you have freedom to use this particular product, freedom to operate free and clear of that.

The timing, again, difficulty in this area. There is an obsolescence issue that needs to be considered, but also the long time to commercialization. The reason we see, for example, a heavier reliance on patents in the biotechnology genomics area is because there is such a long time period that's involved before proof of principle and actual commercial development. On the other side of that spectrum may be something like software development. It's increasingly conventional wisdom that software applications in the patent area, although feasible, may not be the best way to go, because certainly by the time you go through and wind yourself through the patent process, by then your software may be obsolete because things do move so much more rapidly in that area. However, as we have bioinformatics packages and applications, we may see a little bit of an overlap in those two areas.

Lastly, regulatory controls. We understand that certainly for commercialization and marketing of pharmaceutical products that result from earlier-stage inventions, those are subject to regulatory controls

which again can delay the period of time that it would enable somebody to ultimately benefit from patent protection. As a result of that, we allow certain extensions to patent term to recoup some of that administrative delay.

What are some of the concerns that have come up here? Well, certainly in any situation, we talk about the restriction. I can't seem to do something as a result of someone else having a patent right to this area, nor will I likely be able to design around it because things are rather more confined in the biotechnology sphere. Again, to look at an isolated incident like that and to say yes, this is a situation where a patent right has clearly blocked progress, we need to take it in the overall context that that may be true in that specific instance and there may not be any other way to design around or otherwise obtain permission to use this. But in the overall scheme of things, remember that the intent of the system overall is to spur innovation through design-around, if necessary.

Collaboration issues are rather difficult. There are hardly scientists nowadays who feel comfortable picking up the telephone as they might have done even five to ten years ago and calling a colleague at another institution and chatting things through, because effectively everybody has a material transfer agreement that they want you to take a look at and sign off on, or there may be considerations from various home institutions as to what level of disclosure you are providing to one or another of your colleagues. So there has been more of an impact in the practical sense on collegiality and collaboration with regard to research.

How much of that is arguable? There has not been a whole lot of empirical work done on what the true impact is of intellectual property protection on biotechnology advancement. I think that organizations like the NIH and various institutions are trying to take a leadership role in that regard to spur further study about that, because everything is rather anecdotal at this point in time. Again, you have so many different instances where somebody may say, well, if you look at BRCA1 and you look at what Myriad has done, that's an anathema and the patent system is horrible that it allows something like that. Once again, perhaps true, but in the overall scheme of things there may be a number of different other instances that we can point to that show the success of the patent system.

How does business work along these lines? What types of incentives are there for securing intellectual property protection for purposes of financial investment? What happens when there are prohibitions that are involved? How are they overcome? Are there cross-licensing schemes between patent holders in this regard to free up scientific advancement?

I'll conclude with just a couple of comments about some of the horizons. Certainly, whenever there is some controversy with regard to the patent system, there are violent efforts to try to change the patent laws themselves substantively. The problem is there are a lot of laws of unintended consequences that come into play with that. The existing U.S. patent system is based in large part on a law that was written in 1952. It is applicable broadly against all technologies. There have been some minute changes since that period of time, but certainly the law, being written at a time when there was hardly biotechnology and certainly no computer technology in that sense, is grappling with its ability to apply to certain new areas of technology.

Enforcement is another consideration. How are people more or less inclined to enforce their patent rights? Because understand that there are, because this is a private civil matter, lots of considerations about whether patent rights, once they are obtained, will actually be enforced. Because a patent is subject to being invalidated, you put your patent at risk by enforcing it against others. So there is a risk calculus that goes forward as to whether a patent holder will actually try to enforce their patent rights.

One of the examples that's typically referred to as to why patent rights aren't the end of the world with regard to genomics and biotechnology tends to be the Cohen/Boyer patent on early-stage methodology for genetic engineering. However, a lot of legal practitioners might have looked at that early-stage patent and said, well, it was invalid anyway. If you looked at it, there were certainly a lot of things in the public domain that would have suggested that that patent right would not have been upheld if it were enforced aggressively. So perhaps when Stanford had licensed it at reasonable cost, and at times no cost, to certain entities, maybe that was the appropriate resolution of that. So understand that there is a lot of discretion and risk assessment that goes on in the enforcement area as well. Not simply because somebody has a patent will they enforce it in all circumstances.

The last point here is what I will refer to as the research use exemption. Increasingly, there has been a lot of discussion about whether or not base researchers, academics, as well as not-for-profits or non-profits should have the opportunity to have an exemption placed so that they will be exempt from patent infringement liability. The reason that this has taken on a little bit more of a conversational tone these days is because there are certainly a lot of researchers that were shocked in realizing that last year, when the U.S. Court of Appeals for the Federal Circuit issued a case called Mady vs. Duke University, that what they were doing was really an infringement.

Everyone had thought, no, they'll never come after us, we won't have this type of discussion, what I'm doing is not commercial in nature, and the Court put that to rest. It eliminated any exemption as a bona fide exemption against patent infringement. Now, certainly as a practical matter, it is unlikely in many circumstances that private companies will go against academic institutions in this regard, but the exemption itself is something that people would have liked to have an absolute immunity from. The Court of Appeals for the Federal Circuit, in their one-two punch, not just with the Mady decision last year but with a decision called Integra vs. Merck that issued just Friday, has come into it and said even early-stage research, research that may ultimately be used to underlie clinical research, is not going to be exempt from patent infringement.

So we are foreclosing those areas that we may look at under any type of recognized defense in terms of early-stage research, particularly with genomics and biotechnology. So that is definitely having an impact. The Mady vs. Duke University case is on appeal to the U.S. Supreme Court. The stage it's at is that the Supreme Court has asked for comments from the Solicitor General to weigh in on the scope of things, and the Solicitor General has submitted an amicus brief as a result of that. We will be pending resolution of that case going forward.

DR. LANDER: How does the Solicitor General come down?

DR. SUNG: The Solicitor General really is taking a very broad-based approach. You would have imagined that the amicus would have been a little bit more focused in saying whether or not this is going to shape the foundation of science generally. I did not read that to be the case.

DR. LANDER: That is supportive or not supportive of the lower court decision?

DR. SUNG: It is supportive of the lower -- the reason it's hard for me to answer the question is because it's not as focused as that. There's certainly a recognition that the way the law has played out through the Supreme Court and the common law element along those lines does not really support a reversal on the law itself. So in some ways, this almost calls for a legislative remedy as opposed to a judicial one.

DR. LANDER: Are you done? Can I just follow up with that?

DR. SUNG: Sure.

DR. LANDER: You've given us a wonderful tour through the black letter law of all this, and that's all fine; and you've told us that in theory, anything we're unhappy about, any particular event might be outweighed by lots of other good things that make the whole thing fine. But in practice, we all live in practice, right?

DR. SUNG: Yes.

DR. LANDER: So you look at the biotechnology and you'd say have we created a morass where, in fact, work doesn't get done because companies are uncertain about the patent rights of people out there, and therefore they don't work on projects? My observation is that that really does occur, the typical thing. Do we see people increasingly expanding to things like pathway patent claims, all molecules X, undescribed as of today that might affect protein Y for disease Z? Will this block all second- and third-generation products against particular pathways?

Do we get into situations where Francis' $1,000 genome thing comes along and we can do your genome for $1,000, we can't actually peak at the BRCA1 but we can peak at this one but not that one, or whatever? Is it the case that because of the unusual nature of this industry that we have to actually look empirically as to whether we're really serving the public or not? Too often, the patent lawyers who talk about this in general tell us, well, it makes innovation, et cetera, but it is indeed an empirical question whether it does.

DR. SUNG: Yes, absolutely.

DR. LANDER: So what's your take? Are we on the right side right now, or do you think it's out of balance?

DR. SUNG: The funny thing is that everyone is on the right side on this issue. Yes, you can look at instances where there is a block in certain cases to progress. I think it's fair to say that. However, it's not just about saying whether there is forward progress or not in that area, but also whether or not certain instances of commercial exploitation would not have occurred but for patent rights that were in the mix. So not being able to just focus on one particular aspect is the difficulty here.

DR. LANDER: Sure. But again, you're saying it could be. So are there fruitful changes to the patent system, whether by law, by PTO change in regulations or whatever, that you would recommend to improve things given your read of what's going on?

DR. SUNG: I think there can be improved administration of what happens within the patent office itself. At this point in time the patent office is certainly loathe, because the courts essentially placed this on top of them, that you cannot make certain practices special. You cannot look at biotechnology inventions and say we are going to apply the law differently in that context. However, it does call for that, and really there are special circumstances where biotechnology inventions pull into place certain areas of the law that really require somewhat different considerations

So I think if there is an incremental improvement to be had here, that's probably it, to give the patent office the ability to really examine these inventions in a somewhat different light. Now, that may take an organic change within the law, so it's not something that has a great deal of momentum at this point in time. But again, I think that addresses your question.

DR. McCABE: Actually, this is a nice segue, because what I'd like to do is have all the speakers come to the table now.

Thank you very much, Dr. Sung.

(Applause.)