**Ethical, Legal, and Social Issues of Large Population Studies**
***Mylène Deschênes, LL.M.***

DR. TUCKSON: So with that, let us turn to Mylène to see the ethical, legal, and social issues of large population studies. Thank you so much. As we mentioned, and I don't know if you were here earlier, but there is a little timer there in case you need to time yourself.

DR. DESCHÊNES: Good morning. Thank you for the opportunity to talk to you about biobanks. As you mentioned, I learned yesterday afternoon that I would be giving this presentation because Bartha's plane was canceled. So I hope that I will be able to convey her ideas, because this is her presentation.

The presentation is divided into three parts. I will first talk about the legal and ethical framework. I think we're still in search of an adequate one, so I will comment on these. I will kind of skip the second part, because I think Teri Manolio earlier on talked a lot about these existing projects. I will focus right around the third part, which are the challenges and issues with respect to population biobanks. I will also talk to you, lastly, about P3G, Public Population Projects in Genomics, at the end of my presentation.

So let's start with a small, brief introduction. I think it is clear now that the way we do research has changed in recent years. We first looked into more single gene disorders, and now we're into more complex diseases. We are really now focused on national and international collaboration. In fact, they are pivotal to researching complex diseases.

We went from what we call research on traditional biobanks, the small fridge in the researcher's lab, towards human genetic research databases per se. Finally, it's interesting to notice that some issues were at some point considered almost waste. Now they are kind of sacralized to the level of becoming almost equivalent to the person from whom they came.

We should also note that there has been some recent bureaucratization of the ethics review. I don't think the IRB process was initially intended to be maybe as complex and bureaucratized as it is right now, but it is certainly an element we need to take into account.

Human genetic research database. What are we talking about? What is it? For the purpose of this presentation, we'll certainly focus on collection of information that is organized and searchable. It is not just a large bulk of samples. You really need to have a way to search through it.

It is interesting to note that in the legal and ethical literature, oftentimes biobanks, collection, and cohorts are words that are used as if they were all synonyms. We ought to make sure that we use the appropriate wording.

Also I will focus in this presentation on really the new reality of human genetic research databases, meaning large-scale population databases including at least 10,000 individuals.

So the first section of the presentation, what is the legal and ethical framework, and what struggles do we have in those? I can see two things. First, there is really the trend towards the proliferation and specialization of national and international policies. I will tell you a little bit more about this in a minute.

I think through this we see that this demonstrates the need for harmonization of some of the principle, but most importantly, of the terminology. I will tell you more about this too in a second.

So talking about the proliferation and specialization of law and policy, here you see at the international level within the past three years some of the international guideline legislation or declarations, I should say, that has been adopted by various organizations like HUGO, or the World Health Organization. If you look now at the national level, the title says it all. It is a very uneven playing field. You can see a great disparity between all jurisdictions.

Here you have a few countries that have implemented legislation that specifically regulates human genetic research databases, and this is very specific legislation. Interestingly enough, the examples we have here all come from the northern part of Europe.

If you look at other jurisdictions, some of them just rely on the current data legislation, public health, and traditional legislation. This really creates some confusion and conflicts, and has overlapped. Some areas are sometimes left even unregulated.

I think this quote from France really says it all. It says, "Several systems co-exist so that the problems are approached from different angles which ignore each other." That's really what can happen. I mean, you try to regulate it by pieces that are maybe not well adapted to the need of human genetic research databases.

However, you can see an increased interest surrounding human genetic research databases. These are just, again, examples of very recent documents that were issued by advisory committees or law reform commissions in various countries. The Canadian Biotechnology Advisory Committee being the most recent one that we have here.
So we see that there's an interest and some discomfort at least in the countries with respect to the current situation.

Now, if we go to the second part, the challenge of our harmonization, I think that at the international level, it is very clear that there is an increased need for harmonization. I think the lack of internationally agreed upon rules, but most importantly, common taxonomy, is really detrimental to research collaboration. It is really an impediment to be able to exchange your sample with other countries, or even just to transfer information. So we need to acknowledge this problem. It is already being acknowledged by various organizations, such as the WHO.

Here you have the Babel tower. Really I think that's how researchers out there feel right now. The Secretary General U.N. quote really says it all. It says, "Despite the existence of numerous declarations, guiding principles, and codes dealing with the issue of genetic data, the changing conditions of genetic research call for the establishment of an international instrument that would enable states to agree on ethical principles, which they would then have to transpose into their legislation." This is really a wish, but I think it is a tool that we really need right now for the type of genetic research that we want to do.

At the national level now, there is a need really to recognize the specificity of human genetic research databases. These are no longer just research projects that you're trying to regulate. These are really research resources that will be used for multiple future uses. So it's quite the different thing.

There are limits to the traditional consent and personal data privacy legislation. These legislation oftentimes were created again in the context of research for genes for Mendelian diseases, and are not really appropriate in the case of databases like the one that we're talking about here.

There is also a need in personal data and privacy legislation to have a more common language. We know that there is a huge problem with the vocabulary that's being used right now for coded, deanonymized, delinked, and deidentified. And in one country and another country, the same word will mean something different.

So when you want to respect participants and make sure that the consent that follows the sample will really show your partners how they should use the sample, it's a problem. We're not even sure how it is understood between each partner. So there is also a call for the implementation of a more comprehensive regulatory framework so that it will be more easy, I would say, to conduct these types of research.

Well, at least there is some consensus on what we should be working on. The first thing is certainly to work on the tailoring of traditional consent mechanisms to the specificity of human genetic research databases. Again, we can no longer use the traditional consent models. I don't think it's appropriate, neither for participants, nor for the researchers.

We need to have a better correlation between the degree of data identifiability and all the obligations that comes with it. It is more interesting, of course, to have data that are coded and that we can link to a participant, but it comes with obligation. What are we going to do 20 years from now? Will we have the obligation to bring results to these participants? That's something that we need to clarify.

The need for adequate ethical oversight from the inception of a database, as well as monitoring mechanisms, that is certainly something we need to work on as fast as we can. Initiating, promoting, and strengthening the professional and public dialogue. This is fundamental to the type of enterprise we're talking about. We certainly need to work on it.

It is kind of related to the last point also, the need to develop a benefit sharing policy. We need to do, I think, a better job at really being able to identify the benefits. It's difficult, because we know the benefits are long term. But for the participants, for the funders to be able to justify such an important investment, we need to be able to have better communication with the public about this.

Some controversial issues. Funding. This is a very sensitive issue. If we want these human genetics research databases to stay in the public domain, the way they will be funded has a tremendous impact. This issue about original consent form and secondary use of sample is also one that is controversial. Are we going to go into this blanket consent? We have very big doubts that that is something that is going to be accepted in the legal system, but it could be possible.

There are suggestions about the authorization model. Maybe it is a new way we should explore. But certainly what is the appropriate type of consent we need here is something we need to further discuss. It is really something that's a sensitive issue, because it will have an impact not only in genetic research, but any other types of research that we're doing out there.

Protecting privacy. Again, the choice of words is very important. Personal feedback. As I said, what are we going to do in large-scale settings. Is it appropriate to think that we're going to be able to bring back individual results? Is this something that is reasonable and feasible?

The status of genetic material. Ownership. Who owns these databases, the tissue? In certain jurisdictions, the mere fact that you would own tissue is counterintuitive, I would say, and against most basic fundamental principles.

Government structure. Looking into checks and balance is also something I will talk a little bit more about in a second. Ethical review for multi-centered research projects is also quite challenging these days.

I will skip this part and go right through now to the challenges. So if you were to establish a human genetic research database right now, what would you consider? What are the fundamental elements you need to think about?

We think there are at least three elements you'd like to go through. The first one is ensuring legitimacy of your human genetics research database. You'd like to look into the adequate protection, building trust, making sure that it's well protected, and you like to make sure that there are appropriate checks and balances. Let me go into more detail into these three elements.

So if we are looking into legitimacy, as I mentioned earlier, you need to justify putting so much research, money, and resources into these huge human genetics research databases. What are the benefits? How do we need to explain these benefits? So this is key into the funding and support of the community. We need to work on this, I think.

Legitimacy can come in different ways. In some countries, they have chosen the democratic forum through Parliament and legislation to start these types of human genetic research databases. So here, for example, you have Estonia and Iceland where in these countries, they have adopted the legislation to really create their human genetics research database.

Now, is Parliament the most appropriate way? Or is it the appropriate democratic forum by which you could engage the public and make sure that there is legitimacy there? The question that we had is if there is not enough public consultation, public communication prior to this Parliament enactment of the legislation, we might have questions with respect to the process. But nevertheless, in many countries, at least it is very clear. Whenever there is a legislation, you know the rules, and you know what is being done.

Another project like CARTaGENE, U.K. Biobank, HapMap, and others, the initiative, instead of going through Parliament, is a project that was started by scientists themselves. They are adapting the science to the community's needs and the population's desires through discussion. Again, in this case, it is more, I would say, self-regulated, but the participants have really again here discussed the regulatory framework that is being built.

So these are two different ways in which you could approach it. Now, for a transnational enterprise, it is a little bit more complex, like GenomeEUtwin, P3G, or HapMap. These are transnational international collaborations. Here, the success really depends on trust and communication between members, and based on common understanding of the issues and agreements on the scientific, ethical, legal, social issues and common philosophy. So this is quite challenging, but at the same time, the benefits are I think incredible.

Now, the second part is about building trust. Building trust at different levels. First, ensuring public representation, and ideally, inclusion of all the groups that could be representing the sample population. But we know that there are financial constraints, and it's not always possible.

Building trust with the community really depends on your communication strategy. We cannot emphasize enough how important it is to really create a communications strategy that will really include the community from the start, and that will really enable bilateral communication, if I should say so.

Ensure data collector's participation and expertise, making sure that the people that will collect the data are properly trained, and that the researchers also are sensitive to all these ethical, legal, and social issues. That's something you'll want to think about.

Privacy consent issues. Again, privacy is oftentimes the thing that worries I would say, communities. That's the first thing that will come. In a way, it's legitimate, because you are in these human genetic research databases, you're putting in all of this sensitive information, and really concentrating in one spot. So it is legitimate that they have questions, but I think we have to just be able to answer with appropriate tools, choosing an appropriate consent process, looking into our security mechanism, and looking into the types of identifiability of the samples that you are going to look into.

Individual feedback and general results. Again, that is something that the research team will have to make a decision about. You see here different options. In Estonia, they chose to really respect the right to know in a way, and in other projects, there will be no research results except for the medical examination from the start. So that's another element you'll need to consider.

Is it possible? That's the question that we're wondering. Is it even possible in such large-scale projects to get the appropriate genetic counseling to really make sure that you don't fall into the potential problems in genetic discrimination or misinterpretation of results.

Finally, stigmatization and discrimination are really issues you want to consider in the commercial aspect. This is a very tough one, making sure that you get free public access, yet at the same time, we need to respect all these intellectual property rights that are involved.

The involvement of the industry, I think there is the financial resource needed for these types of projects. Often we will for sure need the involvement of the industry, but how to do it, at what level, and how to appropriately make it, that's the question.

Finally, checks and balance. Thinking about checks and balance, you need to think about it from the start to get approval of not only the protocols that will use your huge human genetic research database, but you need to look into the framework itself. You need to get a stamp of approval.

We learned from the authorities it could be anybody from the ethics community to other types of authorities, making sure that the public is recognized, again, as a true partner, and will have its say in the establishment and creation of the framework itself, and need to build a mechanism for the review procedure. It needs to be there from the start.

If you look into the research project review and monitoring, this is really I think a quite challenging area. We want to set mechanisms to really make sure that there will be appropriate ongoing monitoring not only of the research project, but again, of these public resources, and how it will be set.

The U.K. Biobank did something very interesting. I think there are very innovative solutions out there, but we need to still work on those.

Finally, the management structures. In each of these projects, they have built interesting charts on how the project would be managed and appropriately balanced. So we need to ensure transparency, independence, and integrity. But to create, conceive, and conceptualize these management structures is quite challenging for researchers as well.

I will go through just before I say it, and talk about the conclusion. I want to talk to you a little bit about the P3G project. I thought through the presentation I have been talking about some of the challenges, the problem of organization, and the problem of having different taxonomy to designate similar things.

Public Population Project in Genomics is a non for profit organization that is currently building an international consortium to really promote the type of discussion and collaboration that we need in the field of population genetics research. We want to foster this international organization and discussion at all levels.

At the scientific level first to be able, for instance, to have common words to designate the type of research, common ways to collect data, and also at the ethical/legal/social level to make sure that people are provided with the types of tools, and that we can benefit from the experience also of other population genetic research databases that are already out there.

We want ultimately to create a body of knowledge that will be publicly available so that all the human genetic research databases that are out there will have an opportunity to really be able to communicate with each other, to be able to compare data if it is interesting, and to be able to exchange data, because they will have had an advance talk about this organization of taxonomy, and dealt with some of these issues of making sure that we have a common approach and common vocabulary.

The current partners in the P3G project, and I'll just go back in the slides to show you the website if you're interested to know more, the current partners are GenomeEUtwin, the Estonian Genome Project, CARTaGENE, and CIMGR, which is a Manchester project. We have other partners that are coming up in the project right now. The Chair of the board for this project is Bartha Knoppers. So if you'd like to know a little bit more about P3G, I invite you basically to go see our website.

So just in conclusion, I think we're building really unprecedented, very interesting research tools that will be used for generations to come. But I think the legal and ethical tools right now might not really deal appropriately with all the issues that are raised. I think oftentimes they were created, as I mentioned earlier, for drug research, or Mendelian research. I think if we want these biobanks to really span the test of time, we need to look at three things.

We need to probably revisit the current ethical/legal framework. We certainly need to make sure that participants are on board, and communities are on board very early on in these types of projects. I think ultimately the success of these types of human genetic research databases will rely on their trust in these types of tools.

We have a common goal here. It is really to benefit the health of everybody. I think we then should have common vocabulary, and we still don't have this yet. So we need to work on this.

Thank you very much.

DR. TUCKSON: Thank you very much, Mylène. That was terrific on its own merit, but even more terrific for having stepped in at the last second.