Q&A: SickKids' Scherer Moves Up to 'Bigger Rink' as New McLaughlin Centre Director

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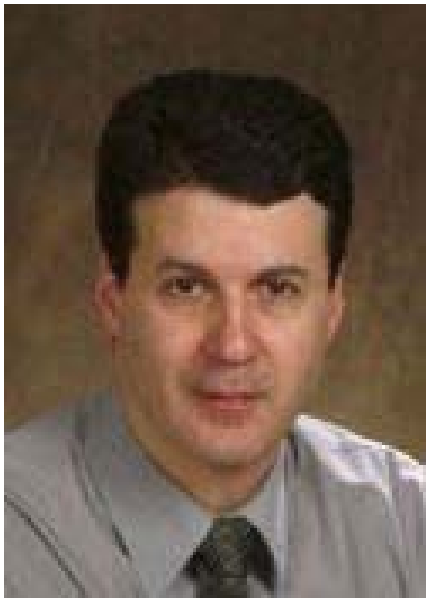

Name: Stephen Scherer

Titles: Director, McLaughlin Centre for Molecular Medicine, University of Toronto; Director, The Centre for Applied Genomics, The Hospital for Sick Children (SickKids), Toronto; senior scientist, SickKids; professor, medicine, University of Toronto

Professional background: 2007-2009, Interim Director, McLaughlin Centre for Molecular Medicine; 2006-present, Professor, Molecular and Medical Genetics, University of Toronto; 2003-present, Program Director, Computational Genomics, McLaughlin Centre for Molecular Medicine, University of Toronto; 2002-2010, Associate Chief, Research Institute, SickKids; 2002-present, Director, The Centre for Applied Genomics; 2001-2006, Associate Professor, Molecular and Medical Genetics, University of Toronto; 2001-present, Senior Scientist, Genetics and Genomic Biology, SickKids; 1998-2002, Associate Director, The Centre for Applied Genomics; 1998-2002, Founding Scientist, Ellipsis Biotherapeutics; 1998-2001, Assistant Professor, Molecular and Medical Genetics, University of Toronto; 1997-1998, Director, Canadian Genetic Disease Network DNA Sequencing Centre; 1997-2001, Scientist, Genetics, SickKids

Education: 1995, PhD, Medical Genetics, University of Toronto; 1990, MSc, Medical Genetics, University of Toronto; 1987, BSc, Biology, University of Waterloo, Canada

Last week the McLaughlin Centre, a decade-old University of Toronto institution that aims to advance genomic medicine through research and education, appointed Stephen Scherer as its new director. Scherer, who has been the center's interim director for the past two years, is also currently Director at The Centre for Applied Genomics at The Hospital for Sick Children and a professor of Medicine at the University of Toronto.

The McLaughlin appointment gives Scherer the ability to play a larger role in encouraging Canadian clinicians to adopt genomic technologies. Armed with a C$50 million ($48.8 million) bequest from the R. Samuel McLaughlin Foundation, Scherer's plans for the McLaughlin Centre include investing in research, education, and training in genomic medicine. The center will have a specific focus on the clinical use of microarray and next-generation sequencing data.

BioArray News spoke with Scherer last week about the immediate goals of the McLaughlin Centre, and how he envisions newer genomic technology platforms like microarrays and sequencing will be adopted by clinicians. Below is an edited transcript of that interview.

Now that you are the director of the McLaughlin Centre, what are some of your goals for it, and what will your work as its director entail?

There are 10 fully affiliated hospitals and their research institutes as well as the Health Sciences faculty at the University of Toronto that the McLaughlin Centre will work between. Our mission statement is to advance genomic medicine through research and education. That's our tag line.

The major programs that will have an impact in the first couple years are to expand the MD-PhD program at the university medical school, with a focus that the PhD component would be conducted within the area of genomic medicine. Along with this will be enhancing genetics and genomics in the undergraduate medical program curriculum. The second thing is to expand the impact of genetic counseling and clinical genetics. There is a strong history here in Toronto, but we now need to support bringing the front line people who have to deal with these types of information up to speed on what's happening in the areas of databasing and technologies. The third part of the effort is to have resources to attract and retain the top postdoctoral fellows in genomic medicine, and to roll out an open, peer-reviewed grant competition. For success, we need to make the whole of the McLaughlin Centre greater than the sum of its parts. I will continue to be [on] staff of The Hospital for Sick Children, which is a teaching hospital of the University of Toronto's Faculty of Medicine. My SickKids research group and the McLaughlin Centre are in the MaRS-Toronto Discovery Tower central to the University of Toronto Health Sciences complex, which should all help to facilitate our objectives.

How does your role as director differ from your role as interim director?

My role as interim director was to reel in the budget from the first phase of the McLaughlin Centre, weather the recession, and also plan for this next phase. Now the fun begins and I get to build teams and spend the money.

Will this administrative role affect in any way your research at SickKids?

I consider myself to be nearing mid-career and would have only accepted this position if I thought it would actually enhance my own research, as well as that of others in Toronto. In Canada, the philosophy for research has always been a bit different than the US. I think, as a result of a more developed social system, Canadians tend to collaborate more often than not. Over the years my research approach has followed the 'goal is only equal to an assist' philosophy. Maybe it's just a hockey thing, with hockey being one of the few sports where a goal is equal to an assist, but it has worked for me. With the McLaughlin Centre appointment I get to play on a bigger rink.

What kind of projects are you looking to fund through the center?

It's going to be a little unique in that it's going to be what I like to call an accelerator grant competition. These are typically short-term, potentially high-impact grants that essentially help move primary exploration or discovery to the next stage and quickly. Importantly, the project also needs to be close to the patient. The grants will also be viewed as impactful if more than two institutions are involved, and include partners from government and/or industry, but the latter will not be a deal-breaker. We'd also like to see new faces with new solutions.

The scope of this effort seems broad. What are some concrete projects you hope to first address as director?

Our first efforts will be focused on data analysis and interpretation, mainly for microarrays, but it's also now rapidly moving to sequencing. For example, we have the *Database of Genomic Variants* that we run and we have organized monthly calls with all the molecular diagnostics labs across Canada that are doing genome-wide microarrays to set up a mechanism for them to ask questions and discuss things.

The impact has been tremendous. Some groups have benefited on everything from the technologies to advice on vendors to supply them. Everyone needs help interpreting the data, including often comparing case reports and control data. People often ask, 'Is genomic medicine here?' The answer is absolutely yes, you don't have to go too far to see the impact. Moreover, the applications are increasing every single day. In the SickKids molecular diagnostic lab – the largest DNA diagnostic lab in Canada – run by Peter Ray, they run several thousand genome-wide clinical microarrays each year, and the Centre for Applied Genomics, supported by the McLaughlin Centre, is running tens of thousands of research arrays. The clinical or research users come from traditional clinical genetics, but also neurology, cardiology, orthopedics, cancer, and actually all divisions of both pediatric and adult hospitals. Of course, the quantity of the data is increasing now from a few dozen data points to millions of data points. In our experience, an accurate interpretation of the genome-wide data can only come when you bring the expertise from all of these people together. It is incredible how professionals with different training see different things in the data, and that's precisely what the McLaughlin Centre wants to facilitate.

Where do you see some of the more cutting-edge technologies, like high-density genotyping arrays and next-generation sequencing, fitting into the objective to advance genomic medicine?

The promise of genome-wide experiments, such as high-density genotyping arrays or [next-generation] genome sequencing, is that you will only have to do the experiment once and get all of the data and then, somehow, just re-annotate it as the clinical databases get better. I think single-scan experiments will come at some point in the future, but we still have a way to go. The microarrays will continue to get better and for this reason the clinicians will always want to run the latest version. We see this over and over here. It doesn't matter if you tell them the last array run is pretty good, they want the latest data; their practice demands it. For this reason, NGS will ultimately prevail and take the market share, but it will likely never entirely replace some single-gene tests that may be more sensitive, specific, or economical. I think in five years the arguments we often hear – of there being too much data to deal with – will seem silly. Can you image where we would be if the early cytogeneticists, the first genome diagnosticians, squinted for only partial viewing of the genome karyotype because there were too many chromosome bands too look at? Again, how this all plays out will depend on who is at the table. The McLaughlin Centre will try to bring as many of the end-users of the data to the decision-making table [as possible].

For what indications are these technologies being used clinically?

There is a trend I am seeing for researchers and clinicians to seek the answer to some complex clinical cases by just running an array, and now in a few cases sequencing. Some of this has to do with the recognition of a growing number of examples where rare and apparently high-penetrant variants are being found in what are categorized as common disease. I am not saying this is wrong and, in fact, [I] usually advocate it, but the thing that keeps popping up is that while some of these variants seem to be susceptibility factors, they are often found in a host of conditions sometimes only distantly related in clinical presentation and there [are] often complexities in penetrance.

What this means is that the genomic data needs to be fully contextualized with the family history, the stage of screening – adult, infant, prenatal, pre-implantation, high-risk setting, and the families need for it to have utility.

These kinds of efforts are underway around the world. Where does Canada fit into this mix? Is it a leader? Is it behind other efforts? What needs to be done?

I am very proud to say that with massive investments in genomics research from agencies like Genome Canada, the Canadian Foundation for Innovation, and the Canadian Institutes for Health Research, in the past decade our country has moved into the very top echelon of genomics research in the world. With continued commitment from our governments, now our scientists need to step up and deliver in transferring that knowledge to benefit all aspects of society.

A great example is found in the cover story in *Nature* this week, where Brendan Frey and Ben Blencowe [from the University of Toronto] came up with an algorithm to break the splicing code of genes in different tissues. I can see how this basic research will have all kinds of clinical impact if the project is now shepherded in the right direction for applications in genomic research. There are many other examples. I also think that with what is probably the healthiest economy in the world right now, it's Canada's turn to step up and take the lead on more international genome projects, mainly because we can, but also because we want to take some of the load from countries like the US and the UK and others who have made so many contributions and helped us so much in the past.

You have done a lot of work using genomic research tools to study the causes of autism spectrum disorder. Will this also become a focus of the center?

Much of what we are learning in genome-wide studies is coming from our work on autism spectrum disorder. ASD is a good model since there seem to be monogenic forms and also multigenic forms of the disorder and everything in between. This reflects really where genomic medicine needs to go – in other words from harnessing the knowledge and experiences of Mendelian genetics to help make sense of complex clinical traits.

Most of the new technologies like dense microarrays and NGS are initially tested in our well-characterized ASD cohort since we usually have the money to do these experiments. For example, we are now sequencing 1,000 exomes from individuals with autism. Our experiences will then filter out to the Toronto and Canadian community through these research studies ongoing in the genome center. While there will be no specific 'disease' focus of the McLaughlin Centre, I hope it will facilitate experiences gained and autism and equally other disorders, will ultimately benefit from the new ideas it brings through its open membership.

Why do you think sequencing will be used clinically in the future?

When I think about the Neandertal paper that just came out in *Science*, it is hard to imagine sequencing will not become ubiquitous. If a little bit of DNA taken from a bone tens of thousands of years old can be used to generate a draft sequence of a genome, it is just a matter of time before genome sequencing will be ubiquitous. The naysayer will challenge that even with a genome sequence it doesn't tell you that much. The cells in our body are smart enough to read and write the genome code over and over again, passing the most important traits, and sometimes, unfortunately, diseases, down from generation to generation. As a community, we just have to become as smart as our cells. To this day the most important question a physician will ask you is, "Do you have a family history of this or that?" Studies of the genome give us the most important form of family history: our DNA sequence. We hope the new investments through the McLaughlin Centre will speed up getting useful and understandable genomic data to the families who will most benefit from it.