ResearchConnection
An e-newsletter for cancer researchers

December 2010. Volume 3, Issue 2

Genomics – will it usher in an age of personalized medicine?

When the Human Genome Project was completed and published 10 years ago, it was met with a great deal of fanfare, hope and expectation. An extraordinary feat had been accomplished with the sequencing of an entire human genome. Would this massive amount of information help doctors to personalize the practice of medicine to each individual, leading to the prediction, control or even cure of diseases like cancer?

Did the Human Genome Project (HGP) achieve everything it was expected to?

"When it was published, people said, 'this will change everything,'" says Huntsman. "This has proven to be true, it's just that it was impossible to predict at the time how those changes would occur."

"The HGP created a map, or an accrued atlas, on which all of our voyages of exploration take place now. All of the projects we're engaged in now are derivatives of the HGP – everything from cancer prevention studies to the identification of risk factors for cancer, through to the development of new drugs and predictive biomarkers. The HGP has had a massive impact on all of this research."

What has been the impact on patients?

"By the time patient care is changed," says Huntsman, "we are so many steps removed from the HGP that it's hard to actually directly attribute it. But, just as one example, the most exciting new treatments for breast and ovarian carcinomas are Parp inhibitors, [which generally target mutations in the BRCA1 and BRCA2 genes] and this is very much underpinned by the HGP effort."

Some people remain skeptical. One reason for the skepticism is that, for the average person to have their own genome sequenced, it was originally estimated to cost as much as $30 million. While this estimate is much, much lower now, there is still a huge appetite from both researchers and the public for less expensive and faster ways to do complete genome sequencing

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In fact, several large prizes have been offered to inspire scientists to achieve this complex task. For example, the Archon Genomics X Prize[1] is currently offering $10 million to the first research team to sequence 100 human genomes in 10 days.

Despite the skeptics, tremendous advances have been made and the promise of genomics in the field of cancer is bright. In the past, the diagnostic classification of a cancer was based on the organ or

site location, such as liver, lung or blood. But now, thanks to genomics, many forms of cancer can be characterized by their molecular profile. These molecular characteristics provide insights into how quickly the cancer might spread or how it might respond to specific treatments.

> "The opportunities presented by genomics are so great … that I think we have to move in this direction."

Scientists still have much more to learn about how cells function and how they interact with each other and with the environment. This information is crucial to our understanding of how genes keep us healthy, predispose us to disease, or even help predict how we will respond to treatment.

Now that scientists have mapped and sequenced each gene, they are better equipped to search out the "abnormal" genes – the ones that may cause cancer or other problems.

And it is widely believed that the future of medicine will rely on genetic-based approaches to help develop smarter treatments for diseases such as cancer, and reduce their risk of developing in the first place.

Next generation sequencing

Dr David Huntsman is the director of the Centre for Translational and Applied Genomics at the BC Cancer Agency in Vancouver. He says that there was a "bit of a lull after the initial flurry" when the human genome was first sequenced. That lull now appears to have ended. In the past couple of years, the pace of change in genomic discovery has really taken off and is now accelerating at breakneck speed. "We're able now to discuss research projects that would have been insane even to consider two years ago, such as sequencing full genomes of

Dr David Huntsman,
Photo credit Vancouver Sun files.

multiple cancers taken from clinical trials, which should lead to new predictive biomarkers," he says.

The reason for this recent acceleration is the advent of "next generation sequencing" (see previous article *A Genomics Primer*). "There's been a sea change in technology in the last 2 to 3 years," says Huntsman. "There are now many platforms of next generation sequencing technologies that are becoming more and more available, and that will dramatically change the way research is done but will also change the way medicine is practiced."

Future directions and dilemmas in genomics

The practice of medicine could change dramatically in the future to the point where, ultimately, a patient might come into the doctor's office with their sequenced genome on their iPod.

But even if that were an affordable option today, doctors wouldn't yet know what to do with the information – both how to interpret it and how to deal with the enormous ethical considerations.

"Society has to decide whether it wants medicine to change in this way."

"This is very personal information and there is great scope for misuse," says Huntsman. Determining specific therapies based on a genetic profile could significantly improve the way some diseases are managed in certain groups of people; however, it will also mean that the same treatment options are not available to everyone. And then there is the possibility of workplace, insurance and other discrimination against those with genetic susceptibilities to disease. "Before it becomes main stream, there will have to be broad-based, community-wide discussions because society has to decide whether it wants medicine to change in this way," he says.

Personalized medicine?

The dawning of the age of "personalized medicine" does present exciting opportunities for cancer patients. As we become better able to group these patients in more sophisticated ways, we can treat them more specifically for their own form of the disease. Those who will respond to a drug will be offered it, and those who won't respond will be spared unnecessary toxic side-effects.

"Ultimately, a patient might come into the doctor's office with their sequenced genome on their iPod."

The term "personalized medicine" is, however, beginning to shift somewhat as scientists speak more in terms of groups or stratification of care. "We often talk about progress in cancer care as being a movement along a continuum from a generic approach to cancer control to an individualized approach. This is certainly going to happen for some problems, such as identifying individuals with a dramatically increased risk of some cancers. But what is more likely to happen is, rather than becoming entirely individualized, cancer care will become highly stratified and genomic tools will be used for that stratification," says Huntsman.

The role of the Canadian Cancer Society

The Canadian Cancer Society has a long history of funding fundamental research, which has made it possible to get to the threshold of a genomics era.

We have also made a significant difference in the rapidly changing field of genomics, and we are well positioned to continue to do so in the future.

"The Canadian Cancer Society has greatly contributed to research that has led to greater stratification of cancer control, in terms of risk reduction, early detection and treatment. Often the funds required for large-scale genomics projects are outside the normal range of Society grants, since genomics research is often very expensive, but the Society has developed a cancer genomics panel [*which Huntsman chairs*], and we've been very pleased to be able to fund several genomics projects that focus on specific cancer-related questions," says Huntsman.

"I look forward to working with the Society closely to ensure that the Canadian Cancer Society, with its strong translational research history, becomes a major player in the development of cancer genomics in the Canadian research landscape."

Rethinking the solutions, right here in Canada

Another hurdle to overcome in the future of genomics, according to Huntsman, is that the current system of testing new cancer drugs and other treatments will have to continue to evolve in order to adapt to the new knowledge and technology. "If you're going to use a new treatment plan, you have to prove it in a clinical trial, but if we're individualizing cancer care, or creating very small groups of cancer patients to be treated in the same fashion, the current clinical trial set-up with large phase III trials cannot address these questions. So we have to not just rethink what the solutions are going to be, but also how we're going to test possible answers."

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Despite the obstacles, Huntsman sees Canada as the ideal place for progress to be made in this burgeoning and promising field. "The community of cancer researchers in Canada is quite small and tends to be collegial and knows each other well. There's a great opportunity for us to work together to align platforms that can rapidly engage in genomic-driven clinical trials, which will enable the further stratification of treatment and maybe, in some cases, individualization of care."

"The opportunities presented by genomics are so great in terms of improving outcomes, decreasing the numbers of people who develop cancer, and making sure that people don't get exposed to side effects if they're going to derive no benefits from intervention, that I think we have to move in this direction."

The Canadian Cancer Society is currently funding several promising genomics projects. For example:

- Dr Michael Taylor is trying to better understand the molecular genetics and epigenetics of medulloblastoma and ependymoma, two of the most common malignant childhood brain tumours, in order to develop better treatments.
- Dr Steven Jones is leading a project on genomic sequencing and analysis to characterize, for the first time, molecular changes underlying thyroid cancer.
- Dr Wan Lam is studying the genes and genetic mutations involved in the development of lung cancer in people who have never smoked – a group that represents an increasing proportion of lung cancer sufferers.

[1] http://genomics.xprize.org/