BULLETIN

CANADIAN GENETIC DISEASES NETWORK

"SOLUTIONS" FOR FINDING GENETIC MUTATIONS

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Thanks to improved technology, people living with retinoblastoma, a rare cancer of the retina that occurs in infants, can now have genetic mutations traced faster and more effectively, leading to earlier detection and treatment.

Retinoblastoma is caused by mutations in the RB gene, and is heritable in 40 percent of families, but inherited in only 10 percent. Molecular testing of blood relatives can determine which family members are at risk for retinoblastoma, which is a significant advantage since early detection and treatment of the cancer can save the vision and the life of the patient. Children who do not carry the RB mutation found in one member of the family are not at risk. Children who do carry the RB gene mutation are watched for tumours and treated early.

In 1999, Dr. Brenda Gallie and Kirk Vandezande formed a company in Toronto called Solutions by Sequence that tests for the RB mutations. Dr. Gallie does much of the research, while Vandezande's mission is to reduce the time and cost required for molecular tests. The University Health Network of Toronto is an equity partner.

The company is a spin-off of research supported by The Canadian Genetic Diseases Network's (CGDN) 'strategic fund,' which is designed to provide early-stage funding to projects with commercial potential. As part of their mandate to catalyze commercial competitiveness in genetic diseases research, CGDN assists in developing spin-off companies such as Solutions by Sequence.

"We know the gene very well, we know the disease very well. We understand how the protein works and therefore have found types of mutations that routine genetic labs can not look for," says Dr. Gallie.

Dr. Gallie says that she always wanted the opportunity to take molecular genetic information and apply it to patients, and retinoblastoma is the pilot case that demonstrates how valuable and efficient this can be. As of right now, they are

only testing retinoblastoma, which is the pilot “proof of principle” through which Solutions by Sequence has been able to develop the technology to test for other difficult gene mutations.

Difficult genes are big genes where mutations are found all over the place and every different kind of mutation disrupts the gene, as is the case with retinoblastoma. Dr. Gallie says that the scientific challenge lies in finding all of the different mutations, unlike in diseases such as cystic fibrosis, where there is predominantly one common mutation.

The goal of Solutions by Sequence is to optimize its test sensitivity so that it can more reliably detect a mutation in diseases where detection would have a benefit to the health of the family. Another of the company’s goals is to reduce the turnaround time between testing and the issuing of a report. Solutions by Sequence is now able to identify 90 percent of mutations, and the entire test procedure takes only an average of 3.7 weeks.

“The focus on optimizing for retinoblastoma has let Solutions leap ahead in efficiency and sensitivity,” says Dr. Gallie.

In the next year or two, Dr. Gallie says that Solutions will start testing two or three new genes in addition to retinoblastoma. Possible new genes are hereditary hemorrhagic telangiectasia (HHT) and the often overlooked multiple endocrine neoplasia (MEN) genes. She says they will also be looking at breast cancer genes. Much of the company’s work will likely end up being focused on cancer genes.

In the lab, Dr. Gallie says they are using human genome data to study the non-coding regions around the gene to find the 10 percent of mutations that people aren’t finding in the coding regions. This bio-informatics project may find how genes are regulated and find the mutations that cause disease. Solutions’ technology has also been used in research on tumours, leading to the discovery of a new oncogene and a new tumour suppresser gene, which may have importance in the progression of retinoblastoma, bladder cancer and other cancers.

In support of its business interests, Solutions by Sequence is about to file several patent applications and is also applying to license other genes. Dr. Gallie says that although they have already begun to generate revenue from the retinoblastoma testing, they have not yet made a profit. However, they are optimistic and are now looking for early investors, which would allow them to hire more people and build the business side so that she and Vandezande can continue doing science.

“If we identify the mutation in a baby, we can make a lifetime of vision and save them from a lethal cancer, so it’s really, really valuable to do that,” Gallie says.

The Canadian Genetic Diseases Network (CGDN) has been a member of the federal Networks of Centres of Excellence program since 1989. This program is a federal initiative administered jointly through the Natural Sciences and Engineering Research Council (NSERC), the Canadian Institutes of Health Research (CIHR), and the Social Sciences and Humanities Research Council (SSHRC) in partnership with Industry Canada.

To learn more about Solutions by Sequence, visit
http://www.solutionsbysequence.com