

# THE BURRILL REPORT

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## FINANCE

Variations on a Theme

[Crohn's discovery points to the power of a Canadian company's approach to unraveling genetic players in complex diseases.](#)

### DANIEL S. LEVINE

Between 1608 and 1760, a group of rather prolific immigrants from France made their way to Quebec. One couple alone, Pierre and Anne Tremblay, married in 1657 and now are credited with more than 260,000 descendants.

The Quebec founder population grew rapidly from a start of about 2,600 people to up to 6 million today, a fact that is of interest to Genizon BioSciences.

"The population is of importance because they had large families that fueled population growth with very little intermarriage between the French immigrants and other populations in Quebec due to cultural and language differences," said Tim Keith, chief scientific officer of biotech Genizon. "It is a group of people of particular interest to geneticists because it underwent a so-called bottleneck effect where a small group of people gave rise to a large population with genomes that are more homogenous than the general population."

Privately held Genizon, a Quebec-based firm with about 135 employees, is using DNA collected from descendants of the Quebec founder population to unlock the genetic origins of complex diseases. Though single genes can be identified as the underlying cause of simple genetic diseases such as cystic fibrosis, many diseases involve an array of genes as well as environmental triggers. Because of the lack of variation in the genome of the Quebec founder population, DNA collected from the group provides a unique opportunity to unravel the genetic causes underlying certain complex diseases.

A genome-wide association study for Crohn's disease in the Quebec founder population from researchers at Genizon and elsewhere identified multiple genes not previously known to underlie Crohn's. The study just published in the *Proceedings of the National Academy of Sciences* also confirmed the role of three other genes known to be involved in the disease.

Crohn's disease is an inflammatory bowel disorder with a strong genetic component. Because of its complex origins, it has been difficult for scientists to pinpoint the best targets for drug therapy. A genome-wide association is a means of finding genes at work in a complex genetic disease such as Crohn's. The process involves taking a set of individuals known to have the disease and comparing their genomes to a group of people without the disease to find significant points of variation.

#### A New Model

Genizon licensed rights to its Crohn's disease GeneMap to Genentech in August 2006. Under the terms of the agreement, Genizon will receive an upfront payment, research funding and milestone payments for each therapeutic product that may emerge from the collaboration. Financial terms were not disclosed.

That is the model for Genizon as it moves forward. It plans to use the

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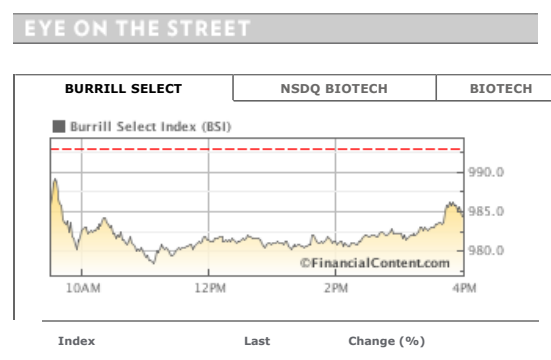
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information on specific complex diseases it is able to coax out of the Quebec founder population and license it to makers of diagnostics and therapeutics. Already the company has completed six genome-wide associations to date and earlier this year licensed diagnostic rights to GeneMaps for Attention Deficit Hyperactivity Disorder, endometriosis, and Alzheimer's disease to the drug giant Pfizer.

The GeneMap consists of a collection of all of the genes that make someone susceptible to a disease along with their biochemical pathways and drug targets. Genizon said it expects its discoveries relating to Crohn's will lead to the development of new therapeutics to treat the disease more effectively. The discoveries were actually made in 2004, when the company performed what it dubbed the first comprehensive genome-wide association study of a common disease.

In the journal publication, researchers replicated and refined Genizon's findings by comparing the information gleaned from the Quebec founder population to two general patient populations from Germany. Of the novel genes identified by Genizon, none were known to be connected to Crohn's disease, but some were involved in pathways relevant to Crohn's disease. This includes pathways involved in such things as immune response, the epithelial cells that line the gastrointestinal tract, and repair and remodeling of tissue.

**Novel Treatments Seen**

"These discoveries provide new and exciting information on how tissue repair, epithelial defense, and immune response may be targeted producing more effective therapies," said Genizon's German collaborator, Professor Stefan Schreiber, director of the Institute for Clinical Molecular Biology at the University Hospital Schleswig-Holstein. "They open the door to truly understand the mechanisms of the disease and how therapies ideally should work."

Genizon said it has identified additional genes that complement the genes in the journal article. These and their interactions are also under study for the development of novel treatments for Crohn's disease.

Leading to Genizon's breakthroughs were advances in computing and the development of sophisticated DNA analysis that has made genome-wide associations feasible. But as the Quebec founders population begins to become more integrated with other populations, it also may represent a window of opportunity that will only remain open so long.

"There's no doubt about it," said Genizon's Keith. "This will go away in the next several generations."

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