Gene discovery made easier with powerful new networking technique

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The identification of disease-causing genes will be much easier and faster using a powerful new gene-networking model developed by researchers at The University of Texas at Austin.

Edward Marcotte and his colleague, postdoctoral researcher Insuk Lee, used the gene network technique to identify new genes that regulate life span and are involved in tumor development in the nematode worm.

In collaboration with Andrew Fraser's group at The Wellcome Trust Sanger Institute, the researchers manipulated the newly found genes and were able to extend the lives of the worms by 55 percent and reverse the onset of tumors.

Marcotte hopes to extend the technique to identifying genes for disease and other disorders in humans. The human genome has been sequenced, but very little is known about what more than half of about 20,000 genes do.

"This is a big step forward in the rational discovery of disease genes," says Marcotte, a professor in the Institute for Cellular and Molecular Biology. "We can use this gene modeling technique to predict the function of new genes and then run experiments to confirm the findings.

"The process could greatly improve our ability to pinpoint specific genes involved in disease and aid in the development of drugs."

Marcotte's research was published January 27 online in *Nature Genetics*.

Gene networks are models of the connections between all of the genes within an organism, and Marcotte uses them like an online social network. He learns what new genes do by the genes' connections to others in the network, much like people use online social networking systems to connect with friends and others with similar interests.

"You can think of it like six degrees of separation or a Facebook.com for genes," says Marcotte. "If you know of a few genes and what they do, their 'friends' probably do something similar, and we can find these through the network."

To build the worm gene network, Lee, a postdoctoral researcher in Marcotte's group, synthesized data from about 20 million experiments from around the world. A visual representation of the network—which has the appeal of a work of modern art—is a complex web of lines interconnecting the worm's 16,000 genes.

In one set of studies, the researchers looked for genes that cause tumors in the worms. The tumors are a model for human eye cancer (retinoblastoma) and appear as growths along the length of the worms' bodies.

By searching the network, they found about 170 new genes that could have been involved in the development of tumors.

Then Marcotte's colleagues at the Wellcome Trust Sanger Institute in Cambridge in the United Kingdom tested the function of the new genes by inactivating them with a technique known as RNAi. The technique mimics the action of a potential drug by knocking out the function of individual genes.

They found that inactivating 16 of the 170 genes reversed tumors in the worms.

In similar studies, the researchers identified genes that regulate life span in the worms and manipulated the genes to extend the worms' lives by 55 percent.

"This sets the stage for making equivalent networks for the mouse and human genome," Marcotte says. "Then we hope we can discover genes that are causal for disease conditions in humans."

Source: University of Texas at Austin