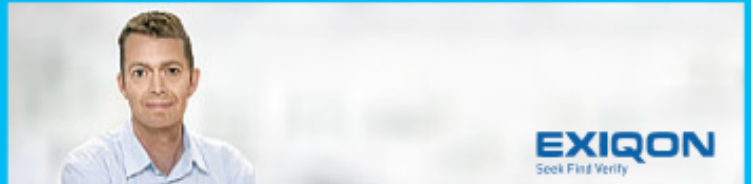


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Rule-Breaker Genes Identified

By Elizabeth Pennisi
ScienceNOW Daily News
30 November 2007

The battle of the sexes extends all the way to our chromosomes. In some cases, the copy of a gene inherited from one parent shuts down, leaving just the copy from the other parent active and upsetting the classic rules of inheritance. Now researchers have come up with the first comprehensive map of these so-called imprinted genes in humans. Many of them lie in regions of chromosomes implicated in disease and may be involved in problems such as autism and obesity.

Geneticists discovered imprinting in 1991 and now know that defects in imprinted genes lead to abnormal development and to diseases such as Angelman and Prader-Willi syndromes, both characterized by mental retardation. Imprinting involves chemical modification of the relevant DNA, alterations that can be strengthened or undone by diet, toxicants, or other environmental factors. But imprinted genes have been hard to find because imprinting can occur in just one tissue, whereas in the rest of the body, two copies are active, making the gene appear normal. Indeed, until now, geneticists knew of only 40 such genes.

To track down more, geneticist Randy Jirtle of Duke University in Durham, North Carolina, enlisted Duke computer scientist Alexander Hartemink and his graduate student Philippe Luedi to develop a computer program that can learn. It improved its search ability by distilling common features of known imprinted genes and contrasting them with characteristics of 552 genes that are never imprinted. One difference is in the distribution of bits of repetitive DNA that bulk up the genome near the gene in question, for example.

Jirtle and colleagues used that program, along with commercially available software as a further check, to scan the human genome. The software predicted the existence of 156 more imprinted genes among the 20,770 human genes. More than one-third of the genes function in development. Several chromosomal regions have relatively high concentrations of these genes, the researchers report online 30 November in *Genome Research*. One such region, on chromosome 11, has quite a few: two previously known imprinted genes and five unrecognized ones, including a gene possibly involved in lung cancer.

In the lab, the group confirmed that two genes on the list were imprinted as predicted, boosting Jirtle's confidence in the software. Located on chromosome 8, both are associated with cancer, and one, which is expressed in the brain, is implicated in epilepsy.

Geneticist Benjamin Tycko of Columbia University cautions that more of the predicted genes need to be verified as truly imprinted. But no matter what, says quantitative geneticist Jason Wolf of the University of Manchester, U.K., the map "is an important starting point for studies of gene expression and gene functions. It will provide a valuable database for human geneticists."

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