Study finds one percent of human genes switched off

Kate Kelland, Reuters

Scientists studying the human genome have found that each of us is carrying around 20 genes that have been completely inactivated, suggesting that not all switched-off genes are harmful to health.

A team at Britain's Wellcome Trust Sanger Institute is developing a new catalogue of so-called "loss-of-function" (LoF) gene variants to help identify new disease-causing mutations, and say their work will help scientists better understand the normal function of human genes.

Working as part of larger study called the 1000 Genomes Project, the team developed a series of filters to identify common errors in the human genome, which maps the entire genetic code.

"The key questions we focused on for this study were how many of these LoF variants were real and how large a role might they play in human disease," said Daniel MacArthur of the Sanger Institute, who worked on the team.

The researchers looked at nearly 3,000 possible LoF variants in the genomes of 185 people from Europe, East Asia and West Africa. Their findings were published in the journal Science on Thursday.

Loss of function variants are genetic changes that are predicted to severely disrupt the function of genes. Some are known to cause severe human diseases such as muscular dystrophy and cystic fibrosis.

Previous genome sequencing projects have suggested there are hundreds of these variants in the DNA of even perfectly healthy individuals, but researchers were not able to tell exactly how many.

In this study, the filters revealed that 56 percent of the 3,000 possible LoFs analyzed were unlikely to seriously affect gene function.

But of the true LoF variants, 100 are typically found in the genome of each European, the researchers said, and 20 affect both copies of the gene - meaning they are likely to result in complete loss of gene function.

"This shows that at least 1 percent of human genes can be shut down without causing serious disease," said Mark Gerstein, a professor of biomedical informatics from Yale University in the United States, who also worked on the study.

"We were able to use the differences between such 'LoF-tolerant' genes and known human disease genes to develop a way of predicting whether or not a newly

discovered change in a gene is likely to be severely disease-causing."

Chris Tyler-Smith, who led the team at the Sanger Institute, said the findings would prove immediately useful for current DNA sequencing studies in patients with particular diseases.

The results produced a list of more than 1,000 LoF variants, he said, "and in most cases little or nothing is known about how these genes work or what they do.

"By studying the people carrying them in detail, we should get new insights into the function of many poorly known human genes."

(Reporting by Kate Kelland)