Many genes are switched on by default

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Contrary to common scientific belief, many genes are switched "on" by default. These findings are from a study by Prof. Dr. Frank Holstege of University Medical Center (UMC) Utrecht that has been published in the April 24 edition of *Cell*.

Genetic differences between individuals affect the origin and treatment of diseases, a fact that has prompted more and more wide-scale genetic research. However, it seems that we sometimes lack very basic genetic knowledge.

Holstege's research shows that contrary to common opinion, many genes are by default actually switched "on". Given that DNA is wrapped in proteins, most scientists assumed that it could not be read by the cell. Transcription can only begin when so-called transcription factors bind to the DNA. Holstege and his colleagues show that nearly half of the transcription factors actually prevent the DNA from being read. It would seem that in most circumstances these genes should first be actively switched "off".

1,600 genes analyzed

Holstege and his colleagues used yeast as the model organism for their research. Yeast may seem far removed from humans, but its genes are controlled in exactly the same way as in human cells. Holstege et al. analyzed the role played by 1,600 genes, a quarter of all known yeast genes. They studied the effect that mutations in all those genes have on the gene expression of all other genes. This is the largest systematic

study of the effect of mutation on gene expression to date.

Holstege has previously demonstrated that it is actually not necessarily useful to look at the effect of changes in just one gene. All genes are active in networks that are often organized in such a way that they can replace defective genes (Cell, December 10, 2010). The new study is the first step to mapping out the entire genetic control network.

"Comparative genetic research into patients and healthy subjects is very important," says Holstege. "It provides information on the cellular pathways associated with diseases. Our research shows, however, that it's hard to understand cells if you don't take the simultaneous activity of all genes into account."

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