MedicalXpress

Non-coding DNA implicated in type 2 diabetes

January 12 2014

Variations in non-coding sections of the genome might be important contributors to type 2 diabetes risk, according to a new study.

DNA sequences that don't encode proteins were once dismissed as "junk DNA", but scientists are increasingly discovering that some regions are important for controlling which genes are switched on.

The new study, published in *Nature Genetics*, is one of the first to show how such regions, called regulatory elements, can influence people's risk of disease.

Type 2 diabetes affects over 300 million people worldwide. Genetic factors have long been known to have an important role in determining a person's risk of type 2 diabetes, alongside other factors such as body weight, diet and age.

Many studies have identified regions of the genome where variations are linked to diabetes risk, but the function of many of these regions is unknown, making it difficult for scientists to glean insights into how and why the disease develops. Only around two per cent of the genome is made up of genes: the sequences that contain code for making proteins. Most of the remainder is shrouded in mystery.

"Non-coding DNA, or junk DNA as it is sometimes known, is the dark matter of the genome. We're only just beginning to unravel what it does," said leading author Professor Jorge Ferrer, a Wellcome Trust

Senior Investigator from the Department of Medicine at Imperial College London.

In the new study scientists mapped the regulatory elements that orchestrate gene activity in the cells of the pancreas that produce insulin, a hormone that regulates blood sugar.

In type 2 diabetes, the tissues become less responsive to insulin, resulting in blood sugar levels being too high. Most people can compensate when this happens by producing more insulin, but in people with type 2 diabetes, the pancreas cannot cope with this increased demand.

"The cells that produce insulin appear to be programmed to behave differently in people with type 2 diabetes," said co-author Mark McCarthy, a Wellcome Trust Senior Investigator at the University of Oxford. "This study provides some important clues to the mechanisms which are disturbed in the earliest stages of the development of type 2 diabetes, and may point the way to novel ways of treating and preventing the disease."

The team identified genome sequences that drive gene activity in insulin-producing cells specifically. They found that these sequences are located in clusters, and that genetic variants known to be linked to diabetes risk are also found in these clusters.

"Many people have small DNA variants in such regulatory elements, and these variants affect gene expression in the cells that produce insulin. This knowledge will allow us to understand the detailed mechanisms whereby specific DNA variants predispose to diabetes," said Professor Ferrer.

More information: L. Pasquali et al. 'Pancreatic islet enhancer clusters enriched in type 2 diabetes risk-associated variants.' *Nature*

Genetics, 12 January 2014. dx.doi.org/10.1038/ng.2870