

Scientists offer new clues to genetics of type 2 diabetes

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An international collaboration of scientists from Europe and the US has identified six new genes which play a role in the development of type 2 diabetes, extending the total number of genes implicated in common forms of the disease to sixteen.

The findings provide valuable new insights into the mechanisms responsible for the control of sugar levels in the blood and how malfunctions in this mechanism can result in type 2 diabetes. The research, of which the major UK funders were the Wellcome Trust, Medical Research Council, Diabetes UK and the EU, may lead to new ways of treating and preventing diabetes.

The main feature of type 2 diabetes is a sustained abnormal elevation of blood sugar levels. This results from a failure of the systems (involving the production of insulin from the pancreas) which usually keep those levels within tight limits. Exposure to high levels of glucose over years can result in serious damage to the heart, kidneys and other major organs. There are currently over two million people with diabetes in the UK and as many as 750,000 others who have the condition but are unaware.

Ninety researchers from over 40 centres analysed genetic data gathered from over 70,000 people in search of differences in our genetic code that make some people more susceptible than others to type 2 diabetes. Previous work from these groups and others had identified ten genes contributing to type 2 diabetes risk, to which the new findings, published

online today in the journal *Nature Genetics*, add a further six new genes.

“None of the genes we have found was previously on the radar screen of diabetes researchers,” says Professor Mark McCarthy from the University of Oxford, one of the authors of the paper. “Each of these genes therefore provides new clues to the processes that go wrong when diabetes develops, and each provides an opportunity for the generation of new approaches for treating or preventing this condition.”

The research backs up previous studies suggesting that a key process in the development of type 2 diabetes is the failure to regulate the number of insulin-producing cells in the pancreas.

In addition, the researchers have identified a surprising association between type 2 diabetes and the gene known as JAZF1, which has recently been shown to play a role in a very different condition, prostate cancer.

“Genetic studies of this kind are revealing new and unsuspected connections between diseases,” says Dr Eleftheria Zeggini from the University of Oxford, first author on the paper. “This is now the second example of a gene which affects both type 2 diabetes and prostate cancer. We don’t yet know what the connections are, but this has important implications for the future design of drugs for these conditions”.

Each of the new genes only increases the risk of diabetes by a small amount, though when combined, their effects can be more impressive. However, the scientists caution against any immediate rush to use this information to give individual predictions of disease risk.

“Once we more fully understand the large numbers of genes now implicated in diabetes risk, it might become possible to identify people

at particularly high risk before the disease takes root,” says Professor David Altshuler of the Broad Institute of Harvard and MIT in Cambridge, USA, who led one of the three groups behind the research. “However, until we have evidence that using such information results in better health outcomes, widespread genetic testing would be premature.”

The research was made possible through an unprecedented collaborative effort that brought together many groups active in the field of diabetes research. This international collaboration provided access to large data samples, ensuring that the results are robust.

The findings have been welcomed by Professor Simon Howell, Chair of Diabetes UK, which funded the original collection of samples from people with diabetes within the UK.

“It’s remarkable that we still know so little about such a major condition as type 2 diabetes,” says Professor Howell. “By revealing new pathways by which the body normally keeps blood glucose levels under control, this research offers new opportunities for more effective ways of treating and preventing this condition.”

Source: Wellcome Trust

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