Largest ever study of genetics of common diseases published today

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The Wellcome Trust Case Control Consortium, the largest ever study of the genetics behind common diseases such as diabetes, rheumatoid arthritis and coronary heart disease, today publishes its results in the journals *Nature* and *Nature Genetics*.

The £9 million study is one of the UK's largest and most successful academic collaborations to date. It has examined DNA samples from 17,000 people across the UK, bringing together 50 leading research groups and 200 scientists in the field of human genetics from dozens of UK institutions. Over two years, they have analysed almost 10 billion pieces of genetic information.

"Many of the most common diseases are very complex, part 'nature' and 'nurture', with genes interacting with our environment and lifestyles," says Professor Peter Donnelly, Chair of the Consortium, who is based at the University of Oxford. "By identifying the genes underlying these conditions, our study should enable scientists to understand better how disease occurs, which people are most at risk and, in time, to produce more effective, more personalised treatments."

The study has substantially increased the number of genes known to play a role in the development of some of our most common diseases. Many of these genes that have been found are in areas of the genome not previously thought to have been related to the diseases.

"Just a few years ago it would have been thought wildly optimistic that it

would be possible in the near future to study a thousand genetic variants in each of a thousand people," says Dr Mark Walport, Director of the Wellcome Trust, the UK's largest medical research charity, which funded the study. "What has been achieved in this research is the analysis of half a million genetic variants in each of seventeen thousand individuals, with the discovery of more than ten genes that predispose to common diseases.

"This research shows that it is possible to analyse human variation in health and disease on an enormous scale. It shows the importance of studies such as the UK Biobank, which is seeking half a million volunteers aged between 40 and 69, with the aim of understanding the links between health, the environment and genetic variation. New preventive strategies and new treatments depend on a detailed understanding of the genetic, behavioural and environmental factors that conspire to cause disease."

Amongst the most significant new findings are four chromosome regions containing genes that can predispose to type 1 diabetes and three new genes for Crohn's disease (a type of inflammatory bowel disease). For the first time, the researchers have found a gene linking these two autoimmune diseases, known as PTPN2.

The study has also confirmed the importance of a process known as autophagy in the development of Crohn's disease. Autophagy, or "self eating", is responsible for clearing unwanted material, such as bacteria, from within cells. The may be key to the interaction of gut bacteria in health and in inflammatory bowel disease and could have clinical significance in the future.

"The link between type 1 diabetes and Crohn's disease is one of the most exciting findings to come out of the Consortium," says Professor John Todd from the University of Cambridge, who led the study into type 1

diabetes. "It is a promising avenue for us to understand how the two diseases occur. The pathways that lead to Crohn's disease are increasingly well understood and we hope that progress in treating Crohn's disease may give us clues on how to treat type 1 diabetes in the future."

Research from the Consortium has already played a major part in identifying the clearest genetic link yet to obesity and three new genes linked to type 2 diabetes, published in April in advance of the main study. It has found independently a major gene region on chromosome 9 identified by independent studies on coronary heart disease.

Researchers analysed DNA samples taken from people in the UK – 2,000 patients for each disease and 3,000 control samples – to identify common genetic variations for seven major diseases. These are bipolar disorder, Crohn's disease, coronary heart disease, hypertension, rheumatoid arthritis and type 1 and type 2 diabetes. For each disease, the researchers will study larger population samples to confirm their results.

Although the human genome is made up of more than three billion sub-units of DNA, called nucleotides (or bases), most of these show little in the way of differences between individuals. A substantial part of the variation in DNA sequence between individuals is due to single-nucleotide polymorphisms (differences), also known as SNPs. There are approximately 8 million common SNPs in European populations. Fortunately, because SNPs that lie close together on chromosomes often tell quite similar stories, researchers in the Consortium were able to explore this variation through analysing a subset of these SNPs (in fact approximately 500,000).

"Human genetics has a chequered history of irreproducible results, but this landmark collaboration of scientists in Britain has shown conclusively that the new approach of analysing a large subset of genetic

variants in large samples of patients and healthy individuals works," says Professor Donnelly. "We are now able to effectively scan most of the common variation in the human genome to look for variants associated with diseases. This approach will undoubtedly herald major advances in how we understand and tackle disease in the future."

Further analysis as part of the Consortium will be looking at tuberculosis (TB), breast cancer, autoimmune thyroid disease, multiple sclerosis and ankylosing spondylitis. The results are expected later this year.

Source: Wellcome Trust