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A new light shed on genetic regulation's role in the predisposition to common diseases

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An international team of researchers from King's College, Oxford University, Wellcome Trust Sanger Institute and Faculty of Medicine of University of Geneva, has discovered several thousands new genetic variants impacting gene expression some of which are responsible for predisposition to common diseases, bringing closer to the biological interpretation of personal genomes.

Genetic disease risk differences between one individual and another are based on complex aetiology. Indeed, they may reflect differences in the genes themselves, or else differences at the heart of the regions involved in the regulation of these same genes.

By gene regulation we mean the decision that the cell makes as to when, where and at what level to activate or suppress the expression of a gene. In theory, two people could thus share a gene that is perfectly identical and yet show differences in their predisposition to a disease due to genetic differences concerning the regulation (overexpression or underexpression) of this same gene.

Numerous teams are currently trying to draw up a map of regions involved in gene regulation. Not an easy task, but invaluable since it allows us to understand all the genetic causes that can explain the predisposition to certain diseases.

Working with twins

Emmanouil Dermitzakis, Louis-Jeantet Professor at the Faculty of Medicine and member of the NCCR Frontiers in Genetics and the Institute of Genetics and Genomics of Geneva (IGE3), is a specialist in what is called the genetics of complex traits. With an international team co-led by Professor Tim Spector (Kings College), Professor Mark McCarthy (Oxford University) and Dr. Panos Deloukas (Wellcome Trust Sanger Institute), he publishes a study highlighting thousands of these genetic variants that seem to explain individual differences in gene expression.

For this work, the researchers used samples of three different tissue types (adipose tissue, skin and blood cells) collected from more than 800 homozygotic (identical) and dizygotic twins.

"Identifying variants which control the activity of many genes is a greater challenge than we anticipated but we are developing appropriate tools to uncover them and understand their contribution to disease," comments Panos Deloukas. "Modern human genetics combined with samples donated by the participants in studies such as TwinsUK is making great strides towards finding the genetic culprits behind human disease."

The method researchers followed allowed them to uncover nearly 358 variants apparently involved in the predisposition to certain diseases including quantifying the contribution of rare regulatory variants that was previously not possible to identify by conventional analysis methods.

"Our work adds to those who have previously demonstrated the contribution of common variants in the predisposition to these disorders", explains Emmanouil Dermitzakis. "Thanks to this new level of knowledge, and if we manage to adapt this methodology to search for these variants in each individual, this will be a powerful tool to help prognose the predisposition to certain diseases and more importantly

understand the biological aetiology in order to develop and employ individualized treatments."

Provided by University of Geneva