

Researchers discover 'master switch' gene for obesity, diabetes

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A team of researchers, led by King's College London and the University of Oxford, have found that a gene linked to type 2 diabetes and cholesterol levels is in fact a 'master regulator' gene, which controls the behaviour of other genes found within fat in the body.

As fat plays a key role in susceptibility to [metabolic diseases](#) such as obesity, heart disease and diabetes, this study highlights the [regulatory gene](#) as a possible target for future treatments to fight these diseases.

Published today in [Nature Genetics](#), the study was one part of a large multi-national collaboration funded by the Wellcome Trust, known as the MuTHER study. It involves researchers from King's College London, University of Oxford, The Wellcome Trust Sanger Institute, and the University of Geneva. DeCODE Genetics also contributed to the results reported in this paper.

It was already known that the KLF14 gene is linked to [type 2 diabetes](#) and [cholesterol levels](#) but, until now, how it did this and the role it played in controlling other genes located further away on the genome was unknown.

The researchers examined over 20,000 genes in subcutaneous fat biopsies from 800 UK female twin volunteers. They found an association between the KLF14 gene and the expression levels of multiple distant genes found in fat tissue, which means it acts as a master switch to control these genes. This was then confirmed in a further

independent sample of 600 subcutaneous fat biopsies from Icelandic subjects.

These other genes found to be controlled by KLF14 are in fact linked to a range of metabolic traits, including [body-mass index](#) (obesity), cholesterol, insulin and [glucose levels](#), highlighting the interconnectedness of metabolic traits.

The KLF14 gene is special in that its activity is inherited from the mother. Each person inherits a set of all genes from both parents. But in this case, the copy of KLF14 from the father is switched off, meaning that the copy from the mother is the active gene – a process called imprinting. Moreover, the ability of KLF14 to control other genes was entirely dependent on the copy of KLF14 inherited from the mother – the copy inherited from the father had no effect.

Professor Tim Spector from the Department of Twin Research at King's, who led the MuTHER project, said: 'This is the first major study that shows how small changes in one [master regulator](#) gene can cause a cascade of other metabolic effects in other genes. This has great therapeutic potential particularly as by studying large detailed populations such as the twins we hope to find more of these regulators.'

Professor Mark McCarthy from the University of Oxford, who co-led the study, said: 'KLF14 seems to act as a master switch controlling processes that connect changes in the behaviour of [subcutaneous fat](#) to disturbances in muscle and liver that contribute to diabetes and other conditions. We are working hard right now to understand these processes and how we can use this information to improve treatment of these conditions.'

Provided by King's College London

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