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Obesity genes identified by worldwide research team

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A massive worldwide analysis of genetic data from almost 340,000 people around the world has brought understanding of the genetic basis of obesity a step closer.

Associate Professor Dale Nyholt, from QUT's Institute of Health and Biomedical Innovation and QIMR, is one of 483 scientists in 363 research centres across the world who contributed data for a meta-analysis of genetic differences in people's BMI (body mass index), the commonly used measure of obesity and fatty tissue stored by the body.

The findings, published in *Nature*, give new insights into possible weight-loss therapies and the prevention of metabolic-associated diseases.

"Obesity is heritable and predisposes people to many other diseases," Professor Nyholt said.

"It is a worldwide epidemic which imposes an enormous burden on individual and public health."

"To better understand the genetic basis of obesity, we conducted the world's largest genome-wide association study and Metabochip meta-analysis of body mass index (BMI) in up to 339,224 people."

Professor Nyholt said that while it was known that 40 to 70 per cent of the difference in BMI in the population could be attributed to genetic factors, most of the genetic variability was still unexplained.

"While analyses of previous genetic association results have suggested some intriguing biological processes underlying a person's susceptibility to obesity, few specific genes were involved in a defined biological pathway, which represents a series of actions among molecules in a cell that leads to a certain product or a change in a cell.

"This means that for most of the implicated genomic regions (loci) the likely causal gene or genes and their pathways remained unknown until now."

Professor Nyholt said the global team of scientists identified 97 genetic markers strongly associated with influencing BMI, and 56 of these were completely new, after meta-analysing more than 2.5 million single variations of nucleotides, the molecules that make up DNA.

"These analyses pointed to particular genes and biological pathways that affect BMI.

These genes include neurotransmitters that respond to changes in eating and fasting whose pathways could reveal more targets for weight-loss therapies."

Professor Nyholt said BMI-associated genetic markers also overlapped with genes and pathways affecting the brain's development and had a role in the central nervous system in regulating BMI.

"Together, these findings highlight the diverse causes of obesity and its link with many other related metabolic diseases.

"When we better understand these mechanisms, it may help explain why not all obese individuals develop metabolic disease and suggest possible mechanisms to prevent people who are obese developing metabolic disease."

More information: "Genetic studies of body mass index yield new insights for obesity biology." *Nature* 518, 197–206 (12 February 2015) DOI: 10.1038/nature14177