

New insight into the link between genetics and obesity

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Scientists have acquired new insight into how the 'obesity gene' triggers weight gain in some individuals. Their findings, reported online today in *Science Express*, could have implications for the future treatment of obesity as well as adult onset diabetes.

Earlier this year a team of British geneticists discovered that variation in a gene called FTO influence people's risk of becoming obese. While genetic defects causing human obesity had been previously described, the FTO discovery was of considerable interest because the genetic variant in FTO that predisposes to obesity is very common.

About half the UK population carry a copy of the variant and they are on average 1.6 kilograms heaver than those who don't have the variant, while 16% of the population carry two copies of the variant and are on average three kilograms heavier. Carriers of the variant also had an increased risk of diabetes. However the function of FTO was completely unknown.

Researchers from the University of Cambridge, Oxford University and Cancer Research UK, London, have found that the FTO gene, codes for an enzyme that can act directly on DNA to modify it – suggesting that it might have a role in controlling the turning on and off of other genes.

They also found that FTO is highly expressed in a region of the brain, called the hypothalamus, which has important roles in the control of hunger and satiety and that, in certain parts of the hypothalamus, the



levels of FTO are influenced by feeding and fasting.

This work benefited from an unusual and exciting collaboration. Initially, the Cambridge/London and the Oxford teams were working independently on this problem but recently pooled their complementary expertise to ensure that the findings were reliably repeatable using different approaches in different laboratories.

Professor Stephen O'Rahilly, who led the Cambridge part of the collaboration, said: "This is the first glimpse into the possible mechanisms whereby this very common genetic variant might influence a person's risk of obesity. The finding that FTO is an enzyme with these actions on DNA is very surprising and a lot of work is still needed to work out how its actions influence body weight.

"The finding that FTO may have some involvement in the control of the function of the hypothalamus suggest that, like other obesity genes previously discovered, it may play some role in the influencing how well the brain senses hunger and fullness. As the activity of FTO can be altered by small molecules like metabolites, it is possible, in the future, that FTO could be manipulated therapeutically to help treat obesity."

Sara Hiom, director of health information at Cancer Research UK, said: "This is an important piece of research. We know that obesity increases people's risk of developing a range of cancers as well as other diseases, and the increasing number of people who are overweight will have significant implications for cancer in the future. Unravelling how this gene works is very exciting and may one day lead to new treatments for obesity. However maintaining a healthy body weight through a balanced diet and regular physical activity is important for general health as well as reducing the risk of many cancers."

Source: University of Cambridge



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