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## Gene making Indians fat found 6 May 2008, 0047 hrs IST, Kounteya Sinha, TNN

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NEW DELHI: British scientists may have an answer to why, despite best efforts, you are constantly putting on weight, especially around the waist. Well, it's all in your "Indian" genes.

A new large scale British study has identified genetic variations, occurring commonly among Indian Asians, that make them heavier and more prone to diabetes.

The findings shows that Indian Asian adults carrying these genetic variations are, on average, 3.8kg heavier than people of European ancestry.

The scientists also found that the variants - found in a gene called FTO and another close to a gene called MC4R - cause a 2cm expansion in waist circumference and a tremendous tendency to become resistant to insulin, leading to Type 2 diabetes.

Dr Anoop Mishra from Fortis Hospital said, "The study led by Jaspal Kooner of Imperial College, London, has found that the variant is significantly more common among people of Indian ancestry. This is a very important finding for the Indian population, both in India and abroad. It shows that these genetic variations causing obesity occur more often in Indians. When added with bad diet and exercise, Indians are at a far greater risk of cardiovascular diseases and diabetes."

MC4R protein plays a pivotal role in many aspects of physiology, including regulation of appetite and energy expenditure. The severe form of MC4R-related obesity is a consequence of alterations in the gene sequence resulting in an inactive or less active MC4R protein.

By contrast, the new variants discovered lie some distance from the MC4R gene. The team suspects that the variant changes activity of the MC4R gene, perhaps by disrupting DNA regions required for normal activity of MC4R.

Dr Ruth Loos, leading author from the Medical Research Council Epidemiology Unit said, "Several studies had shown that rare, highly disruptive variants in the MC4R gene were responsible for very severe, genetic forms of obesity. This latest collaboration has uncovered more common variants that affect more people."

The study was led by investigators from the Cambridge GEM consortium (Genetics of Energy Metabolism) and Oxford University and was a collaboration between 77 institutions from the UK, USA, France, Germany, Italy, Finland and Sweden.

The team studied more than 77,000 adults and found that two copies of genetic variants resulted in an average increase in weight.

The team now plans to uncover how the DNA variants affect activity of the MC4R protein, which is a key player in orchestrating information from the body to control appetite and energy expenditure to keep body weight in balance.

The team proposes that altered activity of MC4R, imposed by the variants, might reduce its ability to carry out this important role.

"The team, however, has also emphasized that, although gene variants can affect weight, body mass index and obesity, they are only part of the story. Lifestyle actions such as good diet and regular exercise are vital to control weight," Dr Mishra added.

Dr Ines Barroso from Welcome Trust Sanger Institute added, "The precise role in obesity of genetic variants in FTO and near MC4R remains to be discovered, but we can now begin to understand the biological consequences of these variants. This is where this research will make a difference."

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