

# New Risk Factor for Obesity Discovered

Institutes of Epidemiology and Human Genetics, Genome Analysis Centre

It is currently estimated that 40 to 70 per cent of all cases of obesity are linked with an underlying genetic component. Meanwhile many chromosomal loci and genes are known, whose activation or elimination is linked with the development of obesity (adiposity). However, only a fraction of these genes can cause overweight by themselves, it is the combination of various genetic factors as well as a lifestyle with a high-energy diet and lack of exercise which makes us put on too much weight. Among other things adiposity is associated with an elevated risk of high blood pressure, type 2 diabetes, heart attack and some cancers. A genetic variant has now been identified, which is found in approx. 10 per cent of the population and which increases the risk of overweight and adiposity in children and adults.

An analysis of a total of about 100,000 gene variants in the human genotype from samples of the Framingham Study carried out by a group of scientists from Boston University (Prof. Christman) looked

specifically for characteristics which are found more frequently among overweight people. A change in the genotype was discovered near a gene which controls the fat metabolism. The gene variant classified as rs7566605 is on chromosome 2 in the immediate vicinity of the "insulin-induced gene2" (INSIG2) and is found in people of both Western European and Afro-American descent. The protein product of the INSIG 2 gene slows down the synthesis of fatty acids and cholesterol. The changed activity of this gene could result in more fat being deposited in the tissue. In a representative sample of approx. 4000 people from the Augsburg Region (KORA) scientists from the GSF Institutes of Epidemiology and Human Genetics could show that people who carry this gene variant are significantly heavier (measured by body mass index) than those who do not carry it. In parallel a team from the University of Duisburg-Essen studied this gene variant in almost 400 severely overweight children and their parents. It could be shown that the risk variant is



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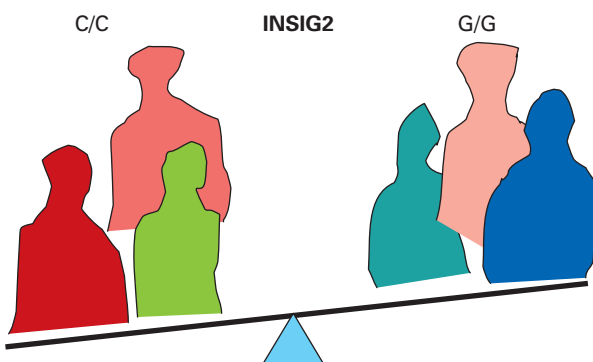
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significantly more often passed on by parents to their overweight children.

This insight can contribute to the elucidation of the molecular processes leading to overweight, which, in turn, is a prerequisite for the development of effective medication to help patients suffering from adiposity.



### Balance of sequence variants in the INSIG2 gene:

In a comparison of large groups of people (n > 1000) sequence variant C in the INSIG2 gene is associated with significantly higher weight than sequence variant G.

### Literature:

- Herbert, A., Gerry, N.P., McQueen, M.B., Heid, I.M., Pfeufer, A., Illig, T., Wichmann, H.-E., Meitinger, T., Hunter, D., Hu, F.B., Colditz, G., Hinney, A., Hebebrand, J., Koberwitz, K., Zhu, X., Cooper, R., Ardlie, K., Lyon, H., Hirschhorn, J.N., Laird, N.M., Lenburg, M.E., Lange, C., Christman, M.F.: A common genetic variant 10 kb upstream of INSIG2 is associated with adult and childhood obesity. *Science* 312, 279-283, 2006.