Overweight affects DNA methylation

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The extra pounds you gain during the holidays will not only show up on your hips but will also affect your DNA. This is the result of a large-scale international study coordinated by Helmholtz Zentrum München, a partner in the German Center for Diabetes Research, which has now been published in *Nature*. The study shows that a high BMI leads to

epigenetic changes at nearly 200 loci of the genome – with effects on gene expression.

While our genes do not change in the course of life, our lifestyle can directly influence their surroundings. Scientists speak here of the epigenome (Greek epi: over, outside of, around), which refers to everything that happens on or around the genes. Up to now there has not been much research on how the epigenome is altered as a result of being overweight. "This issue is particularly relevant because an estimated one and a half billion people throughout the world are overweight," said first author Dr. Simone Wahl of the Research Unit Molecular Epidemiology (AME) at Helmholtz Zentrum München, "especially considering that being overweight can have adverse consequences and lead to diabetes and diseases of the cardiovascular and metabolic systems."

World's largest study on BMI and epigenetics

For this reason, the international research team led by Dr. Christian Gieger and Dr. Harald Grallert of the AME (as well as Jaspal Kooner and John Chambers of Imperial College London) examined possible correlations between body mass index (BMI) and epigenetic changes. Using state-of-the-art technology, the team carried out the world's largest study so far on the subject.

The scientists examined the blood samples of over 10,000 women and men from Europe. A large proportion of these were inhabitants of London of Indian ancestry, who according to the authors are at high risk for obesity and metabolic diseases. In a first step with 5,387 samples, the research team identified 207 gene loci that were epigenetically altered dependent on the BMI. They then tested these candidate loci in blood samples of an additional 4,874 subjects and were able to confirm 187 of these. Further studies and long-term observations also indicated that the changes were predominantly a consequence of being overweight – not

the cause.

Significant changes also in the expression of inflammatory genes

"In particular, significant changes were found in the expression of genes responsible for lipid metabolism and substrate transport, but inflammation-related gene loci were also affected," said group leader Harald Grallert. From the data, the team was also able to identify epigenetic markers that could predict the risk of type 2 diabetes.

"Our results allow new insights into which signaling pathways are influenced by obesity", said Christian Gieger, head of the AME. "We hope that this will lead to new strategies for predicting and possibly preventing type 2 diabetes and other consequences of being overweight." Next, within the framework of translational research in the German Center for Diabetes Research, the researchers want to investigate in detail how the epigenetic changes affect the expression of the underlying genes.

More information: Simone Wahl et al. Epigenome-wide association study of body mass index, and the adverse outcomes of adiposity, *Nature* (2016). DOI: 10.1038/nature20784

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