Genetic alteration can cause obesity among Greenlanders

Credit: University of Copenhagen

Four per cent of the Greenlandic population are, due to a specific genetic alteration, in the risk of developing obesity and diabetes, a new study from the University of Copenhagen, the University of Southern Denmark, the University of Greenland and the Steno Diabetes Center Copenhagen concludes. The gene represent a possible treatment target, the researchers argue.

Greenland is like many other countries struggling with overweight and obesity. Both environment and genetics play a role in development of obesity. However, it is not fully known which specific genes that are causing obesity. Researchers from the University of Copenhagen, among others, now appear to have found one of these genes.

‘We have found a gene, ADCY3, which predisposes Greenlanders to obesity and diabetes when it is inactive. This appears to be unique to the Greenlandic population’, says Associate Professor Niels Grarup from the Novo Nordisk Foundation Center

for Basic Metabolic Research at the University of Copenhagen.

In the study, which has just been published in the scientific journal *Nature Genetics*, the researchers have examined the genes of 5,000 Greenlanders, corresponding to around nine per cent of the entire population in Greenland. In 4.4 per cent of the test subjects this specific gene was inactive.

The activity of the gene is important because everyone has two copies of all their genes. This means that the gene may be expressed in full, in part or not at all. In around four per cent of the Greenlanders the gene is only expressed in part. On average this increases their weight by two kilos, their waist circumference by two centimetres and their BMI by 1 unit compared to the rest of the population.

And the risk of developing diabetes also increases when the gene is not fully active: 11 per cent of those where the gene is expressed in part suffer from diabetes; the figure is 43 per cent for those where the gene is not expressed at all. Around seven per cent of all Greenlanders in whom the gene is expressed in full have diabetes.

‘We are pretty convinced that it is this Greenlandic gene that impacts on obesity and the risk of developing diabetes. Because in seven individuals the gene is not expressed at all, and this really causes problems. On average it increases their weight by 15 kilos, their waist circumference by 17 centimetres and their BMI by seven units, of course with some statistical uncertainties, as we are talking about a very small number of people’, Professor Torben Hansen from the Novo Nordisk Foundation Center for Basic Metabolic Research at the University of Copenhagen explains.

The conclusions of the study are further supported by previous research results, as tests on mice have shown that increasing the activity of the gene causes the mice to become slender and develop a well-functioning metabolism. Thus, they do not

develop overweight and diabetes, even if they are given a fat diet.

‘These findings pave the way for more studies of whether this knowledge can be used to develop new drugs, which may also be used elsewhere in the world. At any rate, we now have several clear indications that expression of this gene is closely connected with obesity and diabetes’, Torben Hansen says.

‘It may not sound significant that we have found seven Greenlanders in whom this gene is not expressed at all. But when we look at a group of 140,000 Europeans we are unable to find a single person in whom the gene is not expressed. This means that this is strongly over-represented in Greenland’, Niels Grarup explains.

The genetic variation may be over-represented in the Greenlandic population, because it genetically has been cut off and isolated from other populations for several thousands of years.

In the future the researchers will explore the possible positive effects of activating the gene.

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More information:
Niels Grarup et al, Loss-of-function variants in ADCY3 increase risk of obesity and type 2 diabetes, *Nature Genetics* (2018). DOI: 10.1038/s41588-017-0022-7

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