OBESITY

Can genetic susceptibility to obesity be overcome?

A genetic predisposition to obesity can be overcome, in part, by having a physically active lifestyle. Writing in the *American Journal of Clinical Nutrition*, Vimalaswaran and co-investigators show that physical activity attenuates the BMI-increasing effects of an *FTO* (fat mass and obesity-associated) risk allele.

The susceptibility to obesity conferred by *FTO* risk alleles is strong. For example, individuals who carry two *FTO* risk alleles have a 60–70% increased risk of obesity compared with noncarriers. Vimalaswaran *et al.* wanted to find out whether the association between the *FTO* locus and obesity risk is influenced by an individual's physical activity level; several studies have examined such a gene–environment interaction, but the findings have been inconclusive.

As gene–lifestyle interaction analyses require large sample sizes for unambiguous observations, the researchers genotyped the *FTO* variant rs1121980 in 20,374 white individuals aged 39–79 years; questionnaire responses were used to determine these individuals' physically

activity level. In the cohort, the risk allele (T) of rs1121980 was significantly associated with increased BMI and waist circumference. Physical activity attenuated the effect of the *FTO* risk allele on BMI and waist circumference. “The most important finding is that the *FTO* risk allele increases BMI, in particular, in those who are physically inactive,” explains lead investigator Ruth Loos of the MRC Epidemiology Unit, Institute of Metabolic Science, UK.

The researchers now plan to conduct a meta-analysis of all studies on *FTO* that also include data on physical activity, to see if they observe the same interaction. In addition, they hope to examine the interaction between overall genetic susceptibility to obesity (to include all currently identified obesity-related loci) and physical activity.

Loos highlights that their findings carry an important public health message. “You may be genetically susceptible to become obese, but it doesn't mean that you are destined to become obese” she concludes. “We showed that you can overcome, at

least in part, the genetic susceptibility by living a healthy lifestyle. It will, however, be harder to stay lean compared to those who are genetically protected from becoming obese.”

Carol Wilson

Original article Vimalaswaran, K. S. Physical activity attenuates the body mass index-increasing influence of genetic variation in the *FTO* gene. *Am. J. Clin. Nutr.* **90**, 425–428 (2009).