# Team discovers why people who lack a specific blood group are genetically predisposed to be overweight or obese

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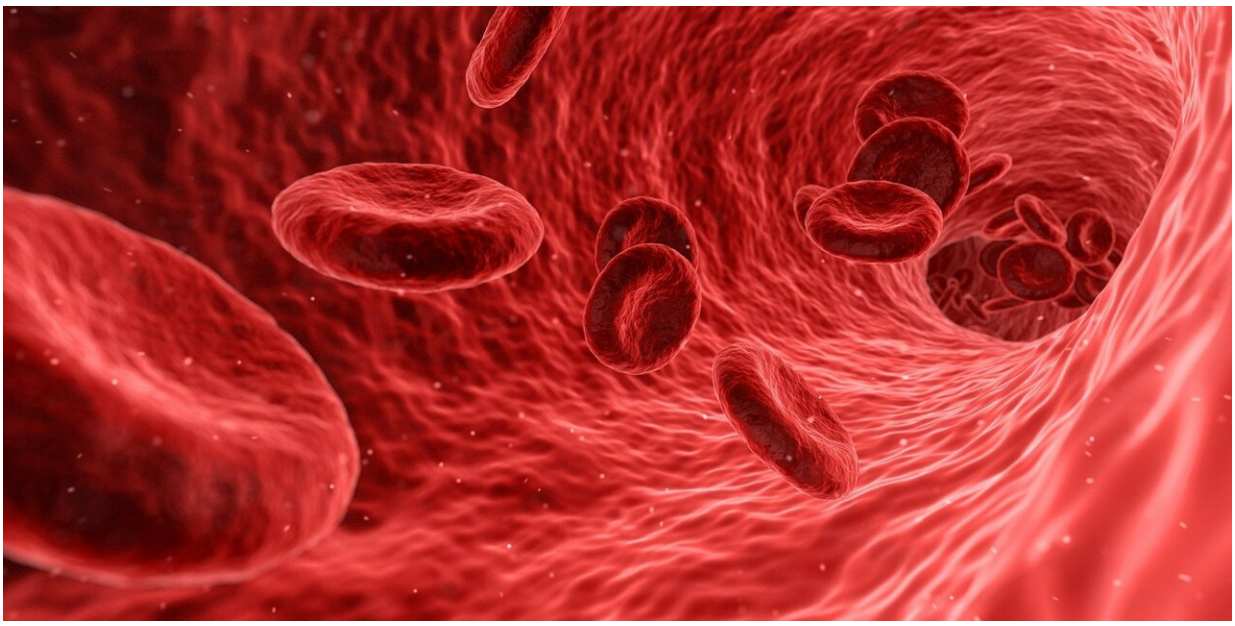

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A team of international researchers, led by the University of Exeter, has discovered that people with a genetic variant that disables the SMIM1 gene have higher body weight because they expend less energy when at rest.

SMIM1 was only identified 10 years ago, while researchers were

searching for the gene encoding a specific blood group, known as Vel. One in 5,000 people lack both copies of the gene, making them Vel-negative. The findings from the new research suggest that this group is also more likely to be overweight, a conclusion that could one day lead to new treatments.

The study found that people without both copies of the gene have other measures linked to obesity, including high levels of fat in the blood, signs of fat tissue dysfunction, increased liver enzymes as well as lower levels of thyroid hormones.

The study is published in *Med* The collaboration included partners at the University of Cambridge, the Sanger Institute, the Copenhagen University in Denmark, and Lund University in Sweden.

Lead author Mattia Frontini, Associate Professor of Cell Biology at the University of Exeter Medical School, said, "Obesity rates have nearly tripled in the past 50 years, and by 2030, more than one billion individuals worldwide are projected to be obese. The associated diseases and complications create a significant economic burden on health care systems.

"Obesity is due to an imbalance between energy intake and expenditure, often a complex interplay of lifestyle, environmental, and genetic factors . In a small minority of people, obesity is caused by genetic variants. When this is the case, new treatments can sometimes be found to benefit these people. Our findings highlight the need to investigate the genetic cause of obesity, to select the most appropriate and effective treatment, but also to reduce the social stigma associated with it."

To make the discovery, the team analyzed the genetics of nearly 500,000 participants in the UK Biobank cohort, identifying 104 people with the variant that leads to loss of function in the SMIM1 gene (46 females and

44 males). The team also used the NIHR National BioResource to obtain fresh blood samples from both Vel negative and positive individuals. The NIHR National BioResource worked in partnership with NHS Blood and Transplant (NHSBT)—which includes more than 100,000 blood donors who signed up to support genetic research studies.

Extrapolating the frequencies identified in these cohorts would mean the SMIM1 variant could be a significant factor contributing to obesity for around 300,000 people across the world.

The team investigated the effects they found in four additional cohorts of people with the SMIM1 gene variant. They found that having the variant had an impact on weight, equating to an average extra 4.6 kg in females and 2.4 kg in males.

Co-author Jill Storry, Adjunct Professor at Lund University, Sweden, said, "SMIM1 was only discovered a decade ago, as a long-sought blood group protein on red blood cells, but its other function has remained unknown until now. It's very exciting to find that it has a more general role in human metabolism."

Co-author Professor Ole Pedersen, at University of Copenhagen, Denmark, added, "The whole team is very much looking forward to seeing how this new knowledge can be translated into practical solutions for people with this genetic makeup.".

First author Dr. Luca Stefanucci, at the University of Cambridge, remarked, "With the increased availability of genetic data, and more information on SMIM1 mechanism, we would like to see that when individuals lacking SMIM1 are identified, they receive information and support."

**More information:** SMIM1 absence is associated with reduced energy expenditure and excess weight', *Med* (2024). DOI: 10.1016/j.medj.2024.05.015. www.cell.com/med/fulltext/S2666-6340(24)00219-8

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