# Blocking a gene reduces fat

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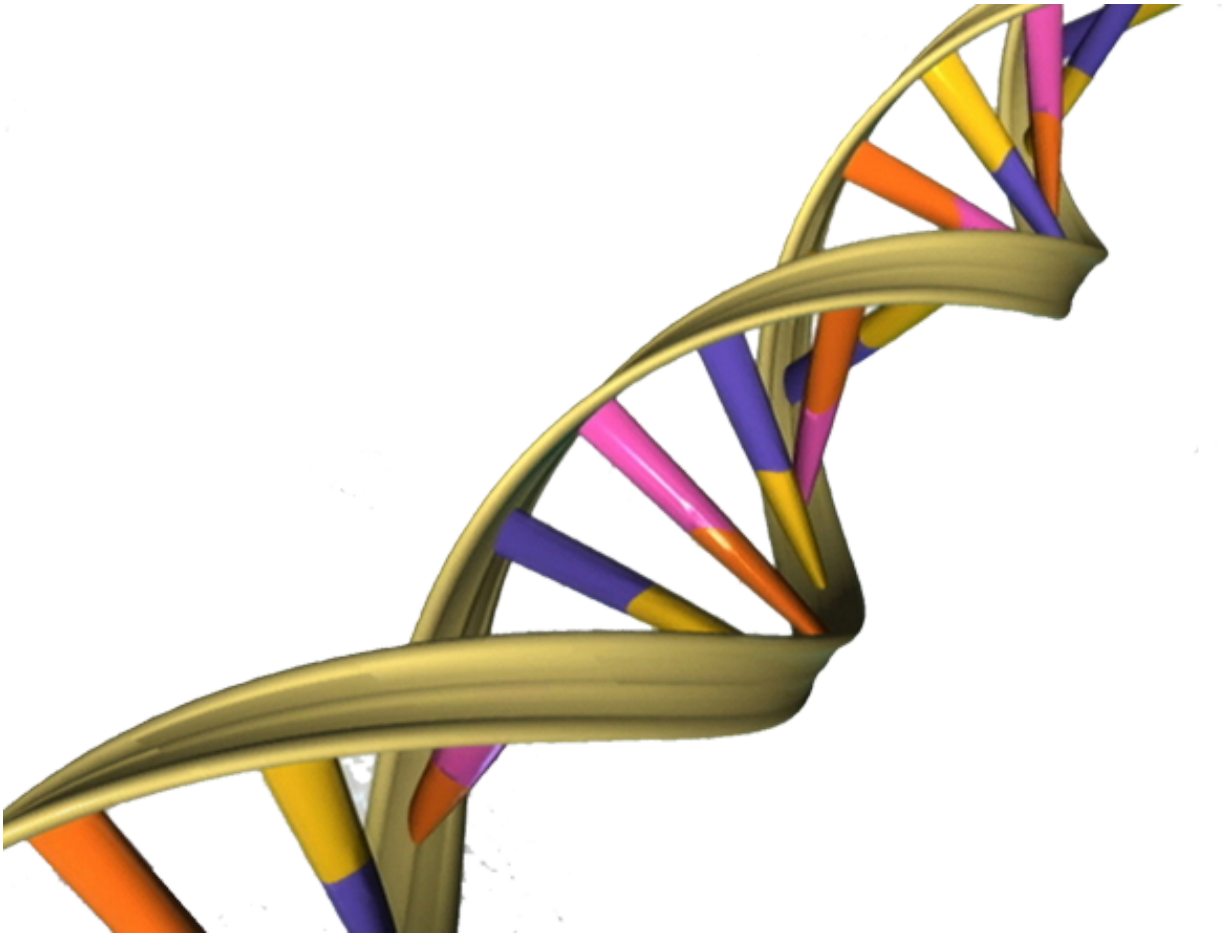

A depiction of the double helical structure of DNA. Its four coding units (A, T, C, G) are color-coded in pink, orange, purple and yellow. Credit: NHGRI

By blocking the expression of a certain gene in patients, University of Montreal researchers have contributed to the demonstration of great

decreases in the concentration of triglycerides in their blood, even in various severe forms of hypertriglyceridemia and regardless of the base values or the treatment the patient usually receives. The gene in question codes for the apoC-III protein.

"Our study suggests that the proteine apoC-III plays a key role in the management of triglycerides. Triglycerides, like cholesterol, are lipids. They come from fats carried by our food or produced by our bodies. Depending on the cause, the accumulation of triglycerides in blood is associated with an increased risk of cardiovascular and pancreatic illnesses, and other complications," explained Dr. Daniel Gaudet, first author of the study. "Our conclusions are promising in terms of the prevention of the risk associated with the accumulation of fat in blood."

The research was published today in the *New England Journal of Medicine*.

Although rare forms of genetic triglyceride accumulation exist, for which there are few effective treatments, hypertriglyceridemia is the one most often associated with frequent health issues, such as obesity or diabetes. Last December, the same research team demonstrated blocking the expression of the gene that encodes apoC-III led to major relief of triglyceridemia in patients suffering a rare and extreme form of hypertriglyceridemia, which in turn opened the door for the identification of unexpected mechanisms that govern blood fat.

Both studies were published in the *New England Journal of Medicine* and are the result of a broad collaboration between researchers at the ECOGENE-21 Clinical and Translational Research Center-linked to the Centre de médecine génique communautaire and the University of Montreal's Department of Medecine in Saguenay, Que.-and ISIS Pharmaceuticals, a Carlsbad, Calif., based company specialised in the development of medications that interfere specifically with the

expression of targeted genes.

The results demonstrate apoC-III's important contribution to the complex mechanisms by which our bodies manage blood fat. "Decoding mechanisms opens the door to precise, individual interventions for the prevention of residual risk associated with the various causes of severe hypertriglyceridemia," Dr. Gaudet said. "The results of these studies enable the acceleration of research targeting better understanding and control of the risk trajectory associated with various forms of severe hypertriglyceridemia."

**More information:** Daniel Gaudet, M.D., Ph.D., Veronica J. Alexander, Ph.D., Brenda F. Baker, Ph.D., Diane Brisson, Ph.D., Karine Tremblay, Ph.D., Walter Singleton, M.D., Richard S. Geary, Ph.D., Steven G. Hughes, M.B., B.S., Nicholas J. Viney, B.Sc., Mark J. Graham, M.S., Rosanne M. Crooke, Ph.D., Joseph L. Witztum, M.D., John D. Brunzell, M.D., and John J.P. Kastelein, M.D., Ph.D. published "Antisense Inhibition of Apolipoprotein C-III in Patients with Hypertriglyceridemia" in the *New England Journal of Medicine* on July 29, 2015.

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