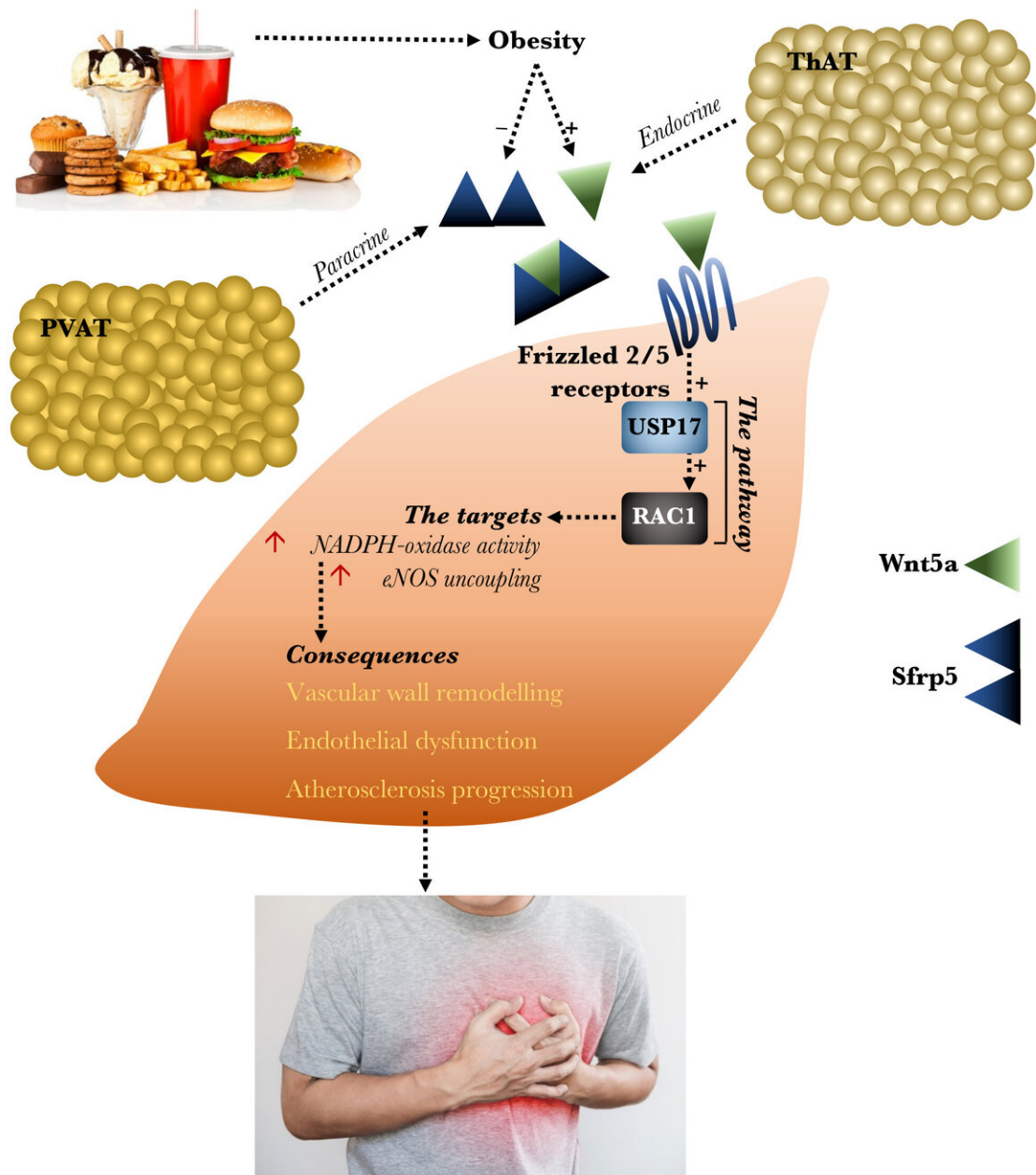


# Scientists discover new way fat harms your arteries

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Obesity results in increased production of Wnt5a from perivascular adipose tissue (PVAT) and visceral adipose tissue (such thoracic adipose tissue, ThAT) resulting in increased bioavailability of Wnt5a relative to its inhibitor Sfrp5. This could be a novel target against obesity-associated cardiac events such as heart attacks. Credit: Division of Cardiovascular Medicine, Radcliffe Department of Medicine, University of Oxford, UK

Scientists may have found a way that obesity directly damages the arteries and contributes to heart disease—a discovery that they say could eventually lead to new treatments.

The British researchers found that in [heart disease](#) patients who are obese, body fat surrounding the arteries tends to secrete high amounts of a protein called WNT5A. The protein, in turn, appears to have "toxic" effects within the [blood vessels](#).

The findings, published in the Sept. 18 issue of *Science Translational Medicine*, are an early step.

But they suggest that WNT5A is a good target for new drugs aimed at treating or preventing heart disease, according to lead researcher Dr. Charalambos Antoniades.

"If we develop a treatment to 'switch off' the production of WNT5A from fat cells, or block its effects on the [[blood vessel](#)] wall, then we may be able to 'neutralize' obesity and prevent heart attacks and stroke," said Antoniades, a professor of cardiovascular medicine at the University of Oxford.

Many studies have shown [obese people](#) have a higher risk of developing

heart disease, compared to thinner people. The American College of Cardiology (ACC) says that's partly due to "indirect" reasons: Obesity promotes conditions that can lead to heart problems—such as type 2 diabetes, [high blood pressure](#) and sleep apnea.

The new findings, Antoniades said, shed light on how obesity directly damages the blood vessels.

For the study, he and his colleagues analyzed blood and tissue samples from about 1,000 [heart disease patients](#) who had undergone cardiac surgery. Overall, they found, obese patients had much higher levels of WNT5A in their blood.

The protein was specifically released in large amounts from fat around the blood vessels, Antoniades said.

In addition, patients with higher WNT5A levels tended to show a faster progression of "plaque" buildup in their arteries in the next three to five years. Plaques are deposits of fat, calcium and other substances that clog the arteries and can trigger a heart attack or stroke.

Those findings alone do not pinpoint WNT5A as a culprit in causing heart disease. But researchers did find more direct evidence in the lab, according to Antoniades. It turns out that when blood vessel cells are exposed to the protein, they churn out more "toxic products" and enter a state that promotes plaque buildup.

Two U.S. cardiologists reviewed the findings from the study.

"This protein is not only significantly elevated in obese patients, but also exerts injury to blood vessels," said Dr. Benjamin Hirsh, director of preventive cardiology at Northwell Health's Sandra Atlas Bass Heart Hospital in Manhasset, N.Y.

Hirsh said the WNT5A "pathway" is probably only one way in which obesity damages blood vessels. He called the findings an "important step forward to improving our understanding of the specific mechanisms by which obesity is harmful."

Dr. Salim Virani is a cardiologist at the Michael E. DeBakey VA Medical Center in Houston and head of the ACC's Prevention Section and Leadership Council.

Virani agreed that understanding the mechanisms that link obesity and heart disease is important, because it could lead to new, more targeted treatments. That said, no medication will replace a [healthy lifestyle](#), he emphasized.

"Diet and exercise will always come first," Virani said.

Even modest weight loss can benefit [heart](#) health, he pointed out. Beyond that, Virani added, obesity is also related to heightened risks of other conditions, including certain cancers. So aiming for a healthier weight will always be important.

And no matter how much weight you lose, Virani said, a healthier lifestyle that includes regular exercise can boost your physical and mental well-being.

"Being obese and physically active is better than being obese and sedentary," he said.

The "greatest challenge," according to Hirsh, is persuading people to make healthier choices and avoid [obesity](#) in the first place. But addressing it, he said, "will yield far greater benefits" than any medication can bring.

**More information:** I. Akoumianakis et al., "Adipose tissue–derived WNT5A regulates vascular redox signaling in obesity via USP17/RAC1-mediated activation of NADPH oxidases," *Science Translational Medicine* (2019). [stm.sciencemag.org/lookup/doi/...  
scitranslmed.aav5055](https://stm.sciencemag.org/lookup/doi/10.1126/scitranslmed.aav5055)

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