

Study sheds light on triglyceride metabolism

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New findings reported in the July issue of *Cell Metabolism* are offering new leads as to why some people might suffer from high levels of triglycerides. High triglycerides are a risk factor for atherosclerosis and cardiovascular disease. They can also lead to inflammation of the pancreas, the researchers said.

The team led by Loren Fong and Stephen Young of the University of California, Los Angeles, has identified the component responsible for bringing a key triglyceride-processing enzyme (called lipoprotein lipase or LPL for short) into the capillaries, where it does its work.

"LPL is required for normal metabolism of triglycerides in blood," Fong said. "If there is no LPL, triglycerides accumulate."

Scientists have known for decades that the LPL enzyme is produced in fat and muscle before it makes its way into [blood vessels](#). What they didn't know until now was how it got there.

It seems that a protein known as GPIHBP1 is the key. Mice lacking that protein end up with LPL built up outside of their muscle and fat tissue instead of where it belongs in capillaries. They show that GPIHBP1 normally sits on the surface of capillary cells, where it actively transports LPL.

The new findings offer an explanation for what had been a surprising finding; *Gpihbp1*-deficient mice develop severe hypertriglyceridemia, even when they eat a normal diet of mouse chow. Very recently, other

researchers have also shown that some people with elevated triglyceride levels carry mutations in their GPIHBP1 gene.

Fong and Young say they don't yet know exactly how GPIHBP1 does its job of transporting LPL into capillaries. It's likely that other as-yet unknown players are involved. Their team also suspects that GPIHBP1 may influence triglyceride metabolism in other ways, aside from its transport function.

There is also much left to learn about how the process is regulated in response to diet or other factors. For instance, "if you eat a fatty meal with more lipids, does this transport go faster?" Fong asked.

The findings may help sort out the causes of hypertriglyceridemia, which in many instances remain unclear.

"In humans, mechanisms for severe cases of hypercholesterolemia have come into focus, but the same cannot be said for many cases of severe hypertriglyceridemia," the researchers wrote. Many patients with very high [triglyceride levels](#) don't have mutations in any of the genes with known links to the condition and some have no obvious abnormalities in LPL levels either.

"It seems possible that defective transport of LPL into the capillaries could underlie at least some cases of [hypertriglyceridemia](#) in humans," they said.

More information: Davies et al.: "GPIHBP1 Is Responsible for the Entry of Lipoprotein Lipase into Capillaries." Publishing in Cell Metabolism 12, 42-52, July 7, 2010. [DOI:10.1016/j.cmet.2010.04.016](https://doi.org/10.1016/j.cmet.2010.04.016)

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