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Lipid raft components offer potential cholesterol-lowering drug target

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Approximately 1 in every 4 deaths in the United States is caused by heart disease, according to the Centers for Disease Control and Prevention. Hypercholesterolemia, or high cholesterol, is a major risk factor for cardiovascular disease. However, cholesterol is also an essential component of cell membranes.

Mammals can either synthesize cholesterol or absorb it from food using the intestinal transmembrane protein Niemann-Pick C1-like 1, or NPC1L1. This transporter resides in lipid rafts, membrane microdomains used for cell-cell interaction and cell signaling that are enriched in cholesterol as well as gangliosides—a group of galactose-containing glycolipids.

In a paper in the *Journal of Lipid Research*, Jin-ichi Inokuchi from Tohoku University in Japan and colleagues show that NPC1L1-dependent intestinal cholesterol uptake requires a particular ganglioside called GM3 and the enzyme that synthesizes it, GM3S.

Cholesterol uptake is decreased in GM3S-deficient cells, and GM3S-deficient mice fed a high-cholesterol diet show a lower susceptibility to high blood cholesterol. This research proposes a new viable target for cholesterol reducing therapies.

More information: Wataru Nihei et al, NPC1L1-dependent intestinal cholesterol absorption requires ganglioside GM3 in membrane microdomains, *Journal of Lipid Research* (2018). DOI:

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