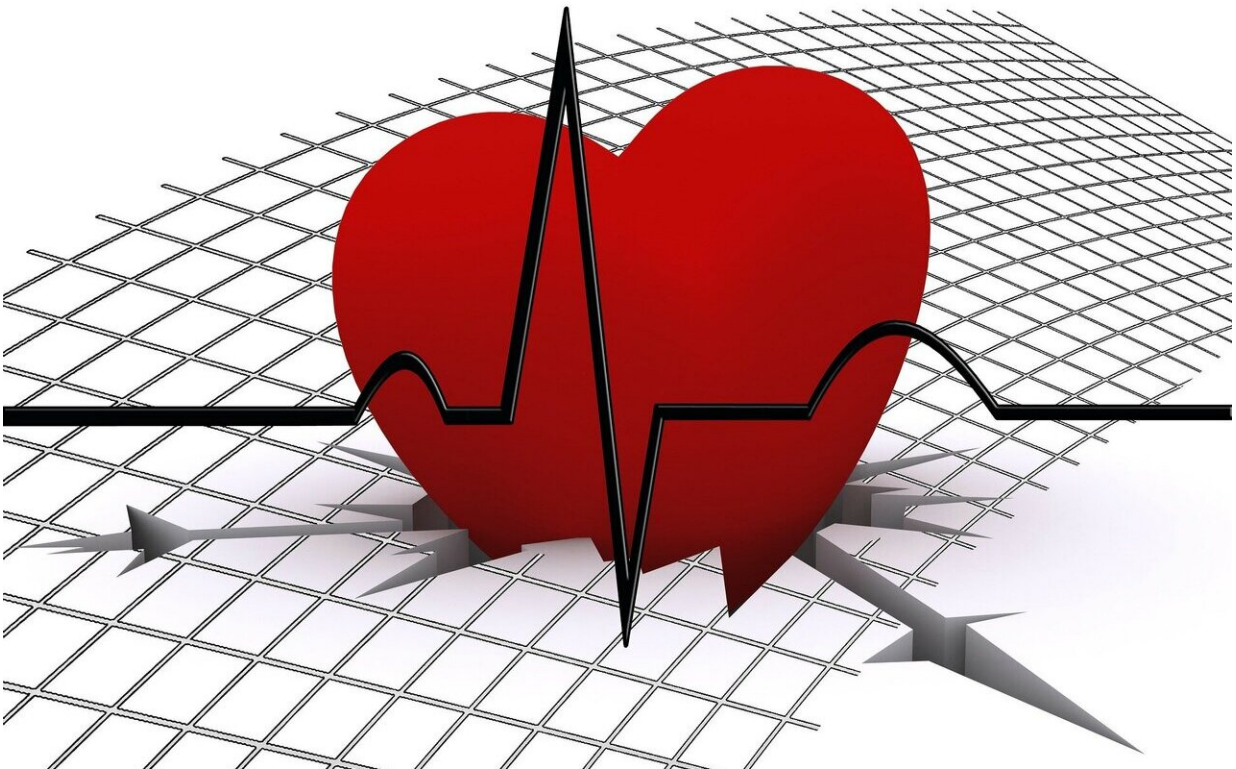


Experimental 'gene silencing' therapy reduces lipoprotein(a), an important risk factor of heart disease, by up to 98%

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Findings from a new Cleveland Clinic-led phase 1 trial show that an experimental "gene silencing" therapy reduced blood levels of

lipoprotein(a), a key driver of heart disease risk, by up to 98%.

Findings from the "APOLLO Trial: Magnitude and Duration of Effects of a Short-interfering RNA Targeting Lipoprotein(a): A Placebo-controlled Double-blind Dose-ranging Trial" were presented today during a late-breaking science session at the American College of Cardiology's 71st Annual Scientific Session and simultaneously published online in the *Journal of the American Medical Association*.

In the trial, participants who received higher doses of SLN360—a small interfering RNA (siRNA) therapeutic that "silences" the gene responsible for lipoprotein(a) production—saw their lipoprotein(a) levels drop by as much as 96%-98%. Five months later, these participants' lipoprotein(a) – also known as Lp(a) – levels remained 71%-81% lower than baseline.

The findings suggest this siRNA therapy could be a promising treatment to help prevent premature [heart disease](#) in people with high levels of Lp(a), which is estimated to affect 64 million people in the United States and 1.4 billion people worldwide. It is estimated that nearly 20 to 25% of the world's population has elevated Lp(a).

"These results showed the safety and strong efficacy of this experimental treatment at reducing levels of Lp(a), a common, but previously untreatable, genetically-determined risk factor that leads to premature heart attack, stroke and [aortic stenosis](#)," said the study's lead author Steven E. Nissen, M.D., Chief Academic Officer of the Heart, Vascular & Thoracic Institute at Cleveland Clinic. "We hope that further development of this therapy also will be shown to reduce the consequences of Lp(a) in the [clinical setting](#) through future studies."

Lp(a) has similarities to LDL, also known as [bad cholesterol](#). Lp(a) is made in the liver, where an extra protein called apolipoprotein(a) is

attached to an LDL-like particle. Unlike other types of cholesterol particles, Lp(a) levels are 80 to 90% genetically determined. The structure of the Lp(a) particle causes the accumulation of plaques in arteries, which play a significant role in heart disease. Elevated Lp(a) greatly increases the risk of heart attacks and strokes.

Although effective therapies to reduce the risk of [heart](#) disease by lowering LDL cholesterol and other lipids exist, currently there are no approved treatments to lower Lp(a). Since Lp(a) levels are determined by a person's genes, [lifestyle changes](#) such as diet or exercise have no effect. In the current study, the siRNA therapy reduces Lp(a) levels by "silencing" the gene responsible for Lp(a) production and blocking creation of apolipoprotein(a) in the liver.

In the APOLLO trial, researchers enrolled 32 people at five medical centers in three countries. All participants had Lp(a) levels above 150 nmol/L, with a median level of 224 nmol/L (75 nmol/L or less is considered normal). Eight participants received a placebo and the remaining received one of four doses of SLN360 via a single subcutaneous injection. The doses were 30 mg, 100 mg, 300 mg and 600 mg. Participants were closely observed for the first 24 hours after their injection and then assessed periodically for five months.

Participants receiving 300 mg and 600 mg of SLN360 had a maximum of 96% and 98% reduction in Lp(a) levels, and a reduction of 71% and 81% at five months compared to baseline. Those receiving a placebo saw no change in Lp(a) levels. The highest doses also reduced LDL cholesterol by about 20%-25%. There were no major safety consequences reported and the most common side effect was temporary soreness at the injection site. The study was extended and researchers will continue to follow participants for a total of one year.

More information: Single Ascending Dose Study of a Short

Interfering RNA Targeting Lipoprotein(a) Production in Individuals With Elevated Plasma Lipoprotein(a) Levels, *Journal of the American Medical Association* (2022). [DOI: 10.1001/jama.2022.5050](https://doi.org/10.1001/jama.2022.5050)

Provided by Cleveland Clinic

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