

New drug found to increase lipoprotein cholesterol in monkeys and humans

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A team of researchers at British Pharmaceutical company AstraZeneca has developed a new antibody drug that increases the level of lipoprotein cholesterol (HDL-C) in test monkeys and humans. In their paper published in the journal *Science Translational Medicine*, the group describes the drug and how well it worked when tested in monkeys and humans.

For many years, medical researchers have been touting the benefits of reducing so-called "bad" cholesterol in the bloodstream—such low-density lipoproteins (LDLs) are believed to lead to dangerous cardiovascular events when they build up in the bloodstream. Many drugs have been developed to treat patients with high amounts of LDL. At the same time, medical researchers have also been suggesting that so-called "good" cholesterol in the blood should be boosted. Unfortunately, efforts to develop drugs to do so have met with limited success. In this new effort, the researchers at AstraZeneca have come up with a new drug that showed promise of overcoming problems seen with other efforts during initial testing.

The drug, currently called MEDI5884, was developed by the company as an experimental antibody drug—then testing showed it to reduce HDL-C in monkeys. The researchers found that it neutralized endothelial lipase, which has been associated with <u>coronary heart disease</u>, and it did so by boosting HDL-C. Experiments showed it could double the levels of HDL-C in monkeys in just two weeks, and it did not seem to have any negative effects.

Emboldened by their findings, the researchers tested the drug on a small group of human volunteers. They found that the drug also increased HDL-C levels in humans, though not as much as with the monkeys. Unfortunately, they also found that the drug boosted the levels of <u>bad cholesterol</u> slightly, so they pretreated test <u>monkeys</u> with a PCSK9 inhibitor before giving them MEDI5884. That seemed to do the trick—HDLC-C levels rose but LDL levels did not. The researchers also found that combining the two drugs seemed to increase the efficacy of both. They suggest that the combination of the two could lead to a means for controlling cholesterol in patients with cardiovascular problems.

More information: John E. Le Lay et al. Blocking endothelial lipase with monoclonal antibody MEDI5884 durably increases high density lipoprotein in nonhuman primates and in a phase 1 trial, *Science Translational Medicine* (2021). DOI: 10.1126/scitransImed.abb0602

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