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New pathway discovered in cellular cholesterol regulation

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Researchers at two laboratories at NYU Langone Medical Center have collaborated to identify a tiny micro-RNA, miR-33, that regulates key genes involved in cellular cholesterol transport. The study, published online May 13, 2010 in *Science*, found that inhibitors of miR-33 may be beneficial because they could enhance cholesterol removal from tissues and raise levels of HDL -- shown in clinical trials to promote regression of human atherosclerotic plaques. This discovery could lead to the development of new treatments for atherosclerosis that would eliminate cholesterol accumulation in the artery wall.

"High density lipoprotein (HDL), 'the good cholesterol', is thought to protect against atherosclerotic vascular disease and treatments to raise HDL are at the forefront of cardiovascular research. Our study identifies a new pathway to regulate HDL levels and suggests that antagonists of miR-33 have exciting potential for use in conjunction with traditional LDL lowering therapies to raise HDL," says Kathryn J. Moore, PhD, associate professor in the Departments of Medicine and Cell Biology at NYU Langone Medical Center and one of the senior authors of the study.

MicroRNAs have recently emerged as important regulators of genes involved in physiological pathways. This study found that inhibiting miR-33 in mice could increase HDL levels by as much as 25%, which is similar to what can be accomplished by the drug Niacin, also known as vitamin B3 or nicotinic acid.

"Our work identifies miR-33 as a key regulator of intracellular cholesterol homeostasis. In atherosclerosis, macrophages in the artery wall accumulate cholesterol, leading to plaque formation. MiR-33 regulates this process by targeting pathways involved in cholesterol efflux from the cell and the formation of HDL," adds co-senior author Carlos Fernandez-Hernando, PhD, assistant professor in the Departments of Medicine and Cell Biology at NYU Langone Medicine, who was recently awarded the American Heart Association's Irvine H. Page Young Investigator Award for this discovery.

This exciting collaboration between the labs of Dr.'s Moore and Fernández-Hernando emerged as a result of their participation in the Marc and Ruti Bell Vascular Biology and Disease Program, a component of the Leon H. Charney Division of Cardiology at NYU Langone Medical Center. Edward A. Fisher, PhD, MPH, MD, the Leon H. Charney Professor of Cardiovascular Medicine and professor in the Departments of Medicine, Pediatrics and Cell Biology, is the director of this program and a co-author of the study. Additional co-authors of the study include Katey Rayner, PhD, Yajaira Suárez, PhD, Alberto Dávalos, PhD and Saj Parathath PhD of NYU Langone Medical Center.

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