Novel therapeutic target identified to decrease triglycerides and increase 'good' cholesterol

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Researchers at NYU Langone Medical Center today announce findings published in the October 20 issue of *Nature* that show for the first time the inhibition of both microRNA-33a and microRNA-33b (miR-33a/b) with chemically modified anti-miR oligonucleotides markedly suppress triglyceride levels and cause a sustained increase in high density lipoprotein cholesterol (HDL-C) "good" cholesterol.

"The discovery of microRNAs in the last decade has opened new insights for up new avenues for the development of therapies targeted at these potent regulators of gene pathways," said lead author Kathryn Moore, PhD, associate professor in the Department of Medicine, The Leon H. Charney Division of Cardiology and The Marc and Ruti Bell Vascular Biology and Disease Program at NYU Langone Medical Center. "The current study is the first to show that inhibition of miR-33a, as well as miR-33b which is only found in larger mammals can suppress plasma triglyceride levels and increase circulating levels of HDL-C. This study highlights the benefits of modulating miR-33a/b and its downstream metabolic pathways for the treatment of conditions that increase cardiovascular disease risks, such as dyslipidemias and metabolic syndrome."

Metabolic syndrome is a combination of medical disorders that increase the risk of developing cardiovascular disease and diabetes. Cholesterol is a growing public concern worldwide characterized by an increase in triglycerides, decrease in plasma HDL-C, obesity and resistance to insulin that can lead to both cardiovascular disease and diabetes.

Recent studies have indicated miR-33a/b regulate genes involved in cholesterol and fatty acid metabolism pathways. miR-33a/b strongly represses the cholesterol transporter ABCA1, resulting in decreased generation of HDL-C and reverse cholesterol transport. In addition, miR-33a/b also inhibit key genes involved in fatty acid metabolism resulting in the accumulation of triglycerides. The ability to inhibit miR-33a/b to reverse these events provides a novel therapeutic approach to correct dyslipidemia and metabolic syndrome.

"This study represents a significant advance from our proof-of-concept studies in mice showing that anti-miR-33 can both raise HDL and improve existing atherosclerotic vascular disease," said Katey Rayner, PhD in the Department of Medicine at NYU Langone Medical Center and co-author of the study. "These exciting results now bring the use of miR-33 inhibitors one step closer to the clinic."

Provided by New York University School of Medicine