

HDL cholesterol controls blood glucose

October 30 2013

High density lipoprotein cholesterol (HDL), the so-called "good" cholesterol improves blood glucose levels by enhancing skeletal muscle function and reducing adiposity, scientists of the Helmholtz Zentrum München report in the current issue of the American Heart Association Journal *Circulation*.

Atherosclerotic <u>cardiovascular disease</u> rates are markedly increased in individuals with type 2 diabetes. One of the strongest independent predictors of cardiovascular disease in these patients is a low circulating level of <u>high density lipoprotein</u> (HDL) cholesterol and its major protein constituent apolipoprotein A-I (ApoA-I). An international team of scientists led by Dr. Susanna Hofmann from the Institute of Diabetes and Regeneration Research at the Helmholtz Zentrum München (HMGU), Partner of the German Center for Diabetes Research (DZD), and Dr. Maarit Lehti from the LIKES Research Center for Sport and Health Sciences, Jyväskylä, Finland, have now determined that normal circulating HDL levels are required for proper skeletal muscle metabolism and function.

In their study, Hofmann and her team observed that without ApoA-I, burning of calories is reduced in <u>skeletal muscle</u> resulting in increased <u>blood glucose</u> and weaker <u>muscle function</u>. The scientists then determined that HDL cholesterol and its protein ApoA-I both enhance usage of glucose and calories inside muscle cells. Raising HDL and ApoA-I levels in animal models resulted in protection against hyperglycemia and age-related symptoms such as decline of muscle performance or fat mass gain. Improved calorie burning in mitochondria



(the "power plants" in each cell) was further indicated by a marked reduction of circulating Fibroblast Growth Factor 21, a novel biomarker for mitochondrial dysfunction.

"Our results link for the first time low HDL-cholesterol with impaired use of glucose and burning of calories in type 2 diabetes. ApoA-I analogues are now clinically tested for the prevention and regression of atherosclerosis. Based on our findings described herein, these analogs may offer underappreciated potential for therapeutic opportunities in diabetes", explains Hofmann, who investigates interactions of fat and glucose metabolism with her international team. She adds: "Most importantly, our results are highly relevant for women with type 2 diabetes. Their risk for cardiovascular diseases compared to men with type 2 diabetes is significantly increased, because these women have low concentrations of HDL-cholesterol and ApoA-I."

The numerous conditions associated with overweight and obesity, such as T2D, are among the major widespread diseases in Germany. They are the focus of the research at the Helmholtz Zentrum München.

More information: Lehti, M. et al (2013). High-density lipoprotein maintains skeletal muscle function by modulating cellular respiration in mice, *Circulation*, DOI: 10.1161/CIRCULATIONAHA.113.001551

Provided by Helmholtz Association of German Research Centres

Citation: HDL cholesterol controls blood glucose (2013, October 30) retrieved 6 May 2024 from https://medicalxpress.com/news/2013-10-hdl-cholesterol-blood-glucose.html

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