CIRCULATING HDL AS A MODULATOR OF FATTY ACID METABOLISM

Lehti M\(^1,2\), Donelan E\(^2\), Ress C\(^2\), Krishna R\(^2\), Hofmann S\(^2,3\)

\(^1\)LIKES Research Center for Sport and Health Sciences, Jyväskylä, Finland; \(^2\)University of Cincinnati, OH, USA; \(^3\)Helmholtz Centrum München, Germany

Physical activity is recommended as a treatment for unbalanced cholesterol profile. The most prominent and sustained effect of exercise on lipoproteins is increase in circulating high-density-lipoprotein-cholesterol (HDL) and its major protein constituent apolipoprotein A1 (apoA1).

Herein we used apoA1 human transgenic (apoA1-tg) mouse model to test hypothesis that HDL may modulate lipid homeostasis in sedentary and exercising mice. ApoA1-tg mice have markedly increased HDL levels compared to wild type (wt) mice. In addition, the levels of circulating triglycerides and neutral fatty acids (FFA) were increased in apoA1-tg compared to wt mice. Fasting increased circulating FFA levels of apoA1-tg mice further as well as difference between genotypes. While exhaustive exercise moderated difference between genotypes and lowered FFA levels immediately after running. Oral fat tolerance test showed impairment of FFA removal from circulation of apoA1-tg mice. Circulating level of an inhibitor of lipolysis, FGF21, was decreased in apoA1-tg. But exhaustive exercise increased FGF21 plasma levels in both genotypes. In ageing, sedentary apoA1-tg mice did not show increase in body fat mass that was observed in sedentary wt mice but their fat mass was close to trained wt mice (running 1h/5 d/ wk for 10 months).

Circulating HDL levels modulate body lipid metabolism. Greater reduction in blood FFA levels in apoA1-tg than wt mice after single bout of endurance exercise may point to higher fat consumption during exercise in apoA1-tg mice. At the same time, slow clearance of FFA after lipid load and decreased fat mass in ageing apoA1-tg mice may indicate impaired fat storing. One of the underlying mechanisms of differences in FFA metabolism of wt and apoA1-tg mice may be alterations in FGF21 levels. FGF21 is also known as a biomarker for mitochondrial deficiencies that designates more extensive changes in energy metabolism related to increased circulating HDL.