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HDL mimetics enhances mitochondrial function via stimulation of PGC1-alpha.

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Objectives: Various large clinical trial has been shown that high-density lipoprotein (HDL) has pleiotropic effects for antiatherosclerosis, and an enhanced HDL by CETP inhibitor improves glucose metabolism. In addition, HDL and apolipoprotein A-I (ApoA-I), the major protein of HDL had been demonstrated to enhance mitochondrial function in skeletal muscle *in vitro*.

Materials and Methods: One of the HDL mimetics, Fukuoka University ApoA-I Mimetic Peptide (FAMP) was developed as a low-amino acid residues peptide preserving human ApoA-I activity without phospholipids and has been reported to enhance HDL functions. C57BL6J mice were intraperitoneally administered 50 mg/kg/day of FAMP or saline for 4 weeks. After 4weeks, plasma samples were collected, and HDL was extracted by ApoB-depleted method. The mitochondrial functions were evaluated with the extracellular flux analyzer in C2C12 mouse myoblast cells *ex vivo*.

Results: HDL induced oxygen consumption rate changes that was the significant elevation of basal respiration, maximal respiration, ATP production and spare respiratory capacity (+35%, +54%, +35%, +68%, respectively). Moreover, HDL from mice treated with FAMP has further increasing maximal respiration and spare respiratory capacity, significantly. In addition, mice HDL from 4 weeks treatment with FAMP significantly increased PPARg-coactivator 1-a mRNA expression (HDL, 9.6±2.0; HDL treated with FAMP, 12.2±3.6; $P<0.01$).

Conclusion: Our results reveal that treatment with HDL mimetics improves mitochondrial function in skeletal muscle cells through stimulation of PGC1-a expressions. These findings may suggest that HDL prevents cardiovascular disease by enhancement of skeletal muscle functions.