Apolipoprotein A2 induces structural changes in HDL leading to increased antioxidant activity

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Aim: Recent data indicate that the apolipoprotein content of high-density lipoprotein (HDL) influences its functionality. Apolipoprotein A2 (APOA2) is the second most abundant protein of HDL. Despite studies aiming at understanding its biological functions, currently our knowledge on the impact of APOA2 on HDL functions remains limited. To this direction, here we investigated the effects of APOA2 expression on HDL composition and functionality.

Methods: C57BL/6 mice were infected with an adenovirus expressing human APOA2 (AdGFP-APOA2) or a control adenovirus (AdGFP). Five days post-infection plasma samples were collected from the two groups and HDL was isolated by ultracentrifugation and analyzed.

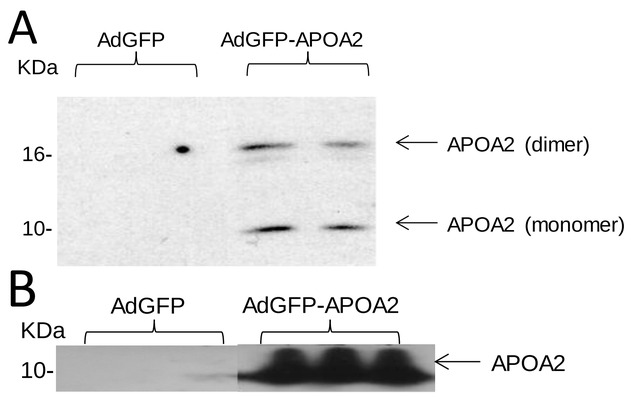

Fig. 1. Validation of human APOA2 expression in vitro and in vivo. A: Representative western blot analyses of media collected from cultures of HTB13 cells infected with AdGFP-APOA2 or control AdGFP; B: Representative western blot analysis of plasma isolated from mice infected with AdGFP-APOA2 or the control AdGFP.

Results: Hepatic APOA2 production and subsequent APOA2-HDL formation leads to:

- Increased plasma cholesterol, triglycerides and phospholipid levels.
- Increased apolipoprotein levels in the APOA2-HDL
- Discoidal HDL particles in the plasma of AdGFP-APOA2 infected mice.
- Increased antioxidant and anti-inflammatory activity of the APOA2-HDL
- Increased levels of CYTC and decreased levels of UCP1 in WAT isolated from AdGFP-APOA2 infected mice

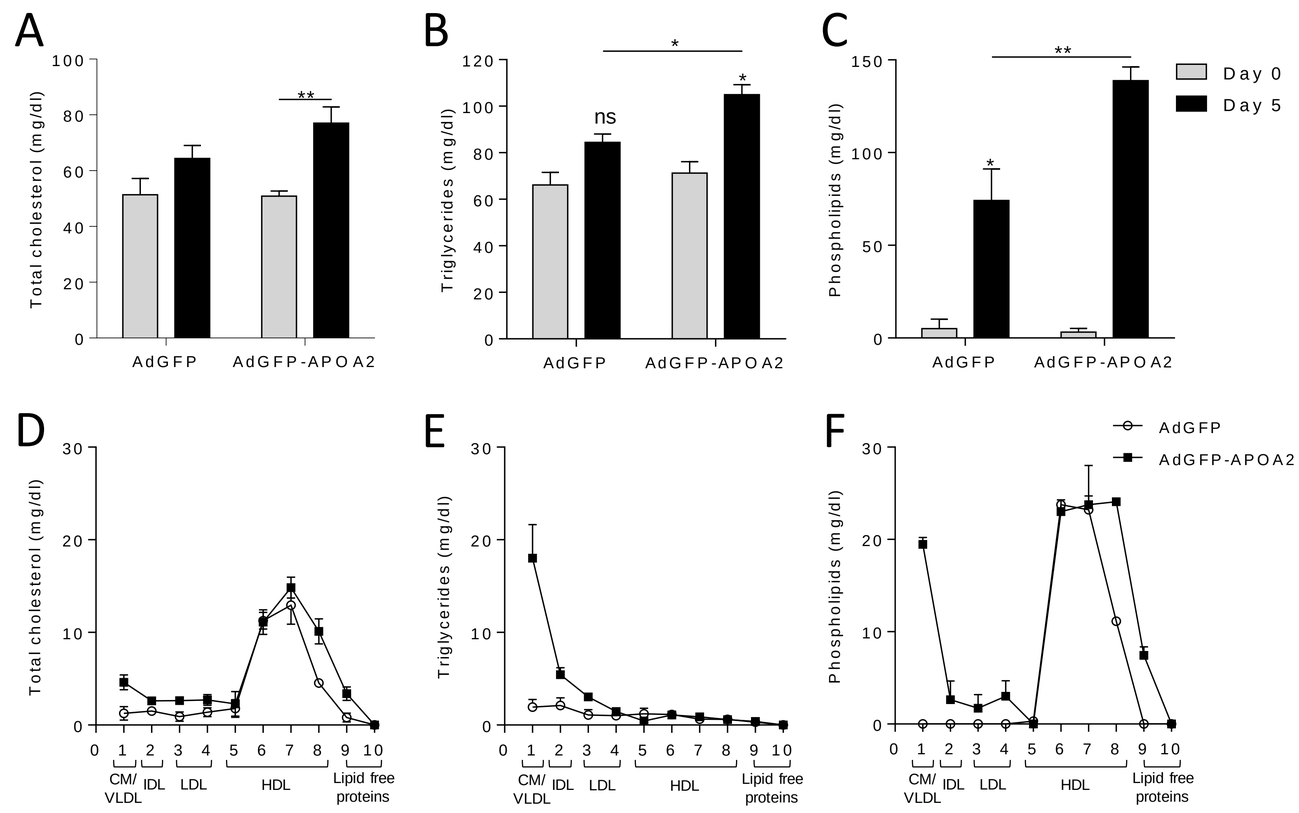

Fig. 2. Plasma and lipoprotein cholesterol, triglyceride and phospholipid content. A: Plasma total cholesterol levels; B: Plasma triglyceride levels; C: Plasma phospholipid levels; D: Lipoprotein cholesterol levels; E: Lipoprotein triglyceride levels; F: Lipoprotein phospholipid levels.

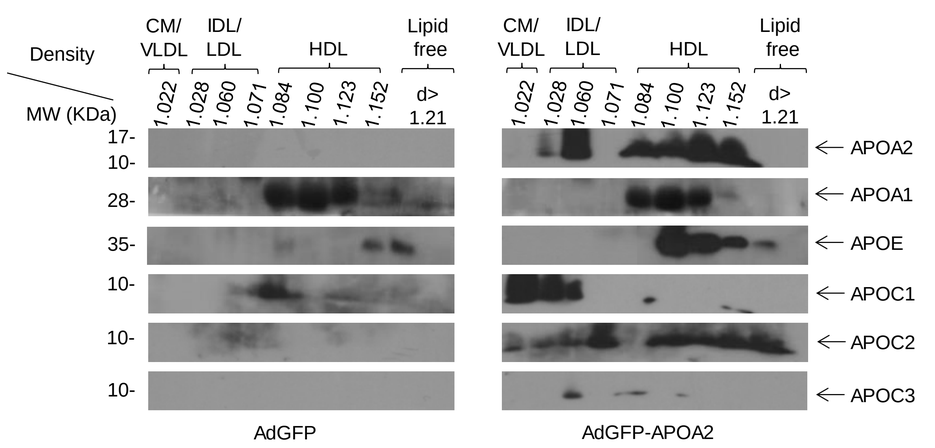

Fig. 3. Distribution of human APOA2 and murine APOA1, APOE, APOC1, APOC2 and APOC3 in various lipoprotein fractions isolated by UCF.

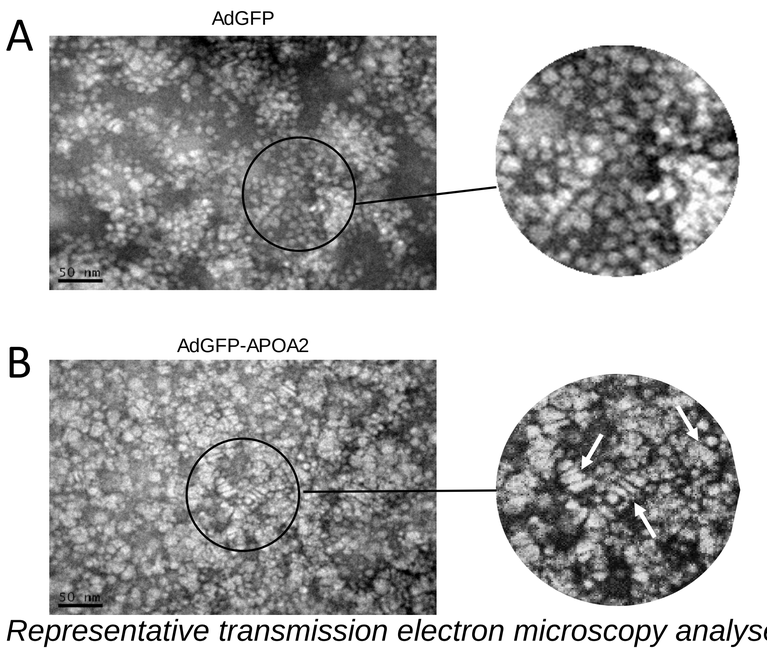

Fig. 4. Representative transmission electron microscopy analyses of HDL.

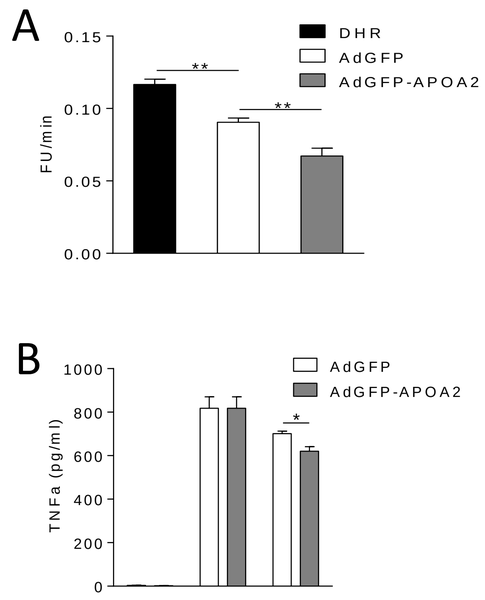

Fig. 5. Functional properties of HDL A: Antioxidant potential of HDL; B: Effects of APOA2-HDL on LPS-induced (100 ng/ml) TNFα production in cultured RAW 264.7 macrophages.

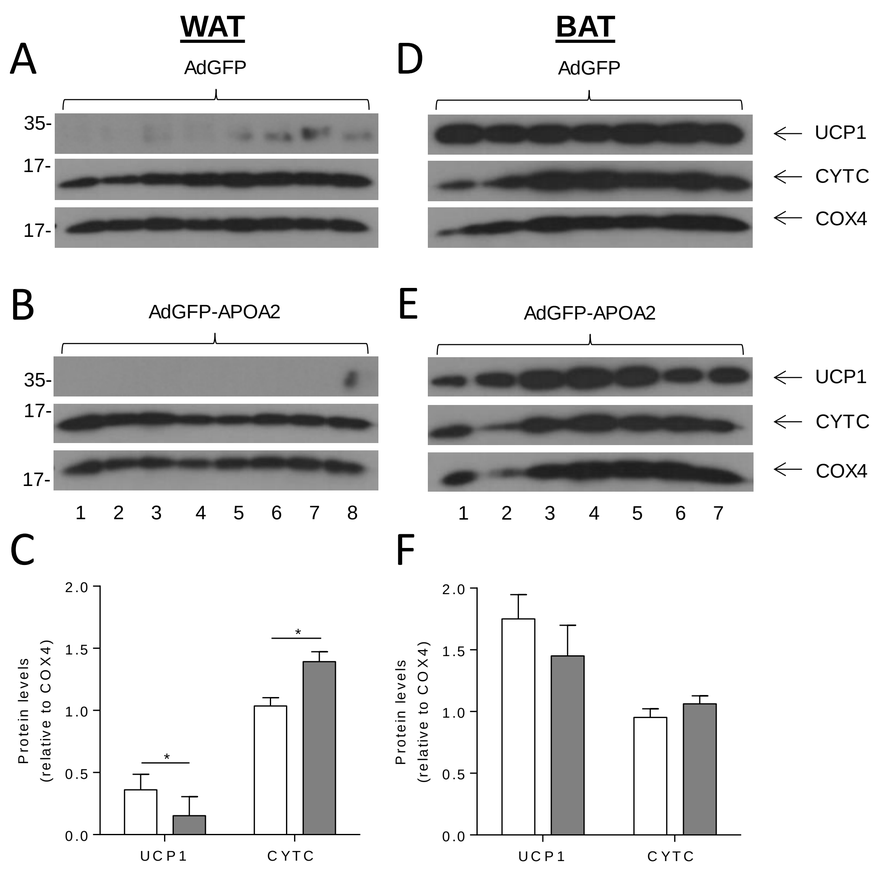

Fig. 6. Representative western blot analyses and semiquantitative determination of CYTC and UCP1 relative to COX4 in mitochondrial extracts.

Conclusions: Transient expression of APOA2 in C57BL/6 mice induces changes in HDL apolipoprotein composition and geometry, leading to improved HDL functionality. Moreover, APOA2 stimulates ATP production in WAT. Overall our data indicate that APOA2 expression results in pleiotropic effects, which are beneficial for human health.

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