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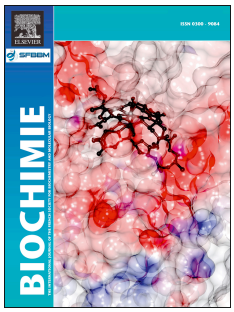


Oleic acid induces the novel apolipoprotein O and reduces mitochondrial membrane potential in chicken and human hepatoma cells.

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**Abstract**

Non-alcoholic fatty liver disease (NAFLD) is marked by hepatic fat accumulation and reflects a spectrum of chronic liver diseases associated with obesity, impaired insulin sensitivity and dyslipidemia.

Apolipoprotein O (ApoO) is a new member of the plasma apolipoprotein family that may play a role in lipid metabolism and electron transport activity of the mitochondrium. However, its physiological functions have not been elucidated yet. Based on our previous data in a non-mammalian experimental system [1], we hypothesized that hepatic expression of ApoO is tightly linked not only to diet-induced hepatosteatosis, but also to increased lipoprotein-production induced by, e.g., hormones and oxidative stress.

To gain insight into a mammalian experimental system, we compared the effects of lipid loading on ApoO regulation in chicken hepatoma LMH cells with those in the human hepatoma cell line HepG2. Incubation of the cells with BSA-complexed oleic acid (OA-Alb) induced triglyceride accumulation, but did not affect cell viability. qPCR using specific primer pairs and Western blot analysis with in-house produced rabbit anti-ApoO antisera demonstrated significant increase in ApoO transcript and protein levels in both cell lines. ROS formation due to OA-Alb treatment was only slightly altered in LMH cells, indicating an intact antioxidant defense system of the cells.

Oxidative stress applied by addition of $H_2O_2$ revealed induction of ApoO transcript and protein level in the same or even higher extent as monitored in the presence of OA-Alb. Upon treatment with estrogen for 24 h quantitative analysis of ApoO transcript and protein revealed increases of ApoO expression supporting the assumption that estrogen affects lipoprotein metabolism at various points. Furthermore, both cell lines showed a significant decrease of the mitochondrial membrane potential upon incubation with OA-Alb. Therefore, we assume that our findings support a role of ApoO as an effector of compromised mitochondrial function that likely accompanies the onset of non-alcoholic fatty liver disease.