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Non-alcoholic fatty liver disease (NAFLD) reflects a spectrum of chronic liver diseases characterized by hepatic fat accumulation. Apolipoprotein O (ApoO) is a new member of the apolipoprotein family that may play a role in lipid metabolism and mitochondrial electron transport activity. We hypothesized that hepatic expression of ApoO is tightly linked not only to diet-induced hepatosteatosis, but also to oxidative stress and hormones. Therefore, we compared the effects of lipid loading on ApoO regulation in chicken (LMH) with those in human (HepG2) hepatoma cells. Incubation with oleic acid (OA) induced triglyceride accumulation but did not affect cell viability. RT-qPCR and Western blot analyses showed significant increase in ApoO transcript and protein levels in both cell lines. Oxidative stress applied by H_2O_2 revealed induction of ApoO in the same or even higher extent as monitored by OA. ApoO increased upon treatment with estrogen supporting the assumption that estrogen affects lipoprotein metabolism. Furthermore, both cell lines showed a significant decrease of the mitochondrial membrane potential upon incubation with OA. We assume that our findings support a role of ApoO as an effector of compromised mitochondrial function that likely accompanies the onset of NAFLD.

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http://dx.doi.org/10.1016/j.freeradbiomed.2018.04.358

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Influence of hemoglobin S on metabolic homeostasis of human erythrocytes – partial results

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This is an initial study regarding the influence of redox imbalance of sickle cells on erythrocyte metabolism. Thus, the study is carrying out on ten patients with sickle cell anemia (SCA) and ten individuals without any hemoglobinopathies, as control group (CG). We assessed markers of membrane stability, hemolysis and antioxidant capacity, as well as metabolic enzymes and subproducts. We observed a typical increased osmotic resistance of sickle cells when compared to the healthy ones ($P < 0.01$), along with higher acetylcholinesterase activity ($P = 0.02$), indicating membrane impairment. SCA patients also showed higher hemolysis degree than CG, according to the levels of free hemoglobin ($P = 0.03$) and lactate dehydrogenase (LDH) ($P < 0.01$) in plasma. We did not find any alteration on total antioxidant capacity, both in plasma ($P = 0.57$) and intracellularly ($P = 0.54$). On the other hand, sickle cells showed twice the levels of NADPH ($P < 0.01$) and LDH activity ($P < 0.01$) than healthy erythrocytes, suggesting an up-regulation of both the pentose phosphate pathway and glycolysis. Thus, we concluded that the hemoglobin S presence promotes the disruption of erythrocyte metabolic homeostasis in a way far more complex than it was explored to date.

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http://dx.doi.org/10.1016/j.freeradbiomed.2018.04.359

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Structural and functional characterization of the acid and alkaline transition of cytochrome b5

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We have described, very recently, that cytochrome b5 (Cb5) is able to acquire a peroxidase-like activity in extreme alkaline media, when a hemichromic state is attained. At pH 4, Cb5 is mainly in a high-spin state (protein unfolding occurs and heme is released from the peptide chain) and its peroxidase activity is weak when compared with the one measured to pH 12. A structural characterization of Cb5 alkaline transition allowed us to reveal several parameters that might affect its stability and activity. H1NMR studies above pH 11 indicate the existence of a heme spin alterations that correlates with formation of tyrosinate anion, suggesting conformational changes at the heme crevice. Spectroscopic data support the interaction of Cb5 with imidazole above pH 11 and suggest the appearance of a binding site in the protein that allows accessibility of substrates to the heme. Our study, accordingly with other reports, shows acquisition of enzymatic activities when non-native states are acquired, before unfolding.

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Acknowledgements

Work supported by LAQV-REQUIMTE, FCT/MEC (UID/Multi/04378/2013) and co-financed by the ERDF under the PT2020 Partnership Agreement (POCI-01–0145-FEDER-007728), AKSA and LBM thank FCT/MEC, for fellowship grants SFRH/BPD/100069/2014 and SFRH/BPD/111404/2015

http://dx.doi.org/10.1016/j.freeradbiomed.2018.04.360

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Role of the aryl hydrocarbon receptor (AhR) signaling pathway in exceptional longevity in humans

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Centenarians are the best example of successfully aging in humans. Thus, the characterization of the biological processes and pathways in this population is an excellent strategy to understand the lifespan extension. The aryl hydrocarbon receptor (AhR) is a ligand-activated-transcription factor historically known for regulating expression of several important drug-detoxifying proteins. But recently its role in the immune response and in cellular homeostasis has been recognized. Furthermore, AhR is activated in *C. Elegans* in extreme longevity due to a dietary restriction. We report here results of a whole transcriptome analysis of centenarians. The main biological process was the immune response and we have highlighted the role of the AhR signaling pathway in exceptionally longevity. These results suggest that the AhR signaling have a role in the