Abstract

Mitochondria play a central role in the regulation of cellular energy homeostasis. These organelles provide the majority of cellular adenosine triphosphate (ATP) through the process of oxidative phosphorylation (OXPHOS) and match the bioenergetic requirements of the cell in response to a host energy demands. However, how mitochondrial energy metabolism could adapt to different environmental conditions in order to maintain cellular homeostasis is still not clear.

Recent studies highlighted the mitochondrial acetylation state as a possible regulatory mechanism in the bioenergetic adaptation of mitochondrial function. It has been shown that the majority of mitochondrial proteins could be acetylated and that the mitochondrial acetylation state is susceptible to metabolic perturbations. Moreover, several proteins involved in different mitochondrial metabolic pathways (e.g. mitochondrial translation and OXPHOS system) have been identified as targets of the major mitochondrial deacetylase, sirtuin 3 (Sirt3).

In this study we genetically modified the mitochondrial acetylation state *in vitro* as well as *in vivo* and assessed the adaptation of mitochondrial translation and OXPHOS function in response to a broad range of metabolic challenges. We provided indications of a novel role of mitochondrial acetylation state as a possible regulator in the nutrient sensing of *de novo* mitochondrial translation. Furthermore, we showed *in vitro* that the mitochondrial acetylation state is involved in the adaptation of cellular respiration in response to galactose-treatment. However, this effect might not result from the alteration of the enzymatic activity of specific OXPHOS complexes. Moreover, *in vivo* experiments further confirmed the role of Sirt3 in the tissue-specific regulation of OXPHOS function in physiological condition. In contrast, no major indications of a possible role of Sirt3 in the bioenergetic adaptation of OXPHOS in response to the analyzed dietary interventions were detected. Additionally, our *in vivo* data suggested a possible involvement of Sirt3 in the regulation of hepatic acetylation state in response to an inflammatory insult.