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World Yeast Congress

May 14-15, 2018 | Montreal, Canada

Regulation of the mitochondrial functions by phosphorylation in the yeast *Saccharomyces* cerevisiae

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The mitochondrion is an organelle of which the most important function is to provide energy to the cell generated by oxidative phosphorylation catalyzed by the respiratory enzymes. In humans, deregulation of mitochondrial functions, particularly with regard to the respiratory chain, is associated with several pathologies. The activity of the respiratory enzymes may be modulated in response to metabolic demand and various types of stress. Several levels of regulation may be conceived, including post-translational modifications such as phosphorylation. The steadily increasing number of identified mitochondrial phosphoproteins suggests that reversible protein phosphorylation could be an important level of regulation in mitochondria. However, this hypothesis cannot be tested without quantitative data on variations in the abundance of mitochondrial proteins and their level of phosphorylation under different growth conditions. The yeast *Saccharomyces cerevisiae* is a powerful tool for studying various energetic and physiological states. We realized for the first time a quantitative study of both protein abundance and phosphorylation levels in yeast mitochondria under respiratory (lactate) and fermentative (glucose or galactose) conditions. Protein abundances were quantified using a label-free method. The phosphoproteome was analyzed quantitatively using the multiplex stable isotope dimethyl labeling procedure. Label free quantitative analysis of protein accumulation revealed significant variation of 176 mitochondrial proteins. We highlighted significant differences of the proteome between the two fermentative substrates.This study enlarges significantly the map of yeast mitochondrial phosphosites as 670 phosphorylation sites were identified, of which 214 were new and quantified. Above all, we showed that 90 phosphosites displayed a significant variation according to the medium. This proteomic and phosphoproteomic study is the first extensive study providing confident quantitative data on mitochondrial phosphosites responses to different carbon substrates in the yeast *S. cerevisiae* mitochondria. The significant changes observed in the level of phosphorylation according to the carbon substrate open the way to the study of the regulation of mitochondrial proteins by phosphorylation in fermentative and respiratory media. In addition, the identification of a large number of new phosphorylation sites show that the characterization of the yeast mitochondrial phosphoproteome is not yet completed.

Speaker Biography

Lemaire Claire is expert in the biochemistry of membrane proteins. Her scientific interests have always been focused on energy-transducing systems and in particular those evolved in organelles. She began her career in the photosynthesis field on the assembly and regulation of photosynthetic complexes (Institute of Physico-Chemical Biology, Paris). She then joined the C.N.R.S. (French National Center for Scientific Research) where she has acquired an excellent appreciation of the mitochondrial system through the study of the biogenesis of respiratory complexes in yeast and human using various biochemical and genetic approaches. These last years, she has developed a new research project with her group focusing on the regulation of the mitochondrial functions by post-translational modifications.

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