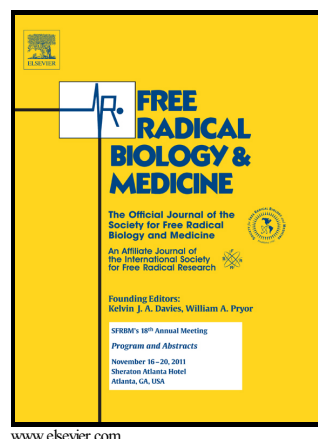


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FUNCTIONAL ROLE OF MITOCHONDRIAL REACTIVE OXYGEN SPECIES IN PHYSIOLOGY

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ABSTRACT

The major energy generator in the cell – mitochondria produce reactive oxygen species as a by-product of a number of enzymatic reactions and the production of ATP. Emerging evidence suggests that mitochondrial ROS regulate diverse physiological parameters and that dysregulated ROS signalling may contribute to a development of processes which lead to human diseases. ROS produced in mitochondrial enzymes are triggers of monoamine-induced calcium signal in astrocytes, playing important role in physiological and pathophysiological response to dopamine. Generation of ROS in mitochondria leads to peroxidation of lipids, which is considered to be one of the most important mechanisms of cell injury under condition of oxidative stress. However, it also can induce activation of mitochondrial and cellular phospholipases that can trigger a variety of the signals – from activation of ion channels to stimulation of calcium signal. Mitochondria are shown to be the oxygen sensor in astrocytes, therefore inhibition of respiration by hypoxia induces ROS production which leads to lipid peroxidation, activation of phospholipase C and induction of IP₃-mediated calcium signal. Propagation of astrocytic calcium signal stimulates breathing activity in response to hypoxia. Thus, ROS produced by mitochondrial enzymes or electron transport chain can be used as a trigger for signalling cascades in central nervous system and deregulation of this process leads to pathology.

Introduction

Although mitochondria have multiple important functions, these organelles are mainly high efficient engine for conversion of the products of glucose or fatty acid metabolism into

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