中山大學孫逸仙紀念医院
SUN YAT-SEN MEMORIAL HOSPITAL,SUN YAT-SEN UNIVERSITY

A Mitophagic Response to Iron Overload-induced Oxidative Damage Associated with the PINK1/Parkin Pathway in Pancreatic Beta Cells

ZHANG Lina, HOU Lele, LIU Zulin, OU Hui, JIANG Zhuanna, HUANG Siqi, MENG Zhe, LIANG Liyang*
Department of Pediatrics, Sun Yat-sen Memorial Hospital, Guangzhou China

Highlights

First study of direct impact from iron overload on pancreatic beta cells

First investigation of mitochondrial defect in iron overloaded pancreatic beta cells

Mitophagy occurs in iron overloaded pancreatic beta cells

Introduction: An increased iron overload led to a disorder in glucose metabolism. However, the mechanism through which iron overload induces beta cell death remains unknown.

Methods: INS-1 cells were cultured with different concentrations (0, 80,160μM for 48 h respectively) of ferric ammonium citrate (FAC) and INS-1 cells (FAC 160μM for 48h) were pretreated with N-acetylcysteine (NAC 5 mM for 1 h) as the drug intervention groups. Cell proliferation was accessed using CCK8. Reactive oxygen species (ROS) level was further detected by flow cytometer after fluorescent probe staining. The mitochondrial membrane potential was detected by jc-1 kit, and the mitochondrial changes were observed by transmission electron microscopy. The proteins expression related to autophagy was detected by western bolt.

Results: The present study revealed that ferric ammonium citrate treatment inhibited cell viability in vitro, induced a decline in mitochondrial membrane potential, increased oxidative stress and suppressed mitophagy. These effects could be alleviated by a reactive oxygen species scavenger.

Conclusions: we demonstrated that increased iron overload induced cytotoxicity in INS-1 cells primarily by activating oxidative stress and further suppressed mitophagy in the PTEN-induced putative kinase 1/Parkin pathway.

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