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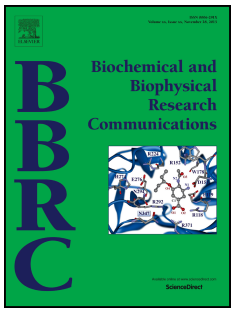

AMPK alleviates endoplasmic reticulum stress by inducing the ER-chaperone ORP150 via FOXO1 to protect human bronchial cells from apoptosis

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AMPK alleviates endoplasmic reticulum stress by inducing the ER-chaperone ORP150 via FOXO1 to protect human bronchial cells from apoptosis

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Abstract:

Chronic obstructive pulmonary disease (COPD), is characterized by inflammation of airways accompanied by a progressive destruction of lung parenchyma. This process is initiated in most cases by cigarette smoking. In this study we investigated the role of AMP activated protein kinase (AMPK) in cigarette smoke extract (CSE)-induced airway epithelial cell apoptosis as a consequence of endoplasmic reticulum stress (ER stress). Exposure of human bronchial epithelial cells (HBEpC) to CSE resulted in apoptosis as detected using Annexin V-PI flow cytometry. However, co-treatment with N^1-(β-D-ribofuranosyl)-5-aminoimidazole-4-carboxamide (AICAR), a pharmacological activator of AMPK, significantly increased cell protection against ER stress-induced apoptosis by upregulating the 150 kDa oxygen-regulated protein (ORP150), which functions as an ER-associated chaperone, with concomitant elevation of FOXO1, a critical transcription factor regulating ORP150 expression. Lentiviral silencing of AMPK or FOXO1 using short hairpin (sh) RNA resulted in a significant decrease of ORP150 and an elevation of CCAAT/enhancer-binding protein-homologous protein (CHOP) resulting in ER stress and apoptosis of HBEpC. Together, our results strongly suggest that AMPK can activate ORP150 through FOXO1 pathway and confer protection against ER stress-induced apoptosis of airway epithelial cells following exposure to CSE. Thus, AMPK may serve as a likely therapeutic target for clinical and sub-clinical interventions in COPD.