Genetics and Molecular Research

PI3K-Akt-mTOR signal inhibition affects expression of genes related to endoplasmic reticulum stress

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Genet. Mol. Res. 15 (3): gmr.15037868
Received October 21, 2015
Accepted January 18, 2016
Published July 25, 2016
DOI http://dx.doi.org/10.4238/gmr.15037868

ABSTRACT. PI3K-Akt-mTOR signaling pathway is associated with endoplasmic reticulum (ER) stress. However, it is not clear how this signaling pathway affects the ER stress. The present study aimed to determine whether the PI3K-Akt-mTOR signaling pathway regulates tunicamycin (TM)-induced increases in mRNA levels of genes involved in the ER stress, to help elucidate the mechanism by which this pathway affects the ER stress in primary goose hepatocytes. Primary hepatocytes were isolated from geese and cultured *in vitro*. After 12 h in a serum-free medium, the hepatocytes were incubated for 24 h in a medium with either no addition (control) or with supplementation of TM or TM together with PI3K-Akt-mTOR signaling pathway inhibitors (LY294002, rapamycin, NVP-BEZ235). Thereafter, the expression levels of genes involved in the ER stress (*BIP*, *EIF2a*, *ATF6*, and *XBP1*) were assessed. The results indicated that the mRNA level of *BIP*

was up-regulated in 0.2, 2, and 20 μM TM treatment group ($P < 0.05$), whereas the mRNA levels of *EIF2a*, *ATF6*, and *XBP1* were up-regulated in the 2 μM TM treatment group ($P < 0.05$). However, the TM mediated induction of mRNA levels of genes involved in the ER stress (*BIP*, *EIF2a*, *ATF6*, and *XBP1*) was down-regulated after the treatment with PI3K-Akt-mTOR pathway inhibitors (LY294002, NVP-BEZ235, and rapamycin). Therefore, our results strongly suggest that the PI3K-Akt-mTOR signaling pathway might be involved in the down-regulation of the TM-induced ER stress in primary goose hepatocytes.

Key words: Endoplasmic reticulum (ER) stress; Tunicamycin (TM); Goose primary hepatocytes; Unfolded protein response (UPR); PI3k-Akt-mTOR signaling pathways