Hypoxia-induced apoptosis and mitochondrial dysfunction in chondrocytes arising from CREB phosphorylation reduction

Y.Y. Qiu, Y. Chen, T.H. Zeng, W.H. Guo, W.Y. Zhou and X.J. Yang

Department of Spine Surgery, The 2nd Shenzhen People's Hospital, Shenzhen, China

Corresponding author: X.J. Yang
E-mail: jian_xinyang@163.com

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ABSTRACT. Chondrocytes, which are embedded within the growth-plate or the intervertebral disc, are sensitive to environmental stresses, such as inflammation and hypoxia. However, little is known about the molecular signaling pathways underlying hypoxia-induced mitochondrial dysfunction and apoptosis in chondrocytes. We first examined the apoptosis, caspase-3 activity, and apoptosis-associated markers in human chondrocyte cell line C28/I2 under normoxia or hypoxia. We then investigated mitochondrial dysfunction and the activation of cyclic adenosine monophosphate response element-binding protein (CREB) signaling in the same human chondrocyte cell line. Our results indicated that hypoxia induced apoptosis and reduced CREB phosphorylation in chondrocytes. Upregulated mitochondrial superoxide and reactive oxygen species levels, and reduced mitochondrial membrane potential and complex IV activity were observed in hypoxia-treated C28/I2 cells. In conclusion, the present study confirmed reduced CREB phosphorylation, apoptosis induction, and mitochondrial dysfunction in the hypoxia-treated chondrocyte

cells. This implies the key role played by CREB signaling in hypoxia-induced mitochondrial dysfunction and apoptosis in chondrocytes.

Key words: Hypoxia; Apoptosis; Mitochondrial dysfunction; Chondrocytes; CREB phosphorylation

