Abstracts

ACTIVATION OF MAPK/ERK1/2 PATHWAYS IS AN IMPORTANT MECHANISM OF OXIDATIVE STRESS-INDUCED APOPTOSIS IN MESENCHYMAL STEM CELLS OF RATS

Jianfeng Xu 1, Juying Qian 1, Xinxing Xie 1, Jianying Ma 1, Li Lin 2, Mingqiang Fu 1, Aijun Sun 1, Yunzeng Zou 1, Junbo Ge 1 1Zhongshan Hospital, Shanghai, China 1eastern Hospital, Hong Kong, China

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Objective To investigate the role of MAPK/ERK1/2 pathways in oxidative stress-induced apoptosis of mesenchymal stem cells.

Methods Hydrogen peroxide (H2O2) was used to induce apoptosis of mesenchymal stem cells (MSCs) of adult Sprague-Dawley rats to establish the oxidative stress damage model in vitro. MSCs were treated with H2O2 in different concentration (0, 0.2 mmol/l, 0.5 mmol/l, 1 mmol/l, 2 mmol/l) for 6 h, and were divided into five groups. The percentages of total MSCs apoptosis were analysed by flow cytometry; the expression of proteins related with MAPK/ERK1/2 pathways, such as phosphorylation of ERK1/2 and caspase-3 were compared by Western-Blot assay. With the use of U0126, an inhibitor of phosphorylation of ERK1/2, all above detections in moderately treated concentration group (0.5 mmol/l) were observed.

Results H2O2 significantly induced accumulation of ROS in MSCs in a concentration-dependant manner (control group, (2.34±0.55)%; 0.2 mmol/l group, (6.25±1.23)%; 0.5 mmol/l group, (16.52±2.30)%; 1 mmol/l group, (25.8±4.51)%; and 2 mmol/l group, (56.87±6.25)%, p value all<0.05). Flow cytometry indicated that the percentages of total apoptosis of MSCs gradually increased as the concentration of H2O2 rose ((7.2±3.9)%, (11.4±5.8)%, (13.8±7.1)%, (20.5±6.3)%, (24.6±7.9)%, respectively, p value all<0.05). More interestingly, phosphorylation of ERK1/2 was up-regulated gradually as the concentration of H2O2 increased (11.31±0.25, 1.56±0.36, 2.81±1.03, 3.25±1.39 (folds of internal control), respectively; p value all<0.05). Similar effects occurred with the expression of caspase-3 (11.64±0.31, 1.87±0.41, 3.56±0.65, 5.45±1.30 (folds of internal control), respectively; p value all<0.05). In U0126 group, the percentages of total apoptotic MSCs dramatically decreased compared with 0.5 mmol/l group ((10.1±3.4)% vs (24.6±7.9)%, p<0.05); the expression of caspase-3 downregulated synchronously (1.12±0.57 vs 1.87±0.41 (folds of internal control), p<0.05).

Conclusion The above results suggested that activation of MAPK/ERK1/2 pathways is an important mechanism of oxidative stress-induced apoptosis in mesenchymal stem cells.