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

Methods Hydrogen peroxide (H_2O_2) 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 H_2O_2 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 H_2O_2 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 H_2O_2 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 H_2O_2 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.

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

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