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, $(2.34\pm0.55)\%$; 0.2 mmol/l group, $(6.25\pm1.23)\%$; 0.5 mmol/l group, $(16.52\pm2.30)\%$; 1 mmol/l group, $(25.8\pm4.51)\%$; and 2 mmol/l group, $(56.87\pm6.25)\%$, 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 $((7.2\pm3.9)\%$, $(11.4\pm5.8)\%$, $(13.8\pm7.1)\%$, $(20.5\pm6.3)\%$, $(24.6\pm7.9)\%$, 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 $((10.1\pm3.4)\%$ vs $(24.6\pm7.9)\%$, 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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