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HIGH DENSITY LIPOPROTEIN CHOLESTEROL PROMOTES THE PROLIFERATION OF BONE-DERIVED MESENCHYMAL STEM CELLS VIA BINDING SCAVENGER RECEPTOR-B TYPE I AND ACTIVATION OF PI3K/AKT, MAPK/ERK PATHWAYS

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Objectives To investigate the effect of high density lipoprotein (HDL) on the proliferation of mesenchymal stem cells (MSCs), and to elucidate the molecular mechanisms involved.

Methods MSCs derived from rats was treated with HDL in different concentration or for different periods. The proliferation of MSCs was measured with MTT and BrdU assay. The expressions of p21 and phosphorylation of Akt, ERK1/2 were evaluated by western blot. The activity of pathways was down-regulated by the respective specific inhibitor, and the gene of Scavenger Receptor-B Type I (SR-BI) was knocked down by RNA interference.

Results We found that HDL promoted MSCs proliferation in a time- and concentration-dependent manner, in which the phosphorylation of Akt, ERK1/2 were up-regulated and the level of p21 was down-regulated. When MSCs was preconditioned with the specific inhibitor to respective pathways, the decrease of p21 induced by HDL was significantly attenuated compared with that without preconditioning (LY294002: 1.03±0.16 vs 0.691±0.13, $p<0.05$; U0126: 1.68±0.17 vs 0.76±0.15, $p<0.05$). SR-BI contributed to HDL-induced proliferation of MSCs, which was effectively abolished by the knock-down of SR-BI. Compared with respective PBS-treatment groups, MSCs transfected with mock siRNA displayed a higher BrdU incorporation rate after administration of HDL (0.98±0.16 vs 1.57±0.23, $p<0.05$), while the MSCs transfected with SR-BI siRNA showed no change (1.08±0.15 vs1.08 ±0.14, $p > 0.05$).

Conclusions HDL improves the proliferation of MSCs in a time- and concentration-dependent manner through PI3K/Akt and MAPK/ERK1/2 pathways and binding SR-BI receptor.