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Investigating the effect of statin on the expression of PGC1-α and NRF2 genes on neural stem cells derived from bone marrow stromal stem cells in laboratory conditions

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Introduction

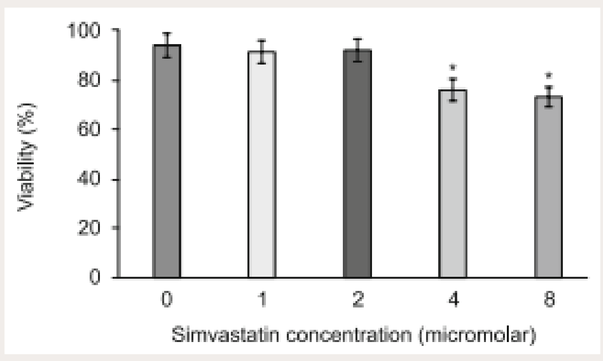
Stem cell knowledge provide new opportunities to scientists in using bone marrow stem cells and its derived tissue in replacement damaged tissue. In this field neural stem cells had specific roll in researches in traumatic brain injury and brain damages. But unfortunately damages to new derived cells due to oxidative stress secondary to free oxygen radicals after differential from bone marrow stem cells are one of obstacles in this process. New researches showed that simvastatin one of anti-lipid agents can play important role in inhibit cell death due to its anti-oxidant effects and can activate gene transcription pathways to awake intrinsic antioxidant defense. In this study we examine this theory with putting in place with simvastatin and hydrogen peroxide as oxidant agent.

Material and Methods

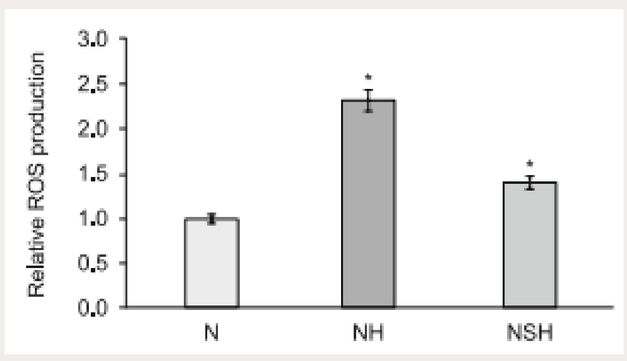
This experimental study was conducted on neural like stem cells (NLSCs) derived from bone marrow stem cell. After cell differentiation and immune histochemical staining, cells divided into three groups: neural like stem cells (NLSCs), NLSCs+ H2O2 100 micro molar, NLSCs+H2O2 100 micro molar +simvastatin 2 micro molar. Then via viability test with triptan blue detect viable cells.

Results

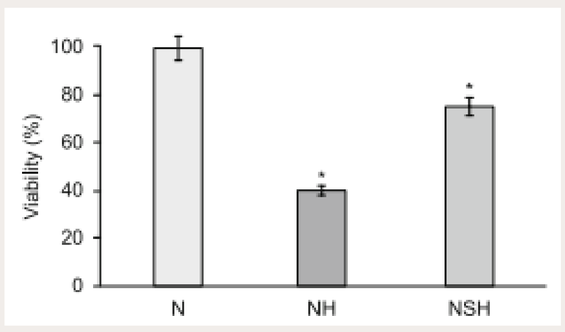
Seventy-six percent of NLSCs+ H2O2+ simvastatin and 40% of NLSCs+H2O2 was alive after exposure to H2O2 P<0/05. Thus NRF-2 and PGC-1α gene expression was increase in NLSCs+H2O2 100 micro molar +simvastatin 2 micro molar despite of NLSCs+H2O2.



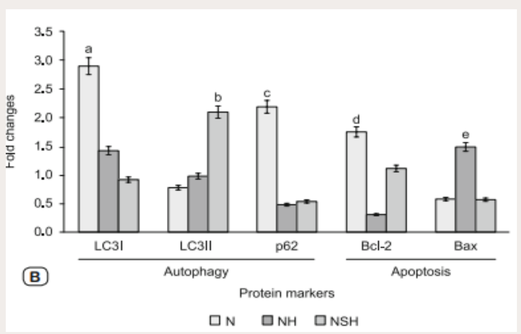
Dose-dependent effects of SIM on BMSCs-derived NSCs. Cell viability was determined using trypan blue assay. Asterisk denotes a statistically signifi cant difference in cell viability among 0, 4, and 8 μM concentrations.



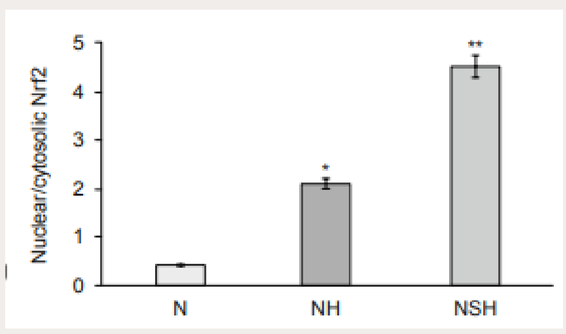
The effect of SIM on the reduction of ROS generation in BMSCs-derived NSCs. The BMSCs-derived NSCs were pretreated with SIM (2 μM) for 48 hours, and the ROS level was determined using the DCFH-DA dye.



Protective effects of SIM pretreatment on cell viability. The cell viability was determined using trypan blue assay. The N, NH and NSH indicate group of BMSCs-derived NSCs (untreated group), group of BMSCs-derived NSCs treated with 100 μM of H2 O2 , and group of BMSCs-derived NSCs pretreated with 2 μM of SIM and then treated with 100 μM of H2 O2 , respectively. Cell death was induced by H2 O2 (100 μM) in BMSCs-derived NSCs, however, 2 μM of SIM pretreatment protects NSCs against H2 O2 -induced cell death.



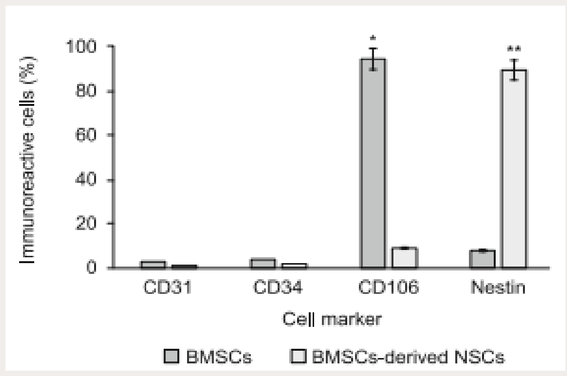
Western blotting analyses of apoptosis (Bcl-2 and Bax) and autophagy (LC3I, LC3II, p62) proteins. Representative Western blots (A) and quantifi cation of autophagic and apoptotic mediators (B). The expression of LC3I, LC3II, p62, Bcl-2 and Bax assays in N, NH and NSH groups.



Nrf2 protein level assessment using immunocytochemistry. SIM pretreatment increased the Nrf2 activation in the NSH group (BMSCsderived NSCs + SIM pretreatment + H2 O2). The BMSCs-derived NSCs were pretreated with 2 μM of SIM for 2 hours and were further treated with 100 μM of H2 O2 for another 48 hours.

Discussion

Pretreatment neural stem cells with simvastlower cellular death and more cellular suatin causes rvival in comparison to other cells.



Mean percentage of immunoreactive cells to CD31, CD34, CD106 and nestin in BMSCs. The fi gure shows BMSCs and BMSCsderived NSCs with black and white solid patterns, respectively.

Keywords

Stem cell, Oxidative stress, Simvastatin, Neural like stem cells