

The Improved Therapeutic Effect of Trans-Cinnamaldehyde on Adipose-Derived Stem Cells without Chemical Induction

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Abstract : Assuring cell quality is an essential parameter for the success of stem cell therapy, utilization of various components to improve this potential has been the primary goal of stem cell research. The aim of this study was not only to demonstrate the capacity of trans-cinnamaldehyde (TC) to reverse stress-induced senescence but also improve the therapeutic abilities of stem cells. Because of the availability and the promising application potential in regenerative medicine, adipose-derived stem cells (ADSCs) were chosen for the study. We found that H₂O₂ treatment resulted in the expression of senescence characteristics in the ADSCs, including decreased proliferation rate, increased senescence-associated- β -galactosidase (SA- β -gal) activity, decreased SIRT1 (silent mating type information regulation 2 homologs) expression and decreased telomerase activity. However, TC treatment was sufficient to rescue or reduce the effects of H₂O₂ induction, ultimately leading to an increased proliferation rate, a decrease in the percentage of SA- β -gal positive cells, upregulation of SIRT1 expression, and increased telomerase activity of the senescent ADSCs at the cellular level. Further recently it was observed that the ADSCs were treated with TC without induction of senescence, all the before said positives were observed. Moreover, a chemically induced liver fibrosis animal model was used to evaluate the functionality of these rescued cells in vivo. Liver dysfunction was established by injecting 200 mg/kg thioacetamide (TAA) intraperitoneally into Wistar rats every third day for 60 days. The experimental rats were separated into groups; normal group (rats without TAA induction), sham group (without ADSC transplantation), positive control group (transplanted with normal ADSCs); H₂O₂ group (transplanted with H₂O₂ -induced senescent ADSCs), H₂O₂+TC group (transplanted with ADSCs pretreated with H₂O₂ and then further treated with TC) and TC group (ADSC treated with TC without H₂O₂ treatment). In the transplantation group, 1 \times 10⁶ human ADSCs were introduced into each rat via direct liver injection. Based on the biochemical analysis and immunohistochemical staining results, it was determined that the therapeutic effects on liver fibrosis by the induced senescent ADSCs (H₂O₂ group) were not as significant as those exerted by the normal ADSCs (the positive control group). However, the H₂O₂+TC group showed significant reversal of liver damage when compared to the H₂O₂ group 1 week post-transplantation. Further ADSCs without H₂O₂ treatment but with just TC treatment performed much better than all the groups. These data confirmed that the TC treatment had the potential to improve the therapeutic effect of ADSCs. It is therefore suggested that TC has potential applications in maintaining stem cell quality and could possibly aid in the treatment of senescence-related disorders.

Keywords : senescence, SIRT1, adipose derived stem cells, liver fibrosis

Conference Title : ICLSE 2015 : International Conference on Life Science and Engineering

Conference Location : Paris, France

Conference Dates : December 30-31, 2015