Biomedical Research & Therapy

ISSN: 2198-4093
www.bmrat.org

POSTER

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Adipose-derived stem cells and platelet rich plasma ameliorate liver cirrhotic circumstance in CCl_4-induced mice: a new approach for liver cirrhosis treatment

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Abstract

Background: Stem cell therapy in liver cirrhosis treatment is attracting the attention of the scientific community. Adipose tissue-derived mesenchymal stem cells are a potential source of cells because they have self-renewal, high proliferation, and differentiation into a variety of cell types, including hepatocytes as potential cell sources for cirrhosis treatment. Platelet-rich plasma (PRP) growth factors contribute to regeneration and wound healing. We test the hypothesis that PRP co-administration enhances MSC treatment for mouse cirrhosis.

Method: Male Swiss mice were treated orally with olive oil or CCl_4 for 11 weeks. PRP was obtained from healthy mice. Mouse adipose-derived stem cells (mADSCs) from adipose tissue of 3 weeks CCl_4 mice were cultured for three passages (P3-mADSCs) before the transfer by tail vein injection with or without PRP into 11 weeks CCl_4 mice. Mice were divided into six groups (n=10 each group). 1) normal, 2) cirrhotic, 3) cirrhotic /PBS; 4) cirrhotic/PRP (0.2 ml/mice with PRP from healthy mice), 5) cirrhotic/mADSCs (5 x 105 cells/mice), and 6) cirrhotic/mADSC-PRP.

Result: mADSCs were highly positive for CD44, CD90, and CD105. Relative to liver cells, P3-mADSCs highly expressed Alb, Ck18, Ck19, Tnf, c-met, Cyp1a1, Afp, Muc1, Ldl receptor. mADSCs were strongly positive for Cyp1a1 (98.21±1.57%) and Hgf (95.55±3.11%); moderately positive for alfa-fetoprotein (45.99±2.08%), Aat (44.43±7.79%), Alb (57.81±8.49%) and differentiated into hepatocyte-like cells under induction medium. After transplantation, CFDA-transplanted cells into CCl_4-treated mice were found in the liver at day 21 st. Compared to mADSCs, mADSCs and PRP co-treatment most effectively improved serum AST/ALT/bilirubin and albumin levels in day seven cirrhotic mice ($p<0.05$); and significantly down-regulated procollagen (104-fold less) and TGF-beta 1 (10-fold less) in day 21 cirrhotic liver. Histology index and collagen deposition were improved in 100% of mADSC/PRP- and mADSCs- cirrhotic mice compared to 33.3% of PBS- or PRP- cirrhotic liver ($p<0.05$).

Conclusion: Cultured mADSCs express hepatocyte enriched markers. PRP coadministration enhances mADSC effects to improve liver function further, and further reduce fibrosis.

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Competing interests: The authors declare that no competing interests exist.

Received: 2017-02-07
Accepted: 2017-08-19
Published: 2017-09-05

DOI 10.15419/bmrat.v4iS.330

Biomedical Research & Therapy

ISSN: 2198-4093
www.bmrat.org

Keywords

Adipose-derived stem cells, liver cirrhosis, liver disease, mesenchymal stem cells, stem cell therapy

Funding

This study was funded by VNU-HCM and Center of Science and Technology Development for Youth - Ho Chi Minh city

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