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Comparative Evaluation of Differentiation Potential of Menstrual Blood- Versus Bone Marrow- Derived Stem Cells into Hepatocyte-Like Cells

Sayeh Khanjani[1-], Manijeh Khanmohammadi[1-], Amir-Hassan Zarnani[2,3], Mohammad-Mehdi Akhondi[1], Ali Ahani[1], Zahra Ghaempanah[1], Mohammad Mehdi Naderi[1], Saman Eghtesad[4], Somaieh Kazemnejad[1]*

1 Reproductive Biotechnology Research Center, Avicenna Research Institute, ACECR, Tehran, Iran, 2 Nanobiotechnology Research Center, Avicenna Research Institute, ACECR, Tehran, Iran, 3 Immunology Research Center, Iran University of Medical Sciences, Tehran, Iran, 4 Department of Biochemistry and Molecular Biology, University of Maryland School of Medicine, Baltimore, Maryland, United States of America

Abstract

Menstrual blood has been introduced as an easily accessible and refreshing stem cell source with no ethical consideration. Although recent works have shown that menstrual blood stem cells (MenSCs) possess multi lineage differentiation capacity, their efficiency of hepatic differentiation in comparison to other stem cell resources has not been addressed so far. The aim of this study was to investigate hepatic differentiation capacity of MenSCs compared to bone marrow-derived stem cells (BMSCs) under protocols developed by different concentrations of hepatocyte growth factor (HGF) and oncostatin M (OSM) in combination with other components in serum supplemented or serum-free culture media. Such comparison was made after assessment of immunophenotye, trans-differentiation potential, immunogenicity and tumorigeicity of these cell types. The differential expression of mature hepatocyte markers such as albumin (ALB), cytokeratin 18 (CK-18), tyrosine aminotransferase and cholesterol 7 alpha-hydroxylase activities (CYP7A1) at both mRNA and protein levels in differentiating MenSCs was significantly higher in upper concentration of HGF and OSM (P1) compared to lower concentration of these factors (P2). Moreover, omission of serum during differentiation process (P3) caused typical improvement in functions assigned to hepatocytes in differentiated MenSCs. While up-regulation level of ALB and CYP7A1 was higher in differentiated MenSCs compared to driven BMSCs, expression level of CK-18, detected level of produced ALB and glycogen accumulation were lower or not significantly different. Therefore, based on the overall comparable hepatic differentiation ability of MenSCs with BMSCs, and also accessibility, refreshing nature and lack of ethical issues of MenSCs, these cells could be suggested as an apt and safe alternative to BMSCs for future stem cell therapy of chronic liver diseases.

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* E-mail: s.kazemnejad@avicenna.ac.ir

- These authors contributed equally to this work.

Introduction

Cell therapy, using human hepatocytes, is being regarded worldwide as an alternative approach to organ transplantation for liver failure. Major obstacles, including donor organ shortage have encouraged scientists and physicians to take advantage of stem cells for cell therapy of liver disorders [1]. Adult bone marrow has commonly been known as the most conventional stem cell source in the field of regenerative medicine and tissue engineering, including liver tissue engineering, because bone marrow-derived mesenchymal stem cells (BMSCs) do not present the ethical issues of embryonic stem cells (ESCs), have hepatogenic differentiation ability in vitro and in vivo [2,3] and exhibit immunosuppressive capabilities [4,5]. However, problems such as less availability, invasive methods for sample collection and lower proliferation capacity in comparison with ESCs limit applicability of BMSCs for clinical therapy of liver diseases. Pertaining to other sources of stem cells and regardless of great achievements in generating terminally-differentiated hepatocyte-like cells from human induced pluripotent stem (iPS) cells, limitations such as the risk of tumor formation are yet to be addressed in this stem cell type [6,7].

Several studies have reported that menstrual blood (MB) contains a unique population of cells with properties similar to adult stem cells [8–11]. It has been proposed that MB contains circulating BMSCs, which contribute to endometrial regeneration [12]. Menstrual blood-derived stem cells (MenSCs) exhibit a long term self-renewal ability, greater proliferation capacity compared to BMSCs and have minimal risk of karyotypic abnormalities [8–11,13]. In addition, recent studies have showed that reprogramming efficiency for generation of iPS cells could be increased using MenSCs as a cell source even in the absence of ectopic expression of c-Myc [14,15]. These characteristics, as well as the ease of access and the possibility of cyclic sample collection, make MB an appropriate stem cell supply for tissue engineering and regenerative medicine.