The differentiation of MSCs into functional hepatocyte-like cells in a liver biomatrix scaffold and their transplantation into liver-fibrotic mice

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1. Introduction

Liver transplantation remains the definitive treatment option for end-stage liver disease. However, the surgical complications, chronic rejections, critical shortage of donor organs and high cost of this procedure have sparked tremendous interest in finding new treatments [1]. Cell-based therapies, such as cell transplantation and bioartificial liver devices, have emerged as alternative therapies [2,3]. Because of the difficulties associated with obtaining autologous hepatic tissue and maintaining the phenotype of the primary hepatocytes in culture, the scarcity of human hepatocytes remains a serious roadblock for the development of cell-based therapies [4]. Therefore, the promise of a renewable supply of functional hepatocytes from an alternative source represents an important goal in current studies.

Stem cells are considered an alternative cell source for functional hepatocytes. Increasing evidence suggests that the differentiation of stem cells into hepatocytes is achieved in the appropriate microenvironment following stimulation with hepatic growth factors [5–7]. Mesenchymal stem cells (MSCs) are a type of adult stem cell and, compared to hepatocytes, are more suitable for cell therapy because of their adequate availability, easy accessibility, rapid proliferation, multipotent differentiation, and successful integration and immunological tolerance in the host tissue [8]. Meanwhile, MSCs could be derived from a patient’s own tissues rather than blastocyst or embryos, and are considered more appropriate for clinical use [9]. In addition, it has been shown that the transplantation of MSCs or MSC-derived hepatocyte-like cells improves the liver function in rodents [10,11] or patients [12] suffering from liver damage. However, the several traditional protocols used to date have had limited success, and these hepatocyte-like cells exhibit only a portion of the markers and...