Effect of mesenchymal stem cells administered by two different routes on experimentally induced liver fibrosis in rats
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Background
Liver fibrosis is a progressive pathological process involving multiple cellular and molecular events that ultimately lead to deposition of excess matrix proteins in the extracellular space. Adult bone marrow mesenchymal stem cells (BM-MSCs) have the potential to open a new frontier in medicine. BM-derived MSCs can be differentiated into various lineage cells including hepatocyte-like cells.

Aim of the work
This study was conducted to investigate the effect of MSCs introduced by two different routes on experimentally induced liver fibrosis in rats.

Material and methods
In this study 45 adult male rats were divided into four groups. Fifteen rats served as the control group (group I). In group II (the affected group), 10 rats were injected intraperitoneally with carbon tetrachloride (CCl4; 0.15 ml/100 g body weight) dissolved in an equal volume of castor oil twice a week for 10 weeks. In group III (the intravenous stem cell group), 10 rats were injected intraperitoneally with CCl4 twice a week for 10 weeks and then given a single intravenous dose of MSCs in the sixth week. In group IV (the intrahepatic stem cell group), 10 rats were injected intraperitoneally with CCl4 twice a week for 10 weeks and then administered a single intrahepatic MSC dose in the sixth week. Liver samples were taken after 10 weeks from the first dose of CCl4 for processing of paraffin sections and for staining with H&E, Sirius red, and immunohistochemistry staining for detection of matrix metalloproteinase-13 (MMP-13) and tissue inhibitors of matrix metalloproteinases-1 (TIMP-1). The slides stained by Sirius red were quantitatively analyzed for collagen fibers.

Results
CCl4 induced liver necrosis and fibrosis after 10 weeks (ballooning of hepatocytes, moderate-to-severe cytoplasmic vacuolation, massive accumulation of collagen fibers, weak expression of MMP-13, and strong expression of TIMP-1). Intrahepatic MSCs reduced the impact of CCl4 on the liver more than those injected by the intravenous route (minimal cytoplasmic vacuolation of hepatocytes, significant decrease in collagen fiber accumulation, strong expression of MMP-13, and weak expression of TIMP-1).

Conclusion
BM-derived MSCs can protect against liver fibrosis, and the route of transplantation affects the results. The intrahepatic route is better than the intravenous route in reducing the hepatic necrosis and fibrosis induced by CCl4.

Keywords:
liver fibrosis, mesenchymal stem cells, route of injection

Introduction
Liver is a highly regenerative organ with the ability to restore its mass even in the face of massive parenchymal cell loss. Liver regeneration and reconstitution is associated with fibrosis in chronic liver injury [1].

Hepatic fibrosis is considered to be a wound-healing response characterized by persistent tissue damage and activation of multiple cell types that produce extracellular matrix (ECM), culminating in tissue scarring, loss of normal parenchyma, and eventually organ failure [2]. Its main feature is an imbalance in the synthesis and degradation of the ECM, which leads to a great deal of precipitation in the perisinusoidal space (space of Disse). It is currently believed that activation of hepatic stellate cells is not only the key link in the development of hepatic fibrosis but also the main source of ECM [3].
ECM turnover is regulated by matrix metalloproteinases (MMPs) and their inhibitors, the tissue inhibitors of matrix-metalloproteinases (TIMPs). Whether fibrosis results from increased synthesis of ECM, decreased degradation of ECM, or a combination of both has not been clearly established, although the TIMP : MMP ratio may determine the net balance of ECM turnover [2].

The initial cause of the injury determines the loss of hepatocytes as a result of both apoptotic and necrotic phenomena; the immune system as well can participate in hepatocyte loss either by inducing apoptotic signals or by directly mediating hepatocyte cell destruction [4]. However, during hepatocyte regeneration, the ECM undergoes a process of remodeling due to the persisting inflammatory stimulus, which leads to abnormal collagen deposition and consequently to fibrosis of the parenchyma [5].

The ECM is one of the most important regulators of cellular and tissue function in the body. Tightly controlled ECM homeostasis is essential for development, wound healing, and normal organ homeostasis, and sustained deregulation can result in life-threatening pathological conditions [6]. In healthy livers, collagen is mainly of types I and III, which are present in equal amounts and are limited to the capsule, around big vessels, and in the portal areas [7]. When a fibrogenic injury occurs, both type I and type III collagen increase. Moreover, fibrillar type IV collagen is deposited within perisinusoidal spaces [8]. A further phase is eventually characterized by the bridging fibrosis, connecting portal spaces to the central vein. Liver fibrosis is a dynamic process, in which progression and regression phases can be present alternatively during its evolution [9].

Tissue mesenchymal stem cells (MSCs) exist in almost all tissues, such as bone marrow (BM), muscle, fat, hair follicles, tooth root, placenta, brain, peristeum, dermis, perichondrium, umbilical cord, lung, liver, and spleen [10]. They were initially identified by their potential for induced differentiation into several mesenchymal lineages: bone, cartilage, adipose tissue, muscle, and tendon [11]. However, it has been shown that some types of MS-like cells isolated from both human and mouse can be induced into cells of endodermal and neuroectodermal lineages, including endothelium, neurons, and hepatocytes [12]. The most intensely studied MSCs are those derived from the adult BM [13]. Human BM-derived MSCs can be cloned and expanded in vitro more than a million-fold and still retain the ability to differentiate into several cell lineages. Thus, it is possible to produce sufficiently large numbers of MSCs for cell therapy from a single modest BM aspirate [14].

**Aim of the work**
This study was conducted to investigate the effect of MSCs introduced by two different routes (intravenous and intrahepatic) on experimentally induced liver fibrosis in adult male albino rats.

**Material and methods**
In this study, 45 adult male albino rats of average weight 150–200 g were used. The animals were housed in special cages and maintained under standard laboratory conditions in the experimental animal unit of the Faculty of Medicine, Cairo University. They were fed with tap water and a commercial diet ad libitum. All ethical protocols for animal treatment were followed and were supervised by the animal facilities. All animal experiments received approval from the Institutional Animal Care Committee.

Carbon tetrachloride (CCl4) solution was obtained from Sigma (Saint Louis, Missouri, USA). It was dissolved in an equal volume of castor oil and injected intraperitoneally twice a week at a dose of 0.15 ml/100 g body weight [15].

**Preparation of bone marrow-derived mesenchymal stem cell** [16]
BM was harvested by flushing the tibiae and femurs of 6-week-old male, white, albino rats with Dulbecco’s modified Eagle’s medium (Gibco/BRL; Gel Company Inc., San Francisco, California, USA) supplemented with 10% fetal bovine serum (Gibco/BRL). Nucleated cells were isolated with a density gradient (Ficoll/Paque; Pharmacia New Jersey, USA) and resuspended in complete culture medium supplemented with 1% penicillin-streptomycin (Gibco/BRL). Cells were incubated at 37°C in 5% humidified CO2 for 12–14 days. The medium was changed every 2–3 days. When large colonies developed (80–90% confluence), cultures were washed twice with PBS and the cells were trypsinized with 0.25% trypsin in 1 mmol/l EDTA (Gibco/BRL) for 5 min at 37°C. After centrifugation (2400 rpm for 20 min), cells were resuspended with supplemented medium and incubated in a 50 cm² culture flask (Falcon, Becton, Dickinson and Company, Lovetone Circle, Sparks, Maryland, USA). On day 14, the adherent colonies of cells were trypsinized and counted. MSCs were injected at a dose of 3 × 10⁶ cells (3 ml) per rat.

Cells were identified as being MSCs by their morphology, adherence, and by detection of CD29, a surface marker of rat MSCs, through reverse transcriptase-PCR. The PCR product was separated by electrophoresis through a 1% agarose gel, stained, and photographed under ultraviolet light.

**Tracking of intravenous stem cells** [16]
PKH26 is a red fluorochrome. The linkers are physiologically stable and show little to no toxic side effects on cell systems. Labeled cells retain both biological and proliferating activity and are ideal for in-vivo cell tracking. In the current work, undifferentiated MSCs were labeled with PKH26 according to the manufacturer's recommendations (Sigma-Aldrich, Saint Louis, Missouri, USA). Cells were injected intravenously into the tail vein. After 1 month, liver tissue was examined with a fluorescence microscope to detect the cells stained with PKH26.

**Animals were divided into four groups as follows:**
Group I (*the control group*): Fifteen rats were injected intraperitoneally with castor oil (0.15 ml/100 g body weight)
twice a week for 10 weeks. Five of them received a single intravenous (3 ml) saline injection (in the tail vein) and another five rats received a single intrahepatic (3 ml) saline injection in the sixth week.

Group II (the affected group): Ten rats were injected intraperitoneally with CCl₄ (0.15 ml/100 g body weight) dissolved in an equal volume of castor oil twice a week for 10 weeks.

Group III (the intravenous stem cell group): Ten rats were injected intraperitoneally with CCl₄ twice a week for 10 weeks and received a single intravenous (in the tail vein) dose of BM-derived MSCs in the sixth week.

Group IV (the intrahepatic stem cell group): Ten rats were injected intraperitoneally by CCl₄ twice a week for 10 weeks and received a single intravenous (in the tail vein) dose of BM-derived MSCs in the sixth week.

Liver samples were taken at 10 weeks for processing of paraffin sections and for staining with H&E [17] and Sirius red [18]. The slides stained by Sirius red underwent quantitative analysis for collagen by means of an imaging analyzer using an imaging system constituted by a digital Q-color 5 camera (Olympus, Tokyo, Japan) coupled to an epifluorescence Axiosvert 100 microscope (Carl Zeiss, Thornwood, New York, USA). Randomly picked fields of Sirius red sections were captured from each animal, using an objective lens of magnification ×40. Quantification was estimated by the percentage of stained area in comparison with the total area of fields examined, using Image-Pro Plus 5.0 (Media Cybernetics Inc., Bethesda, Maryland, USA) image analysis software. All data were expressed as mean area %. Difference between groups was compared using the F-test, with $P < 0.05$ selected as the level of statistical significance. Statistical analyses were carried out using Microsoft excel 2010 (Microsoft Egypt, Cairo, Egypt).

Also, liver tissues were examined by immunohistochemistry for detection of MMP-13 and TIMP-1, using the ultravision detection system Anti-polyvalent HRP/DAB (ready to use) IHC staining technique (Midco Trade Co., Cairo, Egypt). Sections were counterstained with hematoxylin [19].

The mean area % for brown cytoplasmic staining (MMP-13 and TIMP-1 expression) was quantified in 10 images for each group using Image-Pro Plus program version 6.0 (Media Cybernetics Inc.).

The control group (group I) showed cords of hepatocytes radiating from a central vein, each of a single cell thickness, which bifurcated and fused to give a network. Hepatocytes were approximately cubical in shape with central nuclei. Some cells showed two nuclei. Blood sinusoids were present between the cords of hepatocytes (Fig. 4). In the affected group (group II), it showed ballooning of hepatocytes, moderate-to-severe cytoplasmic vacuolation, and disorganized hepatic architecture. The central vein was dilated and congested (Fig. 5). In the intravenous stem cell group (group III), hepatocytes showed cytoplasmic vacuolation with a dilated congested central vein and a disorganized hepatic architecture (Fig. 6). In the intrahepatic stem cell group (group IV), there was minimal cytoplasmic vacuolation of hepatocytes, dilated congested sinusoids, and nearly normal liver architecture (Fig. 7).

**Results**

**Bone marrow mesenchymal stem cells characterization and tracking**

Cells were identified in culture as being MSCs by their spindle-shaped appearance (Fig. 1) and by detection of CD29, a surface marker of rat MSCs, through reverse transcriptase-PCR (Fig. 2). MSCs labeled with PKH26 injected into the tail vein were observed in liver tissue using a fluorescent microscope (Fig. 3).

**H&E stain**

The control group (group I) showed cords of hepatocytes around the central vein (Fig. 8). The affected group (group II) showed massive accumulation of collagen fibers around dilated central veins, which extended between cords of hepatocytes (Fig. 9). The intravenous stem cell group (group III) showed moderate accumulation of collagen fibers around the dilated central vein (Fig. 10). The intrahepatic stem cell group (group IV) showed mild collagen accumulation around the central vein (Fig. 11).

The mean area % for collagen fiber accumulation for all groups is presented in Table 1 and Histogram 1.

There was a nonsignificant decrease ($P < 0.05$) in collagen fiber accumulation in group III (the intravenous stem cell group), whereas there was a significant decrease ($P < 0.05$) in collagen fiber accumulation in group IV (the intrahepatic stem cell group) compared with group II (the affected group).

**Sirius red stain**

The control group (group I) showed minimal accumulation of collagen fibers around the central vein (Fig. 8). The affected group (group II) showed massive accumulation of collagen fibers around dilated central veins, which extended between cords of hepatocytes (Fig. 9). The intravenous stem cell group (group III) showed moderate accumulation of collagen fibers around the dilated central vein (Fig. 10). The intrahepatic stem cell group (group IV) showed mild collagen accumulation around the central vein (Fig. 11).

The mean area % for brown cytoplasmic staining (MMP-13 and TIMP-1 expression) was quantified in 10 images for each group using Image-Pro Plus program version 6.0 (Media Cybernetics Inc.).

**Immunohistochemistry stain for matrix metalloproteinase-13 and tissue inhibitors of matrix metalloproteases-1**

The control group showed weak expression of MMP-13 (Fig. 12) and absent expression of TIMP-1 (Fig. 13) in the hepatocyte cytoplasm. The affected group showed weak expression of MMP-13 (Fig. 14) and strong expression of TIMP-1 (Fig. 15) in the hepatocyte cytoplasm. The intravenous stem cell group showed moderate expression of both MMP-13 (Fig. 16) and TIMP-1 (Fig. 17) in the hepatocyte cytoplasm. The intrahepatic stem cell group showed strong expression of MMP-13 (Fig. 18) and weak expression of TIMP-1 (Fig. 19) in the hepatocyte cytoplasm.

The mean area % of MMP-13 expression for all groups is presented in Table 2 and Histogram 2 and of TIMP-1 expression for all groups in Table 3 and Histogram 3.
Effect of MSCs on liver fibrosis

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Figure 1.

Mesenchymal stem cells (arrow) in culture. Characterized by their spindle shape. × 200.

Figure 2.

An agarose gel electrophoresis shows PCR products of CD29 gene expression in mesenchymal stem cell (MSC) culture [lane M: DNA marker; lane 1: MSC culture (261 bp)].

Figure 3.

Fluorescent microscopy showing mesenchymal stem cells labeled with PKH26 (double arrows) in liver tissue after injection into the rat tail vein. × 200.

Figure 4.

A photomicrograph of a section of liver obtained from group I (the control group) showing cords of normal hepatocytes radiating from the central vein (C). Hepatocytes (H) are cubical in shape with a central nucleus (N) and blood sinusoids (S) in between the cords. H&E, × 400.

Figure 5.

A photomicrograph of a section of liver from group II (the affected group) showing ballooning (arrow) and moderate-to-severe vacuolation (V) of hepatocyte cytoplasm, and a dilated congested central vein (C) with disorganized hepatic architecture. H&E, × 400.

Figure 6.

A photomicrograph of a section of liver from group III (the intravenous stem cell group) showing vacuolation (V) of the hepatocyte cytoplasm, and a dilated congested central vein (C). Disorganized hepatic architecture is noticed. H&E, × 400.
Figure 7.

A photomicrograph of a section of liver from group IV (the intrahepatic stem cell group) showing minimal vacuolation (V) of hepatocyte cytoplasm, a normal-appearing central vein (C), and nearly normal liver architecture. Dilated congested blood sinusoids (S) are noticed. H&E, × 400.

Figure 8.

A photomicrograph of a section of liver from group I (the control group) showing minimal collagen fibers (double arrow) around the central vein. Sirius red, × 400.

Figure 9.

A photomicrograph of a section of liver from group II (affected group) showing extensive collagen fiber accumulation (double arrows) around a dilated central vein that extends between cords of hepatocytes. Sirius red, × 400.

Figure 10.

A photomicrograph of a section of liver from group III (the intravenous stem cell group) showing collagen fiber accumulation (double arrows) around the dilated central vein. Sirius red, × 400.

Figure 11.

A photomicrograph of a section of liver from group IV (the intrahepatic stem cell group) showing few collagen fibers accumulated (double arrows) around the central vein. Sirius red, × 400.

Figure 12.

A photomicrograph of a section of liver from group I (the control group) showing weak matrix metalloproteinase-13 (MMP-13) expression in the hepatocyte cytoplasm (arrowhead). Immunohistochemistry stain for MMP-13, × 400.
Figure 13.

A photomicrograph of a section of liver from group I (the control group) showing absent expression of tissue inhibitors of matrix metalloproteases-1 (TIMP-1) in the hepatocyte cytoplasm (double arrowheads).

Immunohistochemistry stain for TIMP-1, × 400.

Figure 14.

A photomicrograph of a section of liver from group II (the affected group) showing weak matrix metalloproteinase-13 (MMP-13) expression in the hepatocyte cytoplasm (arrowhead).

Immunohistochemistry stain for MMP-13, × 400.

Figure 15.

A photomicrograph of a section of liver from group II (the affected group) showing strong expression of tissue inhibitors of matrix metalloproteases-1 (TIMP-1) in the hepatocyte cytoplasm (double arrowheads).

Immunohistochemistry stain for TIMP-1, × 400.

Figure 16.

A photomicrograph of a section of liver from group III (the intravenous stem cell group) showing matrix metalloproteinase-13 (MMP-13) expression in the hepatocyte cytoplasm (arrowhead).

Immunohistochemistry stain for MMP-13, × 400.

Figure 17.

A photomicrograph of a section of liver from group III (the intravenous stem cell group) showing expression of tissue inhibitors of matrix metalloproteases-1 (TIMP-1) in the hepatocyte cytoplasm (double arrowheads).

Immunohistochemistry stain for TIMP-1, × 400.

Figure 18.

A photomicrograph of a section of liver from group IV (the intrahepatic stem cell group) showing strong matrix metalloproteinase-13 (MMP-13) expression in the hepatocyte cytoplasm (arrowhead).

Immunohistochemistry stain for MMP-13, × 400.
Discussion

Liver is a central organ for homeostasis because of its numerous functions. Because it is such an essential organ, diseases related to it are often fatal [20]. Liver fibrosis and cirrhosis result from the majority of chronic liver insults and represent a common and difficult clinical challenge of worldwide importance. The only curative treatment for end-stage cirrhosis is transplantation,
but even in the developed world the number of donor organs available and the clinical condition of the potential recipient limit the applicability of this technique [21].

CCl₄ was used in the present study because it is considered as an experimental model for studying liver necrosis and fibrosis [22]. CCl₄ was given for 10 weeks (continued for 4 weeks after stem cell injection) to avoid the spontaneous reversibility state after cessation of CCl₄ to study the therapeutic effect of stem cells; this agreed with the results of some researchers [23] who reported that liver had a spontaneous reversibility state after cessation of CCl₄.

In the present study, the hepatocytes in the affected group showed ballooning (H&E), accumulation of collagen fibers with bridging between central veins (Sirus red), weak MMP-13 expression, and strong TIMP-1 expression (on immunohistochemistry) 10 weeks after starting administration of CCl₄. This agreed with the results of some authors [24] who reported that these changes in hepatocytes were most frequent and that the most conspicuous changes were seen in liver injury on CCl₄ administration. Others [25] mentioned that centrilobular necrosis of liver cells was found following a single administration of CCl₄ (single dose per week), and slight accumulation of fibers in the necrotic area, as demonstrated by Sirius red, was observed at this time. By the sixth week, the presence of connective tissue became prominent at the necrotic central areas and formed bridging fibrosis between central and portal areas. However, one researcher [26] claimed that hepatocytes showed fatty metamorphosis in rats treated with CCl₄ for 4 weeks (two doses per week), but liver fibrosis was not observed until they were treated for 8 weeks, at which time the liver showed moderate fibrosis. Some scientists [27] demonstrated that differential expression of both MMPs and TIMPs occurs in fibrotic liver disease. The balance between MMPs and TIMPs is the key factor for liver fibrogenesis. In this respect, increased TIMP expression is more critical than MMPs in CCl₄-induced fibrogenesis. Understanding the balance between MMP and TIMP activity may identify the prevention strategies for liver fibrosis. Others [28] reported that, in CCl₄-induced rat liver fibrosis, MMP-13 expression increased during the development of fibrosis but dropped to normal values thereafter, and TIMP-1 expression severely increased compared with control mice.

Cell therapy offers exciting promise for future treatment of liver cirrhosis and metabolic liver diseases. Several types of cells including mature hepatocytes, adult liver progenitor cells, human embryonic stem cells, fetal liver progenitor cells, BM-derived hematopoietic or MSCs, and umbilical cord blood cells have been reported to be capable of self-replication, giving rise to daughter hepatocytes, both in vivo and in vitro [29,30]. MSCs are undifferentiated multipotent stem cells that reside in the BM and in many other adult tissues. These cells can be easily isolated and they possess a high proliferative and differentiated capacity as they are able to differentiate into many cell lineages [31]. Stem cell therapy seems to hold tremendous promise in the treatment of liver cirrhosis [32]. In the present study, BM-MSCs were isolated and expanded in adult rats. The antifibrosis effects of the experimental groups were evaluated by infusion of BM-MSCs by two routes of administration, either intrahepatic or intravenous, to rats with CCl₄. The results showed that MSC treatment through both routes could decrease the ballooning of hepatocytes and reduce fibrosis, as shown by H&E and Sirius red stains. MMP-13 expression was markedly increased in the stem cell group, whereas TIMP-1 expression decreased during the healing process to react with MMP-13. These agreed with the results of some researchers [33] who demonstrated the ability of BM-MSCs to reverse liver fibrosis. MSCs caused a decrease in liver fibrosis 4 weeks after transplantation. The reduction in liver collagen was confirmed by quantitative analysis. Administration of MSCs has a significant antifibrotic effect, as evidenced by the decrease in expression of liver collagen and increase in MMP-13 in the CCl₄/MSC group when compared with the CCl₄ group 4 weeks after transplantation. The expression of TIMP-1 was also downregulated in the CCl₄/MSC group. Others [34] have reported that transplantation of MSCs can strongly alleviate acute or chronic liver injury and reduce fibrosis.

The beneficial effect of MSC therapy described in these previous studies could have a different explanation. MSCs could secrete a wide array of arteriogenic cytokines and contribute to reducing fibrosis through paracrine mechanisms [35]. MSCs may protect against CCl₄ injury by altering the microenvironment of the liver at sites of engraftment [36]. Immune response might play a major role in fibrosis establishment as macrophages and lymphocytes participate in the fibrogenic process. In addition, MSCs possess toll-like receptors that respond to danger signals and drive their migration and immunomodulatory responses [37]. Thus, it is possible that the immunomodulatory properties of MSCs function by regulating the immune response when injury is promoted concurrently with cell transplantation in the liver [38].

In contrast, some authors [39] found that MSCs do not reduce liver fibrosis. Although there was a reduction in fibrosis over time, which is an expected and already described phenomenon of tissue remodeling in the murine injured liver, no difference was found between placebo and cell-treated groups, indicating that MSCs did not participate in this process. Possible explanations are that cells failed to engraft and/or died, as they could not find labeled cells even 2 months after injection.

In the present study, fibrosis reduced in the intrahepatic group (significantly decreased fibrosis compared with the affected group) more than in the intravenous group (insignificantly decreased fibrosis). This agreed with the results of some researchers [40], who demonstrated that the direct delivery of MSCs into the liver resulted in both a higher level of hepatocytes and a more widespread distribution of these hepatocytes throughout the parenchyma compared with intravenous injection. Also, other researchers [41] have reported that intravenous transplantation of MSCs results in no more than a small percentage of donor-derived hepatocytes. It is possible that
in the animal model, MSCs transplanted intravenously do not preferentially migrate to the liver, and this results in fewer cells giving rise to hepatocytes.

**Conclusion**

BM-MSCs can protect against liver fibrosis, and the route of transplantation affects the result. The intrahepatic route is better than the intravenous route in alleviating the hepatic necrosis and fibrosis induced by CCl4.

**Acknowledgements**

Conflicts of interest

There is no conflict of interest to declare.

**References**


تأثير الخلايا الجذعية الميزنشيمية المضادة للفيبروز الكبدى في الفئران

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تأثير الخلايا الجذعية الميزنشيمية المضادة للفيبروز الكبدى في الفئران

تليف الكبد هو عملية مرضية تشمل العديد من الفعاليات الخلوية والجزيئية التي تؤدي في النهاية إلى تورسب البروتينات المصورة الفائضة في الفضاء خارج الخلية. الخلايا الجذعية المستمدة من نخاع العظام للبالغين تتيح فتح جبهة جديدة في الطب والعلاج. هذه الخلايا تستطيع أن تعزز إصلاح سلالات خلوية مختلفة، وتشمل الخلايا مثل الكبدية. يهدف هذا العمل لدراسة تأثير الخلايا الجذعية الميزنشيمية المضادة للفيبروز الكبدى المستحث تجريبياً في الفئران البالغة.

نستخلص من هذه النتائج أن الخلايا الجذعية الميزنشيمية لها الأمل في تقليل تليف الكبد وتمكين الفئران من السفر الممكن دون أي علاج تقليدي.

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