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Markers for the Characterization of Liver Mesenchymal Stem Cell

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Abstract

Mesenchymal stem cells (MSCs) show promise for use in regenerative medicine and tissue engineering. Bone marrow mesenchymal stem cells (BMSCs) are considered to be the standard, but MSCs can be isolated from many sources. Liver mesenchymal stem cells (LMSCs) are a promising alternative to BMSCs. One challenge in MSC research is immunophenotypic characterization of the cells, since there is no specific marker for MSCs to date; in addition, markers may differ among sources and among species. In this review, we will discuss the markers that have been tested on LMSCs from different species.

Keywords: Liver; Mesenchymal Stem Cells; Characterization; Bone Marrow; Human; Animals

Introduction

Mesenchymal stem cells (MSCs) have the characteristics of self-renewal, immune regulation and multipotency. Due to their multi-lineage differentiation potential [1], MSCs can be induced to differentiate into adipocytes, osteoblasts, chondrocytes, muscle cells, nerve cells, liver cells and pancreatic beta cells *in vivo* and *in vitro*. These characteristics make MSCs promising candidates for use in cell therapy and regenerative medicine [2-4]. MSCs were first described as stromal stem cells from the bone marrow that have a spindle shape in culture. However, although the bone marrow is considered the standard source for MSCs, MSCs isolated from other sources have different features in terms of surface markers, proliferation rates, and differentiation capability [5-7]. MSCs have been isolated from a number of other sources, such as adipose tissue, dental pulp, umbilical cord blood, and amniotic fluid [8-10]. One alternative source for MSCs is liver tissue. Scientists have isolated liver mesenchymal stem cells (LMSCs) from different species and attempted to characterize them in hopes that these cells could be a better alternative to bone marrow mesenchymal stem cells (BMSCs), especially for liver diseases [8]. One of the challenging aspects concerning MSCs in general is their characterization. In this mini-review, we will focus on studies that characterized LMSCs from different species, such as humans, mice, rats, rabbits, sheep, chickens and cattle.

Human LMSCs and human BMSCs

The International Society of Cell Therapy (ISCT) states that cultured human BMSCs are positive for expression of CD105, CD73, and CD90 and negative for expression of CD11b or CD14, CD19 or CD79a, CD34, CD45, and HLA-DR (11). CD105 is TGF-beta receptor III, which plays a role in TGF-beta signalling during differentiation into chondrocytes [12]. CD73 is known to be involved in MSC migration and to modulate adaptive immunity [13,14].

CD90 plays roles in mediating cell-cell interactions and leukocyte adhesion to endothelial cells [15,16]. Human LMSCs are also positive for expression of CD105, CD73 and CD90 Table 1. However, Najimi et al. [17] reported that LMSCs have low expression of CD105, and most other studies reported that LMSCs are positive for CD105. Additionally, LMSCs are positive for expression of CD44, CD29, CD166, and CD146, which is consistent with BMSC expression patterns [18-20].

LMSCs and BMSCs from other species

In mice, LMSCs and BMSCs have nearly identical markers since both cell types are positive for CD44, CD29 CD105, CD49e, CD90 and Sca-1. However, mouse LMSCs are positive for CD73 [21], and mouse BMSCs have low expression of CD73 [22]. In rats, there are no studies on LMSCs; however, Payushina et al. [23] indicated that LMSCs are positive for expression of CD90.

Jones et al. [24] reported that bovine BMSCs are positive for expression of CD166. In addition, bovine LMSCs are negative for expression of CD166 but positive for expression of CD44, CD29, CD73, CD90, and CD106 [25-43].

Table 1: Surface antigen expression on cultured LMSCs from different species.

Surface Antigen	Human	Mouse	Rat	Rabbit	Chicken	Bovine
CD44	+(27) ++(17) +(28) +(29) ++(30) ++(31) ++(32) +++(33) ++(34) ++(35) ++(36) ++(37)	++(21)	++(38)		+(26)	++(25)
CD71					+(26)	
CD29	++(27) ++(17) + (28) +(29) ++(30) ++(31) ++(32) ++(33) ++(35) ++(36) ++ (37) +(39)	++(21)	++(38)		+(26)	++(25)
CD73	++(17) +(28) ++(29) ++(30) ++(31) ++(32) +++(33) ++(35) ++(36)	++(21)	+(23) ++(38)		+(26)	++(25)
CD49e	+(17)	++(21)				
CD105	- (17) +(30) ++(31) ++(32)	++(21) ++(40)	++(38)			

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	+++(33) ++(35) ++(36) ++(37) ++(41)					
CD14	-(30) +(32) -(33) -(37)	+/-(21)				
CD80		+/-(21)		+(42)		
Ter119		+/-(21)				
CD45	+/-(27) +/-(17) -(30) - (31) +(32) -(33) -(34) -(37) -(39) -(41)	+/-(2) ++(40)				-(25)
CD86		+/-(21)		-(42)		
CD133	+/- (17) -(30)	+(40)				
CD34	+(17) - (28) -(30) -(31) -(32) -(33) -(34) -(37) -(41)	+(40) – (43)			-(26)	-(25)
CD90	++(27) ++(17) +(28) ++(30) ++ (31) ++(32) ++(33) ++(34) ++(35) ++(36) ++(41)	++(40)	++(23) ++(38)			++ (25)

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Sca-1		++(40)				
CG117	-(33)	+(40)				
Thy-1		-(43)				
c-kit		-(43)				
CD106	++(36)		+/-(23)			
HLA Class I	++(17)					
CD13	++(17) +++(33)					
HLA-DR	+/-(17) -(33) -(41)					
CD49b	+(17)					
CD49f	+(17)					
MHC I	+(31)		++(42)			
MHC II	-(31) -(35)		+(42)			
CD26	++ (31) ++(32)					
CD107	+(28)					
CD117	+/- (17) -(28) -(30) -(31) -(32) -(33)					
CD166	++(31) ++(32) ++(34) ++(35) ++(36) ++(37) ++(41)		++(38)			- (25)
CD146	+(30) ++(35) ++(36)					
CD3	-(33)					
CD4	-(33)					
CD38	-(33)					
CD39	-(36)					
CD19	-(33) +(27)					
CD227	++(34)					
CD54	++(36)	++(38)				

Symbols indicate marker expression levels: −: no expression; +/−: <5% expression; +: 5−50% expression, ++: 50−100% expression.

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Conclusion

Many markers have been tested on LMSCs, especially on human and mouse samples, and BMSCs and LMSCs have been reported to share most markers. However, additional studies are required to establish a standard panel of positive/negative markers for LMSCs, and studies are also required for further characterization of LMSCs from other species, especially species that are used as in vivo models for many diseases.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors have no conflicts of interest.

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