

The Anti-Inflammatory Properties of Osteoarthritis-Synovial Membrane Conditioned Media Induced Mesenchymal Stromal Cell Derived Secretome

Tarini V¹; Krishnamurthy G²; Kamarul.T¹

¹Department of Orthopaedic Surgery, Faculty of Medicine, University of Malaya, KL

²Department of Physiology, Faculty of Medicine, University of Malaya, KL

INTRODUCTION:

Mesenchymal stromal cells (MSCs) exert their immunomodulatory effects via their paracrine components, namely secretome. In a naïve state, soluble factors of MSCs-secretome (MSCs-S) plays a role in maintaining tissue homeostasis. The content and composition of MSCs-S can be regulated by pretreatment of MSCs. Studies have shown that induction of MSCs with specific pro-inflammatory factors such as IL-1 β , exerts anti-inflammatory properties necessary for restoration of immune homeostasis in inflammatory condition¹. In our preliminary study, osteoarthritis (OA)-synovial membrane derived conditioned media has been profiled to contain abundance of pro-inflammatory factors. However, if exposure of MSCs to this cocktail of inflammatory factors, influences its secretion of immunomodulatory factor supporting the restoration of synovial joint homeostasis is yet to be explored.

MATERIALS & METHODS:

Human bone marrow derived MSCs (N=7) were cultured and induced by OA-synovial membrane conditioned media. Each MSCs culture had two types of secretome harvested: naïve MSCs-secretome (nMSCs-S) and induced MSCs-secretome (iMSCs-S). All the harvested nMSCs-S and iMSCs-S were pooled into its respective groups and profiled for its protein content using LCMS/MS QTOF. The data were then hierarchically analyzed using PEAKS, DAVID and Cytoscape softwares.

RESULTS:

The finding shows that iMSCs-S contains 54 more differential proteins in comparison to the nMSCs-S. While, both nMSCs-S and iMSCs-S had 17 proteins in common (Figure 1).

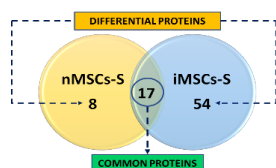


Figure 1: Venn Diagram summarizing the number of proteins identified in nMSCs-S and iMSCs-S.

Differential Proteins of Naïve MSCs-S	Common Proteins	Differential Proteins of Induced MSCs-S		
8	17	54		
ACTN1	ACTB	ABI3BP	HSPA1B	SERPINE2
EEF1A	ACTG1	ALDOA	HSPA1L	SERPINH1
ITIH2	ALB	ANXA2	HSPA2	TF
KRT2	COL1A1	ANXA5	HSPA6	TGFBI
MMP2	COL1A2	BGN	HSPA7	TIMP1
PKM2	EEF1A1	CKB	HSPA8	TUBA1A
PS1TPSBP1	EEF1A1P5	COL3A1	IGHG1	TUBA1B
TTR	EEF1A2	COL6A1	INA	TUBA1C
	FN1	COL6A3	LDHA	TUBB
	KRT1	DCTPP1	LUM	TUBB2C
	KRT10	DPYSL2	NAMPT	TUBB3
	KRT9	ELSPBP1	NEFH	TUBB4A
	PKM	ENO1	NEFL	TUBB4B
	PTX3	FLNA	NEFM	TUBB7
	SPARC	GDI1	PLS3	TUBD1
	THBS1	H4C1	RTN4	VCL
	VIM	HEL-S-17	SERPINA1	VHCH1
		HSPA1A	SERPINE1	WDR1

Figure 2: Shows the list of differential and common proteins identified in nMSCs-S and iMSCs-S.

DISCUSSIONS:

Several differential proteins of iMSCs-S such as, biglycan (BGN), tissue inhibitor of metalloproteinase 1 (TIMP1), tubulin (TUBB) alongside with the common proteins such as actin (ACTB), vimentin (VIM), thrombospondin 1 (THBS1) (Figure 2), could contribute to synthesis of articular cartilage extracellular matrix, cytoskeletal network of articular cartilage chondrocytes and aids in suppressing inflammation, respectively.

CONCLUSION:

In conclusion, MSCs induced by the cocktail of inflammatory factors derived from OA condition does secrete selective differential proteins that could restore synovial joint homeostasis.

REFERENCE(S):

1. Su et al., (2023). *International journal of molecular sciences*, 24(2), 1277.