

Senescence-Driven Inflammatory and Trophic Microenvironment Imprints Mesenchymal Stromal/Stem Cells in Osteoarthritic Patients

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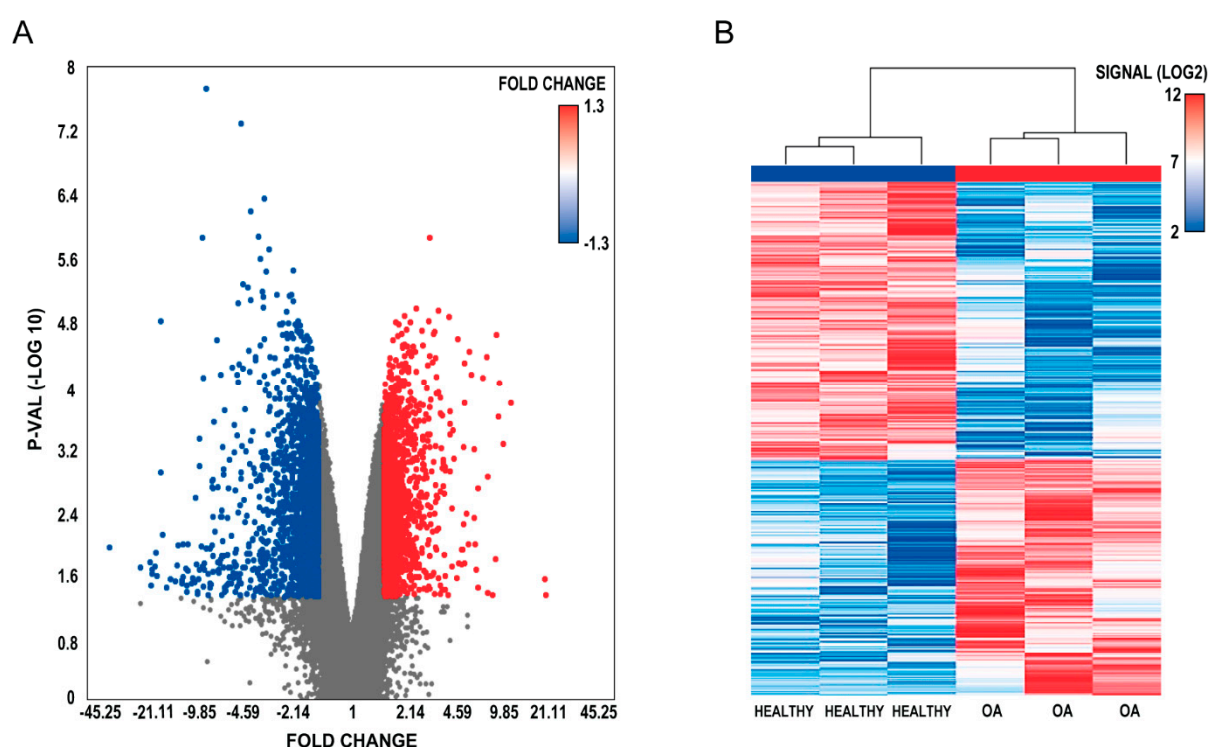


Figure S1. Differential gene expression in MSC from patients with Osteoarthritis (OA) and MSC from healthy donors. (A) Volcano plot for MSC isolated from patients with OA, showing the distribution of significance for all genes. Blue and red dots represent genes with significantly different relative expression (p-value < 0.05 and |Fold Change| > 1.3) compared with healthy

donors. (B) Heatmap showing that MSC isolated from patients with OA and from healthy donors can be differentiated based on the gene expression profile. Heatmap constructed using only significantly differentially genes (p-value < 0.05 and |Fold Change| > 1.3). Blue and red dots represent genes with significant relative expression changes (p-value < 0.05 and |Fold Change| > 1.3) in OA MSC compared with healthy MSC.

Supplementary Table S1. List of common differentially expressed genes between both IFN- γ and TGF β 1 MSC senescent models. (Probes bound to uncharacterized encoding genes were excluded).

Gene Symbol	IFN- γ vs NT		TGF β 1 vs NT	
	Fold Change	p-value	Fold Change	p-value
ROR1	1,7	0,0014	2,17	0,0004
G0S2	1,89	0,0002	1,48	0,0042
LOC100287497; LOC101926980	1,57	0,0082	1,57	0,0091
ERRFI1	2,18	0,0011	1,65	0,016
LOC105376694	1,73	0,0284	1,58	0,0481
FAM129A	1,67	0,0213	1,39	0,0333
AKR1C3	1,32	0,0138	1,34	0,019
ADIRF	2,15	0,0016	2,47	0,0005
AGAP11; BMS1P3; ADIRF	1,4	0,0051	1,37	0,0013
ITGA8	11,49	0,0042	7,81	0,043
ANK3	2,29	0,0002	3,62	0,0001
LRP5	1,7	0,0046	1,33	0,0283
DYNC2H1	1,73	0,0124	1,48	0,025
AHNAK	1,67	0,0082	1,44	0,0121
CD248	1,4	0,015	2,18	0,0308
TXNRD1	1,37	0,0238	1,7	9,68E-05
APPL2	1,99	0,0001	1,52	0,0114
CEMIP	2,22	0,0053	1,78	0,0368
ACAN	8,5	6,34E-05	16,4	0,0028
MNS1	1,72	0,0005	1,5	0,0025
ADAMTS7	2,75	0,0003	1,85	0,002
FBXW10	1,45	0,046	1,49	0,0291
ANKRD20A5P	2,16	0,001	1,76	0,0161
ANKRD20A5P	2,25	0,0037	2,44	0,0424
MIR3975	2,33	0,0113	1,87	0,0014
NOTCH3	2,57	0,0005	1,31	0,0259
SOCS5	1,53	0,0104	1,79	0,002
ARL4C	1,36	0,0271	2,2	0,0076
MCTS2P	1,44	0,0018	1,43	0,0029
COL6A1	1,56	0,0006	1,33	0,0052
PTPRG	2,16	0,0218	1,6	0,0064
CSTA	1,82	0,0005	1,61	0,0016
PDIA5	1,47	0,0199	1,75	0,0009
PTX3	1,58	0,0028	5,33	0,0007
SNAR-I	1,38	0,0408	2,74	0,0083
TBL1XR1	1,31	0,0065	1,31	0,0203
LOC220729	1,39	0,0003	1,54	0,0379
PDE5A	2,11	0,0003	2	0,0011
MARVELD2	1,65	0,0004	1,91	0,0011
MYCT1	1,94	0,0147	2,1	0,0042
SNX9	1,62	0,0077	2,43	0,0004
TUBE1	1,4	0,0287	1,34	0,0232

MTURN	1,32	0,0291	1,4	0,0329
ELN	6,04	2,73E-06	2,04	0,0003
DPYSL2	1,41	0,0109	1,43	0,0069
DEPTOR	3,13	9,10E-07	1,97	3,08E-05
COL14A1	9,09	9,04E-06	3,25	0,0006
PNMA2	1,3	0,0403	1,87	3,64E-05
PABPC1	1,64	0,0098	1,58	0,0008
EIF3E	1,33	0,0318	1,31	0,0293
CNTNAP3B	1,39	0,0198	1,42	0,0216
LOC100287497; LOC101926980	1,77	0,0199	1,98	0,0138
EPHB2	-2,15	0,0003	-1,33	0,032
PALMD	-1,74	0,0006	-1,42	0,0293
ADAMTS4	-1,91	0,0094	-1,47	0,0024
SNORA23	-1,62	0,0413	-2,55	0,0382
MIR3160-2	-1,48	0,0066	-1,33	0,0173
ACP2	-1,4	0,0181	-1,46	0,0117
CHST11	-1,46	0,0051	-1,51	0,0012
FKBP11	-1,39	0,0136	-1,35	0,0079
PCDH9	-1,74	0,0126	-1,61	0,0092
PLEK2	-1,37	0,0217	-1,37	0,0043
FRMD5	-2,14	0,0121	-1,34	0,0443
LCTL	-1,96	0,018	-1,33	0,0073
MT1CP	-1,7	0,014	-1,69	0,0221
HS3ST3A1	-1,31	0,0261	-2,56	0,0006
HOXB2	-1,79	0,0013	-1,37	0,0144
PLK5	-1,31	0,0373	-1,3	0,0081
ZNF175	-1,32	0,0317	-1,37	0,0251
TSEN34	-1,42	0,0022	-1,34	0,0027
ZNF569	-1,35	0,0052	-1,42	0,0292
NRP2	-2,37	6,11E-05	-1,66	0,0072
IGKV1-39; IGKC	-1,37	0,0352	-1,63	0,0314
ANKRD44	-1,55	0,0021	-1,34	0,0161
DOCK10	-4,5	2,84E-05	-2,41	0,0189
TGM2	-1,78	0,0002	-1,69	0,0024
MRAS	-1,31	0,0249	-1,34	0,006
IL12A	-2,68	0,013	-6,64	0,0295
APBB2	-1,62	0,0205	-1,32	0,0154
SMIM3	-1,4	0,0094	-1,36	0,0279
OGFRL1	-1,4	0,0418	-2,25	0,0004
DCBLD1	-2	0,0146	-1,41	0,0075
LIMK1	-1,47	0,0024	-1,58	0,0092
GNG11	-3,38	0,0027	-2,81	0,0057
TCAF2	-1,34	0,042	-1,37	0,0117
SCARA3	-1,67	0,0066	-1,31	0,0266
ZNF703	-1,33	0,0065	-1,42	0,034
SGK223	-1,68	0,0001	-1,56	0,0016
CLU; MIR6843	-3,05	0,0038	-1,75	0,0267
ZNF462	-1,89	3,07E-05	-1,32	0,0302

Supplementary Table S2. Analytical clustering of common regulated genes between OA and in vitro induced-senescence MSC.

	Gene Symbol	Matrisome	Canonical Wnt Pathway (DOWN)	AKT/mTOR Pathway (UP)	Cdc42/ROCK Pathway (UP)	Bcl2 activation	ROS production	References
UP	ADAMTS4	X						(1)
	DOCK10				X			(3), (4)
	GNG11			X	X	X	X	(5)
	HS3ST3A1	X						(6), (7), (8)
	LIMK1				X			(9)
	OGFRL1			X				(10)
	PCDH9	X	X		X			(11), (12), (13)
	SCARA3						X	(14)
	ZNF703	X	X	X	X	X	X	(15), (16),(17), (18)
	ACAN	X						(2)
DOWN	ADAMTS7	X						(19)
	ANK3		X					(20)
	ARL4C				X			(21)
	CEMIP	X	X		X			(9), (22)
	DEPTOR			X				(23), (24)
	ELN	X						(2)
	ERRFI1			X				(25)
	G0S2					X		(26), (27), (28)
	ITGA8	X						(29)
	LRP5		X					(30)
	MARVELD2	X						(31)
	MYCT1				X	X		(32), (33)
	PTX3	X						(34)
	ROR1		X					(35)
	TXNRD1		X				X	(36), (37), (38)

OA: Osteoarthritis; MSC: Mesenchymal Stem Cells.

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