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ORIGINAL ARTICLE

Gene Expression Analyses of Human Mesenchymal Stem Cells Cultured in Osteogenic Differentiation Medium for 3, 7, 14 and 21 Days by Genome Focus DNA Microarray and Real-time PCR

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SYNOPSIS

The purpose of this study was to evaluate gene expressions of human mesenchymal stem cells (hMSC) cultured in osteogenic differentiation medium (OM) which contained ascorbic acid, β-glycerophosphate and dexamethasone for 0 (control), 3, 5, 7, 14 and 21 days by 8.5k Genome Focus DNA microarray and real-time PCR. It was confirmed by the DNA microarray analysis that 327 genes of hMSC were significantly up-regulated by culture in OM especially at 14 and 21 days while 156 genes were down-regulated. Up-regulated genes included osteoblast-related genes such as secreted phosphoprotein 1 (osteopontin) gene and hypothetical protein expressed in osteoblast gene, along with angiogenesis-related genes and cell cycle arrest-related genes, while down-regulated genes contained stroma-related genes and keratin-related genes. Expressions of several osteogenic differentiation marker genes such as (down-regulated) osteonectin gene and (up-regulated) BMP2 gene were also evaluated by real-time PCR. Gene expression database identified here might contribute to dental tissue engineering.

***Key words**: Mesenchymal stem cells, Osteogenic differentiation medium, Gene expression, DNA microarray, Real-time PCR*

INTRODUCTION

In dental tissue engineering therapy, culture of mesenchymal stem cells (MSC) collected from iliac-crest-derived bone marrow is regarded as one important clinical technique[1] because MSC can be multiplied, seeded in bio-absorbable scaffold materials and differentiated into osteoblasts[2,3]. Osseous defects could be restored using the *ex vivo* formed complex of scaffold and osteoblasts[4].

Osteogenic differentiation of stem cells and osteoblastic cells has often been inducted by osteogenic differentiation medium (OM), namely, α-minimum essential medium supplemented with ascorbic acid, Na β-glycerophosphate and dexamethasone[5,6]. As for gene expression by stimulation of OM, several osteogenic differentiation marker genes such as osteopontin and bone sialo protein were examined by RT-PCR or

Table 1 Expression levels of 23 osteogenesis related genes and GAPDH (GAPD) gene of hMSC cultured in exclusive medium (day = 0) and in OM for 3, 7, 14 and 21 days.

Gene ID	Gene Identifier	Gene Title	Gene Expression levels					fold-change (21 days/ 0 day)
			0 day	3 days	7 days	14 days	21 days	
AHSG	NM_001622	Alpha-2-HS-glycoprotein	0.006	0.007	0.038	0.009	0.103	18.66
CALCR	NM_001742	Calcitonin receptor	0.002	0.003	0.007	0.004	0.035	17.50
SPP1	M83248	Secreted phosphoprotein 1 (osteopontin, bone sialoprotein I, early T-lymphocyte activation 1)	0.097	0.078	0.255	1.011	0.984	10.11
STATH	NM_003154	Statherin	0.001	0.002	0.025	0.032	0.008	9.42
AMELY	NM_001143	Amelogenin (Y chromosome)	0.005	0.026	0.013	0.008	0.036	7.36
IBSP	NM_004967	Integrin-binding sialoprotein (bone sialoprotein, bone sialoprotein II)	0.011	0.058	0.068	0.051	0.072	6.68
DMP1	NM_004407	Dentin matrix acidic phosphoprotein	0.001	0.014	0.020	0.026	0.004	4.31
HTN1	NM_002159	Histatin 1	0.021	0.018	0.036	0.007	0.056	2.64
HTN3	NM_000200	Histatin 3	0.002	0.022	0.010	0.002	0.004	1.84
ALPL	X14174	Alkaline phosphatase, liver/bone/kidney	0.104	0.694	0.672	0.460	0.188	1.80
AMBN	NM_016519	Ameloblastin, enamel matrix protein	0.021	0.018	0.029	0.016	0.036	1.68
-	NM_000711	Bone gamma-carboxyglutamate (gla) protein (osteocalcin)	0.187	0.189	0.187	0.218	0.254	1.36
TFIP11	AI220627	qg01a03.x1 Soares_placenta_8to9weeks_2NbHP8to9W Homo sapiens cDNA clone IMAGE:1758220 3', mRNA sequence.	0.413	0.356	0.379	0.417	0.558	1.35
MINPP1	AF084943	Multiple inositol polyphosphate histidine phosphatase, 1	0.252	0.283	0.290	0.351	0.323	1.28
AMELX	NM_001142	Amelogenin (X chromosome, amelogenesis imperfecta 1)	0.037	0.051	0.055	0.039	0.042	1.15
-	AF094508		0.046	0.031	0.082	0.039	0.047	1.02
RUNX2	L40992	Runt-related transcription factor 2	0.067	0.108	0.071	0.112	0.064	0.95
CASR	U20760	Calcium-sensing receptor (hypocalciuric hypercalcemia 1, severe neonatal hyperparathyroidism)	0.045	0.008	0.023	0.058	0.024	0.53
OSTF1	NM_012383	Osteoclast stimulating factor 1	0.792	0.755	0.658	0.491	0.407	0.51
SPARC	NM_003118	Secreted protein, acidic, cysteine-rich (osteonectin)	12.26	13.11	9.92	7.77	6.13	0.50
CDH11	NM_001797	Cadherin 11, type 2, OB-cadherin (osteoblast)	4.19	3.22	3.72	5.17	1.97	0.47
PHEX	U87284	Phosphate regulating gene with homologies to endopeptidases on the X chromosome (hypophosphatemia, vitamin D resistant rickets)	0.079	0.037	0.095	0.109	0.032	0.40
TUFT1	NM_020127	Tuftelin 1	0.525	0.523	0.258	0.110	0.183	0.35
GAPD	M33197	glyceraldehyde-3-phosphate dehydrogenase (EC 1.2.1.12); Human glyceraldehyde-3-phosphate dehydrogenase (GAPDH) mRNA, complete cds.	35.74	30.6	29.0	31.1	30.9	0.86

real-time PCR[7,8]. Genome-wide gene expressions were also studied by means of DNA microarray technology by two research groups[9,10]. The effect of OM on gene expressions of MSC has still not been, however, fully clarified, yet.

We have already reported gene expressions of human mesenchymal stem cells (hMSC) cultured in OM for 14 days, and identified several useful marker genes to characterize osteogenic differentiation[11]. The osteogenic differentiation of hMSC is, however, highly time-dependent[7-10]. It appeared necessary to examine expressions of these cells in OM cultured for different period.

The purpose of this study was, therefore, to examine gene expressions of hMSC cultured in OM by 8.5k Genome Focus DNA microarray for 0 (control), 3, 7, 14 and 21 days. Furthermore, the expressions of several osteogenic differentiation-related genes were evaluated and confirmed by real-time PCR.

MATERIALS AND METHODS

hMSC (PT-2501, Takara, Tokyo, Japan) (cell passage number = 5) were cultured in six polystyrene dishes 125mm in diameter (168351, Nunc, Rochester, NY, U.S.A.) with 20 mL exclusive α-minimum essential medium supplemented with 10% exclusive mesenchymal cell growth supplement (serum portion, PT-4106, Takara, Tokyo, Japan) and 1% penicillin/streptomycin (PT-3238, Takara, Tokyo, Japan) in a 5% CO_2 incubator at 37℃. At sub-confluence, the cells (about 10^7 cells) were collected from one dish by a plastic cell scraper (as a control, date = 0 day) following twice cell wash with PBS (-) solution. The cells on five dishes were further cultured with fresh OM consisting of control medium and three additives such as 50 μg /mL L (+) ascorbic acid (012-04802, Wako Chemical, Osaka, Japan), 10mM Na β-glycerophosphate (Sigma Chemical, St. Louis, MO, U.S.A.) and 10^{-8} M dexamethasone (Sigma Chemical, St. Louis, MO, U.S.A.). After 3, 7, 14 and 21 days culture with OM, the cells were collected by a cell scraper following twice cell wash with PBS (-) solution. For the entire cell cultures, the medium exchange was conducted every three days.

Total RNAs (at least 10 μg) were extracted from the cells using TRIZOL reagent (Invitrogen, Carlsbad, CA, U.S.A.). Genomic DNA was removed by DNase treatment (DNase I, 2215A, Takara, Tokyo, Japan). A company (Kurabo, Osaka, Japan) conducted DNA microarray analyses; namely, reverse transcription, labeling, microarray hybridization, scanning and raw data analyses using a software (GeneSpring, GX, Agilent Technologies Japan, Tokyo, Japan). For the hybridization, six human 8.5k Genome Focus GeneChips (Affymetrix, Santa Clara, U.S.A.) were used. The expressions of genes in the time course and in categories of biological functions were further analyzed by a web-based DNA microarray data analysis system (Genesifter Net, VizXlabs, Seattle, WA, U.S.A.).

Real-time PCR analyses were performed to quantitatively identify the amounts (copy numbers) of GAPDH, collagen 1A1 (type I collagen, α 1), osteonectin (SPARC), osteopontin, osteocalcin and BMP2 mRNAs of hMSC cultured in exclusive control medium (day 0) and OM for 3, 5, 7, 14 and 21 days, using a machine (Light Cycler, Roche Diagnostics, Tokyo, Japan) and primer/probe sets (410964 for GAPDH mRNA, 4651456 for collagen 1A1 mRNA, 4410688 for osteonectin mRNA, 4410530 for ostepontin mRNA, 4410521 for osteocalcin mRNA and 4391594 for BMP2 mRNA; Nippon Gene Research Lab., Sendai, Miyagi, Japan) mixed with FastStart DNA master hybridization probes (3 003 248, Light Cycler, Roche Diagnostics, Tokyo, Japan). The thermal heating (denature, amplification and cool) conditions followed the instructions of each primer/probe sets.

RESULTS

Table 1 shows expression levels of 23 osteogenesis-related genes and GAPDH (GAPD) gene of hMSC cultured in exclusive medium (day = 0) and in OM for 3, 7, 14 and 21 days. Well-known osteogenic differentiation-related genes such as alkaline phosphatase (ALPL) and osteonectin (SPARC) are included. The most right column expresses the fold change defined by the gene expression level at 21 days divided by that at 0 day. Early-stage osteogenic differentiation marker genes such as ALPL and SPARC displayed the highest expression at 7 days, followed by gradual decline at 14 and 21 days.

The medium-stage osteogenic differentiation gene such as secreted phosphoprotein 1 (osteopontin) (SPP1) exhibited the highest expression at 14 days while the last-stage osteogenic differentiation marker gene such as bone gamma-carboxyglutamate (gla) protein (osteocalcin) showed the highest expression at 21 days. With the addition of the culture period in OM, the expression of osteoclast stimulating factor 1 (OSTF1) and Tuftelin 1 (TUFT1) declined. The expressions of other genes were quite low, or altering.

We also found 327 genes of hMSC whose expressions were significantly up-regulated by OM especially at 14 and 21 days (Table 2). Although many genes are listed, it was noted that OM caused hMSC to up-regulate (1) osteoblast-related genes such as secreted phosphoprotein (osteopontin) (SPP1) gene and hypothetical protein expressed in osteoblast gene (IFI44L); (2) angiogenesis-related genes such as vascular endothelial growth factor B (VEGFB) gene and vascular cell adhesion molecule 1 (VCAM1) gene; and (3) cell cycle arrest genes such as growth arrest-specific 7 gene and cyclin-dependent kinase inhibitor 2A (CDKN2A) gene. Other interesting up-regulated genes included those of phospholipid transfer protein (PLTP), glycoprotein (transmembrane) nmb (GPNMB) and transforming growth factor, beta 1 (TGFB1). On the other hand, we identified 156 genes whose expressions were significantly down-regulated especially at 14 and 21 days (Table 3). it was noticed that OM caused hMSC to down-regulate (1) stromal cell-related genes such as stromal cell-derived factor (CXCL12) gene and bone marrow stromal cell antigen 1 (BST1) gene; and (2) keratin related genes such as keratin 18 (KRT18) gene and keratin associated protein 1.1 (KRTAP1-1) gene; and (3) antioxidant related genes such as NAD(P)H dehydrogenase, quinone 1 (NQO1) gene and catalase (CAT) gene. Other interesting down-regulated genes included those of cartilage linking protein 1 (HPPLN1), adipose specific 2 (C10orf116), hyaluronan synthase 1 (HAS1) and cysteine-rich protein 1 (CRIP1). Many other up-regulated and down-regulated genes are listed in Tables 2 and 3, respectively, but they cannot be systematically related to the osteogenic differentiation in this study.

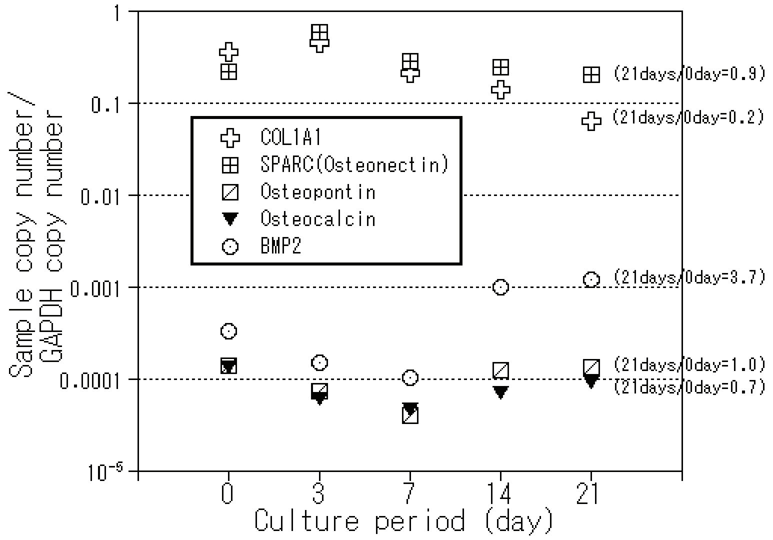

Fig. 1 Real-time PCR analyses results (sample copy number / GAPDH copy number) of five osteogenic differentiation-related genes of hMSC such as COL1A1 (type I collagen alpha 1), SPARC (osteonectin), osteopontin, osteocalcin and BMP2 when cultured in the exclusive medium (day 0) and in osteogenic differentiation medium (OM) for 3, 7, 14 and 21 days.

Fig. 1 shows real-time PCR analyses results (sample copy number / GAPDH copy number) of five osteogenic differentiation-related genes of hMSC such as COL1A1 (type I collagen, α 1), SPARC (osteonectin), osteopontin, osteocalcin and BMP2 when cultured in the exclusive medium (day 0) and in OM for 3, 7, 14 and 21 days. It was pointed out that OM up-regulated BMP 2 gene at 14 and 21 days; little affected osteopontin and osteocalcin genes; and down-regulated COL1A1 and SPARC (osteonectin) genes with increasing the culture period of more than three days. As for osteopontin and osteocalcin genes, expression levels declined from 0 to 7 days in OM, but increased from 7 to 14 days in OM.

DISCUSSION

DNA microarray analyses using GeneChip provides a database from which many researchers can draw new ideas such as pathway analyses[12]. We welcome such approach taken by other investigators. There existed little information concerning genome-wide gene expressions of hMSC when cultured in OM for different period up to 21 days[9,10].

In this study, Genome Focus GeneChip tested the expression levels of about 8.5k (8500) genes but did not cover entire human genes (about 47k[13]). The repetition number of DNA microarray analysis was one at each condition (culture periods = 0, 3, 7, 14 and 21 days, respectively) due to the high cost of DNA microarray analyses conducted by a company. Withal such drawback, we still believe that results obtained here could contribute to dental tissue engineering. There is an opinion that gene expression data by GeneChip is quite reliable even when the test run is once[14], although the test repetition is quite desirable.

hMSC is multi-potent, and can differentiate into several different phenotypes such as osteoblast, chondrocyte and adipocyte, etc[15]. As reported before, OM appeared to cause hMSC to progressively induce osteochondral-ossification with angiogenesis[11]. Therefore, osteoblast-related genes gradually intensified (Table 2) while cartilage, adipose and keratin related genes tended to slowly declined (Table 3). Osteogenic differentiation marker genes sequentially peaked in the manner that initial-stage osteogenic differentiation marker genes such as alkaline phosphatase and osteonectin genes first peaked, followed by middle-stage osteogenic differentiation marker gene such as osteopontin gene, while last-stage osteogenic differentiation marker gene such as osteocalcin peaked last[7,8] (Table 1).

It appears that dentin matrix acidic phosphoprotein (DMP1) gene[16] can be used as another osteogenic differentiation marker, which peaked at 14 days in OM culture (Table 1). In this study, its expression level is too low to make a conclusive statement, and research to verify this assumption is highly expected. Another new potential osteogenic differentiation marker gene was hypothetical protein expressed in osteoblast gene (IFI44L)[17], which peaked at 14 days in OM with moderate signal intensities (Table 2). Research to confirm this idea is also highly probable.

Real-time PCR analyses (Fig. 1) further demonstrated that BMP2 gene[18] could be an additional osteogenic differentiation marker gene. BMP2 gene was unfortunately contained in Genome Focus DNA microarray. Real-time PCR analyses (Fig. 1) succeeded in confirming the down-regulation of SPARC (osteonectin) of hMSC by OM, but failed in proving the up-regulation of osteopontin and osteocalcin genes of hMSC by OM. We plan to conduct DNA microarray analyses of hMSC in OM using complete human gene-labeled GeneChips; and to repeat real-time PCR analyses, especially those of osteopontin and osteocalcin genes whose signals were too low in this study (Fig. 1). Larger sample (total RNA) amount might be helpful for next real-time PCR analyses.

Table 2 Expression levels of 327 up-regulated genes of hMSC cultured in exclusive medium (day = 0) and in OM for 3, 7, 14 and 21 days.

Gene ID	Gene Identifier	Gene Title	Gene expression levels				
			0 day	3 days	7 days	14 days	21 days
SPP1	M83248	Secreted phosphoprotein 1 (osteopontin, bone sialoprotein I, early T-lymphocyte activation 1)	0.1	0.08	0.25	1.01	0.98
PLTP	NM_006227	Phospholipid transfer protein	0.15	0.16	0.23	1.4	1.34
PPL	NM_002705	Periplakin	0.05	0.11	0.21	1.28	1.21
SEPP1	NM_005410	Selenoprotein P, plasma, 1	0.05	0.25	0.38	1.73	1.56
SIAT9	NM_003896	Sialyltransferase 9 (CMP-NeuAc:lactosylceramide alpha-2,3-sialyltransferase; GM3 synthase)	0.44	0.34	0.63	1.99	2.1
WISP2	NM_003881	WNT1 inducible signaling pathway protein 2	0.15	0.21	0.61	3.46	2.7
ARHI	AK021882	Ras homolog gene family, member I	0.07	0.04	0.16	0.39	0.46
IFITM1	AA749101	ny11d02.s1 NCI_CGAP_GCB1 Homo sapiens cDNA clone IMAGE:1271427 3' similar to gb:J04164 INTERFERON-INDUCIBLE PROTEIN 9-27 (HUMAN);, mRNA sequence.	1.65	2.93	3.53	11.01	11.26
-	NM_005890	Growth arrest-specific 7	0.07	0.05	0.12	0.31	0.35
PDGFRL	NM_006207	Platelet-derived growth factor receptor-like	0.04	0.04	0.06	0.17	0.2
SFRP4	AW089415	xd05c09.x1 NCI_CGAP_Brn35 Homo sapiens cDNA clone IMAGE:2592880 3', mRNA sequence.	0.26	0.19	0.22	1.1	1.33
MX2	NM_002463	Myxovirus (influenza) resistance 2, homolog of murine	0.09	0.13	0.21	0.78	0.59
RARRES2	BC000069	Retinoic acid receptor responder (tazarotene induced) 2	0.06	0.07	0.07	0.52	0.63
ARHGEF3	NM_019555	Rho guanine nucleotide exchange factor (GEF) 3	0.14	0.15	0.3	0.71	0.76
IFIH1	NM_022168	Melanoma differentiation associated protein-5	0.01	0.03	0.08	0.21	0.17
MMP11	NM_005940	Matrix metalloproteinase 11 (stromelysin 3)	0.1	0.14	0.11	0.88	0.68
APOD	NM_001647	Apolipoprotein D	0.07	0.03	0.26	5.22	5.42
PCSK1	NM_000439	Proprotein convertase subtilisin/kexin type 1	0	0.03	0.01	0.36	0.35
IFI44L	NM_006820	Hypothetical protein, expressed in osteoblast	0.02	0.04	0.18	0.82	0.57
DSPG3	NM_004950	Dermatan sulphate proteoglycan 3	0	0.01	0.04	0.09	0.07
NACA	AI992187	wt75f11.x1 Soares_thymus_NHFTh Homo sapiens cDNA clone IMAGE:2513325 3' similar to TR:Q13765 Q13765 NASCENT POLYPEPTIDE ASSOCIATED COMPLEX ALPHA SUBUNIT. ;, mRNA sequence.	0.04	0.01	0.05	0.13	0.18
TSGA10	NM_025244	Testis specific, 10	0.01	0.01	0.01	0.05	0.07
PRKY	NM_002760	Protein kinase, Y-linked	0.02	0.02	0.05	0.09	0.09
IFI27	NM_005532	Interferon, alpha-inducible protein 27	0.02	0.09	0.09	0.35	0.26
PLEKHA4	NM_020904	Pleckstrin homology domain-containing, family A (phosphoinositide binding specific) member 4	0.04	0.04	0.03	0.21	0.28
SPON2	NM_012445	Spondin 2, extracellular matrix protein	0.27	0.48	0.78	1.64	1.86
MX1	NM_002462	Myxovirus (influenza) resistance 1, homolog of murine (interferon-inducible protein p78)	0.07	0.06	0.32	2.16	1.42
HERC5	NM_016323	Cyclin-E binding protein 1	0.01	0	0.01	0.11	0.14
GPNMB	NM_002510	Glycoprotein (transmembrane) nmb	1.63	4.02	7.57	14.66	15.86
PTGDS	NM_000954	Prostaglandin D2 synthase (21kD, brain)	0.99	2.08	2.46	6.02	6.21
DPP4	NM_001935	Dipeptidylpeptidase IV (CD26, adenosine deaminase complexing protein 2)	0.04	0.09	0.11	0.26	0.34
BMP2	AA583044	nn80f11.s1 NCI_CGAP_Co9 Homo sapiens cDNA clone IMAGE:1090221 3', mRNA sequence.	0.05	0.01	0.01	0.66	0.52
CHI3L1	M80927	Chitinase 3-like 1 (cartilage glycoprotein-39)	2.18	2.73	4.75	13.77	20.49
SERPING1	NM_000062	Serine (or cysteine) proteinase inhibitor, clade G (C1 inhibitor), member 1	0.59	0.87	0.85	3.09	2.37
ZNF137	NM_003438	Zinc finger protein 137 (clone pHZ-30)	0.03	0.01	0.01	0.07	0.07
CA12	NM_001218	Carbonic anhydrase XII	3.26	2.54	3.75	9.54	9.8
SERPINF1	NM_002615	Serine (or cysteine) proteinase inhibitor, clade F (alpha-2 antiplasmin, pigment epithelium derived factor), member 1	1.94	2.45	2.88	7.07	7.84
ATP1B4	NM_012069	ATPase, (Na+)/K+ transporting, beta 4 polypeptide	0.02	0.01	0.01	0.05	0.06
G1P3	NM_022873	Interferon, alpha-inducible protein (clone IFI-6-16)	0.38	0.51	0.61	1.82	1.38
AEBP1	NM_001129	AE-binding protein 1	1.16	1.86	3.33	7.64	11.7
SOX9	NM_000346	SRY (sex determining region Y)-box 9 (campomelic dysplasia, autosomal sex-reversal)	0.47	0.28	0.46	1.21	1.16
BCL6	NM_001706	B-cell CLL/lymphoma 6 (zinc finger protein 51)	0.53	0.62	0.74	2	1.67
AGT	NM_000029	Angiotensinogen (serine (or cysteine) proteinase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 8)	0.06	0.07	0.05	0.19	0.21
SIAT1	AI743792	wg53h11.x1 Soares_NSF_F8_9W_OT_PA_P_S1 Homo sapiens cDNA clone IMAGE:2368869 3', mRNA sequence.	0.09	0.1	0.13	0.33	0.28
DUSP6	BC003143	Dual specificity phosphatase 6	0.17	0.12	0.28	0.56	0.51
CDKL3	NM_016508	Cyclin-dependent kinase-like 3	0.06	0.08	0.09	0.21	0.24
CALB2	NM_001740	Calbindin 2, (29kD, calretinin)	0.04	0.07	0.2	0.42	0.68
SSPN	AL136756	Sarcospan (Kras oncogene-associated gene)	0.03	0.05	0.1	0.17	0.25
TNFSF4	NM_003326	Tumor necrosis factor (ligand) superfamily, member 4 (tax-transcriptionally activated glycoprotein 1, 34kD)	0.04	0.04	0.07	0.15	0.13
APOE	NM_000041	Apolipoprotein E	0.02	0.21	0.34	0.6	0.78
-	AL138717		0.01	0.02	0.04	0.07	0.1
DBC1	NM_014618	Deleted in bladder cancer chromosome region candidate 1	0.21	0.3	0.4	0.83	1.22
BACH2	NM_021813	BTB and CNC homology 1, basic leucine zipper transcription factor 2	0.04	0.06	0.06	0.14	0.14
CTSK	NM_000396	Cathepsin K (pycnodysostosis)	2.03	4.96	10.5	17.96	16.5
CTSF	NM_003793	Cathepsin F	0.17	0.23	0.3	0.59	0.74
SE57-1	NM_025214	CTCL tumor antigen se57-1	0.02	0.08	0.04	0.18	0.25
SEMA5A	NM_003966	Sema domain, seven thrombospondin repeats (type 1 and type 1-like), transmembrane domain (TM) and short cytoplasmic domain, (semaphorin) 5A	0.45	0.26	0.55	1.17	1.78
COL15A1	NM_001855	Collagen, type XV, alpha 1	0.08	0.02	0.19	0.33	0.53
NBL1	D28124	Human mRNA for unknown product, complete cds.	2.11	1.56	1.77	4.95	6.89
SRPX	NM_006307	Sushi-repeat-containing protein, X chromosome	1.19	1.88	2.94	5.22	7.58
IFIT3	NM_001549	Interferon-induced protein with tetratricopeptide repeats 4	0.15	0.18	0.3	1.15	0.65
TNFRSF1B	NM_001066	Tumor necrosis factor receptor superfamily, member 1B	0.05	0.09	0.15	0.33	0.24
FOXO1A	NM_002015	Forkhead box O1A (rhabdomyosarcoma)	0.1	0.07	0.08	0.23	0.34
G1P2	NM_005101	Interferon-stimulated protein, 15 kDa	0.95	1.5	1.79	5.49	3.56
C10orf10	AL136653	Decidual protein induced by progesterone	0.54	0.8	0.85	2.39	1.77
COMP	NM_000095	Cartilage oligomeric matrix protein (pseudoachondroplasia, epiphyseal dysplasia 1, multiple)	2	0.89	2.86	14.65	7.89
TNFRSF10B	AF016266	Tumor necrosis factor receptor superfamily, member 10b	0.51	0.46	0.68	1.37	1.4
IGSF4	NM_014333	Immunoglobulin superfamily, member 4	0.16	0.17	0.23	1.29	2.21
CDKN2A	NM_000077	Cyclin-dependent kinase inhibitor 2A (melanoma, p16, inhibits CDK4)	0.24	0.25	0.47	0.95	1.61
DKK2	NM_014421	Dickkopf (Xenopus laevis) homolog 2	0	0.03	0.04	0.07	0.07
IRF7	NM_004030	Interferon regulatory factor 7	0.16	0.25	0.18	0.6	0.52
RAB31	BE789881	601476750F1 NIH_MGC_68 Homo sapiens cDNA clone IMAGE:3879493 5', mRNA sequence.	1.51	1.37	1.52	3.56	4.25
BDKRB2	NM_000623	Bradykinin receptor B2	0.2	0.1	0.21	0.43	0.46
-	AF063612	2'-5'-oligoadenylate synthetase-like	0.09	0.1	0.11	0.29	0.23
AKR1C1	NM_001353	Aldo-keto reductase family 1, member C1 (dihydrodiol dehydrogenase 1; 20-alpha (3-alpha)-hydroxysteroid dehydrogenase)	1.3	1.41	3.1	11.15	5.92
-	NM_019847	Ankylosis, progressive (mouse) homolog	0.04	0.01	0.14	0.2	0.19
-	AA576961	nm82d08.s1 NCI_CGAP_Co9 Homo sapiens cDNA clone IMAGE:1074735 3', mRNA sequence.	0.84	0.56	1.47	2.65	2.22
ADA	NM_000022	Adenosine deaminase	0.2	0.21	0.34	0.66	0.59
PDGFRB	NM_002609	Platelet-derived growth factor receptor, beta polypeptide	1.51	1.52	2.17	4.03	4.62
SLC16A6	NM_004694	Solute carrier family 16 (monocarboxylic acid transporters), member 6	0.01	0.01	0.04	0.58	0.32
ARL7	NM_005737	ADP-ribosylation factor-like 7	1.57	1.67	1.55	4.1	4.05
TM7SF1	NM_003272	Transmembrane 7 superfamily member 1 (upregulated in	0.3	0.4	0.52	1	0.98

Gene ID	Gene Identifier	Gene Title	Gene expression levels				
			0 day	3 days	7 days	14 days	21 days
NR1D1	X72631	Homo sapiens mRNA for Rev-ErbAalpha protein (hRev gene).	0.45	0.28	0.38	0.93	0.95
NPC1	NM_000271	Niemann-Pick disease, type C1	0.81	1.76	3.35	4.78	6.49
PELI2	NM_021255	Pellino (Drosophila) homolog 2	0.01	0.05	0.05	0.18	0.1
PTPRE	AA775177	ac79a06.s1 Stratagene lung (#937210) Homo sapiens cDNA clone IMAGE:868786 3', mRNA sequence.	0.1	0.16	0.22	0.37	0.42
AKR1C2	U05598	Aldo-keto reductase family 1, member C2 (dihydrodiol dehydrogenase 2; bile acid binding protein; 3-alpha hydroxysteroid dehydrogenase, type III)	0.81	1.03	2.21	10.59	5.28
IL16	NM_004513	Interleukin 16 (lymphocyte chemoattractant factor)	0.12	0.1	0.11	0.29	0.26
PROS1	NM_000313	Protein S (alpha)	0.21	0.49	0.76	1.2	1.28
SAT	NM_002970	Spermidine/spermine N1-acetyltransferase	0.19	0.22	0.31	0.97	0.55
MITF	NM_000248	Microphthalmia-associated transcription factor	0.1	0.11	0.16	0.27	0.35
ROR2	NM_004560	Receptor tyrosine kinase-like orphan receptor 2	0	0.03	0.03	0.12	0.23
GCLC	BF676980	602084207F1 NIH_MGC_83 Homo sapiens cDNA clone IMAGE:4248744 5', mRNA sequence.	0.1	0.2	0.23	0.41	0.48
NINJ1	NM_004148	Ninjurin 1	0.28	0.37	0.3	0.76	0.86
EVC	NM_014556	Ellis van Creveld syndrome	0.15	0.09	0.19	0.33	0.5
HEY1	R61374	yh15e02.s1 Soares infant brain 1NIB Homo sapiens cDNA clone IMAGE:37665 3', mRNA sequence.	0.06	0.06	0.03	0.14	0.14
SNAP25	NM_003081	Synaptosomal-associated protein, 25kD	0.03	0	0.01	0.06	0.08
PLAU	NM_002658	Plasminogen activator, urokinase	0.43	0.5	0.93	1.35	1.71
ENO2	NM_001975	Enolase 2, (gamma, neuronal)	0.43	0.33	0.31	0.96	0.84
EGR2	NM_000399	Early growth response 2 (Krox-20 (Drosophila) homolog)	0.08	0.06	0.21	0.29	0.29
MMP13	NM_002427	Matrix metalloproteinase 13 (collagenase 3)	0.02	0	0.04	0.37	0.66
TGFBR3	NM_003243	Transforming growth factor, beta receptor III (betaglycan, 300kD)	0.16	0.19	0.22	0.42	0.59
SH3BP5	AL562152	AL562152 LTI_NFL003_NBC3 Homo sapiens cDNA clone CS0DC001YK23 3 prime, mRNA sequence.	0.57	0.34	0.48	1.28	1.01
MMP14	Z48481	H.sapiens mRNA for membrane-type matrix metalloproteinase 1.	1.85	2.01	3.59	5.27	6.7
PCSK5	NM_006200	Proprotein convertase subtilisin/kexin type 5	0.04	0.04	0.05	0.13	0.09
F2R	NM_001992	Coagulation factor II (thrombin) receptor	0.09	0.09	0.16	0.3	0.24
CYP27A1	NM_000784	Cytochrome P450, subfamily XXVIIA (steroid 27-hydroxylase, cerebrotendinous xanthomatosis), polypeptide 1	0.1	0.28	0.3	0.54	0.6
COLEC12	NM_030781	Collectin sub-family member 12	0.39	0.19	0.26	0.78	0.65
CDO1	NM_001801	Cysteine dioxygenase, type I	0.11	0.11	0.12	0.29	0.23
SATB1	NM_002971	Special AT-rich sequence binding protein 1 (binds to nuclear matrix/scaffold-associating DNAs)	0.28	0.24	0.38	0.64	0.75
TENS1	NM_022748	Tumor endothelial marker 6	1.24	2.13	2.79	4.39	5.93
MPDZ	NM_003829	Multiple PDZ domain protein	0.21	0.23	0.31	0.53	0.79
EPHA4	NM_004438	EphA4	0.01	0.03	0.11	0.15	0.27
-	X79067	Zinc finger protein 36, C3H type-like 1	0.38	0.4	0.62	1.41	0.92
CHST1	NM_003654	Carbohydrate (keratan sulfate Gal-6) sulfotransferase 1	0.07	0.02	0.07	0.14	0.13
MME	AI433463	ti65g11.x1 NCI_CGAP_Kid11 Homo sapiens cDNA clone IMAGE:2136932 3' similar to gb:J03779 NEPRILYSIN (HUMAN);, mRNA sequence.	0.04	0.41	0.75	1.27	0.98
GOLPH2	NM_016548	Golgi phosphoprotein 2	0.78	0.64	0.66	1.6	1.63
TNFAIP6	NM_007115	Tumor necrosis factor, alpha-induced protein 6	0.1	0.11	0.22	1.35	0.63
SLC6A8	NM_005629	Solute carrier family 6 (neurotransmitter transporter, creatine), member 8	0.24	0.25	0.27	0.56	0.94
MFHAS1	BF739959	7o41e04.x1 NCI_CGAP_Kid11 Homo sapiens cDNA clone IMAGE:3576678 3' similar to contains element TAR1 repetitive element ;, mRNA sequence.	0.17	0.14	0.15	0.35	0.35
DIAPH2	NM_006729	Diaphanous (Drosophila, homolog) 2	0.22	0.29	0.5	0.71	0.82
UPP1	NM_003364	Uridine phosphorylase	0.12	0.34	0.51	1.43	0.75
GAA	NM_000152	Glucosidase, alpha; acid (Pompe disease, glycogen storage disease type II)	0.42	0.51	0.58	1.03	1.32
PTGFR	NM_000959	Prostaglandin F receptor (FP)	0.04	0.08	0.07	0.18	0.33
CA11	AB018195	Carbonic anhydrase XI	0.05	0.07	0.04	0.15	0.13
RERE	AB036737	Arginine-glutamic acid dipeptide (RE) repeats	0.36	0.44	0.64	0.97	1.21
GARP	NM_005512	Glycoprotein A repetitions predominant	0.8	1.12	2.61	3.2	4.45
ZNF331	NM_018555	Zinc finger protein 331; zinc finger protein 463	0.2	0.16	0.24	0.4	0.48
ASPN	NM_017680	Asporin (LRR class 1)	0.03	0.08	0.2	0.37	0.23
ZNF318	NM_014345	Endocrine regulator	0.13	0.25	0.22	0.43	0.51
LILRA1	NM_006863	Leukocyte immunoglobulin-like receptor, subfamily A (with TM domain), member 1	0.03	0	0.01	0.04	0.05
KCND2	NM_012281	Potassium voltage-gated channel, Shal-related subfamily, member 2	0.02	0.01	0.04	0.05	0.06
KYNU	NM_003937	Kynureninase (L-kynurenine hydrolase)	0.08	0.03	0.05	0.13	0.15
IDUA	NM_000203	Iduronidase, alpha-L-	0.23	0.25	0.31	0.52	0.8
CELSR3	AB011536	seven-times-transmembrane protein containing multiple cadherin and EGF-like motifs; Homo sapiens mRNA for MEGF2, partial cds.	0.06	0.03	0.05	0.1	0.11
FCGRT	NM_004107	Fc fragment of IgG, receptor, transporter, alpha	0.26	0.32	0.62	0.8	1.01
WIG1	NM_022470	P53 target zinc finger protein	0.71	0.6	0.97	1.5	2.55
OAS2	NM_016817	2'-5'-oligoadenylate synthetase 2 (69-71 kD)	0.11	0.13	0.23	0.45	0.29
DDB2	NM_000107	Damage-specific DNA binding protein 2 (48kD)	0.43	0.56	0.82	1.18	1.5
HECA	NM_016217	HHDC for homolog of Drosophila headcase	0.41	0.39	0.71	1.2	0.97
HOXA4	NM_002141	Homeo box A4	0.08	0.01	0.09	0.14	0.18
OAS3	NM_006187	2'-5'-oligoadenylate synthetase 3 (100 kD)	0.14	0.2	0.22	0.58	0.36
CDKN1C	N33167	yy35b09.s1 Soares melanocyte 2NbHM Homo sapiens cDNA clone IMAGE:273209 3', mRNA sequence.	0.09	0.1	0.06	0.46	0.22
AQP1	AL518391	AL518391 LTI_NFL011_NBC1 Homo sapiens cDNA clone CS0DA009YJ21 3 prime, mRNA sequence.	0.02	0.03	0.09	0.14	0.09
HIST1H2BK	BC000893	H2B histone family, member A	0.86	1.3	1.28	2.62	2.34
RELB	NM_006509	V-rel avian reticuloendotheliosis viral oncogene homolog B (nuclear factor of kappa light polypeptide gene enhancer in B-cells 3)	0.13	0.12	0.16	0.27	0.33
ANGPTL4	NM_016109	Angiopoietin-like 4	0.11	0.17	0.2	1.25	0.55
HSPA4L	NM_014278	Heat shock protein (hsp110 family)	0.03	0.06	0.18	0.24	0.2
ADFP	BC005127	Adipose differentiation-related protein	1.65	2.15	2.07	7.44	3.88
EVI2A	NM_014210	Ecotropic viral integration site 2A	0.16	0.28	0.53	0.93	0.61
CUGBP2	U69546	CUG triplet repeat, RNA-binding protein 2	0.06	0.21	0.29	0.38	0.49
SRPX2	NM_014467	Sushi-repeat protein	0.44	0.78	1.07	1.65	1.56
SFRP1	NM_003012	Secreted frizzled-related protein 1	0.06	0.12	0.16	0.23	0.44
HK2	AI761561	wi61h11.x1 NCI_CGAP_Co16 Homo sapiens cDNA clone IMAGE:2394789 3', mRNA sequence.	0.51	0.28	0.26	1.05	0.73
DRD5	NM_000798	Dopamine receptor D5	0.07	0.05	0.11	0.14	0.17
MARCKSL1	NM_023009	Macrophage myristoylated alanine-rich C kinase substrate	0.74	0.48	0.34	1.98	1.13
SERPINI1	NM_005025	Serine (or cysteine) proteinase inhibitor, clade I (neuroserpin), member 1	0.27	0.18	0.16	0.44	0.49
MMP1	NM_002421	Matrix metalloproteinase 1 (interstitial collagenase)	0.03	0.07	0.04	0.68	0.31
SOX4	NM_003107	SRY (sex determining region Y)-box 4	1.7	1.05	0.67	4.04	2.52
USP20	NM_006676	Ubiquitin specific protease 20	0.09	0.02	0.16	0.2	0.22
INSR	AA485908	ab38g07.s1 Stratagene HeLa cell s3 937216 Homo sapiens cDNA clone IMAGE:843132 3' similar to gb:A18658 INSULIN RECEPTOR PRECURSOR (HUMAN);, mRNA sequence.	0.1	0.07	0.07	0.17	0.31
IFI16	NM_005531	Interferon, gamma-inducible protein 16	1.09	1.16	1.44	2.59	2.36
HES1	NM_005524	Hairy (Drosophila)-homolog	0.13	0.08	0.16	0.3	0.22
LAMB1	NM_002291	Laminin, beta 1	1.12	0.96	1.32	2.04	2.87

Gene ID	Gene Identifier	Gene Title	Gene expression levels				
			0 day	3 days	7 days	14 days	21 days
-	BE327172	hw08a05.x1 NCI_CGAP_Lu24 Homo sapiens cDNAclone IMAGE:3182288 3' similarto contains element MSR1 repetitive element ;, mRNAsequence.	0.1	0.07	0.07	0.2	0.16
FGFR1	M60485	Fibroblast growth factor receptor 1 (fms-related tyrosine kinase 2, Pfeiffer syndrome)	1.35	1.55	1.63	2.78	4.55
MAFB	NM_005461	V-maf musculoaponeurotic fibrosarcoma oncogene homolog B (avian)	0.23	0.44	0.2	2.32	1.04
PTGIS	NM_000961	Prostaglandin I2 (prostacyclin) synthase	0.78	0.81	1.16	1.68	3.05
LUM	NM_002345	Lumican	1.86	2.09	2.76	4.98	4.02
WWTR1	AA081084	zn32h12.s1 Stratagene endothelial cell 937223 Homo sapiens cDNAclone IMAGE:549191 3', mRNAsequence.	1.47	1.1	1.53	2.59	2.98
TGFB1	BC000125	Transforming growth factor, beta 1	2.3	1.78	2.25	3.83	5.24
ALAD	BC000977	Aminolevulinate, delta-, dehydratase	0.24	0.2	0.3	0.44	0.62
ZBTB16	NM_006006	Zinc finger protein 145 (Kruppel-like, expressed in promyelocytic leukemia)	0.06	0.09	0.16	0.2	0.37
IRS2	AF073310	Insulin receptor substrate 2	0.39	1.22	0.97	2.09	1.81
MLH3	NM_014381	MutL (E. coli) homolog 3	0.11	0.15	0.09	0.25	0.29
A2M	NM_000014		0.13	0.3	0.21	0.5	0.98
SVIL	NM_003174	Supervillin	0.35	0.32	0.63	0.89	1.89
BACE2	NM_012105	Beta-site APP-cleaving enzyme 2	0.74	1.08	1.55	2.06	2.56
TCF4	NM_003199	Transcription factor 4	0.44	0.35	0.5	0.77	0.98
ZNF142	D87073	similarto Human zinc finger protein(ZNF142); Human mRNA for KIAA0236 gene, complete cds.	0.09	0.08	0.1	0.16	0.23
EPHA3	AF213459	EphA3	0.1	0.03	0.1	0.15	0.21
PMP22	L03203	Peripheral myelin protein 22	3.09	5.51	5.55	8.85	10.73
HLA-E	X56841	Major histocompatibility complex, class I, E	0.83	1.16	1.25	2.17	2.1
COL7A1	NM_000094	Collagen, type VII, alpha 1 (epidermolysis bullosa, dystrophic, dominant and recessive)	0.15	0.08	0.13	0.24	0.25
SEC14L2	NM_012429	SEC14 (S. cerevisiae)-like 2	0.12	0.14	0.15	0.3	0.24
TM4SF6	AF053453	Transmembrane 4 superfamily member 6	0.74	0.88	1.16	2.04	1.62
-	X17013	diaminopimelate decarboxylase (AA 1-327); Bacillus subtilis lys gene for diaminopimelate decarboxylase (EC 4.1.1.20).	0.09	0.1	0.1	0.22	0.48
LY6E	NM_002346	Lymphocyte antigen 6 complex, locus E	1.32	1.02	1.31	2.26	2.6
CD68	NM_001251	CD68 antigen	0.06	0.07	0.07	0.14	0.12
PTPRU	U71075	Protein tyrosine phosphatase, receptortype, U	0.13	0.13	0.15	0.24	0.38
GLI3	NM_000168	GLI-Kruppel family member GLI3 (Greig cephalopolysyndactyly syndrome)	0.37	0.18	0.42	0.58	0.82
CEBPB	AL564683	AL564683 LTI_NFL001_NBC4 Homo sapiens cDNAclone CS0DM007YK12 3 prime, mRNAsequence.	3.72	4.19	4.09	8.87	7.17
-	AW304174	xv61d01.x1 NCI_CGAP_Lu28 Homo sapiens cDNAclone IMAGE:2817601 3', mRNAsequence.	0.06	0.04	0.04	0.09	0.16
LAMA2	NM_000426	Laminin, alpha 2 (merosin, congenital muscular dystrophy)	0.1	0.08	0.09	0.16	0.28
SERPINB9	BC002538	Serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 9	0	0.05	0.05	0.09	0.07
CSDA	AL556190	AL556190 LTI_NFL006_PL2 Homo sapiens cDNAclone CS0DK011YH09 5 prime, mRNAsequence.	1.87	2.02	2.62	3.82	4.81
SESN1	NM_014454	P53 regulated PA26 nuclear protein	0.3	0.29	0.33	0.6	0.6
CTSD	NM_001909	Cathepsin D (lysosomal aspartyl protease)	0.84	1.38	1.6	2.23	3.3
DPT	AI146848	qb92h06.x1 Soares_fetal_heart_NbHH19W Homo sapiens cDNA clone IMAGE:1707611 3' similarto SW:DERM_HUMAN Q07507 DERMATOPONTIN PRECURSOR. ;, mRNAsequence.	0.03	0.07	0.16	0.87	0.34
NFKBIA	AI078167	oz30d08.x1 Soares_total_fetus_Nb2HF8_9w Homo sapiens cDNA clone IMAGE:1676847 3' similarto gb:M69043 MAJOR HISTOCOMPATIBILITY COMPLEX ENHANCER-BINDING PROTEIN (HUMAN);, mRNA sequence.	0.55	0.89	0.8	1.73	1.34
HSD11B1	NM_005525	Hydroxysteroid (11-beta) dehydrogenase 1	0.07	0.04	0.06	0.12	0.26
PBEF1	BF575514	602133090F1 NIH_MGC_81 Homo sapiens cDNAclone IMAGE:4288079 5', mRNAsequence.	0.21	0.14	0.23	0.44	0.33
HS3ST3A1	NM_006042	Heparan sulfate (glucosamine) 3-O-sulfotransferase 3A1	0.11	0.1	0.04	0.23	0.18
-	X98568	H.sapiens type X collagen gene.	0.1	0.21	0.43	1.7	0.67
OPN3	NM_014322	Opsin 3 (encephalopsin, panopsin)	0.09	0.33	0.33	0.71	0.46
GYPC	NM_002101	Glycophorin C (Gerbich blood group)	0.68	0.76	1.25	1.71	1.73
PBXIP1	AI935162	wp14e01.x1 NCI_CGAP_Lu19 Homo sapiens cDNAclone IMAGE:2464824 3', mRNAsequence.	0.36	0.38	0.24	0.66	0.76
ENPP1	NM_006208	Ectonucleotide pyrophosphatase/phosphodiesterase 1	1	0.88	2.31	2.48	3.46
RLF	NM_012421	Rearranged L-myc fusion sequence	0.18	0.15	0.22	0.44	0.3
IRF2	NM_002199	Interferon regulatory factor 2	0.16	0.09	0.09	0.26	0.22
XRCC4	NM_022406	X-ray repair complementing defective repair in Chinese hamster cells 4	0.04	0.02	0.02	0.06	0.07
WHSC2	AF101434	Homo sapiens Wolf-Hirschhorn syndrome candidate 2 protein (WHSC2) mRNA, complete cds.	0.11	0.1	0.15	0.23	0.24
-	AL117536	Popeye protein 3	0.4	0.23	0.33	0.59	0.71
NOX4	NM_016931	NADPH oxidase 4	0.03	0.08	0.07	0.55	0.21
NFAT5	NM_006599	Nuclear factor of activated T-cells 5, tonicity-responsive	0.16	0.1	0.16	0.23	0.36
SFRS16	NM_007056	Suppressor of white apricot homolog 2	0.26	0.27	0.3	0.51	0.55
ZFHX1B	NM_014795	Zinc finger homeobox 1B	0.08	0.06	0.07	0.15	0.13
-	AL353759		0.3	0.24	0.29	0.72	0.44
HEPH	NM_014799	Hephaestin	0.33	0.3	0.33	0.56	0.7
PFTK1	NM_012395	PFTAIRE protein kinase 1	0.48	0.49	0.53	0.86	1.09
FLRT2	NM_013231	Fibronectin leucine rich transmembrane protein 2	0.36	0.36	0.32	0.6	1.01
B3GALT4	AB026730	UDP-Gal:betaGlcNAc beta 1,3-galactosyltransferase, polypeptide 4	0.1	0.04	0.11	0.2	0.15
C1orf24	AF288391	Chromosome 1 open reading frame 24	0.31	0.14	0.3	0.43	0.76
ANK2	BF726212	by03a08.y1 Human Lens cDNA (Un-normalized, unamplified): BY Homo sapiens cDNAclone by03a08 5', mRNAsequence.	0.36	0.28	0.46	0.66	0.73
BAZ2B	NM_013450	Bromodomain adjacent to zinc finger domain, 2B	0.07	0.16	0.13	0.24	0.24
BTG1	NM_001731	B-cell translocation gene 1, anti-proliferative	1.19	1.08	1.19	3.32	1.82
ECGF1	NM_001953	Endothelial cell growth factor 1 (platelet-derived)	0.12	0.14	0.15	0.23	0.31
PTPN2	AI828880	wj37b02.x1 NCI_CGAP_Lu19 Homo sapiens cDNAclone IMAGE:2404971 3' similarto gb:M25393 T-CELL PROTEIN-TYROSINE PHOSPHATASE (HUMAN);, mRNA sequence.	0.4	0.34	0.39	0.65	0.81
SLC7A8	AL365347	Solute carrierfamily 7 (cationic amino acid transporter, y+ system), member 8	0.29	0.21	0.3	0.44	0.67
SPOCK	AF231124	Sparc/osteonectin, cwcv and kazal-like domains proteoglycan (testican)	3.9	2.28	4.37	6.14	7.26
KCNK15	NM_022358	Potassium channel, subfamily K, member 15 (TASK-5)	0.01	0.04	0.07	0.22	0.53
KCNMB4	NM_014505	Potassium large conductance calcium-activated channel, subfamily M, beta member 4	0.06	0.04	0.08	0.1	0.15
CREG1	NM_003851	Cellular repressor of E1A-stimulated genes	1.06	1.07	0.64	1.74	2.25
TERF2	NM_005652	Telomeric repeat binding factor 2	0.56	0.5	0.47	0.94	1.03
GUCY1B3	W93728	zd96a11.s1 Soares_fetal_heart_NbHH19W Homo sapiens cDNA clone IMAGE:357308 3', mRNAsequence.	0.05	0.05	0.11	0.11	0.21
FZD1	NM_003505	Frizzled (Drosophila) homolog 1	0.61	0.58	0.69	1.04	1.39
C1S	M18767	Complement component 1, s subcomponent	2.64	3.25	4.23	7.74	5.28
FBXO9	NM_012347	F-box only protein 9	0.35	0.57	0.66	1.12	0.88
ABR	AL527773	AL527773 LTI_NFL003_NBC3 Homo sapiens cDNAclone CS0DC026YF10 3 prime, mRNAsequence.	0.83	1.1	1.04	1.77	1.94
MAP4K4	NM_004834	Mitogen-activated protein kinase kinase kinase kinase 4	1.29	1.62	4.21	4.26	5.4
SLC20A1	NM_005415	Solute carrierfamily 20 (phosphate transporter), member 1	3.76	3.21	7.41	7.98	10.59

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			0 day	3 days	7 days	14 days	21 days
SLC31A2	NM_001860	Solute carrier family 31 (copper transporters), member 2	0.38	0.45	0.64	0.93	0.84
MDM2	NM_002392	Mouse double minute 2, human homolog of; p53-binding protein	0	0.05	0.03	0.07	0.07
RUNX1	D43967	Runt-related transcription factor 1 (acute myeloid leukemia 1; aml1 oncogene)	0.09	0.04	0.06	0.12	0.14
LOH11CR2A	NM_014622	Loss of heterozygosity, 11, chromosomal region 2, gene A	0.2	0.16	0.3	0.38	0.44
COL4A3BP	NM_005713	Collagen, type IV, alpha 3 (Goodpasture antigen) binding protein	0.24	0.22	0.22	0.38	0.51
LYPLA3	AL110209	LCAT-like lysophospholipase	0.28	0.37	0.39	0.57	0.74
ITPR1	NM_002222	Inositol 1,4,5-triphosphate receptor, type 1	0.07	0.1	0.09	0.39	0.16
PLXDC1	NM_020405	Tumor endothelial marker 7 precursor	0.02	0.02	0.07	0.07	0.16
KIF13B	NM_015254	Kinesin family member 13B	0.18	0.17	0.23	0.3	0.56
FBLN1	NM_006486	Fibulin 1	1.21	3.27	3.63	6.61	4.49
PLXNA2	AI688418	wc94h03.x1 NCI_CGAP_Co3 Homo sapiens cDNA clone IMAGE:2326325 3' similar to TR:P70207 P70207 PLEXIN 2. ;, mRNA sequence.	0.09	0.13	0.11	0.18	0.3
ASAH1	U47674	N-acylsphingosine amidohydrolase (acid ceramidase)	0.33	0.38	0.73	1.38	0.72
EGR3	NM_004430	Early growth response 3	0.07	0.04	0.14	0.22	0.13
WHSC1L1	NM_017778	Wolf-Hirschhorn syndrome candidate 1-like 1	0.05	0.04	0.1	0.1	0.14
PDLIM3	AF002280	Alpha-actinin-2-associated LIM protein	0.12	0.17	0.27	0.42	0.29
ZNF192	NM_006298	Zinc finger protein 192	0.07	0.03	0.06	0.09	0.12
U2AF1L2	NM_005089	U2 small nuclear ribonucleoprotein auxiliary factor, small subunit 2	0.18	0.17	0.17	0.28	0.55
ATRX	U72937	Alpha thalassemia/mental retardation syndrome X-linked (RAD54 (S. cerevisiae) homolog)	0.27	0.27	0.47	0.57	0.65
MNT	NM_020310	MAX binding protein	0.36	0.36	0.56	0.66	1.02
RTN2	AF004222	alternatively spliced; contains sequences derived from exons 1-11; Homo sapiens RTN2-A(RTN2) mRNA, complete cds.	0.13	0.14	0.16	0.23	0.31
POLR2A	NM_000937	Polymerase (RNA) II (DNA directed) polypeptide A (220kD)	0.33	0.25	0.27	0.45	0.79
CLGN	NM_004362	Calmegin	0.01	0.01	0.02	0.02	0.05
FYCO1	NM_024513	FYVE and coiled-coil domain containing 1	0.41	0.43	0.66	0.78	1.17
EDNRA	NM_001957	Endothelin receptor type A	0.19	0.18	0.12	0.29	0.41
VEGFB	NM_003377	Vascular endothelial growth factor B	0.37	0.62	0.64	0.89	1.21
IL1R1	NM_000877	Interleukin 1 receptor, type I	0.97	1.42	1.04	2.79	1.85
LTBP3	NM_021070	Latent transforming growth factor beta binding protein 3	0.55	0.38	0.35	0.81	1.78
-	Z48199	H.sapiens syndecan-1 gene (exons 2-5).	0.26	0.14	0.09	0.35	0.39
DFNA5	NM_004403	Deafness, autosomal dominant 5	0.99	0.85	0.99	1.48	2.27
XPC	D21089	Xeroderma pigmentosum, complementation group C	0.5	0.44	0.57	0.83	1
USF2	NM_003367	Upstream transcription factor 2, c-fos interacting	0.26	0.2	0.28	0.51	0.39
CDKN1A	NM_000389	Cyclin-dependent kinase inhibitor 1A (p21, Cip1)	2.72	2.28	3.15	5.01	4.64
CAMLG	NM_001745	Calcium modulating ligand	1.33	1.22	1.36	2.21	2.51
RGS2	NM_002923	Regulator of G-protein signalling 2, 24kD	0.1	0.13	0.18	2.87	1.06
DAPK2	NM_014326	Death-associated protein kinase 2	0.04	0.06	0.04	0.08	0.1
ZNF177	NM_003451	Zinc finger protein 177	0.05	0.03	0.05	0.07	0.08
SOD2	X15132	Superoxide dismutase 2, mitochondrial	0.1	0.16	0.23	0.61	0.25
GFPT2	NM_005110	Glutamine-fructose-6-phosphate transaminase 2	0.22	0.24	0.37	0.94	0.41
-	NM_022448	Hypothetical protein FLJ21817 similar to Rhoip2	0.04	0.15	0.21	0.25	0.28
SLC2A3	NM_006931	Solute carrier family 2 (facilitated glucose transporter), member 3	0.49	0.57	0.49	1.75	0.8
HIST1H2BD	BC002842	H2B histone family, member B	0.27	0.24	0.2	1.3	0.49
NKRF	NM_017544	Transcription factor NRF	0.15	0.17	0.14	0.27	0.29
RRH	NM_006583	Retinal pigment epithelium-derived rhodopsin homolog	0.03	0.01	0.04	0.04	0.07
KCNMA1	U11058	Potassium large conductance calcium-activated channel, subfamily M, alpha member 1	1.27	0.7	2.32	2.34	3.17
C1R	AL573058	AL573058 LTI_NFL006_PL2 Homo sapiens cDNA clone CS0DI014YC05 3 prime, mRNA sequence.	1.12	1.8	1.94	3.73	2.43
-	AL023584		0.36	0.25	0.34	0.54	0.61
FZD4	NM_012193	Frizzled (Drosophila) homolog 4	0.13	0.32	0.26	0.44	0.46
NCOR2	NM_006312	Nuclear receptor co-repressor 2	1.18	1.18	1.26	1.95	4.3
MMP2	NM_004530	Matrix metalloproteinase 2 (gelatinase A, 72kD gelatinase, 72kD type IV collagenase)	16.02	11.87	18.45	25.23	29.61
BTG2	NM_006763	BTG family, member 2	0.19	0.21	0.2	0.3	0.5
OCLN	U53823	Occludin	0.01	0.04	0.05	0.05	0.07
SCAP2	NM_003930	Src family associated phosphoprotein 2	0.34	0.45	0.54	0.7	0.88
-	AA308853	EST179659 Cerebellum II Homo sapiens cDNA 3' end, mRNA sequence.	0.89	0.75	1.1	1.47	3.48
EDG1	NM_001400	Endothelial differentiation, sphingolipid G-protein-coupled receptor, 1	0.07	0.05	0.05	0.15	0.09
VCAM1	NM_001078	Vascular cell adhesion molecule 1	0.82	0.46	0.56	0.98	1.62
VAT1	BC001913	Membrane protein of cholinergic synaptic vesicles	3.2	3.86	6.33	6.72	9.99
RBBP6	NM_006910	Retinoblastoma-binding protein 6	0.16	0.1	0.2	0.26	0.28
SCG2	NM_003469	Secretogranin II (chromogranin C)	0.02	0.02	0.04	0.15	0.39
DDX58	NM_014314	RNA helicase	0.11	0.12	0.18	0.36	0.19
MXI1	NM_005962	MAX-interacting protein 1	0.68	0.45	0.64	3.9	1.35
C1orf38	AB035482	Basement membrane-induced gene	0.09	0.12	0.21	0.44	0.19
RARRES3	NM_004585	Retinoic acid receptor responder (tazarotene induced) 3	0.16	0.19	0.31	0.38	0.37
EGR4	NM_001965	Early growth response 4	0.12	0.11	0.16	0.22	0.23
SH3BP2	AB000462	SH3-domain binding protein 2	0.27	0.16	0.2	0.39	0.37
HBXAP	NM_016578	HBV pX associated protein-8	0.02	0.04	0.07	0.07	0.08
FOLR3	NM_000804	Folate receptor 3 (gamma)	0.14	0.12	0.21	0.29	0.25
RNMT	NM_003799	RNA (guanine-7-) methyltransferase	0.25	0.17	0.21	0.4	0.35
MAN2A1	NM_002372	Mannosidase, alpha, class 2A, member 1	0.39	0.36	0.67	0.73	0.94
TULP1	NM_003322	Tubby like protein 1	0.05	0.02	0.03	0.06	0.09
CRLF1	NM_004750	Cytokine receptor-like factor 1	1.57	0.51	0.5	1.95	2.03
BRD4	BF718610	KEST81 normal human keratinocytes Homo sapiens cDNA clone S90413.NIH-116-R.ab1 3', mRNA sequence.	0.83	0.87	0.86	1.27	2.29
BTN3A3	NM_006994	Butyrophilin, subfamily 3, member A3	0.74	0.7	1.09	1.22	2.02
MAN2B1	U68567	Mannosidase, alpha, class 2B, member 1	0.34	0.45	0.41	0.63	0.84
ABL1	NM_005157	V-abl Abelson murine leukemia viral oncogene homolog 1	0.91	1	1.16	1.73	1.81
BACE1	NM_012104	Beta-site APP-cleaving enzyme	1.13	0.76	0.93	1.42	2.48
-	X57348	H.sapiens mRNA (clone 9112).	0.08	0.06	0.12	0.13	0.2
B4GALT1	D29805	UDP-Gal:betaGlcNAc beta 1,4- galactosyltransferase, polypeptide 1	0.25	0.14	0.19	0.31	0.69
STAT3	AA634272	ac75h05.s1 Stratagene lung (#937210) Homo sapiens cDNA clone IMAGE:868473 3' similar to contains Alu repetitive element;contains element L1 repetitive element ;, mRNA sequence.	1.26	1.74	1.6	2.7	2.7
SCPEP1	NM_021626	Likely homolog of rat and mouse retinoid-inducible serine carboxypeptidase	0.54	0.64	0.73	1.05	1.14
ST5	NM_005418	Suppression of tumorigenicity 5	0.36	0.44	0.57	0.67	1.43
LRP1	NM_002332	Low density lipoprotein-related protein 1 (alpha-2-macroglobulin receptor)	0.46	0.45	0.41	0.71	1.63
SREBF1	NM_004176	Sterol regulatory element binding transcription factor 1	0.25	0.28	0.4	0.77	0.43
BDKRB1	NM_000710	Bradykinin receptor B1	0.44	0.2	0.28	1.89	0.67
PIM2	NM_006875	Pim-2 oncogene	0.11	0.07	0.09	0.15	0.17
GBP2	NM_004120	Guanylate binding protein 2, interferon-inducible	0.23	0.22	0.31	0.46	0.4
CTNS	AJ222967	Homo sapiens mRNA for cystinosin.	0.24	0.38	0.47	0.55	0.78

Table 3 Expression levels of 156 down-regulated genes of hMSC cultured in exclusive medium (day = 0) and in OM for 3, 7, 14 and 21 days.

Gene ID	Gene Identifier	Gene Title	Gene expression levels				
			0 day	3 days	7 days	14 days	21 days
HAPLN1	U43328	Cartilage linking protein 1	1.05	0.35	0.28	0.23	0.16
-	AK023795	A disintegrin-like and metalloprotease (reprolysin type) with thrombospondin type 1 motif, 1	2.80	1.06	0.83	0.54	0.62
LDB2	NM_001290	LIM domain binding 2	1.34	0.34	0.28	0.26	0.24
CXCL12	NM_000609	Stromal cell-derived factor 1	1.84	0.61	0.57	0.49	0.51
ID1	D13889	Inhibitor of DNA binding 1, dominant negative helix-loop-helix protein	2.95	0.98	0.40	0.65	0.58
C10orf116	NM_006829	Adipose specific 2	1.48	0.57	0.33	0.12	0.18
BDNF	NM_001709	Brain-derived neurotrophic factor	0.38	0.16	0.09	0.13	0.10
KRTAP1-1	NM_030967	Keratin associated protein 1.1	1.46	0.38	0.26	0.08	0.20
ID4	NM_001546	Inhibitor of DNA binding 4, dominant negative helix-loop-helix protein	1.75	0.86	0.20	0.33	0.20
IGFBP3	M31159	Insulin-like growth factor binding protein 3	26.49	10.06	9.28	11.10	8.52
MEST	NM_002402	Mesoderm specific transcript (mouse) homolog	9.69	5.13	2.15	0.87	0.60
PENK	NM_006211	Proenkephalin	9.00	3.84	1.10	0.57	0.50
-	L16895	Lysyl oxidase	13.18	7.42	6.15	4.71	2.68
C17	NM_018659	Cytokine-like protein C17	1.14	0.45	0.41	0.53	0.35
CDH2	M34064	Cadherin 2, type 1, N-cadherin (neuronal)	3.05	0.91	0.75	0.64	1.30
DACT1	NM_016651	Heptacellular carcinoma novel gene-3 protein	2.12	1.39	0.74	0.56	0.57
GREM2	NM_022469	Hypothetical protein FLJ21195 similar to protein related to DAC and cerberus	0.74	0.26	0.21	0.16	0.34
ID3	NM_002167	Inhibitor of DNA binding 3, dominant negative helix-loop-helix protein	3.30	2.02	0.50	0.76	1.00
GATA6	D87811	GATA-binding protein 6	0.20	0.08	0.09	0.07	0.09
HSPB7	NM_014424	Heat shock 27kD protein family, member 7 (cardiovascular)	0.78	0.48	0.15	0.06	0.09
ODC1	NM_002539	Ornithine decarboxylase 1	4.64	3.08	2.30	1.29	1.22
TRIM16	NM_006470	Tripartite motif-containing 16	0.83	0.55	0.39	0.26	0.26
IL6	NM_000600	Interleukin 6 (interferon, beta 2)	1.17	0.76	0.62	0.44	0.23
P4HA1	NM_000917	Procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), alpha polypeptide I	3.41	1.09	0.97	1.88	1.16
PHGDH	NM_006623	Phosphoglycerate dehydrogenase	1.89	0.93	0.96	0.90	0.74
PPAP2B	AB000889	Phosphatidic acid phosphatase type 2B	4.88	3.30	1.83	1.78	1.93
GNG10	NM_004125	Guanine nucleotide binding protein 10	2.51	0.94	1.41	0.99	1.09
EIF4E	NM_001968	Eukaryotic translation initiation factor 4E	0.13	0.05	0.06	0.05	0.07
ASNS	NM_001673	Asparagine synthetase	4.35	2.31	1.43	2.09	1.98
TGFBI	NM_000358	Transforming growth factor, beta-induced, 68kD	32.01	14.74	8.74	19.12	10.52
PSAT1	NM_021154	Phosphoserine aminotransferase	3.03	1.63	1.21	1.80	0.15
DKK1	NM_012242	Dickkopf (Xenopus laevis) homolog 1	3.10	2.15	1.70	1.19	0.99
CRIP2	U36190	Cysteine-rich protein 2	2.24	1.50	1.34	0.90	0.34
RHOB	AI263909	qi08f09.x1 Soares_NhHMPu_S1 Homo sapiens cDNA clone IMAGE:1855913 3', mRNA sequence.	4.53	3.15	1.96	2.01	1.68
EIF1AX	BE542684	601067180F1 NIH_MGC_10 Homo sapiens cDNA clone IMAGE:3453571 5', mRNA sequence.	0.37	0.14	0.22	0.20	0.11
ID2	NM_002166	Inhibitor of DNA binding 2, dominant negative helix-loop-helix protein	2.05	0.62	0.47	1.06	0.91
PRPS1	NM_002764	Phosphoribosyl pyrophosphate synthetase 1	1.71	1.38	0.68	0.43	0.18
ELN	AA479278	zv21b07.s1 Soares_NhHMPu_S1 Homo sapiens cDNA clone IMAGE:754261 3' similar to contains element MER22 repetitive element ;, mRNA sequence.	4.79	3.64	0.79	1.70	1.31
STC2	BC000658	Stanniocalcin 2	2.86	2.36	0.86	0.75	0.63
DSCR1	NM_004414	Down syndrome critical region gene 1	2.27	1.73	0.83	1.13	0.62
GLIPR1	NM_006851	Glioma pathogenesis-related protein	5.38	3.64	3.55	1.93	1.71
BAMBI	NM_012342	Putative transmembrane protein	0.96	0.71	0.48	0.36	0.42
MFAP5	U37283	Microfibril-associated glycoprotein-2	8.62	6.08	5.43	4.03	1.96
XPOT	AI984005	wt52c06.x1 NCI_CGAP_Pan1 Homo sapiens cDNA clone IMAGE:2511082 3' similar to TR:043592 043592 EXPORTIN T. [1] ;, mRNA sequence.	2.93	1.68	1.60	1.73	1.12
-	NM_004353	Serine (or cysteine) proteinase inhibitor, clade H (heat shock protein 47), member 1	11.73	8.92	5.74	4.18	5.14
PYCR1	NM_006907	Pyrroline-5-carboxylate reductase 1	1.74	1.29	0.96	0.70	0.74
FGFR2	M87771	Fibroblast growth factor receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crouzon syndrome, Pfeiffer syndrome, Jackson-Weiss syndrome)	0.35	0.23	0.17	0.15	0.18
LOXL2	NM_002318	Lysyl oxidase-like 2	7.99	4.17	3.38	3.67	4.70
CITED2	AF109161	Cbp/p300-interacting transactivator, with Glu/Asp-rich carboxy-terminal domain, 2	2.03	1.71	1.11	0.56	0.53
SLC7A5	AB018009	Solute carrier family 7 (cationic amino acid transporter, y+ system), member 5	2.35	1.57	1.08	1.22	1.15
TXNRD1	NM_003330	Thioredoxin reductase 1	3.73	2.88	1.85	1.91	1.41
PLCB4	AL535113	AL535113 LTI_FL013_FBm1 Homo sapiens cDNA clone CS0DF008YC23 3 prime, mRNA sequence.	0.43	0.33	0.24	0.12	0.19
-	NM_002219	Integral membrane protein 1	2.67	1.95	1.78	1.24	0.81
NQO1	NM_000903	NAD(P)H dehydrogenase, quinone 1	2.17	1.78	1.07	0.53	0.93
ITGA6	NM_000210	Integrin, alpha 6	0.15	0.10	0.08	0.08	0.07
BPGM	NM_001724	2,3-bisphosphoglycerate mutase	0.43	0.29	0.25	0.22	0.20
POLR3D	NM_001722	BN51 (BHK21) temperature sensitivity complementing	0.43	0.29	0.23	0.22	0.22
COL5A1	AI130969	qc15e01.x1 Soares_fetal_heart_NbHH19W Homo sapiens cDNA clone IMAGE:1709688 3' similar to gb:M76729 PROCOLLAGEN ALPHA 1(V) CHAIN PRECURSOR (HUMAN);, mRNA sequence.	5.37	3.18	2.86	2.63	3.04
HYOU1	NM_006389	Oxygen regulated protein (150kD)	1.55	0.93	0.64	0.60	0.97
-	M10098	Human 18S rRNA gene, complete.	2.46	1.80	1.73	0.95	0.94
RBMS3	NM_014483	RNA binding motif, single stranded interacting protein 3	0.43	0.31	0.28	0.23	0.16
PCOLCE2	NM_013363	Procollagen C-endopeptidase enhancer 2	0.39	0.12	0.23	0.21	0.19
RBM3	NM_006743	RNA binding motif protein 3	1.76	1.59	0.93	0.62	0.44
PFKP	NM_002627	Phosphofructokinase, platelet	3.63	2.76	1.96	2.21	1.21
PRKCSH	NM_002743	Protein kinase C substrate 80K-H	1.91	1.35	0.91	1.16	0.88
CPOX	NM_000097	Coproporphyrinogen oxidase (coproporphyria, harderoporphyria)	0.38	0.21	0.20	0.27	0.12
CBX5	L07515	Chromobox homolog 5 (Drosophila HP1 alpha)	0.48	0.41	0.28	0.19	0.16
MYCBP	AL525412	AL525412 LTI_NFL003_NBC3 Homo sapiens cDNA clone CS0DC011YJ12 5 prime, mRNA sequence.	0.29	0.18	0.17	0.12	0.17
SLC16A3	AL513917	AL513917 LTI_NFL006_PL2 Homo sapiens cDNA clone CL0BA006ZD09 3 prime, mRNA sequence.	2.14	1.41	1.20	1.48	0.30
SEMA3C	AI962897	wt24e04.x1 NCI_CGAP_Ut1 Homo sapiens cDNA clone IMAGE:2508414 3' similar to TR:Q62181 Q62181 SEMAPHORIN E PRECURSOR ;, mRNA sequence.	0.67	0.36	0.56	0.28	0.11
WNT5A	NM_003392	Wingless-type MMTV integration site family, member 5A	3.00	2.40	1.20	1.10	1.71
C1orf41	NM_016126	HSPC034 protein	0.37	0.32	0.19	0.15	0.18
GRP58	D83485	Glucose regulated protein, 58kD	6.70	4.83	4.10	4.50	1.98
LANCL1	NM_006055	LanC (bacterial lantibiotic synthetase component C)-like 1	1.19	0.80	0.61	0.69	0.67
TM4SF13	NM_014399	Tetraspan NET-6 protein	0.25	0.20	0.13	0.13	0.11

Gene ID	Gene Identifier	Gene Title	Gene expression levels				
			0 day	3 days	7 days	14 days	21 days
ADAMTS5	NM_007038	A disintegrin-like and metalloprotease (reprolysin type) with thrombospondin type 1 motif, 5 (aggrecanase-2)	0.41	0.08	0.13	0.23	0.22
ATP6V1C2	BE910010	601498050F1 NIH_MGC_70 Homo sapiens cDNAclone IMAGE:3899869 5', mRNAsequence.	5.38	3.64	3.83	2.63	2.65
IGFBP6	NM_002178	Insulin-like growth factor binding protein 6	6.22	4.61	3.79	3.96	2.43
EN1	NM_001426	Engrailed homolog 1	0.43	0.25	0.27	0.15	0.28
ALDH2	NM_000690	Aldehyde dehydrogenase 2 family (mitochondrial)	0.91	0.46	0.46	0.51	0.57
ALDH18A1	NM_002860	Pyrroline-5-carboxylate synthetase (glutamate gamma-semialdehyde synthetase)	1.90	1.62	1.29	0.95	0.50
TCEA2	NM_003195	Transcription elongation factor A(SII), 2	0.47	0.33	0.27	0.30	0.21
GRB2	L29511	Growth factor receptor-bound protein 2	0.76	0.58	0.47	0.43	0.37
RCN2	NM_002902	Reticulocalbin 2, EF-hand calcium binding domain	0.96	0.74	0.53	0.63	0.39
AD-017	NM_018446	Glycosyltransferase AD-017	0.57	0.35	0.37	0.31	0.32
COPB2	NM_004766	Coatomer protein complex, subunit beta 2 (beta prime)	4.74	3.35	3.30	2.47	2.37
TDG	NM_003211	Thymine-DNAglycosylase	0.43	0.37	0.23	0.21	0.21
CXorf6	NM_005491	Chromosome X open reading frame 6	0.42	0.28	0.25	0.13	0.27
MN1	NM_002430	Meningioma (disrupted in balanced translocation) 1	0.28	0.10	0.10	0.11	0.20
GOSR2	BE730204	601564144F1 NIH_MGC_20 Homo sapiens cDNAclone IMAGE:3833530 5', mRNAsequence.	0.44	0.35	0.30	0.24	0.18
UGCG	NM_003358	UDP-glucose ceramide glucosyltransferase	1.89	1.49	1.26	0.99	0.89
MNAB	NM_018835	Olfactory receptor, family 1, subfamily K, member 1	0.51	0.38	0.36	0.25	0.24
HAS1	NM_001523	Hyaluronan synthase 1	1.42	1.23	0.79	0.77	0.63
CPT1A	BC000185	Carnitine palmitoyltransferase I, liver	0.20	0.15	0.12	0.09	0.12
SNAI2	AI572079	tr73d01.x1 NCI_CGAP_Pan1 Homo sapiens cDNAclone IMAGE:2223937 3', mRNAsequence.	3.61	3.05	1.56	2.10	1.76
SFRS2	BG254869	602369310F1 NIH_MGC_91 Homo sapiens cDNAclone IMAGE:4477371 5', mRNAsequence.	2.87	2.48	2.13	1.15	0.90
PTPN14	NM_005401	Protein tyrosine phosphatase, non-receptor type 14	0.32	0.22	0.23	0.21	0.12
UGDH	NM_003359	UDP-glucose dehydrogenase	1.86	1.49	1.17	0.99	0.95
TOP2B	NM_001068	Topoisomerase (DNA) II beta (180kD)	0.85	0.54	0.56	0.50	0.46
LXN	NM_020169	Latexin protein	0.74	0.39	0.47	0.34	0.50
MTHFD2	NM_006636	Methylene tetrahydrofolate dehydrogenase (NAD+ dependent), methenyltetrahydrofolate cyclohydrolase	2.95	2.40	1.34	1.83	1.48
ARFGAP3	BC005122	ADP-ribosylation factor GTPase activating protein 1	0.93	0.63	0.62	0.61	0.44
MYO10	NM_012334	Myosin X	1.10	0.78	0.80	0.51	0.60
NDUFS2	NM_004550	NADH dehydrogenase (ubiquinone) Fe-S protein 2 (49kD) (NADH-coenzyme Q reductase)	3.81	2.87	2.39	1.93	2.19
HMGN2	BC003689	High-mobility group (nonhistone chromosomal) protein 17	10.35	9.49	6.99	3.92	3.85
CRIP1	NM_001311	Cysteine-rich protein 1 (intestinal)	2.47	2.13	1.91	0.80	0.76
CAT	NM_001752	Catalase	2.50	1.84	1.33	1.63	1.34
WDR44	NM_019045	Similar to rab11-binding protein	0.29	0.17	0.18	0.17	0.18
SMURF2	AY014180	E3 ubiquitin ligase SMURF2	3.01	1.87	2.44	1.00	1.61
LMO7	NM_005358	LIM domain only 7	0.14	0.08	0.09	0.06	0.09
ENC1	NM_003633	Ectodermal-neural cortex (with BTB-like domain)	2.32	1.29	1.05	0.96	1.71
SLC1A5	AF105230	Solute carrier family 1 (neutral amino acid transporter), member 5	1.26	0.95	0.72	0.77	0.69
CBS	BE613178	601452166T1 NIH_MGC_66 Homo sapiens cDNAclone IMAGE:3855712 3', mRNAsequence.	0.46	0.28	0.29	0.24	0.30
ACAA2	NM_006111	Acetyl-Coenzyme A acyltransferase 2 (mitochondrial 3-oxoacyl-Coenzyme A thiolase)	1.44	1.19	0.77	0.67	0.86

Gene ID	Gene Identifier	Gene Title	Gene expression levels				
			0 day	3 days	7 days	14 days	21 days
YIF1	NM_020470	Putative transmembrane protein; homolog of yeast Golgi membrane protein Yif1p (Yip1p-interacting factor)	4.58	3.68	3.01	2.08	2.57
KRT18	NM_000224	Keratin 18	0.71	0.20	0.25	0.12	0.03
KRT16	AF061812	Keratin 16 (focal non-epidermolytic palmoplantar keratoderma)	0.41	0.14	0.05	0.05	0.01
KRT14	BC002690	Keratin 14 (epidermolysis bullosa simplex, Dowling-Meara, Koebner)	0.75	0.28	0.12	0.07	0.01
KRTHA4	NM_021013	Keratin, hair, acidic, 4	0.54	0.25	0.16	0.02	0.04
KRT19	NM_002276	Keratin 19	1.40	0.31	0.36	0.07	0.02
SEMA3B	NM_004636	Sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3B	0.20	0.08	0.02	0.01	0.05
HAS2	NM_005328	Hyaluronan synthase 2	0.61	0.37	0.25	0.10	0.09
CACNA2D1	NM_000722	Calcium channel, voltage-dependent, alpha 2/delta subunit 1	0.29	0.13	0.11	0.15	0.03
SCRG1	NM_007281	Scrapie responsive protein 1	1.31	0.17	0.13	0.07	0.06
BST1	NM_004334	Bone marrow stromal cell antigen 1	0.34	0.22	0.18	0.05	0.02
PODXL	NM_005397	Podocalyxin-like	0.18	0.13	0.10	0.05	0.04
MEOX2	NM_005924	Mesenchyme homeo box 2 (growth arrest-specific homeo box)	0.12	0.09	0.06	0.02	0.01
RAC2	NM_002872	Ras-related C3 botulinum toxin substrate 2 (rho family, small GTP binding protein Rac2)	0.25	0.20	0.08	0.10	0.03
ZNF43	NM_003423	Zinc finger protein 43 (HTF6)	0.11	0.08	0.03	0.06	0.01
AP4S1	AF155159	Adaptor-related protein complex 4, sigma 1 subunit	0.09	0.07	0.04	0.03	0.00
CPS1	AF154830	Carbamoyl-phosphate synthetase 1, mitochondrial	0.11	0.05	0.02	0.05	0.06
-	NM_018678	Lipopolysaccharide specific response-68 protein	0.36	0.22	0.15	0.23	0.04
GALNT4	NM_003774	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 4 (GalNAc-T4)	0.09	0.05	0.05	0.06	0.02
DNMT3L	NM_013369	DNA (cytosine-5-)-methyltransferase 3-like	0.09	0.05	0.00	0.01	0.04
PROL5	NM_012390	Protein homologous to salivary proline-rich protein P-B	0.03	0.01	0.01	0.01	0.01
IL7R	NM_002185	Interleukin 7 receptor	0.14	0.10	0.06	0.02	0.05
NGFB	NM_002506	Nerve growth factor, beta polypeptide	0.27	0.20	0.10	0.02	0.09
RASA3	NM_007368	RAS p21 protein activator (GTPase activating protein) 3 (Ins(1,3,4,5)P4-binding protein)	0.29	0.20	0.18	0.14	0.02
CLIC3	NM_004669	Chloride intracellular channel 3	0.74	0.61	0.19	0.20	0.01
STAC	NM_003149	Src homology three (SH3) and cysteine rich domain	0.26	0.16	0.10	0.18	0.10
PVR	NM_006505	Poliovirus receptor	0.18	0.11	0.14	0.08	0.05
LYPDC1	AL567376	AL567376 LTI_FL013_FBm1 Homo sapiens cDNAclone CS0DF024YO04 3 prime, mRNAsequence.	0.39	0.01	0.02	0.02	0.01
RPL3L	NM_005061	Ribosomal protein L3-like	0.06	0.01	0.01	0.03	0.03
LTC4S	NM_000897	Leukotriene C4 synthase	0.10	0.09	0.03	0.02	0.02
LGMN	D55696	Protease, cysteine, 1 (legumain)	0.63	0.49	0.27	0.29	0.31
CYB561	BC000021	Cytochrome b-561	0.18	0.15	0.12	0.10	0.04
LMAN1	NM_005570	Lectin, mannose-binding, 1	0.34	0.19	0.19	0.24	0.00
HTLF	NM_002158	Human T-cell leukemia virus enhancer factor	0.10	0.08	0.01	0.06	0.01
KRT7	BC002700	Keratin 7	0.57	0.52	0.16	0.10	0.07
RDX	NM_002906	Radixin	0.24	0.20	0.18	0.10	0.03
-	BF061658	7i82e10.x1 NCI_CGAP_Ov18 Homo sapiens cDNAclone IMAGE:3341226 3' similar to SW:TGF2_HUMAN P08112 TRANSFORMING GROWTH FACTOR BETA 2 PRECURSOR ;, mRNAsequence.	0.06	0.04	0.03	0.05	0.02
PDE5A	NM_001083	Phosphodiesterase 5A, cGMP-specific	0.07	0.06	0.03	0.04	0.04
ACTC	NM_005159	Actin, alpha, cardiac muscle	0.51	0.50	0.19	0.12	0.11
CKB	NM_001823	Creatine kinase, brain	0.67	0.67	0.26	0.21	0.07
LIN7C	NM_018362	LIN-7 protein 3	0.53	0.42	0.39	0.30	0.06
KIFC3	BC001211	Kinesin family member C3	0.29	0.20	0.20	0.16	0.16

Due to advance of osteochondra-ossification with angiogenesis, it also appeared reasonable to see up-regulation of angiogenesis-related genes[19], cell cycle arrest-related genes[20] and transforming growth factor beta 1 gene[12] in addition to up-regulation of osteogenesis-related genes, as mentioned in Results. Due to advance of osteochondral-ossification with angiogenesis, it seemed natural to observe down-regulation of other phenotype-related genes such as stromal cell-related genes, keratin related genes, antioxidant related genes, cartilage linking protein 1 gene, adipose specific 2 gene, hyaluronan synthase 1 gene and cysteine-rich protein 1 gene, as mentioned in Results.

We cannot, however, refer to many other genes listed in Tables 2 and 3, which might have meaningful influence on osteogenic differentiation of hMSC caused by OM. We are looking forward other researchers to utilize the database presented here. Time-course analyses of expressions of hMSC genes cultured in OM appear to be quite useful for diagnosis (recovery check) and clinical (gene therapy) treatment of damaged dental oral hard tissues in the future. It should be cautioned here that genes identified in this study considerably differ from those[8,9] listed in pre-existing papers except well-known genes such as alkaline phosphatase and BMP2 genes.

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