

## SUPPLERMENTAL TABLE 9

Up- and down-regulated genes in human embryonic stem cells after exposition with  $^{131}\text{I}$ -iodide or  $^{125}\text{I}$ -dU

Gene	Fold change	p-value	Function of encoded protein	Ref.*
<b><math>^{131}\text{I}</math>-iodide: up-regulated</b>				
DMD	18,93541	1,44E-19	Encoded: protein: dystrophin.  Molecular function: structural constituent of cytoskeleton	(1,2)
REN	18,53966	2,27E-16	Encoded: protein: renin, which is produced in the kidneys. This protein is part of the renin-angiotensin system, which regulates blood pressure and water levels in the body. It converts angiotensinogen into angiotensin. Angiotensin causes blood vessels to narrow (constrict), which results in increased blood pressure. Angiotensin also stimulates the production of the hormone aldosterone, which causes the kidneys to retain salt and water. An increased amount of fluid in the body also increases blood pressure.  Biological process: renin producing	(3)
GRAMD1C	18,4341	3,27E-17	Encodes <b>GRAM domain containing 1C</b> Generally, this domain is likely to be involved in membrane-associated processes such as intracellular protein- or lipid-binding signaling pathways. However, functions for most of these family members are still unknown.  Biological process: cell signaling, lipid metabolism	(4)
OLFM4	16,51863	5,28E-15	Encodes OLFM4, a member of olfactomedin-related protein family. It plays important roles in a variety of cellular functions, including neurogenesis, cell adhesion, cell-cycle regulation, and tumorigenesis, and may serve as modulators of critical signaling pathways. <sup>6</sup> It has been shown that OLFM4 interacts with GRIM-19 (Gene associated with retinoid-interferon-induced mortality-19), which is a component of respiratory complex I of mitochondria, <sup>10</sup> and has an anti-apoptotic role.  Biological process: cell adhesion, cell-cycle regulation,	(5)
CLEC1B Q9P126 (CLC1B_H UMAN)	16,08694	9,96E-18	Encodes cell surface receptor linked to signaling pathway and defense response,  Biological process: defense response	(6-8)

MIA2	15,67657	5,35E-20	Gene with melanoma inhibitory activity 2; MIA2, together with MIA, OTOR and TANGO, belongs to the novel MIA gene family sharing important structural features, significant homology and similar genomic organisation. MIA2 is expressed exclusively in the liver. MIA2 acts as an inhibitor of HCC growth and invasion both in vitro and in vivo, and consequently, as a tumour suppressor of HCC.  Biological process: Tumor-suppressor	(9)
COL3A1	15,03772	1,43E-20	The COL3A1 gene provides instructions for making a component of collagen. The COL3A1 gene produces the components of type III collagen, called pro-alpha1(III) chains.  Molecular function: extracellular matrix structural constituent	(10,11)
MGP	14,86286	1,80E-18	Matrix gla protein (MGP) is a protein found in numerous body tissues that requires vitamin K for its optimum function. It is present in bone (together with the related vitamin K-dependent protein osteocalcin), as well as in heart, kidney and lung. In bone, its production is increased by vitamin D.  Molecular function: extracellular matrix structural constituent extracellular matrix structural constituent	(12)
LMOD1	14,69	1,43E-20	The leiomodlin 1 protein has a putative membrane-spanning region and 2 types of tandemly repeated blocks. The transcript is expressed in different tissues tested, with the highest levels in thyroid, eye muscle, skeletal muscle, and ovary. Increased expression of leiomodlin 1 may be linked to Graves' disease and thyroid-associated ophthalmopathy  Molecular function: tropomyosin binding	(13)
CD86	14,3269	1,70E-20	Has co-stimulatory in T cell activation; CD86 stimulation upregulates the expression of the transcription factor Oct-2 in a protein kinase C and NF-κB1-dependent manner  Molecular function: transcription activator activity	(14-16)
<b><sup>131</sup>I-iodide down-regulated</b>				
DMBX1	-35,22288	1,38E-18	member of the Otx family [5]. Otx3/Dmbx1 expression is craniocaudally limited to the rostral region of the developing brain in mice. It also is expressed in developing eyes, adult cerebellum, and pancreatic islets.  Biological process: negative regulation of transcription from RNA polymerase II promoter	(17)
GALP	-22,54466	2,54E-21	This gene encodes a member of the galanin family of neuropeptides. The encoded protein binds galanin receptors 1, 2 and 3 with the highest affinity for galanin receptor 3 and has been implicated in biological processes involving the central nervous system including	(18,19)

			<p>hypothalamic regulation of metabolism and reproduction. A peptide encoded by a splicevariant of this gene, termed alarin, may have vasoactive properties and serve as a marker for neuroblastic tumors.</p> <p>Biological process: neuropeptide signaling pathway</p>	
MITF	-22,42584	1,11E-15	<p>The MITF gene provides instructions for making a protein called microphthalmia-associated transcription factor. This protein plays a role in the development, survival, and function of certain types of cells. To carry out this role, the protein attaches to specific areas of DNA and helps control the activity of particular genes. On the basis of this action, the protein is called a transcription factor.</p> <p>Biological process: regulation of transcription, DNA-dependent, regulation of cell proliferation</p>	(20, 21)
MED28	-16,58791	4,79E-11	<p>Magicin, a protein that we isolated earlier as an interactor of the neurofibromatosis 2 protein merlin, was independently identified as MED28, a subunit of the mammalian Mediator complex. Mediator complex is an evolutionarily conserved transcriptional cofactor, which plays an essential role in positive and negative gene regulation.</p> <p>Biological process: regulation of transcription from RNA polymerase II promoter, regulation of transcription</p>	(22)
RET	-16,00737	6,32E-17	<p>Aliase: ret proto-oncogene1</p> <p>This gene, a member of the cadherin superfamily, encodes one of the receptor tyrosine kinases, which are cell-surface molecules that transduce signals for cell growth and differentiation. RET induces apoptosis through massive expression of Pit-1 leading to p53 accumulation.</p> <p>Molecular function: protein tyrosine kinase activity, protein kinase activity</p>	(23, 24)
RAX	-14,51574	6,32E-17	<p>This gene encodes a homeobox-containing transcription factor that functions in eye development. The gene is expressed early in the eye primordia, and is required for retinal cell fate determination and also regulates stem cell proliferation.</p> <p>Molecular function: transcription factor activity, RNA polymerase II transcription factor activity</p>	(25, 26)
PRKCB1	-12,52932	1,75E-20	<p>The protein encoded by this gene is one of the PKC family members. This protein kinase has been reported to be involved in many different cellular functions, such as B cell activation, apoptosis induction, endothelial cell proliferation, and intestinal sugar absorption.</p> <p>Biological process: signal transduction, lipoprotein transport</p>	(27, 28)

CDH9	-12,27507	1,17E-15	This gene encodes a type II classical cadherin from the cadherin superfamily, integral membrane proteins that mediate calcium-dependent cell-cell adhesion.  Biological process: cell-cell adhesion	(29, 30)
OSBPL1A	-11,84812	1,62E-07	This gene encodes a member of the oxysterol-binding protein (OSBP) family, a group of intracellular lipid receptors. The, cholesterol homeostasis is absolutely dependent on its distribution along an intracellular gradient. It is apparent that this gradient is maintained by a combination of sterol-lipid interactions, vesicular transport and sterol-binding/transport proteins.  Biological process: cholesterol metabolic process, vesicle-mediated transport	(31-33)
SLCO1A2	-11,72874	1,66E-07	Solute carrier organic anion transporter family member 1A2 is a protein that in humans is encoded by the SLCO1A2 gene. It is a sodium-independent transporter which mediates cellular uptake of organic ions in the liver.  Biological process: organic anion transmembrane transporter activity, bile acid transmembrane transporter activity	(34, 35)
<b><sup>125</sup>I-dU up regulated</b>				
CGA	72,16	6,18E-23	Glycoprotein hormones alpha chain is the protein that in humans is encoded by the CGA gene.[1] CGA codes for the common alpha subunit of the four glycoprotein hormones hCG (human chorionic gonadotropin), LH (luteinizing hormone), FSH (follicle-stimulating hormone) and TSH (thyroid-stimulating hormone).  Biological process: cell-cell signaling, G-protein coupled receptor protein signaling pathway	(36-38)
<b>CD274</b>	42,36216	4,44E-21	<b>CD274</b> also known as <b>PD-L1</b> (Programmed Death Ligand-1) or <b>B7-H1</b> is a protein which in humans is encoded by the <i>CD274</i> gene. <sup>[1]</sup> Programmed death (PD) molecules belong to the B7 family of co-stimulatory proteins and function in adaptive immunity.  Biological process: cell proliferation, programmed cell death	(39)
INSL4	39,74621	8,66E-22	INSL4 encodes the insulin-like 4 protein, a member of the insulin superfamily. Expression of INSL4 products occurs within the early placental cytotrophoblast and syncytiotrophoblast.  Biological process: cell proliferation, cell-cell signalling	(40)

ALDOB	32,83224	5,68E-20	<p>ALDOB encodes aldolase B, fructose-bisphosphate. This is a tetrameric glycolytic enzyme that catalyzes the reversible conversion of fructose-1,6-bisphosphate to glyceraldehyde 3-phosphate and dihydroxyacetone phosphate. There is evidence that aldolase binds specifically to the actin-containing stress fibers and suggest that aldolase may regulate cell contraction through its reversible binding to the filaments in the permeabilized MRC-5 fibroblast.</p> <p>Molecular function: cytoskeletal protein binding</p>	(41)
CEACAM6	19,64276	2,37E-16	<p>CEACAM6 belongs to the cell adhesion molecules (CAMs) of the carcinoembryonic antigen (CEA) family that have been shown to be deregulated in lung cancer and in up to 50% of all human cancers. CEACAM6 acts as an inducer of cellular proliferation in A549 cells, likely by interfering with the contact-inhibiting signal triggered by CEACAM1-4L, leading to undifferentiated anchorage-independent cell growth.</p> <p>Biological process: signal transduction, cell-cell signaling</p>	(41, 43)
CYP19A1	17,30941	5,64E-20	<p>This gene encodes a member of the cytochrome P450 superfamily of enzymes. The cytochrome P450 proteins are monooxygenases which catalyze many reactions involved in drug metabolism and synthesis of cholesterol, steroids and other lipids.</p> <p>Molecular function: oxidoreductase activity, acting on paired donors, with incorporation or reduction of molecular oxygen, reduced flavin or flavoprotein as one donor, and incorporation of one atom of oxygen.</p>	(44, 45)
RBP2	15,19759	1,81E-20	<p>RBP2 is an abundant protein present in the small intestinal epithelium. It is thought to participate in the uptake and/or intracellular metabolism of vitamin A.</p> <p>Biological process: vitamin A metabolic process, epidermis development</p>	(46)
SERPINA3	15,18682	1,75E-20	<p>The protein encoded by this gene is a plasma protease inhibitor and member of the serine protease inhibitor class. Mutations have been identified in patients with Parkinson disease and chronic obstructive pulmonary disease.</p> <p>Biological process: regulation of lipid metabolic process</p>	(47)
MUC15	14,53396	1,67E-20	<p>The glycoprotein MUC15 (mucin 15) was initially isolated from the bovine milk fat globule membrane. Screening of a human multiple tissue expression array showed abundant MUC15 gene expression in placenta, salivary gland, thyroid gland, trachea, esophagus, kidney, testis, and the leukemia K-562 cell line. Furthermore, moderate expression was seen in the pancreas, adult and fetal lung, fetal kidney, lymph node, adult and fetal thymus, and parietal lobe. Structural motifs for interactions (epidermal growth factor receptor and Src homology 2 domains) are identified in the intracellular region.</p> <p>Biological process: cell-signaling</p>	(48)

HSD3B1	13,26469	8,49E-20	<p>3-beta-HSD is a bifunctional enzyme, that catalyzes the oxidative conversion of Delta(5)-ene-3-beta-hydroxy steroid, and the oxidative conversion of ketosteroids. The 3-beta-HSD enzymatic system plays a crucial role in the biosynthesis of all classes of hormonal steroids.</p> <p>Biological process: steroid biosynthetic process</p>	(49)
<b><sup>125</sup>I-dU down regulated</b>				
LRRC34	-56,23273	2,23E-20	<p>This gene encodes the leucine rich repeat containing 34 protein. The leucine-rich repeat (NLR)-containing protein family gained much attention because it was shown that members of this family are critically involved in mounting immune responses to bacterial peptidoglycan fragments and in controlling release of the key inflammatory cytokine interleukin-1<math>\beta</math> (2,-,4). Over 20 NLRs are encoded in the human genome.</p> <p>Biological process: protein binding</p>	(50)
ZNF229	-21,0847	5,24E-12	<p>The zinc finger protein 229 belongs to the krueppel C2H2-type zinc-finger protein family. C2H2 zinc finger genes (C2H2-ZNF) constitute the largest class of transcription factors in humans and one of the largest gene families in mammals. Often arranged in clusters in the genome, these genes are thought to have undergone a massive expansion in vertebrates, primarily by tandem duplication. This class of zinc fingers can have a variety of functions such as binding RNA and mediating protein-protein interactions.</p> <p>Biological process: regulation of transcription, DNA-dependent</p>	(51)
ZNF649	-16,47173	1,18E-20	<p>The zinc finger protein 649 is known as transcriptional repressor. and may suppress transcription activities mediated by growth factor signaling pathways</p> <p>Biological process: regulation of transcription, DNA-dependent</p>	(52, 53)
PAX5	-15,77243	4,83E-10	<p>This gene encodes a member of the paired box (PAX) family of transcription factors. PAX proteins are important regulators in early development, and alterations in the expression of their genes are thought to contribute to neoplastic transformation.</p> <p>Pax5 regulates B cell lineage commitment by concurrently activating cell specific gene expression as well as suppressing the expression of genes associated with non-B cell fates. The identity of the molecular targets of Pax5-mediated gene repression is the subject of much current interest. Recent studies have documented the essential nature of the Pax5 mediated repression of the stem cell transcriptional program, as well as the silencing of lineage inappropriate gene expression, for B cell development.</p>	(54, 55)

			Biological process: transcription from RNA polymerase II promoter	
PNN	-14,32759	9,25E-08	In many studies, the expression of PNN has been found to correlate with greater epithelial and less mesenchymal characteristics. The expression of Pnn has been shown to enhance cell–cell adhesion, inhibit cell migration, suppress tumorigenesis, transcriptionally regulate expression of E-cadherin (CDH1) and p21Waf1/Cip1 genes, and participate in alternative pre-mRNA splicing  Biological process: cell adhesion, regulation of transcription	(56)
ZNF502	-13,39231	2,41E-09	The zinc finger protein 502 is involved in the regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolism.  Biological process: regulation of transcription	(57)
FLJ10178	-13,3205	5,04E-09	FLJ10178 (gene: CXorf57) chromosome X open reading frame 57  Hypothetical protein	
CLEC5A	-12,40957	1,25E-06	This gene encodes a member of the C-type lectin/C-type lectin-like domain (CTL/CTLD) superfamily. Members of this family share a common protein fold and have diverse functions, such as cell adhesion, cell-cell signalling, glycoprotein turnover, and roles in inflammation and immune response. The encoded type II transmembrane protein interacts with dnax-activation protein 12 and may play a role in cell activation.  Biological process: cellular defense response, signal transduction	(58, 59)
FGF16	-12,39458	1,26E-06	The protein encoded by this gene is a member of the fibroblast growth factor (FGF) family. FGF family members possess broad mitogenic and cell survival activities, and are involved in a variety of biological processes, including embryonic development, cell growth, morphogenesis, tissue repair, tumor growth and invasion. In contrast, the proliferation of embryonic cardiomyocytes was significantly decreased, indicating that Fgf16 is a growth factor for these cells. The embryonic heart phenotype is similar to that of the Fgf9 knockout heart, indicating Fgf9 and Fgf16 to synergistically act as growth factors for embryonic cardiomyocytes.  Biological process: cell-cell signaling, response to temperature stimulus	(60, 61)
KIAA0101	-12,07166	2,97E-06	This gene is identical with the p15(PAF) gene and may be involved in protection of cells from UV-induced cell death  After genotoxic stress, normal cells trigger DNA repair or, if unable to repair, undergo apoptosis to eradicate the cells that bear the risk of becoming tumorigenic. The repression of the transcription factor, activating transcription factor 3 (ATF3), after ultraviolet (UV)-mediated	(62)

			<p>genotoxic stress impairs the DNA repair process. There is evidence that ATF3 directly regulates the proliferating cell nuclear antigen (PCNA)-associated factor KIAA0101/p15(PAF). The expressions of ATF3 and p15(PAF) is sufficient to trigger the DNA repair machinery, and attenuation of their expression alters DNA repair mechanisms.</p> <p>Biological process: DNA-repair</p>	
HIST1H1A	-12,06276	7,97E-09	<p>Histones encoded by this gene are basic nuclear proteins responsible for nucleosome structure of the chromosomal fiber in eukaryotes. The linker histone, H1, interacts with linker DNA between nucleosomes and functions in the compaction of chromatin into higher order structures. This gene is intronless and encodes a member of the histone H1 family.</p> <p>Biological process: nucleosome assembly</p>	(63)
GRPR	-11,7773	3,99E-08	<p>The gastrin-releasing peptide receptor or GRP-preferring bombesin receptor is activated by the endogenous ligands gastrin-releasing peptide (GRP), neuromedin B (NMB) and GRP18-27 (neuromedin C). Three subtypes of bombesin receptor are known: a GRP-preferring receptor (BB1 receptor), a NMB-preferring receptor (BB2 receptor) and an orphan receptor (bb3 receptor). The receptors are Gq/11-coupled and are involved in the regulation of many biological functions including sensory transmission, thermoregulation, feeding, pituitary, gastric and pancreatic secretion. They may also be involved in tissue development, proliferation and differentiation.</p> <p>GO) biological process: G-protein coupled receptor protein signaling pathway, cell proliferation</p>	(64, 65)

### References to Supplemental Table 5

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