

Supplementary Table I Signal transduction and growth factor pathways.

Pathway	Gene	Symbol	Unigene
Mitogenic	Early growth response 1	EGR1	Hs.326035
	V-fos FBJ murine osteosarcoma viral oncogene homolog	FOS	Hs.25647
	Jun oncogene	JUN	Hs.525704
Wnt	Cyclin 1	CCND1	Hs.523852
	Jun oncogene	JUN	Hs.525704
	Lymphoid enhancer-binding factor 1	LEF1	Hs.555947
	V-myc myelocytomatosis viral oncogene homolog (avian)	MYC	Hs.202453
	Peroxisome proliferator-activated receptor gamma	PPARG	Hs.162646
	Transcription factor 7	TCF7	Hs.573153
	Vascular endothelial growth factor A	VEGFA	Hs.73793
	WNT1 inducible signaling pathway protein 1	WISP1	Hs.492974
Hedgehog	Bone morphogenetic protein 2	BMP2	Hs.73853
	Bone morphogenetic protein 4	BMP4	Hs.68879
	Engrailed homeobox 1	EN1	Hs.271977
	Forkhead box A2	FOXA2	Hs.155651
	Patched homolog 1	PTCH1	Hs.494538
	Wingless-type MMTV integration site family member 1	WNT1	Hs.248164
	Wingless-type MMTV integration site family member 2	WNT2	Hs.567356
TGF-beta	Cyclin-dependent kinase inhibitor 1A	CDKN1A	Hs.370771
	Cyclin-dependent kinase inhibitor 1B	CDKN1B	Hs.238990
	Cyclin-dependent kinase inhibitor 2A	CDKN2A	Hs.512599
	Cyclin-dependent kinase inhibitor 2B	CDKN2B	Hs.72901
Survival pathway			
PI3 kinase/Akt	B-cell CLL/lymphoma2	BCL2	Hs.150749
	Cyclin 1	CCND1	Hs.523852
	Fibronectin 1	FN1	Hs.203717
	Jun oncogene	JUN	Hs.525704
	Matrix metalloproteinase 7	MMP7	Hs.2256
	V-myc myelocytomatosis viral oncogene homolog (avian)	MYC	Hs.202453
Jak/Src	B-cell CLL/lymphoma2	BCL2	Hs.150749
	BCL2-like 1	BCL2L1	Hs.516966
NFkB	BCL2-related protein A1	BCL2A1	Hs.227817
	Baculoviral IAP repeat-containing 2	BIRC2	Hs.696238
	Baculoviral IAP repeat-containing 3	BIRC3	Hs.127799
	NLR family, apoptosis inhibitory protein	NAIP	Hs.646951
	Telomerase reverse transcriptase	TERT	Hs.492203
p53	BCL2-associated X protein	BAX	Hs.631546
	Cyclin-dependent kinase inhibitor 1A	CDKN1A	Hs.370771
	Fas (TNF receptor superfamily member 6)	FAS	Hs.244139
	Growth arrest and DNA-damage-inducible alpha	GADD45A	Hs.80409
	Insulin-like growth factor binding protein 3	IGFBP3	Hs.450230
	Mdm2, transformed 3T3 cell double minute 2, p53 binding protein	MDM2	Hs.567303
	Tumor protein p53 inducible protein 3	TP53I3	Hs.50649
CREB	Cytochrome P450, family 19, subfamily A, polypeptide 1	CYP19A1	Hs.654384
	Early growth response 1	EGR1	Hs.326035
	V-fos FBJ murine osteosarcoma viral oncogene homolog	FOS	Hs.25647
Jak-Stat	Chemokine (C-X-C motif) ligand 9	CXCL9	Hs.77367
	Interleukin 4	IL4	Hs.73917
	Interleukin 4 receptor	IL4R	Hs.513457

	Interferon regulatory factor 1	IRF1	Hs.436061
	Matrix metalloproteinase 10	MMP10	Hs.2258
	Nitric oxide synthase 2A	NOS2A	Hs.706746
Retinoic acid	Engrailed homeobox 1	EN1	Hs.271977
	Homeobox A1	HOXA1	Hs.67397
	Retinol binding protein 1, cellular	RBP1	Hs.529571
Insulin	CCAAT/enhancer binding protein beta	CEBPB	Hs.517106
	Fatty acid synthase	FASN	Hs.83190
	Glycogen synthase 1	GYS1	Hs.386225
	Hexokinase 2	HK2	Hs.406266
	Leptin	LEP	Hs.194236
Phospholipase C	B-cell CLL/lymphoma2	BCL2	Hs.150749
	Early growth response 1	EGR1	Hs.326035
	V-fos FBJ murine osteosarcoma viral oncogene homolog	FOS	Hs.25647
	Intercellular adhesion molecule 1	ICAM1	Hs.707983
	Jun oncogene	JUN	Hs.525704
	Nitric oxide synthase 2A	NOS2A	Hs.706746
	Prostaglandin-endoperoxide synthase 2	PTGS2	Hs.196384
	Vascular cell adhesion molecule 1	VCAM1	Hs.109225
Calcium and protein kinase C	Colony stimulating factor 2	CSF2	Hs.1349
	V-fos FBJ murine osteosarcoma viral oncogene homolog	FOS	Hs.25647
	Interleukin 2	IL2	Hs.89679
	Jun oncogene	JUN	Hs.525704
	V-myc myelocytomatosis viral oncogene homolog (avian)	MYC	Hs.202453
	Omithine decarboxylase 1	ODC1	Hs.467701
	Protein kinase C, alpha	PRKCA	Hs.531704
	Protein kinase C, epsilon	PRKCE	Hs.580351
	Transferrin receptor	TFCR	Hs.529618
EGF	ELK1, member of ETS oncogene family	ELK1	Hs.701980
	V-fos FBJ murine osteosarcoma viral oncogene homolog	FOS	Hs.25647
	Jun oncogene	JUN	Hs.525704
	Signal transducer and activator of transcription 1	STAT1	Hs.708051
	Signal transducer and activator of transcription 3	STAT3	Hs.463059
	Signal transducer and activator of transcription 5A	STAT5A	Hs.437058
IGF1	ELK1, member of ETS oncogene family	ELK1	Hs.701980
	V-fos FBJ murine osteosarcoma viral oncogene homolog	FOS	Hs.25647
	Jun oncogene	JUN	Hs.525704
Insulin signaling	ELK1, member of ETS oncogene family	ELK1	Hs.701980
	V-fos FBJ murine osteosarcoma viral oncogene homolog	FOS	Hs.25647
	Jun oncogene	JUN	Hs.525704
	Forkhead box O1	FOXO1	Hs.370666
PDGF	ELK1, member of ETS oncogene family	ELK1	Hs.701980
	V-fos FBJ murine osteosarcoma viral oncogene homolog	FOS	Hs.25647
	Jun oncogene	JUN	Hs.525704
	Signal transducer and activator of transcription 1	STAT1	Hs.708051
	Signal transducer and activator of transcription 3	STAT3	Hs.463059
	Signal transducer and activator of transcription 5A	STAT5A	Hs.437058
G-protein coupled r	CAMP responsive element binding protein 1	CREB1	Hs.584750
	ELK1, member of ETS oncogene family	ELK1	Hs.701980
	V-fos FBJ murine osteosarcoma viral oncogene homolog	FOS	Hs.25647
	Jun oncogene	JUN	Hs.525704
	Nuclear factor of activated T-cells, cytoplasmic	NFATC1	Hs.534074
Notch	CREB binding protein	CREBBP	Hs.459759
	Histone deacetylase 1	HDAC1	Hs.88556

MAPK pathway			
Erk1/Erk2	ELK1, member of ETS oncogene family	ELK1	Hs.701980
	V-myc myelocytomatosis viral oncogene homolog (avian)	MYC	Hs.202453
	Signal transducer and activator of transcription 3	STAT3	Hs.463059
P38 signaling	Activating transcription factor 2	ATF2	Hs.705370
	CAMP responsive element binding protein 1	CREB1	Hs.584750
	ELK1, member of ETS oncogene family	ELK1	Hs.701980
	MYC associated factor x	MAX	Hs.285354
	Myocyte enhancer factor 2A	MEF2A	Hs.268675
	V-myc myelocytomatosis viral oncogene homolog (avian)	MYC	Hs.202453
	Signal transducer and activator of transcription 1	STAT1	Hs.708051
Hypoxia signaling	Hypoxia-inducible factor 1	HIF1A	Hs.654600
	Endothelial PAS domain protein 1	HIF2A	Hs.468410
	Hypoxia-inducible factor 3	HIF3A	Hs.420830
	Insulin-like growth factor binding protein 1	IGFBP1	Hs.642938
	Insulin-like growth factor 2	IGF2	Hs.523414
	Dynactin 2	DCTN2	Hs.289123
	Interleukin 1 alpha	IL1A	Hs.1722
	Interleukin 6	IL6	Hs.654458
	Metallothionein 3	MT3	Hs.73133
	Neuropeptide Y	NPY	Hs.1832
	Retinoic acid receptor, alpha	RARA	Hs.654583
	Peroxisome proliferative activated receptor, alpha	PPARA	Hs.103110
	Vascular endothelial growth factor A	VEGFA	Hs.73793
	Notch homolog 1, translocation associated	NOTCH1	Hs.495473
	Nitric oxide synthase 2A	NOS2A	Hs.706746
	CREB binding protein	CREBBP	Hs.459759
	BCL2-associated X protein	BAX	Hs.631546
	Hexokinase 2	HK2	Hs.406266
	Leptin	LEP	Hs.194236

Supplementary Table II Differentially expressed genes in hESCs after exposure to hypoxia.

Gene	Symbol	Fold regulation in both media	Pathway
Baculoviral IAP repeat-containing 2	BIRC2	3.1 ↑	Survival pathway: NFkB
Cyclin-dependent kinase inhibitor 1A	CDKN1A	2.1 ↑	TGF-beta, p53
Colony stimulating factor 2	CSF2	32.0 ↑	Calcium and PKC
Dynactin 2	DCTN2	2.1 ↓	Hypoxia signaling: cell proliferation, cytoskeleton
V-fos FBJ murine osteosarcoma viral oncogene homolog	FOS	2.7 ↑	EGF, IGF1, Insulin, PDGF, Calcium and PKC, CREB, G-protein coupled R signaling, mitogenic, phospholipase C
Interleukin 2	IL2	2.0 ↑	Calcium and PKC
Peroxisome proliferative activated receptor, alpha	PPARA	3.1 ↓	Hypoxia signaling: transcription factor, lipid metabolism
Protein kinase C, epsilon	PRKCE	3.0 ↑	Calcium and PKC
Transferrin receptor	TFRC	2.3 ↓	Calcium and PKC
Vascular endothelial growth factor A	VEGFA	2.8 ↑	Wnt, Hypoxia signaling: cell growth, signal transduction, anti-apoptosis, response to stress
Wingless-type MMTV integration site family member 2	WNT2	2.9 ↑	Hedgehog
Gene	Symbol	Fold regulation hES medium	Pathway
Cyclin 1	CCND1	5.9 ↑	Survival pathway: PI3 kinase/Akt
Histone deacetylase 1	HDAC1	2.9 ↑	Notch signaling
Insulin-like growth factor binding protein 3	IGFBP3	2.4 ↑	p53
Interferon regulatory factor 1	IRF1	5.4 ↑	Jak-Stat
MYC associated factor x	MAX	2.9 ↑	MAPK: p38 signaling
Matrix metalloproteinase 10	MMP10	5.2 ↑	Jak-Stat
V-myc myelocytomatosis viral oncogene homolog	MYC	4.8 ↑	Calcium and PKC, Wnt, Survival pathway: PI3 kinase/Akt; MAPK: p38 signaling
Nuclear factor of activated T-cells, cytoplasmic	NFATC1	11.8 ↑	G-protein coupled R signaling
Gene	Symbol	Fold regulation RegES medium	Pathway
BCL2-associated X protein	BAX	2.8 ↓	p53 , hypoxia signaling: apoptosis, cell cycle
B-cell CLL/lymphoma2	BCL2	2.4 ↓	Survival pathway: PI3 kinase/Akt , Jak/src; phospholipase C
BCL2-like 1	BCL2L1	5.8 ↓	Survival pathway: Jak/src
Baculoviral IAP repeat-containing 3	BIRC3	3.3 ↓	Survival pathway: NFkB

Bone morphogenetic protein 2	BMP2	3.4 ↓	Hedgehog
CCAAT/enhancer binding protein beta	CEBPB	4.6 ↓	Insulin
Engrailed homeobox 1	EN1	5.2 ↓	Retinoic acid
Fas (TNF receptor superfamily member 6)	FAS	3.6 ↓	p53
Hexokinase 2	HK2	3.3 ↓	Insulin, hypoxia signaling: cell cycle, carbohydrate metabolism
Homeobox A1	HOXA1	5.2 ↓	Retinoic acid
Insulin-like growth factor binding protein 1	IGFBP1	3.3 ↓	Hypoxia signaling: signal transduction, growth factor
Insulin-like growth factor binding protein 3	IGFBP3	2.2 ↓	p53
Interleukin 4 receptor	IL4R	2.0 ↑	Jak-Stat
Jun oncogene	JUN	2.1 ↑	Mitogenic, Wnt, Survival pathway:PI3 kinase; Phospholipase C, EGF, IGF1, Insulin, PDGF
Leptin	LEP	2.7 ↓	Insulin, Hypoxia signaling: signal transduction
MYC associated factor x	MAX	6.3 ↓	MAPK: p38 signaling
Metallothionein 3	MT3	4.3 ↓	Hypoxia signaling: response to stress, cell proliferation, superoxide metabolism
Omithine decarboxylase 1	ODC1	4.2 ↓	Calcium and PKC
Protein kinase C, alpha	PRKCA	3.2 ↓	Calcium and PKC
Retinol binding protein 1, cellular	RBP1	3.1 ↓	Retinoic acid
Signal transducer and activator of transcription 3	STAT3	2.9 ↓	MAPK: Erk1/Erk2; PDGF, EGF
Vascular cell adhesion molecule 1	VCAM1	2.8 ↓	Phospholipase C
WNT1 inducible signaling pathway protein 1	WISP1	3.1 ↓	Wnt