

Functional Heterogeneity within the CD44 High Human Breast Cancer Stem Cell-Like Compartment Reveals a Gene Signature Predictive of Distant Metastasis

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RELATED TO FIGURE 1, SUPPLEMENTARY FIGURES S1–S3 AND SUPPLEMENTARY TABLE S1:

Characterization of Single Cell Clones, A4 and G4

The isogenic background of CD44^{hi}/CD24⁺ G4 and CD44^{hi}/CD24^{lo} A4 was shown by G-band karyotyping relative to the parental cell line and revealed identical genetic abnormalities (1) (Supplementary Figure S1). Moreover, the phenotypic stability of the CD44^{hi}/CD24⁺ G4 and CD44^{hi}/CD24^{lo} A4 clones over time, as determined by CD44 and CD24 expression, was analyzed under normal adherent growth conditions. In the presence of growth factors (EGF and FGF) the morphology, CD44 and CD24 expression of the CD44^{hi}/CD24⁺ G4 clones remained unchanged during 3 wks of passages (14 cell doublings). In contrast, in the absence of growth factors, the CD44^{hi}/CD24⁺ G4 clone grew more slowly and increased CD24 expression to the level of the CD44^{hi}/CD24^{lo} A4 clone and the parental cell line, although the morphology remained mesenchymal-like. CD44 levels remained unchanged. For the CD44^{hi}/CD24^{lo} A4 clone, CD44 and CD24 expression remained unchanged in both the presence and absence of growth factors (Supplementary Figure S2).

A4 and G4 are designated Basal A and Basal B phenotypes according to their

transcription profiles, morphology and invasion features, which highly resemble those previously described for Basal A and Basal B cell lines and primary tumors (2-4). A4 is designated Basal A due to the luminal-like morphology and its expression of genes distinct from Basal B (3) including *DDR1*, *SHANK2*, *RBM47*, *F11R*, *ATAD4*, *ESRP1*, *SLC9*, *ERBB3*, *CRABP2*, *SPINT2*, *EFHD1*, *MYO5C*, *SPINT1*, *ANK3*, *DLG3*, *RAB25*, *EPCAM*, *CLDN4*, *PRSS8*, *ELF3*, *CD24*, *GRHL2*. G4 is designated Basal B, due to the mesenchymal-like appearance and higher invasive potential in Boyden chambers (24-well QCM™ Endothelial Cell Invasion Assay; EMD Millipore, Billerica, MA, USA) relative to A4 (Supplementary Figure S3). Further, G4 exhibits higher expression of *ZEB1*, *EMP3*, *FBN1*, *TGFBI*, *VIM* and *SPARC* relative to A4. These genes distinguish the Basal B group from cells with other features (3).

RELATED TO FIGURE 5, SUPPLEMENTARY FIGURE S4 AND SUPPLEMENTARY TABLE S2:

Gene Array Profiling of the CD44^{hi}/CD24^{lo} Subsets Revealed Novel Markers and Pathways Linked to Tumor-Initiating Cells as well as a Prognostic Gene Signature

The outcome of gene array analysis of G4 and A4 showed a total of 3660 differentially expressed genes (FDR 0.01, p<

0.01). A panel of 599 mRNAs was expressed differentially more than two-fold between G4 and A4 (Supplementary Table S2). Ingenuity pathway analysis revealed several networks, including a network of 59 genes that were up-regulated more than three-fold in A4 compared to G4, including genes known to be involved in cancer, reproductive systems and genetic disease (Supplementary Figure S4).

SUPPLEMENTAL REFERENCES

1. Brothman AR, Persons DL, Shaffer LG (2009) Nomenclature evolution: Changes in the ISCN from the 2005 to the 2009 edition. *Cytogenet Genome Res* 127: 1-4.
2. Neve RM, et al. (2006) A collection of breast cancer cell lines for the study of functionally distinct cancer subtypes. *Cancer Cell* 10: 515-527.
3. Blick T, et al. (2010) Epithelial mesenchymal transition traits in human breast cancer cell lines parallel the CD44(hi)/CD24(lo/-) stem cell phenotype in human breast cancer. *J Mammary Gland Biol Neoplasia* 15: 235-252.
4. Shipitsin M, et al. (2007) Molecular definition of breast tumor heterogeneity. *Cancer Cell* 11: 259-273.

HMT3909S13:

43-57,XX,+1,add(1)(p36),dup(1)(q25q44),add(3)(q29),+5,+5,+6,add(9)(p13),add(9)(p24),
add(11)(p15),del(11)(p11),-14,+16,add(16)(q24)x2,-21,-22,-22,+5-9mar[cp18]

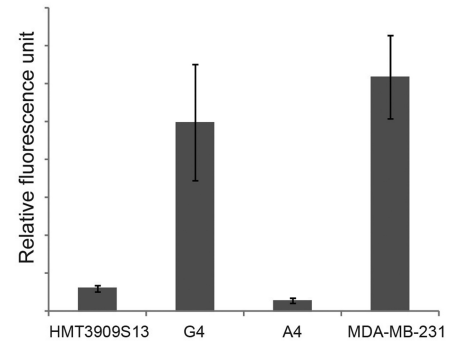
A4:

50-58,XX,+1,add(1)(p36),dup(1)(q25q44),add(3)(q29),+5,+5,+6,add(9)(p13),add(9)(p24),
add(11)(p15),del(11)(p11),-14,+16,add(16)(q24)x2,-21,-22,-22,+5-9mar[cp18]

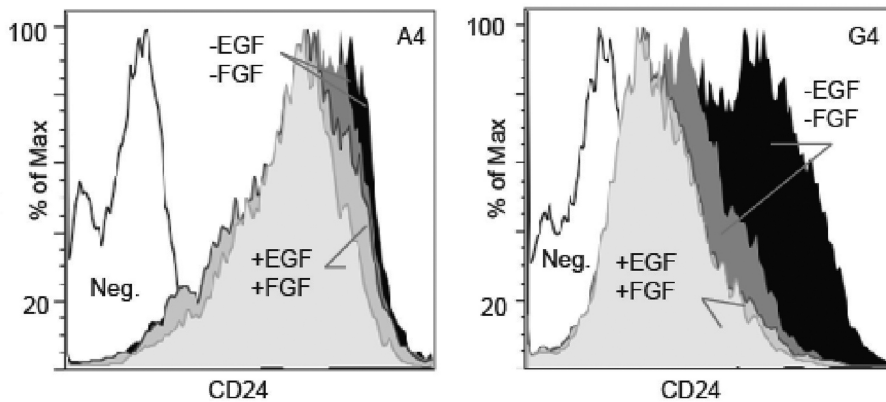
G4:

48-54,XX,+1,add(1)(p36),dup(1)(q25q44),add(3)(q29),+5,+5,+6,add(9)(p13),add(9)(p24),
add(11)(p15),del(11)(p11),-14,+16,add(16)(q24)x2,-21,-22,-22,+5-9mar[cp17]

Supplementary Figure S1. G-band karyotyping of HMT3909S13, A4 and G4 described in accordance with the International System for Human Cytogenetic Nomenclature (ISCN 2005).



Supplementary Figure S3. Boyden chamber invasion assay. Cell invasion assay of HMT3909S13, G4, A4 and MDA-MB-231 was performed according to manufacturer's protocol in 72 h. The figure is representative of four experiments. Cells were grown in MEGM without B27.

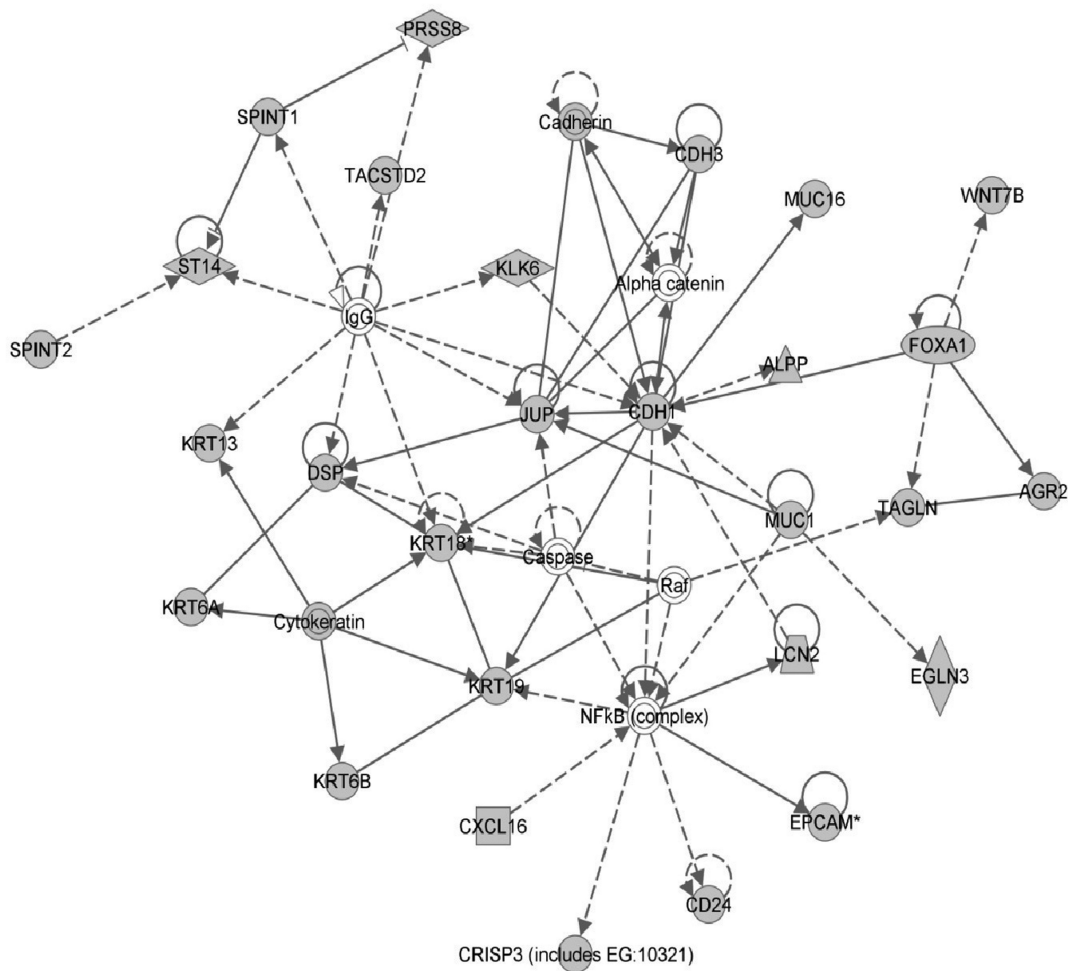


Supplementary Figure S2. Phenotypic stability of the CD44^{hi}/CD24^{lo} G4 and CD44^{hi}/CD24^{lo} A4 clones, as determined by CD24 expression using flow cytometry, were analyzed under normal adherent growth conditions. The chromatogram of the 1st and 14th doublings are depicted with and without growth factors (EGF and FGF).

Supplementary Table S1. Immunocytochemical staining of the CD44^{hi}/CD24⁻ G4 and CD44^{hi}/CD24^{lo} A4 clones and the parental cell line HMT3909S13.

	CD44 ^{hi} /CD24 ⁻ G4	CD44 ^{hi} /CD24 ^{lo} A4	HMT3909S13
ER/PgR/HER2	-	-	-
CD24	-	+(10%)	-
Vimentin	+++ (80%)	++ (5%)	+++ (100%)
E-Cadherin	++ (40%)	+(80%)	-
CK 5/6	++ (50%)	+++ (90%)	++ (70%)
CK 7/8, 18, 19	+++ (100%)	+++ (100%)	+++ (100%)
CK 14	+(100%)	+(100%)	+(100%)
CK17	++ (80%)	+(80%)	+(80%)
CD29/ Integrin β1	++ (100%)	++ (100%)	++ (100%)
CD49f/ Integrin α6	+(50%)	+(50%)	+(50%)
ESA/EpCAM	++ (30%)	++ (100%)	-
HER1/EGFR	++ (70%)	++ (70%)	+(70%)

The staining intensity and percentage of cells expressing protein are listed. The staining intensity is graded: -, +, ++ and +++.



Supplementary Figure S4. Ingenuity Pathway analysis predicted a network of 59 genes that were upregulated more than three-fold in A4 compared to G4, including genes known to be involved in cancer, reproductive systems and genetic disease.

FUNCTIONAL HETEROGENEITY OF CANCER STEM CELL-LIKE CELLS

Supplementary Table S2. Microarray data of 599 mRNAs more than two-fold differently expressed in A4 relative to G4 (FDR 0.01).^{a,b}

Gene assignment	Gene Symbol	p-value	Fold-Change (A4 vs G4)	Gene assignment	Gene Symbol	p-value	Fold-Change (A4 vs G4)
epithelial splicing regulatory protein 1	ESRP1	2.85E-12	71,72	serine peptidase inhibitor, Kunitz type 1	SPINT1	7,03E-09	5,79
urothelial cancer associated 1 (non-protein coding)	UCA1	6,73E-12	59,13	mucin 12, cell surface associated	MUC12	2,22E-05	5,76
plastin 3	PLS3	4,22E-15	54,51	ectonucleotide pyrophosphatase/phosphodiesterase 5	ENPP5	2,28E-07	5,74
epithelial cell adhesion molecule	EPCAM	2,25E-10	48,08	ArfGAP with dual PH domains 1	ADAP1	1,64E-08	5,70
vestigial like 1	VGLL1	2,34E-09	47,76	UDP-GlcNAc transferase	B3GNT3	4,74E-08	5,68
cadherin 1, type 1, E-cadherin	CDH1	1,37E-10	43,55	solute carrier family 6	SLC6A11	4,50E-07	5,65
integrin, beta 6	ITGB6	8,00E-09	32,75	protein kinase, cAMP-dependent, regulatory, type II	PRKAR2B	1,29E-05	5,58
pancreatic lipase-related protein 3	PNLIPRP3	1,57E-11	32,72	sushi, von Willebrand factor type A	SVEP1	7,62E-06	5,42
myelin protein zero-like 2	MPZL2	1,82E-07	26,89	F11 receptor	F11R	2,82E-06	5,41
tandem C2 domains, nuclear	TC2N	8,25E-11	25,00	interferon regulatory factor 6	IRF6	3,66E-08	5,36
grainyhead-like 2	GRHL2	9,76E-11	24,61	transmembrane protein 63C	TMEM63C	2,32E-05	5,35
RAB25, member RAS oncogene family	RAB25	1,18E-10	24,31	microtubule-associated protein 7	MAP7	1,91E-09	5,32
kallikrein-related peptidase 6	KLK6	2,95E-06	23,39	retinoic acid receptor responder	RARRR51	6,00E-05	5,30
anterior gradient homolog 2	AGR2	7,38E-09	21,31	UDP-N-acetyl-alpha-D-galactosamine	GALNT3	7,26E-08	5,28
cadherin 3, type 1, P-cadherin	CDH3	1,06E-07	18,37	myosin VC	MYO5C	3,33E-05	5,20
G protein-coupled receptor 110	GPR110	1,90E-07	18,31	solute carrier organic anion transporter family	SLCO1B3	7,15E-07	5,14
aldo-keto reductase family 1, member B10	AKR1B10	5,72E-08	16,91	exophilin 5	EXPH5	5,76E-10	5,14
claudin 7	CLDN7	7,06E-08	16,68	lipocalin 2	LCN2	4,37E-07	5,12
solute carrier family 7	SLC7A7	2,55E-10	16,20	interleukin 20 receptor	IL20RA	2,62E-06	5,09
adaptor-related protein complex 1, mu 2 subunit	AP1M2	1,61E-10	15,91	epithelial splicing regulatory protein 2	ESRP2	8,93E-07	4,91
coxsackie virus and adenovirus receptor	CXADR	4,80E-09	13,83	protocadherin 7	PCDH7	2,92E-07	4,90
cysteine-rich secretory protein 3	CRISP3	6,14E-06	12,59	plasma membrane proteolipid (plasmolipin)	PLLP	1,42E-05	4,87
peptidyl arginine deiminase, type IV	PADI4	4,69E-07	12,49	endoplasmic reticulum metalloproteinase 1	ERMP1	1,40E-08	4,87
family with sequence similarity 83, member B	FAM83B	2,04E-07	11,49	ATP-binding cassette, sub-family A (ABC1), member 12	ABCA12	1,67E-08	4,85
lipolysis stimulated lipoprotein receptor	LSR	2,77E-12	11,36	CDP-diacylglycerol synthase	CDS1	2,35E-07	4,83
GRAM domain containing 2	GRAMD2	1,10E-08	11,17	membrane protein, palmitoylated 7	MPP7	4,07E-07	4,81
scieillin	SCEL	1,05E-07	10,40	cellular retinoic acid binding protein 2	CRABP2	6,50E-06	4,75
ceruloplasmin	CP	1,62E-06	10,35	annexin A3	ANXA3	4,34E-06	4,72
protease, serine, 8	PRSS8	2,33E-09	10,21	carbonyl reductase 1	CBR1	2,76E-07	4,72
s100 calcium binding protein A14	S100A14	1,34E-10	10,16	alkaline phosphatase, placental	ALPP	3,71E-06	4,67
mucin 16, cell surface associated	MUC16	1,81E-06	9,94	transmembrane protein 30B	TMEM30B	1,20E-08	4,63
serine peptidase inhibitor, Kunitz type, 2	SPINT2	1,91E-05	9,77	aldo-keto reductase family 1, member C2	AKR1C2	4,31E-04	4,62
suppression of tumorigenicity 14 (colon carcinoma)	ST14	3,59E-09	9,42	gap junction protein, alpha 5	GJA5	4,08E-06	4,62
myosin VB	MYO5B	1,70E-09	9,36	lipase, member H	LIPH	1,09E-05	4,59
histone cluster 1, H3i	HIST1H3I	1,48E-05	9,00	kallikrein-related peptidase 10	KLK10	2,04E-06	4,56
fibroblast growth factor receptor 2	FGFR2	7,97E-08	8,62	ets homologous factor	EHF	3,18E-08	4,48
transgelin	TAGLN	3,45E-06	8,52	v-erb-b2 erythroblastic leukemia viral oncogene	ERBB3	1,35E-08	4,21
G protein-coupled receptor 56	GPR56	6,93E-06	8,48	WW and C2 domain containing 1	WWC1	3,91E-08	4,20
chromosome 1 open reading frame 116	C1orf116	1,50E-08	8,43	chromosome 9 open reading frame 152	C9orf152	2,47E-08	4,20
dermokine	DMKN	1,57E-10	8,13	prostate stem cell antigen	PSCA	5,02E-07	4,17
metastasis associated in colon cancer 1	MACC1	2,61E-07	8,02	glutathione S-transferase mu 3	GSTM3	1,37E-05	4,16
mal, T-cell differentiation protein 2	MAL2	6,17E-07	7,64	unc-5 homolog C	UNC5C	7,24E-06	4,16
phosphodiesterase 3B, cGMP-inhibited	PDE3B	6,36E-10	7,26	HRAS-like suppressor 2	HRASLS2	7,93E-09	4,13
desmoplakin	DSP	2,50E-05	7,23	TRAF2 and NCK interacting kinase	TNIK	9,11E-10	4,07
keratin 13	KRT13	4,64E-08	7,19	chromosome 19 open reading frame 46	C19orf46	9,36E-07	4,02
gasdermin C	GSDMC	2,60E-06	7,17	dehydrogenase/reductase (SDR family) member 3	DHRS3	1,08E-04	4,02
sema domain, seven thrombospondin repeats	SEMA5A	1,53E-08	7,16	sortilin-related receptor	SORL1	1,19E-07	4,01
E74-like factor 3 (ets domain transcription factor, epithelial)	ELF3	1,37E-07	6,90	fucosyltransferase 9 (alpha (1,3) fucosyltransferase)	FUT9	2,12E-07	3,98
MARVEL domain containing 2	MARVELD2	3,04E-08	6,88	kinesin family member 13B	KIF13B	4,37E-07	3,96
solute carrier family 7 (cationic amino acid transporter)	SLC7A8	1,97E-05	6,86	chromosome 19 open reading frame 21	C19orf21	1,14E-06	3,94
nephronectin	NPNT	2,45E-07	6,75	ArfGAP with RhoGAP domain	ARAP2	8,13E-05	3,94
complement factor H	CFH	9,83E-06	6,64	creatine kinase, mitochondrial 1A	CKMT1A	2,29E-07	3,93
ladinin 1	LAD1	8,27E-09	6,62	acyl-CoA synthetase family member 2	ACSF2	1,23E-05	3,88
hook homolog 1	HOOK1	4,10E-09	6,47	anoctamin 1, calcium activated chloride channel	ANO1	3,00E-08	3,86
junction plakoglobin	JUP	3,57E-09	6,32	tumor-associated calcium signal transducer 2	TACSTD2	4,75E-07	3,84
FXYD domain containing ion transport regulator 3	FXYD3	2,70E-07	6,28	carcinoembryonic antigen-related cell adhesion molecule	CEACAM1	1,22E-05	3,83
nucleoporin 210kDa	NUP210	1,37E-06	6,25	mucin 12, cell surface associated	MUC12	1,15E-04	3,83
ELOVL family member 7	ELOVL7	2,52E-08	6,22	chromosome 11 open reading frame 70	C11orf70	2,02E-08	3,83
occludin	OCLN	2,87E-07	6,06	wingless-type MMTV integration site family, member 7B	WN7B	3,87E-07	3,80
calcium channel, voltage-dependent, gamma subunit 4	CACNG4	7,83E-08	5,99	organic anion transporter LST-3b	LST-3TM12	2,05E-07	3,74
prominin 2	PROM2	6,40E-11	5,96	PLAUR domain containing 6B	LYPD6B	9,03E-07	3,67
transmembrane protein 156	TMEM156	2,84E-08	5,82	forkhead box A1	FOXA1	2,18E-09	3,63

Continued

Supplementary Table S2. Continued.^a

keratin 6A	KRT6A	1.14E-05	3,61	TIMP metalloproteinase inhibitor 3	TIMP3	4.10E-07	2,82
kallikrein-related peptidase 5	KLK5	1.85E-05	3,61	6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase 2	PFKFB2	9,04E-07	2,81
TIMP metalloproteinase inhibitor 3	TIMP3	4.94E-06	3,60	ATPase, class I, type 8B, member 1	ATP8B1	1,09E-04	2,80
lipase, family member K	LIPK	1.92E-06	3,58	PDZ and LIM domain 1	PDLM1	3,68E-08	2,79
laminin, alpha 3	LAMA3	1.38E-09	3,56	protein phosphatase 2 (formerly 2A), regulatory subunit	PPP2R3A	1,03E-06	2,79
Cas-Br-M ecotropic retroviral transforming sequence	CBLC	1,06E-07	3,55	G protein-coupled receptor 87	GPR87	3,72E-05	2,78
plastin 1	PLS1	1,04E-06	3,54	tripartite motif-containing 31	TRIM31	1,06E-06	2,77
solute carrier family 9	SLC9A7	3,94E-06	3,52	discoidin domain receptor tyrosine kinase 1	DDR1	5,23E-07	2,76
ankyrin 3, node of Ranvier	ANK3	4,80E-06	3,50	lethal giant larvae homolog 2 (Drosophila)	LLGL2	1,55E-06	2,76
retinol binding protein 4, plasma	RBP4	8,24E-07	3,47	calbindin 1, 28kDa	CALB1	1,61E-05	2,75
keratin 6B	KRT6B	1,83E-06	3,45	pregnancy specific beta-1-glycoprotein 4	PSG4	3,28E-05	2,73
xylosyltransferase I	XYLT1	1,08E-08	3,43	semaphorin 7A, GPI membrane anchor	SEMA7A	3,68E-05	2,72
egl nine homolog 3	EGLN3	7,81E-07	3,40	glutathione peroxidase 2 (gastrointestinal)	GPX2	4,44E-06	2,71
tripartite motif-containing 29	TRIM29	5,99E-06	3,38	pregnancy specific beta-1-glycoprotein 7	PSG7	6,49E-05	2,71
complement factor H-related 1	CFHR1	5,00E-06	3,35	tetraspanin 1	TSPAN1	3,42E-05	2,71
chromosome 6 open reading frame 132	C6orf132	2,10E-08	3,35	tripartite motif-containing 31	TRIM31	1,43E-06	2,69
solute carrier family 37	SLC37A1	6,47E-07	3,33	calmin (calponin-like, transmembrane)	CLMN	6,14E-09	2,68
CMT1A duplicated region transcript 1	CDRT1	9,76E-05	3,32	myosin IB	MYO1B	8,88E-06	2,68
RNA binding motif protein 47	RBM47	4,40E-08	3,31	angiotensin I converting enzyme (peptidyl-dipeptidase A) 2	ACE2	1,03E-06	2,67
CD24 molecule	CD24	8,58E-06	3,29	leucine zipper, down-regulated in cancer 1	LDOC1	3,59E-07	2,67
Kallmann syndrome 1 sequence	KAL1	3,15E-05	3,29	ABI family, member 3 (NESH) binding protein	ABI3BP	1,72E-05	2,66
keratin 19	KRT19	1,41E-05	3,27	FYVE, RhoGEF and PH domain containing 3	FGD3	4,25E-07	2,66
histone cluster 1, H1b	HIST1H1B	5,91E-05	3,24	mucin 21, cell surface associated	MUC21	1,54E-04	2,65
actin-related Arp11	ARP11	3,50E-04	3,23	ribosomal protein S6 kinase, 90kDa, polypeptide 6	RPS6KA6	6,95E-07	2,65
odd-skipped related 2	OSR2	8,47E-06	3,23	mucin 21, cell surface associated	MUC21	2,04E-04	2,65
solute carrier family 12 (sodium/chloride transporters)	SLC12A3	3,18E-05	3,22	macrophage stimulating 1 receptor (c-met-related tyrosine)	MST1R	6,08E-06	2,64
transmembrane channel-like 5	TMC5	6,20E-09	3,21	3'-phosphoadenosine 5'-phosphosulfate synthase 2	PAPSS2	2,80E-06	2,63
neuregulin 4	NRG4	4,73E-06	3,21	discoidin domain receptor tyrosine kinase 1	DDR1	3,71E-07	2,63
SH2 domain containing 3A	SH2D3A	2,45E-07	3,20	keratin 17	KRT17	7,12E-05	2,63
chromatin modifying protein 4C	CHMP4C	1,24E-05	3,19	acid phosphatase 6, lysophosphatidic	ACP6	1,25E-04	2,62
StAR-related lipid transfer (START) domain	STAR10	1,60E-07	3,19	ring finger protein 144B	RNF144B	1,43E-04	2,61
keratin 18	KRT18	6,27E-07	3,18	ATPase family, AAA domain containing 4	ATAD4	5,62E-07	2,61
chemokine (C-X-C motif) ligand 16	CXCL16	5,07E-05	3,14	ankyrin repeat domain 2 (stretch responsive muscle)	ANKRD2	2,06E-04	2,61
folliculin	FST	5,43E-06	3,14	hypothetical LOC641928	FLJ16734	1,09E-04	2,60
mucin 1, cell surface associated	MUC1	5,71E-04	3,13	protease, serine, 22	PRSS2	5,04E-08	2,60
family with sequence similarity 84, member B	FAM84B	1,04E-04	3,12	receptor-interacting serine-threonine kinase 4	RIPK4	1,56E-05	2,60
keratin 18	KRT18	1,45E-06	3,12	rhotekin	RTKN	3,31E-06	2,59
phosphoenolpyruvate carboxykinase 2	PCK2	3,30E-04	3,11	discoidin domain receptor tyrosine kinase 1	DDR1	6,89E-07	2,59
InaD-like	INADL	8,45E-08	3,11	sulfotransferase family, cytosolic, 2B, member 1	SULT2B1	1,19E-07	2,59
glycerophosphodiester	GDPD3	5,35E-07	3,10	beta-carotene oxygenase 2	BCO2	1,24E-06	2,59
family with sequence similarity 160, member A1	FAM160A1	6,32E-07	3,06	signal transducing adaptor family member 2	STAP2	7,63E-06	2,58
mucin 21, cell surface associated	MUC21	4,08E-05	3,05	sushi-repeat-containing protein, X-linked 2	SRPX2	5,50E-04	2,58
muscleblind-like 3	MBNL3	6,73E-07	3,05	ATPase, class II, type 9A	ATP9A	3,54E-06	2,56
fyn-related kinase	FRK	5,15E-05	3,05	mannosyl (alpha-1,3-)glycoprotein beta-1,4-N-acetylgluco	MGAT4A	1,01E-04	2,56
myxovirus (influenza virus) resistance 1	MX1	7,85E-04	3,04	transforming growth factor, alpha	TGFA	6,02E-07	2,56
chromosome 4 open reading frame 19	C4orf19	3,20E-07	3,04	nuclear receptor interacting protein 1	NRIP1	1,78E-06	2,56
zinc finger protein 165	ZNF165	1,86E-05	3,03	periplakin	PPL	1,04E-06	2,55
chemokine (C-C motif) ligand 28	CCL28	1,01E-05	3,01	secretory leukocyte peptidase inhibitor	SLPI	4,77E-05	2,52
sterile alpha motif domain containing 12	SAMD12	3,15E-07	3,01	solute carrier family 44, member 3	SLC44A3	3,07E-06	2,52
echinoderm microtubule associated protein like 5	EML5	9,37E-08	2,99	phospholipase A2, group XVI	PLA2G16	4,77E-05	2,52
keratin 8	KRT8	2,84E-07	2,96	tripartite motif-containing 31	TRIM31	3,50E-06	2,52
ATP-binding cassette, sub-family G (WHITE), member 2	ABCG2	3,65E-05	2,96	potassium voltage-gated channel, KQT-like subfamily	KCNQ3	9,44E-06	2,51
keratin 19 pseudogene 2	KRT19P2	9,87E-08	2,95	NK1 homeobox 2	NKX1-2	9,20E-07	2,51
cathepsin H	CTSH	3,49E-06	2,95	inhibitor of DNA binding 3, dominant negative helix-loop-helix	ID3	1,78E-04	2,50
Xg blood group	XG	8,23E-07	2,92	serine incorporator 2	SERINC2	2,65E-05	2,50
ovo-like 2 (Drosophila)	OVOL2	3,43E-06	2,91	transmembrane protein 141	TMEM141	3,85E-08	2,50
myosin ID	MYO1D	4,85E-07	2,91	transcription factor 7-like 1 (T-cell specific, HMG-box)	TCF7L1	1,45E-05	2,50
family with sequence similarity 83, member A	FAM83A	1,48E-05	2,89	scavenger receptor class A, member 3	SCARA3	1,37E-05	2,50
sulfotransferase family 1E, estrogen-preferring	SULT1E1	6,52E-04	2,89	poly(A) binding protein interacting protein 2B	PAIP2B	2,31E-06	2,50
protein tyrosine phosphatase, receptor type	PTPRJ	1,18E-06	2,89	tripartite motif-containing 16	TRIM16	1,81E-05	2,50
beta-site APP-cleaving enzyme 2	BACE2	1,31E-07	2,88	zinc finger protein 704	ZNF704	1,51E-08	2,49
keratin 18	KRT18	9,86E-09	2,85	transmembrane protein 139	TMEM139	1,55E-05	2,49
short chain dehydrogenase/reductase family 42E, member 1	SDR42E1	3,94E-07	2,85	transglutaminase 1 (K polypeptide epidermal type I)	TGM1	1,92E-07	2,48
chromosome 21 open reading frame 87	C21orf87	8,20E-06	2,83	DENN/MADD domain containing 2D	DENND2D	1,05E-04	2,48
osteomodulin	OMD	1,08E-05	2,82	mutated in colorectal cancers	MCC	5,79E-08	2,47
deltex homolog 4 (Drosophila)	DTX4	3,73E-08	2,82	plakophilin 3	PKP3	3,61E-07	2,47
allograft inflammatory factor 1-like	AIF1L	2,20E-06	2,82	transmembrane channel-like 4	TMC4	1,61E-05	2,47

Continued

FUNCTIONAL HETEROGENEITY OF CANCER STEM CELL-LIKE CELLS

Supplementary Table S2. Continued.^a

vesicle-associated membrane protein 8 (endobrevin)	VAMP8	8.39E-06	2.46	SID1 transmembrane family, member 2	SIDT2	8.79E-08	2.18
claudin 8	CLDN8	1.28E-05	2.46	ankyrin repeat domain 30A	ANKRD30A	2.43E-05	2.18
keratin 6C	KRT6C	4.97E-06	2.45	desmoglein 2	DSG2	6.04E-06	2.17
cell adhesion molecule 1	CADM1	5.33E-07	2.45	LPS-responsive vesicle trafficking	LRBA	3.56E-07	2.17
post-GPI attachment to proteins 2	PGAP2	1.95E-08	2.44	cystatin E/M	CST6	6.47E-06	2.17
interleukin 17 receptor B	IL17RB	3.43E-06	2.44	discs, large homolog 3 (Drosophila)	DLG3	1.32E-05	2.17
neurophilin 2	NRP2	3.17E-07	2.43	chromosome 3 open reading frame 57	C3orf57	9.43E-07	2.17
S100 calcium binding protein P	S100P	4.43E-04	2.42	DEP domain containing 6	DEPDC6	1.62E-05	2.16
chromosome 17 open reading frame 28	C17orf28	2.30E-06	2.42	chromosome 1 open reading frame 106	C1orf106	1.17E-06	2.16
myelin protein zero-like 3	MPZL3	2.73E-06	2.41	solute carrier family 20 (phosphate transporter)	SLC20A2	1.45E-05	2.16
nuclear receptor subfamily 3, group C, member 2	NR3C2	4.21E-06	2.41	adaptor-related protein complex 1, sigma 3 subunit	API3	1.32E-05	2.16
RAB15, member RAS oncogene family	RAB15	3.40E-08	2.41	family with sequence similarity 107, member B	FAM107B	5.09E-05	2.16
SH3 and multiple ankyrin repeat domains 2	SHANK2	3.29E-08	2.40	matrix Gla protein	MGP	7.95E-04	2.15
spectrin, beta, non-erythrocytic 2	SPTBN2	3.61E-07	2.40	uncoupling protein 2 (mitochondrial, proton carrier)	UCP2	5.23E-05	2.14
Rho GTPase activating protein 27	ARHGAP27	9.23E-10	2.39	choline dehydrogenase	CHDH	1.51E-04	2.14
prostaglandin E synthase	PTGES	7.92E-06	2.37	caspace 4, apoptosis-related cysteine peptidase	CASP4	1.70E-06	2.14
Rho-type GTPase-activating protein FLJ32810	FLJ32810	7.54E-07	2.37	StAR-related lipid transfer (START) domain	STARSD8	4.91E-05	2.14
chromosome 8 open reading frame 31	C8orf31	3.41E-08	2.37	ovo-like 1 (Drosophila)	OVOL1	7.65E-05	2.13
coiled-coil domain containing 120	CCDC120	8.36E-06	2.37	lipase, endothelial	LIPG	7.04E-04	2.13
synaptotagmin VIII	SYT8	2.47E-06	2.37	myosin, light chain 9, regulatory	MYL9	2.32E-04	2.13
glutathione S-transferase mu 1	GSTM1	1.56E-06	2.33	cytochrome b-561	CYB561	9.99E-07	2.13
erythrocyte membrane protein band 4.1-like 1	EPB41L1	6.99E-07	2.32	heparan sulfate 6-O-sulfotransferase 2	HS6ST2	1.68E-05	2.13
solute carrier family 37 (glycerol-3-phosphate transport)	SLC37A2	2.99E-04	2.32	chloride intracellular channel 3	CLIC3	1.28E-04	2.13
ST6 (alpha-N-acetyl-neuraminy-2,3-beta-galactosyl-5)	ST6GALNAC5	1.35E-05	2.31	signal-induced proliferation-associated 1 like 1	SIPA1L1	1.13E-05	2.12
NEL-like 2 (chicken)	NELL2	8.00E-04	2.31	disvelled associated activator of morphogenesis 1	DAAM1	4.61E-06	2.12
kallikrein-related peptidase 8	KLK8	4.03E-05	2.30	phosphoinositide-3-kinase, class 2, beta polypeptide	PIK3C2B	1.46E-05	2.12
phospholipase A2, group X	PLA2G10	1.82E-05	2.29	Sp6 transcription factor	SP6	1.52E-04	2.11
basic helix-loop-helix family, member e41	BHLHE41	4.00E-06	2.29	solute carrier family 9 (sodium/hydrogen exchanger)	SLC9A2	6.21E-05	2.11
glypican 4	GPC4	6.15E-06	2.29	KIAA1244	KIAA1244	1.59E-04	2.11
ventricular zone expressed PH domain homolog 1 (zebrafish)	VEPH1	3.76E-06	2.28	synaptotagmin-like 2	SYTL2	1.07E-04	2.11
multiple EGF-like-domains 9	MEGF9	5.90E-06	2.28	slingshot homolog 3 (Drosophila)	SSH3	3.06E-06	2.10
CMT1A duplicated region transcript 1	CDRT1	2.25E-04	2.28	biliverdin reductase B (flavin reductase (NADPH))	BLVRB	7.63E-06	2.10
family with sequence similarity 169, member A	FAM169A	4.63E-06	2.28	NLR family, pyrin domain containing 2	NLRP2	6.67E-08	2.10
solute carrier family 2 (facilitated glucose transporter)	SLC2A12	1.06E-08	2.27	KIAA0040	KIAA0040	7.19E-04	2.10
KIAA1161	KIAA1161	9.19E-06	2.27	proprotein convertase subtilisin/kexin type 6	PCSK6	2.77E-08	2.10
peptidyl arginine deiminase, type I	PADI1	8.26E-07	2.27	TBC1 domain family, member 30	TBC1D30	1.20E-06	2.09
mal, T-cell differentiation protein-like	MALL	1.41E-04	2.27	solute carrier family 29 (nucleoside transporters)	SLC29A3	9.32E-06	2.09
endothelin receptor type B	EDNRB	9.26E-05	2.27	aldehyde dehydrogenase 3 family, member B2	ALDH3B2	1.10E-06	2.08
interleukin 1 receptor accessory protein	IL1RAP	4.56E-05	2.26	Rho GTPase activating protein 20	ARHGAP20	2.72E-05	2.08
adaptor-related protein complex 1, gamma 2 subunit	AP1G2	2.04E-06	2.26	nuclear receptor coactivator 7	NCOA7	1.50E-04	2.07
mitochondrial tumor suppressor 1	MTUS1	1.89E-05	2.26	aldehyde dehydrogenase 1 family, member L1	ALDH1L1	4.56E-06	2.07
HLA complex group 4	HCG4	4.66E-06	2.26	keratin 16	KRT16	5.82E-06	2.06
galactosidase, beta 1-like 2	GLB1L2	2.10E-05	2.25	tumor necrosis factor, alpha-induced protein 2	TNFAIP2	5.81E-06	2.06
tumor protein p53 inducible protein 3	TP53I3	1.77E-06	2.25	solute carrier family 1	SLC1A3	9.60E-04	2.06
solute carrier family 16, member 13	SLC16A13	1.13E-04	2.25	low density lipoprotein receptor-related protein 10	LRP10	9.40E-05	2.05
RNA binding protein with multiple splicing	RBPMS	6.25E-05	2.24	bone morphogenetic protein receptor, type IB	BMPRI1B	1.24E-05	2.05
CDC42 small effector 2	CDC42SE2	2.02E-06	2.23	microtubule associated serine/threonine kinase family	MAST4	1.01E-04	2.05
phospholipase A2, group VII (platelet-activating factor)	PLA2G7	1.27E-04	2.23	phosphodiesterase 3A, cGMP-inhibited	PDE3A	1.68E-06	2.05
tumor protein p53 inducible protein 11	TP53I11	2.43E-07	2.23	2',5'-oligoadenylate synthetase 1, 40/46kDa	OAS1	1.25E-03	2.05
protein kinase, AMP-activated, alpha 2 catalytic subunit	PRKAA2	2.51E-06	2.23	epoxide hydrolase 1, microsomal (xenobiotic)	EPHX1	1.88E-05	2.05
alkaline phosphatase, placental-like 2	ALPLP2	2.12E-04	2.22	lymphocyte antigen 6 complex, locus E	LY6E	4.53E-04	2.04
EF-hand domain family, member D1	EFHD1	6.78E-07	2.22	histone cluster 1, H2bm	HIST1H2BM	4.16E-04	2.04
pregnancy specific beta-1-glycoprotein 5	PSG5	4.80E-05	2.22	CKLF-like MARVEL transmembrane domain containing 4	CMTM4	6.66E-06	2.04
CSRP2 binding protein	CSRP2BP	5.30E-06	2.22	Rho GTPase-activating protein	RICS	1.24E-05	2.04
sodium channel, nonvoltage-gated 1, gamma	SCNN1G	3.77E-04	2.21	neogenin homolog 1 (chicken)	NEO1	1.29E-05	2.04
matrix metalloproteinase 15 (membrane-inserted)	MMP15	2.32E-06	2.21	protein kinase C, zeta	PRKCZ	2.77E-06	2.03
claudin 4	CLDN4	2.09E-07	2.21	frizzled homolog 3 (Drosophila)	FZD3	1.07E-05	2.03
chromosome 1 open reading frame 210	C1orf210	9.06E-07	2.21	complement component 3	C3	1.11E-03	2.03
ubiquitin associated and SH3 domain containing, B	UBASH3B	5.47E-05	2.20	T-cell lymphoma invasion and metastasis 1	TIAM1	1.16E-07	2.03
interleukin 6 receptor	IL6R	3.31E-07	2.20	protein phosphatase 1H (PP2C domain containing)	PPM1H	3.14E-05	2.03
junctophilin 1	JPH1	6.18E-05	2.20	chromosome 1 open reading frame 172	C1orf172	1.72E-06	2.02
EPH receptor A1	EPHA1	5.10E-06	2.20	keratin 80	KRT80	2.79E-06	2.02
phosphoglucosyltransferase 2-like 1	PGM2L1	2.71E-04	2.20	pregnancy specific beta-1-glycoprotein 8	PSG8	5.73E-05	2.01
chromosome 7 open reading frame 68	C7orf68	1.47E-07	2.20	epsin 3	EPN3	4.59E-06	2.01
protein phosphatase 1, regulatory (inhibitor) subunit 1	PPP1R13B	1.55E-06	2.19	UDP-N-acetyl-alpha-D-galactosamine	GALNT6	1.85E-05	2.01
acyl-CoA synthetase long-chain family member 5	ACSL5	2.15E-06	2.19	plexin A2	PLXNA2	6.30E-05	2.01
transforming, acidic coiled-coil containing protein 2	TACC2	9.58E-07	2.19	tripartite motif-containing 16-like	TRIM16L	1.05E-05	2.00
insulin-like growth factor binding protein 3	IGFBP3	2.13E-05	2.19	distal-less homeobox 3	DLX3	1.90E-04	2.00

Continued

Supplementary Table S2. *Continued*^b

dual-specificity tyrosine-(Y)-phosphorylation regulated	DYRK3	1,54E-06	-2,00	serpin peptidase inhibitor, clade B (ovalbumin)	SERPINB7	9,88E-05	-2,23
SH3-domain kinase binding protein 1	SH3KBP1	2,74E-04	-2,00	fibrillin 1	FBN1	1,14E-03	-2,23
amylase, alpha 2B (pancreatic)	AMY2B	5,20E-05	-2,00	transcobalamin II; macrocytic anemia	TCN2	1,46E-05	-2,24
CD68 molecule	CD68	4,06E-04	-2,01	thyroid hormone receptor, alpha	THRA	1,87E-05	-2,27
guanine nucleotide binding protein (G protein), gamma 4	GNG4	7,97E-04	-2,01	F-box protein 43	FBXO43	3,56E-05	-2,28
PR domain containing 8	PRDM8	1,04E-03	-2,01	poly (ADP-ribose) polymerase family, member 8	PARP8	1,49E-05	-2,28
chloride intracellular channel 2	CLIC2	4,97E-04	-2,02	solute carrier family 20 (phosphate transporter)	SLC20A1	2,10E-06	-2,28
Cbp/p300-interacting transactivator	CITED2	1,34E-05	-2,02	phosphoglucosyltransferase 3	PGM3	5,61E-06	-2,31
neutral cholesterol ester hydrolase 1	NCEH1	8,37E-08	-2,02	zinc finger protein 117	ZNF117	3,20E-06	-2,31
melanoma antigen family D, 2	MAGED2	3,42E-04	-2,02	tyrosylprotein sulfotransferase 1	TPST1	1,09E-05	-2,31
sorbin and SH3 domain containing 2	SORBS2	1,13E-03	-2,03	gamma-glutamyl hydrolase	GGH	5,40E-06	-2,31
leucine proline-enriched proteoglycan (leprecan) 1	LEPRE1	6,97E-07	-2,03	JAZF zinc finger 1	JAZF1	8,70E-07	-2,31
sprouty homolog 2 (Drosophila)	SPRY2	3,83E-06	-2,03	tetraspanin 5	TSPAN5	6,56E-07	-2,31
retinoic acid early transcript 1E	RAET1E	3,11E-04	-2,04	plasminogen activator, tissue	PLAT	1,28E-05	-2,31
excision repair cross-complementing rodent repair	ERCC1	2,44E-06	-2,04	caprin family member 2	CAPRN2	2,18E-05	-2,34
nephroblastoma overexpressed gene	NOV	1,64E-04	-2,05	neuron navigator 1	NAV1	2,94E-05	-2,34
deleted in malignant brain tumors 1 pseudogene	FLJ46361	1,25E-04	-2,05	spermidine/spermine N1-acetyltransferase 1	SAT1	1,30E-04	-2,35
family with sequence similarity 70, member B	FAM70B	1,72E-05	-2,05	cathepsin L1	CTSL1	8,80E-07	-2,41
sema domain, transmembrane domain	SEMA6D	6,55E-04	-2,06	interferon, gamma-inducible protein 16	IFI16	3,97E-05	-2,41
collagen, type VI, alpha 1	COL6A1	1,65E-04	-2,06	deleted in malignant brain tumors 1	DMBT1	4,30E-09	-2,41
phosphoprotein associated with glycosphingolipid	PAG1	9,67E-06	-2,06	fibulin 2	FBLN2	1,18E-05	-2,43
colony stimulating factor 1 (macrophage)	CSF1	1,45E-05	-2,06	eukaryotic translation initiation factor 5A2	EIF5A2	9,57E-07	-2,43
ADP-ribosylation factor-like 4D	ARL4D	1,13E-05	-2,07	growth arrest-specific 6	GAS6	8,67E-06	-2,43
coiled-coil domain containing 46	CCDC46	4,00E-06	-2,07	apolipoprotein B mRNA editing enzyme	APOBEC3B	1,16E-04	-2,44
zinc finger protein 876 (pseudogene)	ZNF876P	1,94E-05	-2,07	serpin peptidase inhibitor, clade B (ovalbumin)	SERPINB8	1,90E-05	-2,44
armadillo repeat containing, X-linked 1	ARMCX1	4,19E-08	-2,07	acyl-CoA synthetase long-chain family member 4	ACSL4	2,48E-07	-2,45
v-abl Abelson murine leukemia viral oncogene homolog 2	ABL2	1,15E-05	-2,07	absent in melanoma 2	AIM2	1,94E-05	-2,45
protein kinase C, alpha	PRKCA	1,35E-04	-2,07	SWI/SNF related, matrix associated, actin dependent	SMARCA1	4,45E-04	-2,46
G protein-coupled receptor 39	GPR39	9,99E-06	-2,07	decorin	DCN	4,39E-05	-2,47
Lix1 homolog (mouse)-like	LIX1L	1,03E-08	-2,07	PTPRF interacting protein, binding protein 1	PPFIBP1	4,67E-05	-2,47
metallothionein 1E	MT1E	1,21E-04	-2,08	paraoxonase 2	PON2	1,05E-07	-2,52
lymphocyte-specific protein 1	LSP1	2,77E-06	-2,09	endogenous retroviral sequence 3	ERV3	5,32E-05	-2,53
perilipin 2	PLIN2	3,07E-04	-2,09	fibroblast growth factor receptor 1	FGFR1	1,59E-06	-2,54
solute carrier family 39 (zinc transporter)	SLC39A10	4,99E-05	-2,10	family with sequence similarity 114, member A1	FAM114A1	8,35E-05	-2,54
sprouty homolog 4 (Drosophila)	SPRY4	8,06E-05	-2,10	chromosome 5 open reading frame 41	C5orf41	1,34E-05	-2,54
transmembrane protein 154	TMEM154	1,11E-03	-2,10	synapse defective 1, Rho GTPase, homolog 1 (C. elegans)	SYDE1	6,26E-08	-2,55
RNA, U5F small nuclear	RNU5F	1,51E-04	-2,10	S100 calcium binding protein A3	S100A3	9,60E-05	-2,55
RAB7, member RAS oncogene family-like 1	RAB7L1	1,74E-06	-2,10	Kruppel-like factor 12	KLF12	1,00E-05	-2,56
oxysterol binding protein 2	OSBP2	8,03E-07	-2,11	glutaredoxin (thioltransferase)	GLRX	4,07E-05	-2,56
transforming growth factor, beta receptor III	TGFBR3	2,83E-04	-2,11	milk fat globule-EGF factor 8 protein	MFGE8	4,74E-07	-2,58
formin-like 1	FMNL1	4,33E-06	-2,11	solute carrier family 5 (sodium/glucose cotransporter)	SLC5A12	5,09E-04	-2,59
aldehyde oxidase 1	AOX1	1,11E-09	-2,12	ankyrin repeat and sterile alpha motif domain	ANKS1B	2,35E-04	-2,61
CD55 molecule, decay accelerating factor for complement	CD55	4,03E-04	-2,12	TBC1 domain family, member 4	TBC1D4	5,93E-07	-2,62
Rho GTPase activating protein 18	ARHGAP18	1,23E-06	-2,14	RAB31, member RAS oncogene family	RAB31	4,33E-05	-2,64
dystonin	DST	4,98E-06	-2,14	StAR-related lipid transfer (START) domain containing 4	STAR4	5,87E-07	-2,68
p21 protein (Cdc42/Rac)-activated kinase 1	PAK1	1,06E-04	-2,15	solute carrier organic anion transporter family	SLCO4A1	3,55E-05	-2,69
disabled homolog 2, mitogen-responsive phosphoprotein	DAB2	3,28E-06	-2,15	tumor necrosis factor, alpha-induced protein 6	TNFAIP6	6,25E-04	-2,70
chromosome 12 open reading frame 35	C12orf35	4,79E-05	-2,16	L1 cell adhesion molecule	L1CAM	9,63E-05	-2,72
tropomodulin 2 (neuronal)	TMOD2	1,43E-04	-2,17	DENN/MADD domain containing 5B	DENND5B	1,20E-08	-2,74
Ras-related GTP binding D	RRAGD	2,37E-06	-2,17	zinc finger protein 804A	ZNF804A	2,91E-04	-2,76
retinoid X receptor, gamma	RXRG	3,02E-05	-2,17	spastic ataxia of Charlevoix-Saguenay (sacsin)	SACS	2,25E-06	-2,78
ATP-binding cassette, sub-family A (ABC1), member 8	ABCA8	8,73E-05	-2,17	Htra serine peptidase 1	HTRA1	1,08E-07	-2,79
metallothionein 1X	MT1X	7,32E-04	-2,17	programmed cell death 1 ligand 2	PDCD1LG2	8,10E-06	-2,84
AHNAK nucleoprotein 2	AHNAK2	7,68E-05	-2,18	IKK interacting protein	IKIP	1,31E-05	-2,87
kelch-like 24 (Drosophila)	KLHL24	2,75E-04	-2,18	ST3 beta-galactoside alpha-2,3-sialyltransferase 5	ST3GAL5	1,92E-06	-2,87
tumor necrosis factor, alpha-induced protein 3	TNFAIP3	3,03E-04	-2,19	neutrophil cytosolic factor 2	NCF2	3,32E-04	-2,88
STE20-related kinase adaptor beta	STRADB	1,07E-06	-2,19	monoamine oxidase B	MAOB	9,48E-05	-2,88
STE20-related kinase adaptor beta	STRADB	3,14E-07	-2,21	erythrocyte membrane protein band 4.1-like 2	EPB41L2	5,20E-07	-2,90
centrosomal protein 170kDa	CEP170	2,60E-06	-2,21	fibrillin 2	FBN2	3,77E-05	-2,92
leukocyte-associated immunoglobulin-like receptor 1	LAIR1	2,36E-05	-2,21	CD82 molecule	CD82	6,80E-06	-2,92
zinc finger protein 382	ZNF382	1,11E-03	-2,22	acyl-CoA synthetase short-chain family member 3	ACSS3	2,36E-05	-2,94
chromosome 1 open reading frame 21	C1orf21	6,23E-04	-2,22	tumor suppressor candidate 3	TUSC3	8,35E-05	-2,97
carboxypeptidase M	CPM	2,20E-05	-2,22	opioid growth factor receptor-like 1	OGFRL1	4,64E-07	-2,98
methionine sulfoxide reductase B3	MSRB3	1,96E-07	-2,22	major facilitator superfamily domain containing 2	MFS2D2	1,85E-08	-3,04
formyl peptide receptor 1	FPR1	4,67E-05	-2,23	transforming growth factor, beta 1	TGFB1	9,55E-07	-3,10
chromosome 14 open reading frame 139	C14orf139	8,06E-07	-2,23	DnaJ (Hsp40) homolog, subfamily B, member 4	DNAJB4	4,04E-06	-3,12
nexilin (F actin binding protein)	NEXN	7,17E-04	-2,23	proline rich 16	PRR16	1,61E-04	-3,16

Continued

Supplementary Table S2. *Continued.*^b

guanine nucleotide binding protein (G protein), alpha 15	GNA15	2,04E-05	-3,16	lysosomal protein transmembrane 5	LAPTM5	1,29E-04	-4,55
KDEL (Lys-Asp-Glu-Leu) endoplasmic reticulum protein	KDELRL3	2,37E-05	-3,18	ATP-binding cassette, sub-family C (CFTR/MRP)	ABCC4	6,04E-07	-4,62
peripheral myelin protein 22	PMP22	3,94E-06	-3,20	ATP-binding cassette, sub-family A (ABC1), member 6	ABCA6	4,25E-05	-4,64
5'-nucleotidase, ecto (CD73)	NT5E	4,40E-08	-3,20	lysyl oxidase	LOX	1,23E-03	-4,66
ATP-binding cassette, sub-family A (ABC1), member 1	ABCA1	3,94E-06	-3,24	zinc finger E-box binding homeobox 2	ZEB2	4,03E-09	-4,72
serpin peptidase inhibitor, clade E	SERPINE1	3,67E-04	-3,27	neuron navigator 3	NAV3	7,90E-06	-4,79
dedicator of cytokinesis 10	DOCK10	1,10E-03	-3,27	vimentin	VIM	2,81E-06	-4,99
CD302 molecule	CD302	1,80E-05	-3,28	progesterin and adipoQ receptor family member V	PAQR5	4,22E-08	-5,00
potassium large conductance calcium-activated channel	KCNMA1	6,68E-06	-3,37	pleiomorphic adenoma gene-like 1	PLAGL1	1,73E-07	-5,08
ADAM metallopeptidase with thrombospondin type 1 motif	ADAMTS6	5,14E-06	-3,41	microtubule-associated protein 1B	MAP1B	6,30E-07	-5,18
dedicator of cytokinesis 4	DOCK4	2,73E-05	-3,44	N-myc downstream regulated 1	NDRG1	1,79E-06	-5,23
solute carrier family 7 (cationic amino acid transporter)	SLC7A2	1,62E-05	-3,48	anthrax toxin receptor 2	ANTXR2	7,51E-07	-5,37
phosphodiesterase 8B	PDE8B	1,06E-04	-3,51	family with sequence similarity 24, member B	FAM24B	1,02E-07	-5,52
deiodinase, iodothyronine, type II	DIO2	3,65E-04	-3,51	plasma glutamate carboxypeptidase	PGCP	1,76E-05	-5,53
aminoadipate-semialdehyde synthase	AASS	5,59E-08	-3,53	annexin A6	ANXA6	1,15E-08	-5,71
low density lipoprotein-related protein 12	LRP12	1,90E-05	-3,53	glutamine-fructose-6-phosphate transaminase 2	GFPT2	4,03E-05	-6,01
ring finger protein 182	RNF182	2,49E-06	-3,56	apolipoprotein B mRNA editing enzyme	APOBEC3C	2,59E-04	-6,07
dedicator of cytokinesis 11	DOCK11	7,48E-06	-3,56	hypothetical LOC151760	LOC151760	1,13E-04	-6,33
ATPase, Ca++ transporting, plasma membrane 4	ATP2B4	4,25E-07	-3,58	toll-like receptor 4	TLR4	3,70E-08	-6,79
prolactin receptor	PRLR	1,21E-06	-3,62	insulin-like growth factor binding protein 4	IGFBP4	4,19E-07	-7,41
tetratricopeptide repeat domain 28	TTC28	2,15E-07	-3,62	roundabout, axon guidance receptor, homolog 1	ROBO1	2,70E-07	-7,55
HEG homolog 1 (zebrafish)	HEG1	3,01E-10	-3,65	slit homolog 2 (Drosophila)	SLIT2	5,98E-08	-8,58
peptidase M20 domain containing 2	PM20D2	7,56E-07	-3,69	guanine nucleotide binding protein (G protein), gamma 11	GNG11	1,07E-04	-8,64
pop-eye domain containing 3	POPDC3	9,45E-08	-3,79	matrix metallopeptidase 2 (gelatinase A, 72kDa gelatinase)	MMP2	4,37E-04	-8,95
ecotropic viral integration site 2B	EVI2B	1,77E-07	-3,88	syndecan 2	SDC2	1,73E-06	-10,10
mastermind-like domain containing 1	MAMLD1	2,35E-07	-3,99	serpin peptidase inhibitor, clade E	SERPINE2	2,07E-06	-11,22
stanniocalcin 1	STC1	3,38E-06	-4,02	zinc finger E-box binding homeobox 1	ZEB1	1,09E-09	-11,30
solute carrier family 16, member 2	SLC16A2	2,64E-05	-4,21	serglycin	SRGN	6,89E-07	-11,47
adenylate kinase 5	AK5	4,90E-07	-4,25	eyes absent homolog 4 (Drosophila)	EYA4	1,92E-09	-11,77
epithelial membrane protein 3	EMP3	7,08E-07	-4,32	sparc/osteonectin, cwcv and kazal-like domains	SPOCK1	5,07E-06	-15,48
interleukin 7 receptor	IL7R	1,61E-07	-4,41	poliovirus receptor-related 3	PVRL3	3,51E-07	-16,21
leukemia inhibitory factor receptor alpha	LIFR	2,80E-09	-4,48	cadherin 2, type 1, N-cadherin (neuronal)	CDH2	5,04E-07	-17,65
MAM domain containing 2	MAMDC2	7,55E-07	-4,53	collagen, type VI, alpha 3	COL6A3	3,81E-06	-18,44
cyclin-dependent kinase 6	CDK6	9,84E-07	-4,54	carbonic anhydrase VIII	CA8	1,69E-05	-19,57

^aPages S4–S6 show upregulation in A4 relative to G4.

^bPages S7–S8 show downregulation in A4 relative to G4.