

SUPPLEMENTARY INFORMATION

CDK9-Cyclin K Functions in the Replication Stress Response

David S. Yu¹, Runxiang Zhao², Emory Hsu², Jennifer Cayer¹, Fei Ye³, Yan Guo³, Yu Shyr³, & David Cortez²⁺

¹Departments of Radiation Oncology, ²Biochemistry, and ³Biostatistics

Vanderbilt University Medical Center

2215 Garland Avenue

Nashville, TN 37232

⁺Corresponding author. Tel: +1 615 322 8547; Fax: +1 615 343 0704

E-mail: david.cortez@vanderbilt.edu

Contains:

Supplementary methods

Supplementary figure legends

Supplemental figures S1-S5

Supplemental tables S1 and S2

SUPPLEMENTARY METHODS

Individual siRNAs were purchased from Dharmacon or Qiagen. These sequences were as follows:

CDK9-1 (CGGCCAGAAGGTGGCTCTGAA)

CDK9-2 (TAGGGACATGAAGGCTGCTAA)

CDK9-3 (TGGGCACAGTTGGTCCGTTA)

CDK9-4 (GACGTCCATGTTCGAGTACT)

CCNK-1 (ATCCTGGATCTTACTCACAA)

CCNK-2 (AAGCAACTCAAAGGTGATAAA)

CCNK-3 (CAGCCATATTGGCTCAATAAA)

CCNK-4 (AGCCATGTTGGTACTGGGATA)

CCNT1-1 (GACAAGCAACTTAGCACATAA)

CCNT1-2 (ACCCAGACAATAGACTATCAA)

CCNT1-3 (AGGCTTGAACTAACAAATTGA)

CCNT1-4 (TTGGAACATGTCATCAAGGTA)

CCNT2-1 (CTCGATGTAAGGGATCATTAT)

CCNT2-2 (CACCCCTCGTGAAACTGGACAA)

CCNT2-3 (CTGCGGAGTGGAGGCGGATAA)

CCNT2-4 (TGGGAATATGTGGATCCTACA)

Antibodies were purchased from Covance: HA.11; Santa Cruz: ATR (N-19), cyclin T1 (T-18), cyclin T2a/b (S-14), PCNA (FL-261 and PC10); Abcam: claspin (ab3720); Cell Signaling: RPA70 (2267); Bethyl Labs: RPA32 (A300-244A); BD Pharmingen: ORC2

(551178 and 559266); and Millipore: GAPDH (6C5). Rabbit anti-cyclin K (aa 383-400) and anti-CDK9 (aa 329-346) peptide antibodies were custom generated through Open Biosystems.

Microarray analyses. U2OS cells were transfected with NT or CDK9-3 siRNA for 72 hours, treated with or without 3 mM HU for 20 hours, and harvested for RNA extraction using RNeasy mini kit (Qiagen). Targets were prepared with the two-cycle cDNA kit with the WT terminal labelling kit (Affymetrix) and hybridized to the Affymetrix GeneChip Human Exon 1.0 ST Array for genome wide exon level expression profiling and analyzed according to the manufacturer's instructions. Transfections were performed in triplicate. Microarray analysis was done using Linear Model for Microarray Data (LIMMA)(Wettenhall & Smyth, 2004).

SUPPLEMENTARY FIGURE LEGENDS

Supplementary Fig S1 | Primary screen flow diagram. The screen was completed in duplicate, hits ranked by the ratio of the HU-treated to untreated values for each siRNA pool, and analyzed by the weighted flexible compound covariate method (WFCCM). Candidate RSR genes were validated repeating the screen with four individual siRNAs for each gene. Validated genes are listed in Table S1.

Supplementary Fig S2 | Depletion of CDK9 does not affect cell proliferation or apoptosis in the absence of exogenous damage. (A) U2OS cells were transfected with NT or CDK9-3 siRNA and assayed for cell proliferation with WST-1 reagent (Roche) 120

hours after transfection. Mean and standard deviation from four replicas is shown. (B) U2OS cells were treated with or without 150 nM camptothecin for 20 hours or transfected with NT or CDK9-3 siRNA for the indicated time points. Propidium iodide (PI) and annexin V-FITC staining (BD Pharmingen) was analyzed by flow cytometry. Percentage of cells staining positive for annexin V is shown.

Supplementary Fig S3 | Depletion of Cyclin T1 and T2 does not impair cell cycle recovery following replication stress. (A,B) U2OS cells were transfected with NT or both Cyclin T1 and Cyclin T2 siRNA, treated with 3 mM HU for 20 hours, and released into nocodazole for 10 hours. DNA content was analyzed by flow cytometry. (B) The percentage (mean and standard deviation) of cells that completed DNA synthesis in three replicate experiments is shown.

Supplementary Fig S4 | CDK9 is not required for ATR-dependent CHK1 activation but it does regulate CDC25A protein levels. (A) Immunoblot analysis of U2OS cells transfected with NT, ATR, or CDK9-3 siRNA and treated with 3 mM HU for 6 hours. (B) Immunoblot analysis of U2OS cells transfected with the NT, ATR, or CDK9-3 siRNA and treated with 3mM HU for 2h. Lanes 4 and 8 are lysates from cells expressing an siRNA resistant CDK9 cDNA. Cells were harvested 72 hours after transfection with 0.5% NP-40 lysis buffer, separated by SDS-PAGE, and probed with the indicated antibodies. (* = crossreacting protein)

Supplementary Fig S5 | Inactivation of CDK9 with flavopiridol or DRB impairs cell cycle recovery. **(A)** Schematic of cell cycle recovery assay. **(B/C)** U2OS cells were incubated with 50 nM flavopiridol (FP), 25 µM DRB, or no drug for 1 hour prior to and during the recovery assay. Cells were treated with 3 mM HU for 20 hours and released into nocodazole for 10 hours prior to analyzing for DNA content by flow cytometry. Mean and standard deviation from three replicas is shown. * indicates p < 0.05.

Supplementary Table S1 | Validated hits from primary screen.

Supplementary Table S2 | Summary of microarray gene expression analysis following CDK9-silencing and/or treatment with HU. NT, non-targeting.

Reference

Wettenhall JM, Smyth GK (2004) limmaGUI: a graphical user interface for linear modeling of microarray data. *Bioinformatics* **20**: 3705-3706

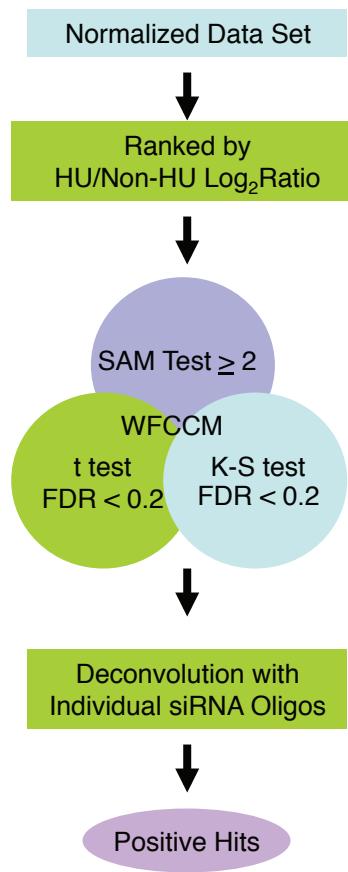


Figure S1

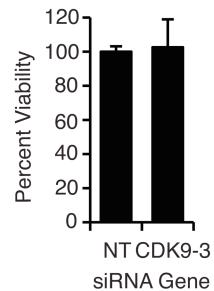
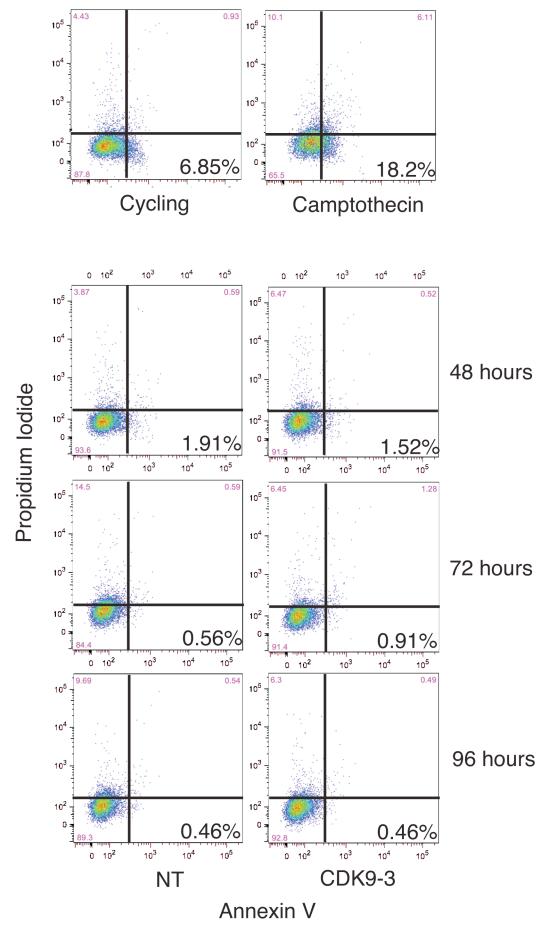
A**B**

Figure S2

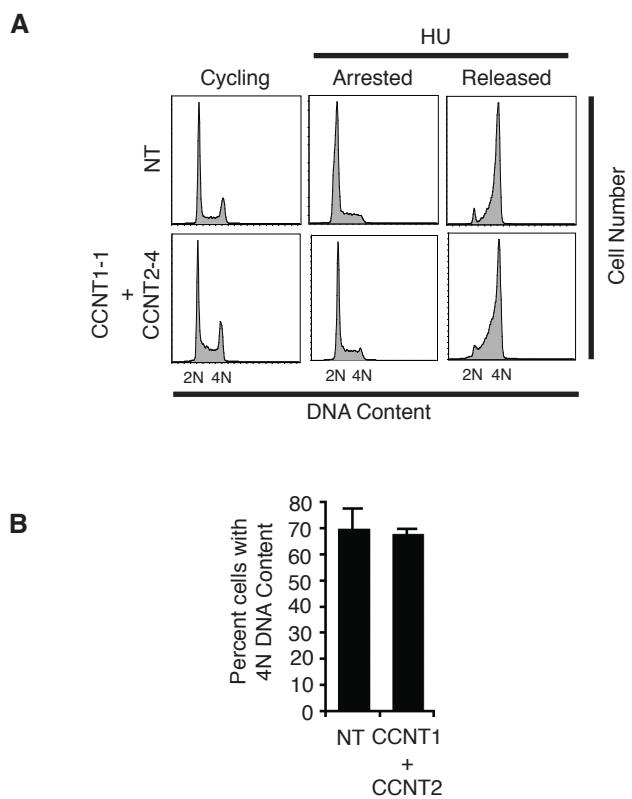


Figure S3

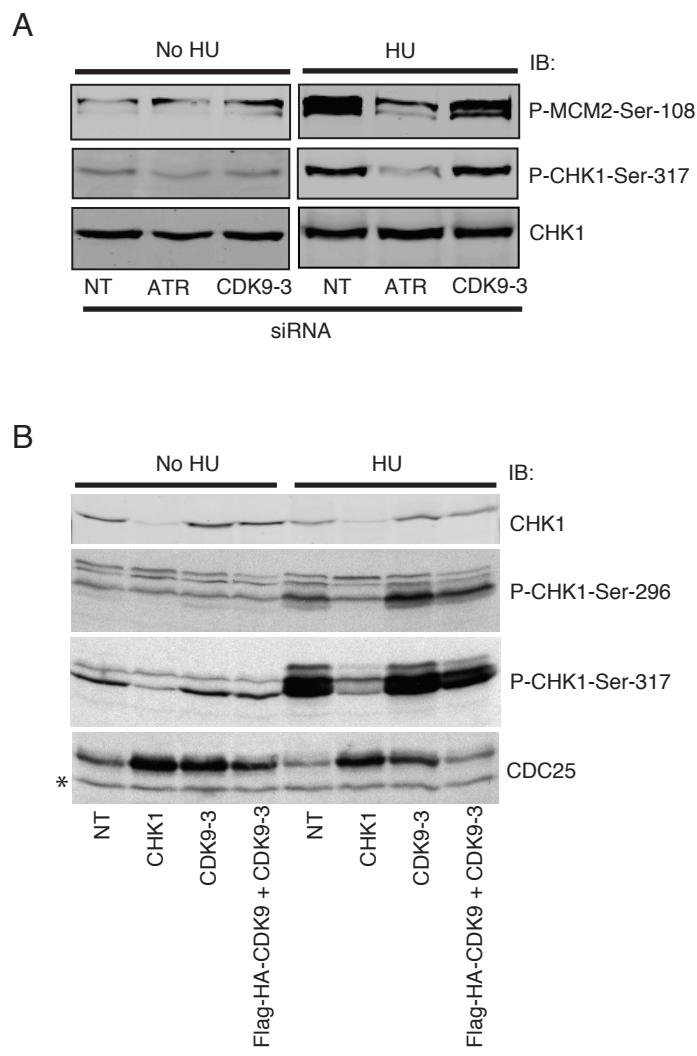
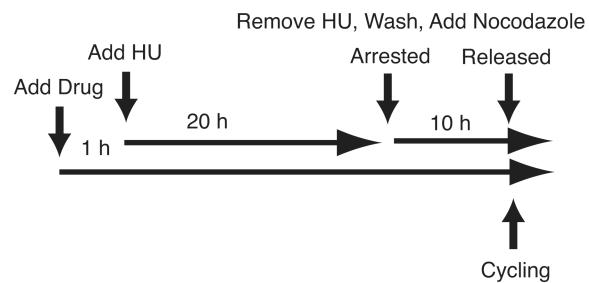
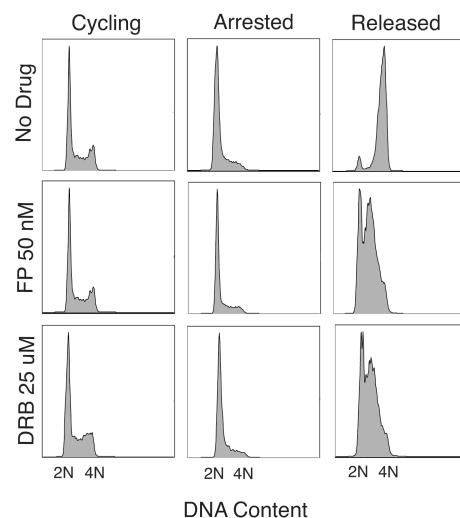
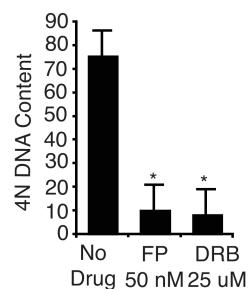


Figure S4

A**B****C****Figure S5**

Supplementary Table S1

Validated HU Sensitivity Genes

Gene	Description	Accession	# siRNA Positive/siRNA Tested
AATK	apoptosis-associated tyrosine kinase	NM_001080395 XM_001128317 XM_927215	2 of 4
AKT2	v-akt murine thymoma viral oncogene homolog 2	NM_001626	3 of 4
AKTIP	AKT interacting protein	NM_001012398 NM_022476	3 of 4
ARFGEF2	ADP-ribosylation factor guanine nucleotide-exchange factor 2 (brefeldin A-inhibited)	NM_006420	3 of 4
AURKB	aurora kinase B	NM_004217	3 of 4
BMP1	bone morphogenetic protein 1	NM_001199 NM_006128 NM_006129 NM_006130 NM_006131 NM_006132	2 of 4
CD40LG	CD40 ligand	NM_000074	2 of 4
CD70	CD70 molecule	NM_001252	3 of 4
CDC2L2	cell division cycle 2-like 2 (PITSLRE proteins)	NM_024011 NM_033527 NM_033528 NM_033529 NM_033531 NM_033532	2 of 4
CDH5	cadherin 5, type 2 (vascular endothelium)	NM_001114117 NM_001795	2 of 4
CDK5RAP1	CDK5 regulatory subunit associated protein 1	NM_016082 NM_016408	4 of 4
CDK9	cyclin-dependent kinase 9	NM_001261	4 of 4
CDKL1	cyclin-dependent kinase-like 1 (CDC2-related kinase)	NM_004196	2 of 4
CDKN1B	cyclin-dependent kinase inhibitor 1B (p27, Kip1)	NM_004064	2 of 4
CDKN3	cyclin-dependent kinase inhibitor 3 (CDK2-associated dual specificity phosphatase)	NM_005192	3 of 4
CNNM2	cyclin M2	NM_017649 NM_199076 NM_199077	3 of 4
DYNL1	dynein, light chain, LC8-type 1	NM_001037494 NM_001037495 NM_003746	3 of 4
EDN1	endothelin 1	NM_001955	3 of 4
ESRRRA	estrogen-related receptor alpha	NM_004451	2 of 4
FCRL2	Fc receptor-like 2	NM_030764 NM_138738 NM_138739	2 of 4
FGFR2	fibroblast growth factor receptor 2	NM_000141 NM_022969 NM_022970 NM_022971 NM_022972 NM_022973 NM_022974	2 of 4
FKBP1A	FK506 binding protein 1A, 12kDa	NM_022975 NM_022976 NM_023028 NM_023029 NM_023030 NM_023031	2 of 4
FRS3	fibroblast growth factor receptor substrate 3	NM_000801	2 of 4
FRZB	frizzled-related protein	NM_006653	2 of 4
GAS8	growth arrest-specific 8	NM_001463	2 of 4
GCKR	glucokinase (hexokinase 4) regulator	NM_001481 NR_023348	2 of 4
GP6	glycoprotein VI (platelet)	NM_001486	3 of 4
GRB2	growth factor receptor-bound protein 2	NM_001083899 NM_016363	2 of 4
GTF3C2	general transcription factor IIIC, polypeptide 2, beta 110kDa	NM_002086 NM_203506	3 of 4
GUCA1A	guanylate cyclase activator 1A (retina)	NM_001035521 NM_001521	3 of 4
	hect (homologous to the E6-AP (UBE3A) carboxyl terminus) domain and RCC1 (CHC1)-like domain (RLD) 1	NM_000409	2 of 4
HERC1	HUS1 checkpoint homolog (S. pombe)	NM_004507	3 of 4
HUS1	interferon, alpha 14	NM_002172	2 of 4
IFNA14	interleukin 18 receptor 1	NM_003855	3 of 4
IL18R1	interleukin 4	NM_000589 NM_172348	2 of 4
IL4	inositol polyphosphate phosphatase-like 1	NM_001567	2 of 4
INPPL1	insulin receptor-related receptor	NM_014215	2 of 4
INSRR	IQ motif containing GTPase activating protein 2	NM_006633	2 of 4
IQGAP2	kinesin family member 11	NM_004523	2 of 4
KIF11	kinesin family member 1C	NM_006612	3 of 4
KIF1C	M-phase phosphoprotein 1	NM_016195	3 of 4
KIF26A	kinesin family member 26A	NM_015656 XM_050278 XM_941210	3 of 4
MAPK15	mitogen-activated protein kinase 15	NM_139021	4 of 4
MLL5	myeloid/lymphoid or mixed-lineage leukemia 5 (trithorax homolog, Drosophila)	NM_018682 NM_182931	2 of 4
NID2	nidoen 2 (osteonidogen)	NM_007361	4 of 4
NUAK2	NUAK family, SNF1-like kinase, 2	NM_030952	2 of 4
PPP2R3B	protein phosphatase 2 (formerly 2A), regulatory subunit B'', beta	NM_013239 NM_199326	2 of 4
PTMA	prothymosin, alpha	NM_001099285 NM_002823	2 of 4
RAD17	RAD17 homolog (S. pombe)	NM_002873 NM_133338 NM_133339 NM_133340 NM_133341 NM_133342 NM_133343	4 of 4
RBKS	ribokinase	NM_133344	2 of 4
RNF31	ring finger protein 31	NM_022128	2 of 4
ROBO1	roundabout, axon guidance receptor, homolog 1 (Drosophila)	NM_017999	2 of 4
	semi-domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3F	NM_002941 NM_133631	2 of 4
SEMA3F	SIVA1, apoptosis-inducing factor	NM_004186	2 of 4
SIVA1	src-related kinase lacking C-terminal regulatory tyrosine and N-terminal myristylation sites	NM_006427 NM_021709	3 of 4
SRMS	SFRS protein kinase 1	NM_080823	3 of 4
SRPK1	tetra-peptide repeat homeobox-like	NM_003137	3 of 4
TPRXL	tumor suppressor candidate 4	NR_022223 XM_496631	2 of 4
TUSC4	vacuolar protein sorting 72 homolog (S. cerevisiae)	NM_006545	3 of 4
VPS72	vacuolar protein sorting 72 homolog (S. cerevisiae)	NM_005997	2 of 4
XCL2	chemokine (C motif) ligand 2	NM_003175	2 of 4

Supplementary Table S2

CDK9 vs NT Downregulated (> 1.5 FC, P < 0.05)			CDK9 vs NT Upregulated (> 1.5 FC, P < 0.05)			CDK9-HU vs NT-HU Downregulated (> 1.5 FC, P < 0.05)			CDK9-HU vs NT-HU Upregulated (> 1.5 FC, P < -0.05)		
Gene	P Value	FC	Gene	P Value	FC	Gene	P Value	FC	Gene	P Value	FC
SEMA3A	0.003598	-3.684497	LCP1	4.84E-10	4.403857	CDK9	2.5E-09	-3.894835	CD274	4.8E-06	2.737874
CDK9	1.83E-05	-3.522216	SPP1	0.001362	2.822405	SEMA3A	6.62E-10	-3.183837	LCP1	4.03E-09	2.690708
CFI	0.021754	-3.220309	C12orf39	0.001451	2.456706	HRSP12	8.85E-08	-3.031601	SPP1	8.77E-09	2.586951
OLR1	0.012776	-3.167604	FAM70A	0.026043	2.309297	COL5A2	2.61E-09	-2.756143	KRT75	3.76E-07	2.480893
HRSP12	1.91E-05	-2.938401	MLLT11	0.002486	2.264048	SEPP1	9.77E-05	-2.701809	PLSCR4	6.15E-07	2.20656
C4orf18	0.005152	-2.845392	CD274	0.000492	2.185713	CFH	9.97E-08	-2.70052	FAM70A	9.53E-08	2.119262
SLC40A1	0.002693	-2.666496	ITGA6	7.86E-06	2.139149	CFI	2.29E-07	-2.621053	CLGN	2.48E-05	2.117351
CFH	0.00176	-2.664318	PDGF	0.004012	2.124432	SLC40A1	1.08E-06	-2.611364	TRY6	0.001342	2.098406
COL5A2	0.000993	-2.455569	PLSCR4	0.007278	2.087193	OLR1	4.84E-08	-2.424885	TMEM40	4.55E-07	2.044354
COL3A1	0.013921	-2.41393	IL8	0.040233	2.062742	FBXO32	2E-07	-2.393501	DMBT1	1.23E-06	2.031809
LOC221442	0.016566	-2.178884	GLP2R	0.007336	2.001267	C3AR1	6.73E-08	-2.378275	KIAA0825	7.5E-06	1.948709
PGM2L1	0.005963	-2.115445	RND3	0.002643	1.984142	NOV	4.78E-07	-2.344247	KIAA0825	3.29E-06	1.947714
C12orf59	0.036429	-2.108929	SLC7A2	1.31E-05	1.965125	COL3A1	4.93E-08	-2.237979	TFEC	6.43E-06	1.934805
MMP2	0.01481	-1.93911	MAP1A	0.000425	1.94641	C4orf18	9.88E-08	-2.199312	FLJ13744	0.000666	1.933195
HMOX1	0.013598	-1.920059	CLGN	0.034317	1.916079	PCDHB5	7.32E-08	-1.999496	NXPH2	3.56E-07	1.925765
P4HB	0.000157	-1.912421	PSG3	0.028668	1.895225	PLXDC2	1.34E-07	-1.992466	PRKACB	1.13E-07	1.91373
P4HB	1.69E-05	-1.901226	SLC1A4	0.000612	1.892018	KLHL24	1.37E-06	-1.986137	HIST1H2BK	5.54E-06	1.903644
BDKRB1	0.002224	-1.881275	FST	0.04532	1.86305	PRR16	9.91E-05	-1.983301	CASP7	1.36E-07	1.890039
SERPINE1	1.08E-05	-1.881051	KIAA0825	0.014728	1.857232	TRIB2	2.2E-07	-1.970495	CCL4L1	1.99E-05	1.878538
VEGFC	0.001221	-1.879586	ANXA3	0.000358	1.854734	RCAN2	7.63E-08	-1.969182	CCL4L1	1.99E-05	1.878538
FER1L3	0.002018	-1.879555	UC41	0.03063	1.853163	COL6A3	8.1E-06	-1.968324	LOC645261	4.51E-05	1.859556
RDH10	0.045035	-1.875367	TRIM16L	7.43E-05	1.844131	NAV3	1.34E-07	-1.96173	MLLT11	1.46E-07	1.845877
NAV3	0.00123	-1.871011	TAGLN	0.015004	1.842838	PCDHB12	7.46E-06	-1.954908	NPPB	6.43E-06	1.843622
AHR	0.036731	-1.8636	PRKACB	0.027019	1.819584	TCP11L2	1.37E-05	-1.940063	IL8	1.37E-06	1.841857
FOSL2	0.002277	-1.826931	ANKRD46	0.001095	1.81701	RGS4	1.74E-06	-1.909203	ADHFE1	1.42E-05	1.841214
PCDHB2	0.027791	-1.811224	MT1E	0.006285	1.795497	ZNF354B	0.000135	-1.906793	CCDC148	2.82E-06	1.839543
ENPP1	0.043874	-1.805319	SCML1	0.005564	1.791898	KCNA1	2.69E-07	-1.906636	PAPPA	2.53E-06	1.834992
CPM	0.042754	-1.783323	FBXO4	0.021567	1.787957	PCDHB11	1.46E-06	-1.894356	SCML2	5.2E-06	1.791915
MAOB	0.028223	-1.781678	LAMB3	0.001969	1.783417	BAMBI	1.4E-06	-1.891722	CYP24A1	1.2E-05	1.791264
GALNT13	0.032585	-1.757209	CYP4F11	0.036659	1.756668	ID2	0.000817	-1.889275	FBXO4	1.62E-06	1.787666
FN1	0.001266	-1.755379	HMMR	0.047745	1.755569	HAS2	5.47E-06	-1.878788	SAR1B	5.79E-07	1.787419
RAB30	0.003767	-1.754904	EGF	0.000855	1.721539	PCDHB16	9.41E-06	-1.875992	TNFSF15	5.28E-06	1.777391
RSPO3	0.012365	-1.743148	SLC7A11	0.002616	1.720378	BMP4	3.51E-06	-1.874667	MFAP3	2.03E-06	1.769236
RIMS1	0.022442	-1.736452	GPX3	0.038056	1.71857	PCDH18	1.02E-05	-1.848271	MYBL1	1.71E-05	1.768044
PLA2G7	0.047668	-1.735862	SAR1B	0.020355	1.684864	PCDHB2	6.97E-07	-1.842822	KRCC1	8.16E-05	1.764462
MICA	0.018422	-1.708783	HSDL2	0.01576	1.677435	TMTC2	3.29E-06	-1.835365	HSDL2	8.64E-07	1.761313
DOCK4	0.020035	-1.705338	C14orf149	0.018637	1.670776	TXNIP	6.83E-07	-1.830029	SCEL	7.89E-05	1.757984
ZNF286A	0.008454	-1.698361	CTH	0.01306	1.660702	PGM2L1	1.69E-06	-1.825465	PRSS2	0.000186	1.749755
ARHGAP12	0.016042	-1.694528	SCML2	0.002251	1.655009	IFIT1	2.53E-06	-1.82213	KLHD1C	7.18E-06	1.749536
CDH11	0.037244	-1.678821	MFAP3	0.010227	1.644087	CXCL14	3.2E-06	-1.814765	HADH	6.63E-06	1.747039
TMTC2	0.005516	-1.676778	RWDD2B	0.007148	1.642076	AHNAK2	3.01E-07	-1.812088	CHRN1	1.14E-06	1.745397
PLAGL2	0.002375	-1.667906	TMEM64	0.01109	1.635954	LRRN1	9.23E-07	-1.80285	WDR69	2.42E-06	1.744831
USP28	0.031698	-1.651487	GLIPR1	0.003392	1.632322	RORB	6.99E-07	-1.792289	LAPTM5	8.07E-06	1.744128
PPIL3	0.028313	-1.650169	PHF11	0.029983	1.630393	MAOB	3.13E-06	-1.78889	GPX3	2E-06	1.74225
SRGAP1	0.002148	-1.647791	PAPPA	0.043226	1.630003	A2M	9.97E-07	-1.767853	SCML1	7.83E-06	1.736888
SGK1	0.02689	-1.635955	GNAQ	0.027839	1.628429	MMP2	1.47E-06	-1.761615	AKR1B10	0.000928	1.722736
BAMBI	0.017872	-1.632652	SERPINB5	0.020585	1.627878	PCDHB3	0.000899	-1.759581	TGM4	2.56E-06	1.715128
SLC16A2	0.031217	-1.625997	CDC6	0.014046	1.619322	FN1	3.1E-06	-1.750297	PSG5	4.43E-06	1.714449
RAB35	0.03392	-1.625896	VGLL3	0.022233	1.613095	FER1L3	5.99E-07	-1.749797	SLC1A4	7.67E-07	1.706964
ANKRD27	0.023379	-1.616565	PCGF5	0.038693	1.608963	TSHZ2	3.53E-07	-1.741246	RNF157	6.86E-05	1.693157
MICA	0.011061	-1.61258	LRP8	0.02336	1.608455	TUBA1A	7.16E-07	-1.740297	CRYAB	4.93E-07	1.687456
GTDC1	0.013785	-1.594923	SLC16A12	0.041824	1.604049	HSD17B3	2.67E-06	-1.737192	ANKRD46	1.1E-05	1.685326
AGPAT9	0.005688	-1.591895	TMEM194B	0.010153	1.602314	ADAMTS5	2.23E-05	-1.722494	NUP210	2.65E-06	1.684152
VKORC1	0.048971	-1.587391	EPB41L4B	0.008986	1.601983	TSHZ2	1.56E-06	-1.720786	RASEF	1.28E-06	1.681839
URM1	0.015721	-1.564548	TLR6	0.019051	1.597534	SFRP1	6.07E-06	-1.718555	CCL4L1	5.25E-05	1.678797
SLC29A4	0.034076	-1.563697	NUP210	0.015042	1.58929	FLG	0.000489	-1.717105	SERPINB5	1.6E-05	1.674265
LTBP1	0.027394	-1.550741	ARL5B	0.018423	1.585456	GJA1	3.61E-06	-1.696043	PSG4	6.2E-06	1.666654
MAP3K13	0.009804	-1.536649	SEC23A	0.029234	1.568435	PDE5A	1.14E-05	-1.69559	EPB41L4B	2.25E-05	1.664578
CENTD1	0.039704	-1.521095	NETO1	0.047937	1.562103	RDH10	6.17E-06	-1.692526	PRRG4	0.000115	1.655344
KITLG	0.045522	-1.513783	GK	0.044246	1.557671	ESM1	1.25E-05	-1.6665918	C9orf46	1.43E-05	1.653366
SOCS2	0.010494	-1.508974	C1orf97	0.036366	1.556133	KLK6	4.89E-07	-1.682824	RND3	6.49E-07	1.653348
			MOSC1	0.033985	1.552395	PLEKHG1	0.000135	-1.680593	GLP2R	2.12E-06	1.649659
			HECW1	0.01288	1.548718	VAMP1	3.22E-06	-1.671029	LOC128102	4.81E-05	1.636683
			CALB2	0.015228	1.547633	FAM46C	9.87E-07	-1.670981	ANXA3	1.18E-05	1.62787
			HTATIP2	0.024344	1.538195	SNORD59B	0.00015	-1.666935	LPL	6.48E-06	1.627416
			TRIM16	0.040463	1.533776	SYTL2	2.69E-06	-1.643225	CYP4F11	1.85E-05	1.609601
			TMEM194B	0.008796	1.523502	SGK1	1.39E-06	-1.630228	TRIM16L	1.91E-06	1.609431
			RECK	0.041932	1.521872	FZD7	1.5E-05	-1.628322	ITGB3	3.71E-06	1.603358
			ASPH	0.007729	1.519095	PCDH7	5.69E-05	-1.660022	MYH15	1.8E-05	1.621003
			WDR69	0.0443	1.51645	DOCK4	5.85E-06	-1.659426	PDGF	6.22E-06	1.616506
						SLC16A2	2.13E-06	-1.654708	ARHGDIB	0.000155	1.616154
						SYTL2	2.69E-06	-1.643225	C9orf46	1.43E-05	1.653366
						ESM1	1.25E-05	-1.6665918	RND3	6.49E-07	1.653348
						P4HB	1.39E-06	-1.66589	GLP2R	2.12E-06	1.649659
						FST	4.37E-06	-1.622643	PDGF	6.22E-06	1.616506
						ITGB3	3.92E-06	-1.627989	ANXA3	1.18E-05	1.62787
						C5	3.56E-06	-1.59791	LPL	6.48E-06	1.627416
						P4HB	3.85E-06	-1.625335	CYP4F11	1.85E-05	1.609601
						URM1	7.96E-06	-1.615669	TRIM16L	1.91E-06	1.609431
						TNFRSF11B	1.19E-05	-1.611439	ITGB3	3.71E	

IRS1	1.7E-06	-1.590049	SLC7A2	4.27E-06	1.581085
EPHA5	4.08E-05	-1.589325	RP11-195B21	0.0002	1.579917
DBP	3.93E-05	-1.585163	SLC4A4	2.9E-05	1.579522
RAB35	5.06E-06	-1.577567	ZNF483	0.00011	1.572603
MEF2C	8.01E-05	-1.576921	GPD2	3.57E-05	1.568172
IGF2	0.000218	-1.576789	FRRS1	7.12E-06	1.562381
CPE	3.89E-06	-1.576045	KLRA1	9.62E-05	1.558884
FAP	0.000762	-1.575621	ARNTL	1.15E-05	1.55876
IGFL2	8.15E-06	-1.570975	JPH1	8.22E-05	1.555216
PDGFRα	5.96E-05	-1.570337	C14orf149	4.25E-06	1.553782
PCDHB8	0.000441	-1.569253	TMEM116	1.46E-05	1.55312
SOX4	1.61E-06	-1.565113	LOC63920	0.001021	1.550884
GTDC1	0.000105	-1.564769	ITGA6	6.18E-06	1.545318
PPIL3	1.82E-05	-1.563413	LOC441233	0.114554	1.544316
KRT23	3.98E-05	-1.554575	SMAP2	4.35E-06	1.544106
HMCN1	5.39E-05	-1.554401	GK	3.49E-06	1.542688
EVI1	7.3E-05	-1.553799	ADAMTS1	1.6E-05	1.542642
SEMA3D	0.004603	-1.551266	PCGF5	3.9E-06	1.539666
PSMAL	7.81E-05	-1.544893	ACSL5	0.001133	1.539213
ENPP1	4.71E-05	-1.542921	TTLL7	6.91E-06	1.538393
TRIM59	0.001619	-1.542314	RNF146	1.14E-05	1.536979
SLIT2	1.65E-05	-1.541595	ACTA2	0.000279	1.535381
ID1	5.43E-05	-1.536005	STK31	1.87E-06	1.53527
ORM2	0.022822	-1.530267	PSG3	0.011505	1.534906
PCDHB10	0.000125	-1.528966	AP1S3	0.000102	1.533445
GNG2	0.000281	-1.528284	MAPK9	8.37E-06	1.533254
FOXO4	0.000135	-1.526368	MAOA	3.16E-06	1.532269
RAB27B	0.0001	-1.526017	GK	2.08E-05	1.531124
DOK5	3.52E-05	-1.525936	CEPT1	1.99E-05	1.529996
CDH6	4.53E-05	-1.524842	SLC22A5	1.26E-05	1.529462
ZCCHC5	4.3E-05	-1.524151	NLRP10	1.74E-05	1.526777
GRAMD3	6.58E-05	-1.523937	C17orf39	4.17E-05	1.525584
LGR4	5.97E-05	-1.521714	TMEM64	2.15E-06	1.524959
IGFBP5	3.11E-06	-1.52036	SLC7A6	5.44E-06	1.524664
SNORD25	0.002875	-1.520047	APOBEC3H	3.95E-05	1.522409
MICA	2.54E-05	-1.517975	CCDC111	0.00018	1.521772
ARHGEF3	2.79E-05	-1.51734	CDC6	3.71E-06	1.521393
PAGE2B	4.24E-06	-1.51731	AFAP1L2	2.26E-05	1.520509
EPYC	3.2E-05	-1.515867	CLCN4	6.15E-06	1.520031
SNAI2	1.63E-05	-1.515434	CCNE2	3.63E-05	1.516388
TOX	0.002184	-1.515281	C12orf39	0.000405	1.515734
PRICKLE1	2.09E-06	-1.512513	PHF11	0.00074	1.515323
TMEM150	6.4E-05	-1.512001	C14orf45	0.000332	1.515106
JARID1B	1.26E-05	-1.511829	KBTBD8	0.00013	1.513992
CPM	0.00011	-1.510835	ENO2	1.62E-05	1.513291
SAT1	0.00011	-1.51017	F2R	9.65E-06	1.512293
CAMK2D	8.23E-06	-1.508909	LRRN4	4.38E-06	1.511664
H1F0	4.24E-06	-1.505709	PKD2	5.25E-06	1.510593
HIST1H1A	1.27E-05	-1.501856	SRR	0.000111	1.508
			MAPRE3	1.96E-05	1.505874
			C8orf46	0.000158	1.502249
			DICER1	3.56E-06	1.501513
			BLVRB	1.39E-05	1.500307
			DPY19L2P2	0.001512	1.500037