Integrated genomic analyses identify WEE1 as a critical mediator of cell fate and novel therapeutic target in acute myeloid leukemia

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Supplemental Information

Contents:

Supplemental Methods:

Genome-wide functional genetic screening:

Total RNA was harvested and reverse transcribed using the vector specific, cDNA Synthesis GNH primer supplied by SBI. The cDNA was amplified by PCR using vector specific, Fwd and Rev GNH primers supplied by SBI. The amplicon was amplified again by nested PCR using vector specific primers customized to include Illumina specific sequences (GNH-ISS).The QIAquick PCR Purification kit (QIAGEN, Valencia, CA) was used to clean up DNA which was then quantified using a 2100 Bioanalyzer (Agilent, Foster City, CA), and diluted to 10nM in EB (QIAGEN) for sequencing. One and one-half pMol was processed on the Genome Analyzer$_{II}$ according to the manufacturer's recommendations using a customized sequencing primer (CSP-GNH; **Supplemental Methods Table 1**).

Image data generated by the IGA was initially processed for base-calling, quality analysis and quantification using the software provided by Illumina. The library of shRNA tags from the genome-wide pool was created by mapping sequence output to the human reference genome (RefSeq GRch37, hg19) by Bowtie [1]. We developed and implemented an innovative solution, for analyzing and interpreting functional genetic screens quantified by deep sequencing (Kim et al, In preparation). We devised a general analytical pipeline that consists of five analytical steps – Preprocessing, Mapping, Statistical Analysis, Post-analysis and Functional analysis. In brief, the preprocessing step filtered out erroneous and low quality reads. Next, we mapped the reads that passed the filtering step against the shRNA reference library using Bowtie. The output from this step is a P x N matrix, where P and N represents the shRNA counts and samples, respectively. We performed secondary filtering step to remove shRNA reads that mapped to sequences that have no gene annotations.

For the BINGS analyses we also filtered out shRNAs where the median raw count in the control group is greater than the maximum raw count in the treatment group if the shRNA is enriched in the control group, and vice versa. This filtering step eliminates shRNA tags for which there is high variability in counts, potentially eliminating false positives. After this secondary filtering step, we use a Negative Binomial as the statistical model in our pipeline to model the count distribution in the NGS data using edgeR [2]. We also compute the q-value of FDR (false discovery rate) for multiple comparisons for these shRNAs [3]. In the post-analysis step, we performed meta-analysis by combining p-values of all the shRNAs representing the same gene using a weighted Z-transformation method that puts more weight to the small-adjusted p-value shRNAs [4]. Using this method, we can collapse multiple shRNAs into genes, with an associated p-value (P(wZ)).

For the RFC analyses we filtered out shRNA tags for which there were not at least 2 replicates of the same condition with read counts $\geq$1. Data were then adjusted for 0 counts by adding 1 to all counts and normalized to the total number of counts per lane. The fold change was calculated as a ratio of the mean tag count of treated divided by that for untreated (i.e. ARA-C/UT). For values less than 1, the negative reciprocal was calculated such that shRNA tags under-represented in cytarabine have negative values. We defined hits as genes with >1 shRNA tag differentially represented by at least 3-fold.

Targeted high-throughput validation: Targeted libraries were created using the known sequences of the included shRNAs from TRC. Bowtie was used to align sequence output to these libraries. Barcoded adapters were prepared by dissolving paired SS oligonucleotides in 10mM Tris pH8.0, 50mM NaCL to 200µM, mixing 1:1 for final concentration of 100µM, heating to 94°, cooling at room temperature overnight, and desalting using Illustra Micro-Spin G25 columns (GE Healthcare, Piscataway, NJ) at 4°. Genomic DNA was isolated using DNeasy Blood & Tissue Kit (QIAGEN) and shRNA coding sequences were amplified using vector specific primers (pLKO.1-Fwd and -Rev; Supplementary Table 2). The amplicon was restriction enzyme digested with XhoI (Fermentas) followed by clean up using the QIAEX II Gel Extraction kit (QIAGEN). One barcoded adapter was ligated to each replicate. The pooled, barcoded samples were then amplified using primers with Illumina specific sequences and specific to the vector and adapter sequences (nFwd- and nRev- pLKO.1-ISS; **Supplemental Methods Table 2**). The PCR product was purified using the QIAquick PCR Purification kit, diluted to 10nM in EB, and processed on the Genome Analyzer$_{ii}$ according to the manufacturer's recommendations using a customized sequencing primer (CSP-pLKO.1; **Supplemental Methods Table 2**).

Data were pre-processed as for the genome-wide screen with the addition of a parsing mechanism to identify replicates according to the barcode. Data were then analyzed in edgeR. Genes were considered validated if 1 of 2 shRNAs or if 2 of 3 or more shRNAs were statistically significantly differentially represented in the expected direction. A p-value of 0.1 was used to identify statistically significant differences.

Supplemental Methods Table 1. Primers for Large Scale FGS using SBI GeneNet 50K (pSIH1)

cDNA Synthesis GNH	5'-ACACACTACTTGAAGCACTCAAGGCAA-3'
Fwd-GNH	5'-TGCATGTCGCTATGTGTTCTGGGA-3'
Rev-GNH	5'-CTCCCAGGCTCAGATCTGGTCTAA-3'
nFwd-GNH-ISS	5'-CAAGCAGAAGACGGCATACGAAGAAGCAAAAAGCAGAATCGAAGAA-3'
nRev-GNH-ISS	5'-AATGATACGGCGACCACCGAGATCTACACTCTTTCCCTACACGACGCTTCCTGTCAGA-3'
CSP-GNH	5'ACACTCTTTCCCTACACGACGCTTCCTGTCAGA-3'

Supplemental Methods Table 2. Primers for high-throughput validation using pLKO.1

Fwd-pLKO.1	5’-CTTGTGGAAAGGACGAAACACCG-3’
Rev-pLKO.1	5’-CCA AAG TGG ATC TCT GCT GTC CC-3’
nFwd-pLKO.1-ISS	5'-CAAGCAGAAGACGGCATACGATGGAAAGGACGAAACACCGG-3'
nRev-pLKO.1-ISS	5'-AATGATACGGCGACCACCGAGATCTACACTCTTTCCCTACACGACGCTCTTCCGATCT-3'
CSP-pLKO.1	5'-ACACTCTTTCCCTACACGACGCTCTTCCGATCT-3'

1. Langmead, B., et al., *Ultrafast and memory-efficient alignment of short DNA sequences to the human genome.* Genome Biol, 2009. **10**(3): p. R25.
2. Robinson, M.D., D.J. McCarthy, and G.K. Smyth, *edgeR: a Bioconductor package for differential expression analysis of digital gene expression data.* Bioinformatics, 2010. **26**(1): p. 139-40.
3. Benjamini, Y., Hochberg, Y., *Controlling the False Discovery Rate: a Practical and Powerful Approach to Multiple Testing.* J. R. Statist. Soc. B, 1995. **57**(1): p. 289-300.
4. Whitlock, M.C., *Combining probability from independent tests: the weighted Z-method is superior to Fisher's approach.* J Evol Biol, 2005. **18**(5): p. 1368-73.

Supplemental Table 1 - Genes Identified by BINGS as mediators of AML cell fate in cytarabine

MV4-11

GeneSymbol	P(wZ)	Rank	E value
Genes which confer chemosensitivity when inhibited			
WEE1	3.35E-05	1	3.35E-05
REEP1	4.93E-05	2	9.87E-05
HSBP1	0.0001153	3	0.0003458
FHL1	0.0001269	4	0.0005076
RAD17	0.000142	5	0.0007098
ABCE1	0.0001525	6	0.000915
PIP5K3	0.0001967	7	0.0013767
TMEM87A	0.0002234	8	0.0017872
ACVR1B	0.0003985	9	0.0035861
DLX4	0.0006295	10	0.0062949
CHAF1A	0.0006774	11	0.0074516
ANAPC5	0.0006914	12	0.0082972
PRKCA	0.0007177	13	0.00933
TUBB1	0.0007223	14	0.0101119
ANKRD28	0.0007749	15	0.0116234
NBS	0.0007942	16	0.0127078
NBN	0.0007942	16	0.0127078
DCLRE1B	0.0010386	18	0.0186948
KRT33B	0.0011624	19	0.0220856
FN1	0.0012063	20	0.024126
CRKL	0.0012122	21	0.0254562
FUSIP1	0.0016807	22	0.0369754
MRPL22	0.0017248	23	0.0396704
CYTH3	0.001725	24	0.0414
FANCL	0.0017251	25	0.0431275
CUL3	0.0017267	26	0.0448942
PRKCQ	0.0017293	27	0.0466911
HUNK	0.0017305	28	0.048454
GORASP1	0.0017317	29	0.0502193
PBRM1	0.0017331	30	0.051993
NSUN5	0.001735	31	0.053785
SPC25	0.0017355	32	0.055536
AKAP9	0.0017366	33	0.0573078
PDIA6	0.0017386	34	0.0591124
ATP6V1C2	0.0017386	34	0.0591124
SPTBN1	0.0017456	36	0.0628416
EMD	0.0017501	37	0.0647537
MAB21L2	0.0017533	38	0.0666254
ACY3	0.0017533	38	0.0666254
ACTL6B	0.0017533	38	0.0666254
FLJ44048	0.0017606	41	0.0721846
LRRC8E	0.0017609	42	0.0739578
CD163	0.0017707	43	0.0761401
ZNF667	0.0018053	44	0.0794332
TPPP3	0.0018093	45	0.0814185
VCL	0.0018195	46	0.083697
KATNA1	0.0018322	47	0.0861134
FANCI	0.0018472	48	0.0886656
ELAC2	0.0018542	49	0.0908558
CAST	0.0018579	50	0.092895
TYRP1	0.0018705	51	0.0953955
E4F1	0.0018751	52	0.0975052
NCOA3	0.0018803	53	0.0996559
RABAC1	0.0018888	54	0.1019952
LPCAT4	0.0019048	55	0.104764
ZNF286A	0.0019209	56	0.1075704
MFN1	0.001931	57	0.110067
MYO9B	0.001933	58	0.112114
GSPT2	0.001933	58	0.112114
GAGE12I	0.0019558	60	0.117348
HTN1	0.0019558	60	0.117348
GAGE7	0.0019558	60	0.117348
GAGE4	0.0019558	60	0.117348
YY1AP1	0.0019629	64	0.1256256
PSTPIP1	0.0019724	65	0.128206
MTFR1	0.0019752	66	0.1303632
SERPINB10	0.0019771	67	0.1324657
PDK2	0.0019958	68	0.1357144
GEM	0.0020162	69	0.1391178
RNF114	0.0020316	70	0.142212
IFT140	0.0020393	71	0.1447903
SUZ12	0.0020418	72	0.1470096
MDC1	0.0020512	73	0.1497376
NPEPPS	0.0020517	74	0.1518258
APPL1	0.0020534	75	0.154005
BZRAP1	0.0020614	76	0.1566664

Molm13

GeneSymbol	P(wZ)	Rank	E value
Genes which confer chemosensitivity when inhibited			
CACNG6	7.81E-05	1	7.81E-05
SPRED2	9.98E-05	2	0.0001996
ATF5	0.0001317	3	0.000395
CLDN20	0.0001332	4	0.0005326
GOLGA2	0.0001889	5	0.0009443
SMPD1	0.0001993	6	0.001196
MAPK8IP3	0.0002157	7	0.0015098
PTPRR	0.0002904	8	0.0023234
FKBP1A	0.0003086	9	0.0027776
KIR2DL1	0.0003171	10	0.0031714
KIR2DL2	0.0003171	10	0.0031714
ZFP42	0.0003299	12	0.0039583
MED21	0.0003642	13	0.0047349
ZBTB7A	0.0004109	14	0.005753
MFF	0.0004296	15	0.0064446
NCOA2	0.0004434	16	0.0070938
STC1	0.0004479	17	0.007614
RWDD2A	0.0006696	18	0.0120526
PPP3CA	0.0008991	19	0.0170831
POLR2C	0.0009127	20	0.018253
RAD18	0.0009557	21	0.0200687
FHL1	0.0010972	22	0.0241384
PAQR6	0.0012476	23	0.0286948
MDGA2	0.0012578	24	0.0301872
SCRN3	0.0014162	25	0.035405
SMOX	0.0016208	26	0.0421408
SFRP1	0.0016388	27	0.0442476
NPAS2	0.0017598	28	0.0492744
CLIC5	0.0020308	29	0.0588932
SLC1A2	0.0020584	30	0.061752
HSP90AA1	0.0020617	31	0.0639127
TMEM97	0.0021573	32	0.0690336
RRAGA	0.0021814	33	0.0719862
ARSD	0.002215	34	0.07531
ITGB8	0.0022314	35	0.078099
ITGB3	0.0022345	36	0.080442
C4orf18	0.0023632	37	0.0874384
HMGB2	0.0023645	38	0.089851
COX15	0.0023753	39	0.0926367
ING5	0.0023825	40	0.0953
PARP10	0.0023825	40	0.0953
SH3KBP1	0.0023903	42	0.1003926
C14orf28	0.0023998	43	0.1031914
COL4A6	0.0024012	44	0.1056528
TLR4	0.0024012	44	0.1056528
SNX6	0.0024018	46	0.1104828
EHMT1	0.0024018	46	0.1104828
UBA5	0.0024299	48	0.1166352
ATP10A	0.0024304	49	0.1190896
ZBTB32	0.0024473	50	0.122365
CTDSPL2	0.0024525	51	0.1250775
PRDM13	0.0024663	52	0.1282476
NEK3	0.0024698	53	0.1308994
LCA5	0.0024937	54	0.1346598
TIMP3	0.0025289	55	0.1390895
ACAD9	0.0025464	56	0.1425984
SLC12A3	0.0025528	57	0.1455096
CCDC18	0.0025528	57	0.1455096
DOCK6	0.0025528	57	0.1455096
C9orf5	0.0025728	60	0.154368
C4orf39	0.0025772	61	0.1572092
LRRC25	0.0026092	62	0.1617704
RUNX2	0.0026416	63	0.1664208
MLX	0.0026416	63	0.1664208
SULT1A2	0.0026422	65	0.171743
SETD2	0.0026622	66	0.1757052
G2E3	0.0026798	67	0.1795466
ALDH6A1	0.0026798	67	0.1795466
GAD2	0.0026798	67	0.1795466
CPNE4	0.0027084	70	0.189588
CFL2	0.0027105	71	0.1924455
PTGS2	0.0027105	71	0.1924455
WIPF1	0.0027387	73	0.1999251
DNAH1	0.0027431	74	0.2029894
C13orf27	0.0027631	75	0.2072325
RXRA	0.0027631	75	0.2072325

Supplemental Table 1 - Genes Identified by BINGS as mediators of AML cell fate in cytarabine

MV4-11				Molm13			
GeneSymbol	P(wZ)	Rank	E value	GeneSymbol	P(wZ)	Rank	E value
PDE4D	0.0020614	76	0.1566664	GLCE	0.0027631	75	0.2072325
PBX2	0.0020614	76	0.1566664	RPS4X	0.0027631	75	0.2072325
ZNF187	0.0020651	79	0.1631429	SNTB2	0.0027824	79	0.2198096
CACNB1	0.0020765	80	0.16612	TAOK3	0.0027961	80	0.223688
AXL	0.0020765	80	0.16612	FAM149A	0.0027961	80	0.223688
TBK1	0.0021308	82	0.1747256	KAZALD1	0.0027961	80	0.223688
PRMT2	0.0021354	83	0.1772382	UGT1A8	0.0028251	83	0.2344833
TCEAL2	0.0021526	84	0.1808184	RNF126	0.0028297	84	0.2376948
FEZ1	0.0021794	85	0.185249	PPP1CB	0.0028338	85	0.240873
MED21	0.0021816	86	0.1876176	SCGB3A2	0.0028338	85	0.240873
SLC39A14	0.0021822	87	0.1898514	SFRS17A	0.0028338	85	0.240873
ASB1	0.0021822	87	0.1898514	CTSS	0.0028338	85	0.240873
CACNA1G	0.0021822	87	0.1898514	DOCK9	0.0028338	85	0.240873
KRR1	0.0022084	90	0.198756	ARHGAP11A	0.0028747	90	0.258723
EVI2B	0.0022088	91	0.2010008	CHIT1	0.0028812	91	0.2621892
ZKSCAN5	0.0022088	91	0.2010008	UBE3A	0.0028822	92	0.2651624
INO80B	0.0022347	93	0.2078271	KIAA1012	0.0028843	93	0.2682399
HAPLN1	0.0022437	94	0.2109078	PAK7	0.002886	94	0.271284
ITPK1	0.0022862	95	0.217189	DPYSL5	0.002886	94	0.271284
EHHADH	0.00229	96	0.21984	DUSP1	0.002886	94	0.271284
LHX5	0.00229	96	0.21984	CYHR1	0.002886	94	0.271284
XRCC5	0.00229	96	0.21984	STYK1	0.0028926	98	0.2834748
ITIH2	0.00229	96	0.21984	RHOQ	0.0029225	99	0.2893275
MAT2A	0.0022902	100	0.22902	MAN1A2	0.0029571	100	0.29571
PKN2	0.0023091	101	0.2332191	SECISBP2	0.0029571	100	0.29571
GK2	0.0023091	101	0.2332191	BZW2	0.0029571	100	0.29571
SERPINB7	0.0023091	101	0.2332191	ABCC4	0.0030012	103	0.3091236
PEX11A	0.0023307	104	0.2423928	SLC38A2	0.00302	104	0.31408
GPI	0.0023355	105	0.2452275	AUP1	0.0030254	105	0.317667
NRIP2	0.0023692	106	0.2511352	ARL6IP5	0.0030569	106	0.3240314
CROP	0.0023828	107	0.2549596	SUFU	0.0030808	107	0.3296456
ABCF2	0.002387	108	0.257796	FJX1	0.003089	108	0.333612
POMP	0.002387	108	0.257796	MAT1A	0.0031004	109	0.3379436
DDX42	0.002387	108	0.257796	BTBD2	0.0031167	110	0.342837
TMEM70	0.0023876	111	0.2650236	GATAD1	0.0031228	111	0.3466308
IRF9	0.0023893	112	0.2676016	DDX17	0.0031274	112	0.3502688
RBBP9	0.0024046	113	0.2717198	LTBP2	0.0031797	113	0.3593061
DDX52	0.0024342	114	0.2774988	FAM111B	0.0031797	113	0.3593061
KIAA0746	0.0024654	115	0.283521	VPS24	0.0031797	113	0.3593061
MAD2L1	0.0024684	116	0.2863344	CALR	0.0032424	116	0.3761184
ANKRD26	0.0024684	116	0.2863344	KLK3	0.003258	117	0.381186
TBC1D4	0.0024684	116	0.2863344	ZSCAN2	0.0032749	118	0.3864382
MFNG	0.0024735	119	0.2943465	PTGS1	0.0032749	118	0.3864382
UCP3	0.0024803	120	0.297636	FERMT1	0.0032909	120	0.394908
FGA	0.0024821	121	0.3003341	RBBP6	0.003327	121	0.402567
PKP4	0.002496	122	0.304512	PSG2	0.0033758	122	0.4118476
H3F3B	0.0024999	123	0.3074877	RNF219	0.0033758	122	0.4118476
TRPC1	0.0025016	124	0.3101984	CARD11	0.0033758	122	0.4118476
LYST	0.0025099	125	0.3137375	HLA-DPA1	0.0033758	122	0.4118476
GAD1	0.0025185	126	0.317331	DCT	0.0033871	126	0.4267746
CSTF1	0.0025185	126	0.317331	SSH3	0.0034094	127	0.4329938
DPP3	0.0025185	126	0.317331	FSD1L	0.0034094	127	0.4329938
TMEM63A	0.0025472	129	0.3285888	PERLD1	0.003447	129	0.444663
SFRS14	0.0025543	130	0.332059	RP1	0.0034617	130	0.450021
ASAH1	0.002562	131	0.335622	BNC2	0.0034769	131	0.4554739
UCHL5IP	0.0025626	132	0.3382632	SLC25A43	0.0034769	131	0.4554739
DDO	0.0025732	133	0.3422356	ZCWPW2	0.0034769	131	0.4554739
ZNF117	0.0025732	133	0.3422356	KLF17	0.003583	134	0.480122
IL11	0.0025732	133	0.3422356	ZNF396	0.003583	134	0.480122
ITGAL	0.0025989	136	0.3534504	ATP6V1A	0.0036127	136	0.4913272
TPBG	0.0026576	137	0.3640912	SLC8A1	0.0036201	137	0.4959537
EFR3A	0.0026868	138	0.3707784	ASPN	0.0036201	137	0.4959537
PLA2G2F	0.0027167	139	0.3776213	LANCL2	0.0036201	137	0.4959537
PAPOLG	0.0027265	140	0.38171	CDC2L5	0.0036201	137	0.4959537
HBG2	0.0027449	141	0.3870309	GNG2	0.0036201	137	0.4959537
HBG1	0.0027449	141	0.3870309	CACNA2D2	0.0036201	137	0.4959537
SMC6	0.0027641	143	0.3952663	MKLN1	0.0036724	143	0.5251532
CARS	0.0028139	144	0.4052016	NDE1	0.0036977	144	0.5324688
HDDC2	0.0028327	145	0.4107415	BCR	0.0037382	145	0.542039
CDYL	0.0028585	146	0.417341	TATDN1	0.0037742	146	0.5510332
ALOX5AP	0.0028809	147	0.4234923	SMARCAD1	0.003805	147	0.559335
LEPR	0.0028809	147	0.4234923	HGF	0.003805	147	0.559335
DBN1	0.0028809	147	0.4234923	CUEDC2	0.003805	147	0.559335
CHRNA5	0.0028809	147	0.4234923	LYRM7	0.0038094	150	0.57141
RAD52	0.0028809	147	0.4234923	PDZD3	0.0039335	151	0.5939585
RSAD2	0.0028809	147	0.4234923	TRIM5	0.0039419	152	0.5991688
KIAA1033	0.0028847	153	0.4413591	CYP3A4	0.0039509	153	0.6044877

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MV4-11

GeneSymbol	P(wZ)	Rank	E value
C1orf63	0.0029354	154	0.4520516
OGFRL1	0.0029377	155	0.4553435
UBE2G2	0.0030341	156	0.4733196
GLRB	0.0030375	157	0.4768875
IL5RA	0.0030666	158	0.4845228
PRSS7	0.003073	159	0.488607
MCM6	0.0030836	160	0.493376
SEC62	0.0030971	161	0.4986331
ITGA7	0.0030971	161	0.4986331
PLAU	0.0030971	161	0.4986331
CPE	0.0031046	164	0.5091544
NPM3	0.0031303	165	0.5164995
ALDH3A2	0.0031308	166	0.5197128
TIMELESS	0.0031447	167	0.5251649
NANOS1	0.0031641	168	0.5315688
TCF3	0.0031792	169	0.5372848
FBXO7	0.0031926	170	0.542742
UNG	0.0032245	171	0.5513895
UBE2D4	0.0032314	172	0.5558008
HMGCL	0.0032936	173	0.5697928
SPAG6	0.0032998	174	0.5741652
IDH3A	0.003302	175	0.57785
PTBP1	0.0033067	176	0.5819792
CDC25B	0.0033172	177	0.5871444
PHYH	0.0033172	177	0.5871444
GRK4	0.0033172	177	0.5871444
WAC	0.0033172	177	0.5871444
GNAL	0.0033172	177	0.5871444
PID1	0.0033172	177	0.5871444
INPP4A	0.0033172	177	0.5871444
PNMAL1	0.0033172	177	0.5871444
GPR175	0.0033172	177	0.5871444
TARP	0.0033172	177	0.5871444
PSMA7	0.0033221	187	0.6212327
CREBZF	0.0033716	188	0.6338608
HUS1	0.0033995	189	0.6425055
TM4SF1	0.0034009	190	0.646171
CACNG2	0.0035807	191	0.6839137
RCN2	0.0035861	192	0.6885312
FBXO9	0.003604	193	0.695572
LAPTM4A	0.003604	193	0.695572
EPM2A	0.003604	193	0.695572
RAB6B	0.003604	193	0.695572
UBXN1	0.003604	193	0.695572
POU1F1	0.0036208	198	0.7169184
FOXP1	0.0036208	198	0.7169184
GAPDH	0.0036661	200	0.73322
SLC34A1	0.0036838	201	0.7404438
SKP1	0.0037284	202	0.7531368
HNRNPD	0.0037518	203	0.7616154
SERPINB13	0.003765	204	0.76806
PSMA2	0.0037711	205	0.7730755
NRD1	0.0037725	206	0.777135
PTCH1	0.0037748	207	0.7813836
NEK1	0.0037978	208	0.7899424
SRGAP2	0.0037978	208	0.7899424
GNAS	0.0039111	210	0.821331
IFI35	0.003917	211	0.826487
KIAA0999	0.0039515	212	0.837718
KCNH2	0.0039515	212	0.837718
EML4	0.0039557	214	0.8465198
AKR7A2	0.0039557	214	0.8465198
CNTNAP2	0.0039557	214	0.8465198
CNBP	0.0039557	214	0.8465198
NPAS2	0.0039557	214	0.8465198
SOX2	0.0039557	214	0.8465198
FLG	0.0039557	214	0.8465198
OBP2A	0.0039849	221	0.8806629
OBP2B	0.0039849	221	0.8806629
MCRS1	0.0040007	223	0.8921561
MFSD7	0.0041451	224	0.9285024

Molm13

GeneSymbol	P(wZ)	Rank	E value
KLHL7	0.0039927	154	0.6148758
KCNK2	0.0039927	154	0.6148758
NRSN1	0.0040106	156	0.6256536
H2AFZ	0.0040106	156	0.6256536
USP12	0.0040106	156	0.6256536
CHD3	0.0041606	159	0.6615354
PLCG1	0.0041949	160	0.671184
SIN3B	0.0042329	161	0.6814969
TTC3	0.0042412	162	0.6870744
ZNF419	0.0042697	163	0.6959611
ANKRD33	0.0042697	163	0.6959611
COPZ1	0.0042697	163	0.6959611
ESF1	0.0043042	166	0.7144972
SETDB1	0.0043047	167	0.7188849
LRRFIP1	0.0043463	168	0.7301784
ARMC2	0.0043463	168	0.7301784
CHMP4A	0.004407	170	0.74919
GUCY1A3	0.0044933	171	0.7683543
FZD9	0.0044952	172	0.7731744
IFIT5	0.0045274	173	0.7832402
ACOT2	0.0045502	174	0.7917348
MTMR12	0.0045502	174	0.7917348
YPEL1	0.0045502	174	0.7917348
LRRC31	0.0045502	174	0.7917348
TMCC1	0.0045502	174	0.7917348
GRM7	0.0045502	174	0.7917348
FAM108B1	0.0045502	174	0.7917348
ACOT1	0.0045502	174	0.7917348
MAP3K8	0.0046489	182	0.8460998
RLBP1L2	0.0046553	183	0.8519199
CPA4	0.0046554	184	0.8565936
C1S	0.0047092	185	0.871202
BBS9	0.0047368	186	0.8810448
OR4D2	0.0047679	187	0.8915973
CCHCR1	0.0047679	187	0.8915973
XPA	0.0048375	189	0.9142875
RICS	0.0048872	190	0.928568
CACNB2	0.0048874	191	0.9334934
FTL	0.0048874	191	0.9334934
C2orf37	0.0048874	191	0.9334934
KRTAP4-12	0.0048874	191	0.9334934
FAM98B	0.0048874	191	0.9334934
CCNT1	0.0048874	191	0.9334934
XPO5	0.0048874	191	0.9334934
ZNF576	0.0049956	198	0.9891288
SS18	0.0050172	199	0.9984228
FEM1B	0.0050405	200	1.0081
CCT4	0.0050626	201	1.0175826
RASGEF1A	0.0050626	201	1.0175826
CXorf40A	0.0051107	203	1.0374721
IL8	0.0051318	204	1.0468872
ZNF544	0.005185	205	1.062925
RPS27L	0.005185	205	1.062925
NCOR2	0.0051935	207	1.0750545
CLDN14	0.0051935	207	1.0750545
CNTN3	0.0051935	207	1.0750545
KIF6	0.0051935	207	1.0750545
SPSB3	0.0051935	207	1.0750545
RGAG1	0.0051935	207	1.0750545
MED13	0.0051935	207	1.0750545
NOP2	0.0051935	207	1.0750545
GPR45	0.0051935	207	1.0750545
GTF2I	0.0052575	216	1.13562
ZMYND8	0.0052656	217	1.1426352
AK2	0.0052656	217	1.1426352
TROVE2	0.0053018	219	1.1610942
PAPPA	0.0053391	220	1.174602
BGN	0.0055003	221	1.2155663
TMC6	0.0055003	221	1.2155663
TOP1	0.0055003	221	1.2155663
SLMO2	0.0055354	224	1.2399296

Supplemental Table 1 - Genes Identified by BINGS as mediators of AML cell fate in cytarabine

MV4-11

GeneSymbol	P(wZ)	Rank	E value
MTMR4	0.0041451	224	0.9285024
UBXN4	0.004168	226	0.941968
RGS13	0.0042129	227	0.9563283
TCEB3	0.0042311	228	0.9646908
SURF2	0.0042311	228	0.9646908
C11orf30	0.0042804	230	0.984492
IL32	0.0043194	231	0.9977814
MTF2	0.0043482	232	1.0087824
ADD2	0.0043945	233	1.0239185
CDH7	0.0044101	234	1.0319634
ARHGEF12	0.0044454	235	1.044669
ZC3H14	0.0044479	236	1.0497044
LONP1	0.0045087	237	1.0685619
OR7A17	0.0045087	237	1.0685619
IRS1	0.0045087	237	1.0685619
CDV3	0.0045087	237	1.0685619
ZNF263	0.0046432	241	1.1190112
PCSK2	0.0046793	242	1.1323906
C8orf79	0.0047591	243	1.1564613
POLE2	0.0047781	244	1.1658564
AK2	0.0048051	245	1.1772495
PAFAH1B3	0.0048245	246	1.186827
RHCE	0.0048344	247	1.1940968
UBE3A	0.0048891	248	1.2124968
SPIN1	0.005068	249	1.261932
CTNND1	0.0050877	250	1.271925
ZZZ3	0.0050877	250	1.271925
STK3	0.0051369	252	1.2944988
LGALS3BP	0.0052066	253	1.3172698
RAD54B	0.0052066	253	1.3172698
ECT2	0.0052066	253	1.3172698
RANBP9	0.0052066	253	1.3172698
AGFG1	0.0052066	253	1.3172698
TTN	0.0052066	253	1.3172698
SHC3	0.005232	259	1.355088
SFRS7	0.0052353	260	1.361178
PAK2	0.0052353	260	1.361178
TUBA1A	0.0052561	262	1.3770982
TUBA1B	0.0052561	262	1.3770982
ARHGAP29	0.0052978	264	1.3986192
DTNA	0.0053188	265	1.409482
GRAMD1C	0.0053315	266	1.418179
MTSS1	0.0053673	267	1.4330691
SLC6A14	0.0053908	268	1.4447344
PLSCR1	0.0054117	269	1.4557473
CBR3	0.0054564	270	1.473228
MIOX	0.0054604	271	1.4797684
STARD5	0.0055598	272	1.5122656
FBXO28	0.0056481	273	1.5419313
NRIP1	0.0056702	274	1.5536348
TAC3	0.0056882	275	1.564255
DZIP3	0.0057405	276	1.584378
IARS	0.0058147	277	1.6106719
ATG5	0.0058404	278	1.6236312
ZDHHC17	0.0058689	279	1.6374231
TIMM10	0.0058689	279	1.6374231
BCAT1	0.0059081	281	1.6601761
WHSC1L1	0.0059345	282	1.673529
CNTN6	0.0059531	283	1.6847273
VSNL1	0.0060158	284	1.7084872
CCND2	0.006109	285	1.741065
PIK3CB	0.0061148	286	1.7488328
TMCC2	0.0061148	286	1.7488328
CYP4F3	0.0061148	286	1.7488328
SLC45A2	0.0061148	286	1.7488328
CYP4F2	0.0061148	286	1.7488328
CDH12	0.0061169	291	1.7800179
SH3TC2	0.0062585	292	1.827482
CACYBP	0.0063776	293	1.8686368
GRIK1	0.0064287	294	1.8900378
PTH	0.0064825	295	1.9123375
ECHS1	0.0065505	296	1.938948
STOML2	0.0065505	296	1.938948
SAFB	0.0066161	298	1.9715978
FCGR2B	0.0066161	298	1.9715978
FCGR2C	0.0066161	298	1.9715978
GATAD1	0.0066161	298	1.9715978

Molm13

GeneSymbol	P(wZ)	Rank	E value
PPARG	0.0055955	225	1.2589875
CXorf40B	0.0056511	226	1.2771486
FUT6	0.005691	227	1.291857
ADCY3	0.0056991	228	1.2993948
CDC2L1	0.0056991	228	1.2993948
RPRD1A	0.0056991	228	1.2993948
WBSCR16	0.0056991	228	1.2993948
CCNJL	0.0056991	228	1.2993948
MYH14	0.0056991	228	1.2993948
SH3BP4	0.0056991	228	1.2993948
PLD1	0.0056991	228	1.2993948
FLRT3	0.0056991	228	1.2993948
RANBP9	0.0056991	228	1.2993948
MTHFR	0.0056991	228	1.2993948
CENPO	0.0056991	228	1.2993948
POLE2	0.0056991	228	1.2993948
VDAC2	0.0056991	228	1.2993948
CDC2L2	0.0056991	228	1.2993948
MYO7A	0.0057403	243	1.3948929
DPEP1	0.0058797	244	1.4346468
NRG1	0.0058871	245	1.4423395
CORO6	0.0059313	246	1.4590998
KLRK1	0.0059594	247	1.4719718
SLC16A3	0.0059594	247	1.4719718
ADAMTS5	0.0060797	249	1.5138453
MLL	0.0060797	249	1.5138453
KIAA1530	0.0061027	251	1.5317777
FGF14	0.0061027	251	1.5317777
BCAT2	0.006137	253	1.552661
PTAFR	0.0061575	254	1.564005
RMND1	0.0061733	255	1.5741915
TPT1	0.006213	256	1.590528
HTATSF1	0.006213	256	1.590528
NIPSNAP3B	0.0062358	258	1.6088364
NAGLU	0.0062358	258	1.6088364
MMP14	0.0062358	258	1.6088364
TAGLN3	0.0062358	258	1.6088364
GPR84	0.0062358	258	1.6088364
CST11	0.0062358	258	1.6088364
JMJD2A	0.0062358	258	1.6088364
SFRS3	0.0062358	258	1.6088364
FERMT2	0.0062358	258	1.6088364
SAP30	0.0062358	258	1.6088364
TAF4	0.0062715	268	1.680762
RASGRP1	0.006362	269	1.711378
ETFDH	0.006362	269	1.711378
MPPE1	0.0064403	271	1.7453213
SLC26A1	0.0064469	272	1.7535568
GRM8	0.0065034	273	1.7754282
RIC3	0.0065295	274	1.789083
KCNJ15	0.0065591	275	1.8037525
NR4A1	0.0066125	276	1.82505
C1orf149	0.0066125	276	1.82505
DCP2	0.0066322	278	1.8437516
DLEC1	0.0066785	279	1.8633015
MBD4	0.006762	280	1.89336
SPANXA1	0.0068254	281	1.9179374
SPANXC	0.0068254	281	1.9179374
SPANXE	0.0068254	281	1.9179374
GRPEL1	0.0068939	284	1.9578676
MYH9	0.0068939	284	1.9578676
PSMAL	0.0069763	286	1.9952218

Supplemental Table 1 - Genes Identified by BINGS as mediators of AML cell fate in cytarabine

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GeneSymbol	P(wZ)	Rank	E value
Genes which confer chemoresistance when inhibited			
DAZ1	0.0008004	1	0.0008004
DAZ3	0.0008004	1	0.0008004
DAZ2	0.0008004	1	0.0008004
DAZ4	0.0008004	1	0.0008004
STRN3	0.0018925	5	0.0094625
MAPK9	0.0018945	6	0.011367
PTPN11	0.0019294	7	0.0135058
SMC3	0.0019299	8	0.0154392
AFF1	0.0020152	9	0.0181368
GATAD1	0.0020758	10	0.020758
NFATC2IP	0.0022614	11	0.0248754
OLFML1	0.0022614	11	0.0248754
ITSN1	0.0023192	13	0.0301496
DMP1	0.0023489	14	0.0328846
CUL5	0.0025691	15	0.0385365
HLA-DPA1	0.0025864	16	0.0413824
RAB3D	0.0027041	17	0.0459697
TLE1	0.0028431	18	0.0511758
BLVRA	0.0029318	19	0.0557042
SPON1	0.003079	20	0.06158
RECQL	0.0031486	21	0.0661206
BANK1	0.0032929	22	0.0724438
BBS10	0.0033994	23	0.0781862
SYPL1	0.003506	24	0.084144
PAFAH1B1	0.0035339	25	0.0883475
MAGEB4	0.0037326	26	0.0970476
CCDC46	0.0037345	27	0.1008315
NUP107	0.0038748	28	0.1084944
PLXNC1	0.0041743	29	0.1210547
NF1	0.0043188	30	0.129564
DST	0.0047386	31	0.1468966
STAG2	0.0049883	32	0.1596256
BCAP31	0.0050364	33	0.1662012
SLC6A6	0.0050773	34	0.1726282
ZC3H11A	0.0052024	35	0.182084
DHX57	0.0053052	36	0.1909872
MAP4	0.0054284	37	0.2008508
DGKQ	0.0057138	38	0.2171244
PARP2	0.0057472	39	0.2241408
DUS4L	0.0059457	40	0.237828
ARG2	0.0059593	41	0.2443313
PPARGC1B	0.0060788	42	0.2553096
BZW1	0.0060788	42	0.2553096
HNRNPK	0.0061535	44	0.270754
TMX1	0.0061543	45	0.2769435
GNRHR	0.0064391	46	0.2961986
RCHY1	0.0064562	47	0.3034414
CD46	0.0068001	48	0.3264048
HNRNPH1	0.0071652	49	0.3510948
AGPAT3	0.0073125	50	0.365625
RRS1	0.0073359	51	0.3741309
UBL3	0.0075037	52	0.3901924
RDX	0.0075514	53	0.4002242
SELENBP1	0.0075947	54	0.4101138
RALA	0.0075947	54	0.4101138
MS4A2	0.007601	56	0.425656
G3BP1	0.0082256	57	0.4688592
CD58	0.0087003	58	0.5046174
TSR1	0.0090563	59	0.5343217
SLC2A14	0.009083	60	0.54498
SLC2A3	0.009083	60	0.54498
PPP3CA	0.0091275	62	0.565905
TFPI	0.0098118	63	0.6181434
IKBKB	0.010187	64	0.651968
SDC2	0.011375	65	0.739375
TUBB	0.011668	66	0.770088
COX7B	0.01217	67	0.81539
SRPK2	0.012622	68	0.858296
DPT	0.013105	69	0.904245
ADM	0.014197	70	0.99379
C6orf106	0.014851	71	1.054421
ICT1	0.01492	72	1.07424
DHPS	0.015183	73	1.108359
NDFIP1	0.016552	74	1.224848
GPRC5B	0.016575	75	1.243125
PKP4	0.016577	76	1.259852

Molm13

GeneSymbol	P(wZ)	Rank	E value
Genes which confer chemoresistance when inhibited			
ALG10	1.90E-06	1	1.90E-06
EPHB2	5.01E-06	2	1.00E-05
FMN2	5.24E-06	3	1.57E-05
ALS2CR11	5.93E-06	4	2.37E-05
ABHD6	8.39E-06	5	4.19E-05
CXorf22	8.75E-06	6	5.25E-05
ANXA4	1.13E-05	7	7.89E-05
RSBN1	1.16E-05	8	9.25E-05
DNAJB12	1.35E-05	9	0.0001219
USP25	1.62E-05	10	0.0001616
CCNL1	1.66E-05	11	0.0001828
CCDC25	1.67E-05	12	0.0002006
SKI	1.84E-05	13	0.0002395
PAX8	2.02E-05	14	0.0002825
TTC22	2.08E-05	15	0.0003123
DR1	2.11E-05	16	0.0003376
TPM4	2.90E-05	17	0.0004925
PSMC1	3.95E-05	18	0.0007102
CYBB	5.25E-05	19	0.000998
EDA	6.74E-05	20	0.0013478
AXL	7.70E-05	21	0.0016163
UNC5C	8.50E-05	22	0.0018704
UBE2L3	8.57E-05	23	0.0019704
RPL13	0.0001004	24	0.0024103
PIAS2	0.000108	25	0.0026998
RUNX1	0.0001141	26	0.0029674
LPCAT2	0.0001239	27	0.0033464
RPS6	0.0001463	28	0.004095
SLC2A3	0.0001608	29	0.0046641
TPT1	0.000212	30	0.0063612
FANCA	0.0002152	31	0.00667
ZNF276	0.0002152	31	0.00667
TRIM33	0.0002275	33	0.0075082
KRT222P	0.000253	34	0.0086006
KSR1	0.0002635	35	0.0092229
CAMTA1	0.0002738	36	0.0098554
RYK	0.0002825	37	0.0104529
U2AF2	0.0002825	37	0.0104529
MEF2C	0.0002836	39	0.0110616
INTS12	0.0002962	40	0.0118468
HNRNPH1	0.0003439	41	0.0140987
OSBPL9	0.0003538	42	0.0148609
FAM62A	0.0003634	43	0.0156279
PLEKHA3	0.0003913	44	0.0172168
CPXCR1	0.0004084	45	0.018378
TRIOBP	0.0004096	46	0.0188434
DNAJC12	0.0004324	47	0.0203242
NEB	0.0004418	48	0.0212059
CEP170	0.0004549	49	0.0222906
HNRPDL	0.0004554	50	0.0227715
PDLIM5	0.0004588	51	0.0233968
PURA	0.0004748	52	0.0246906
TBX5	0.0004757	53	0.0252116
SLC7A9	0.0004857	54	0.0262256
C14orf101	0.0004925	55	0.0270853
SOX11	0.0005012	56	0.028065
ZSCAN5A	0.0005068	57	0.0288887
FCRL4	0.0005096	58	0.0295568
AQP1	0.0005101	59	0.0300947
DKFZP586H2123	0.0005149	60	0.0308916
C10orf90	0.0005232	61	0.0319128
SETDB1	0.0005292	62	0.0328079
CACYBP	0.0005399	63	0.0340112
AFF3	0.0005649	64	0.0361542
TRAPPC4	0.0005669	65	0.0368472
DIAPH1	0.0006167	66	0.0407042
FBXO11	0.0006558	67	0.0439406
PIGR	0.0006774	68	0.0460625
RNF160	0.0007004	69	0.0483297
ZNF77	0.0007012	70	0.0490847
LPIN1	0.0007026	71	0.0498867
HSFY1	0.0007268	72	0.0523282
CSTF2T	0.0007331	73	0.0535148
TNFRSF19	0.0007604	74	0.0562711
GTSE1	0.000762	75	0.0571493
SLC6A8	0.0007776	76	0.0590946

Supplemental Table 1 - Genes Identified by BINGS as mediators of AML cell fate in cytarabine

MV4-11

GeneSymbol	P(wZ)	Rank	E value
PIP4K2A	0.017157	77	1.321089
CLEC1A	0.017401	78	1.357278
PCDHGA11	0.017466	79	1.379814
CLASP2	0.0176	80	1.408
ACTR3	0.01847	81	1.49607
CREBZF	0.018479	82	1.515278
MARCH7	0.018723	83	1.554009
ABAT	0.018797	84	1.578948
CD93	0.019235	85	1.634975
B3GALNT1	0.020069	86	1.725934
NR1I2	0.020069	86	1.725934
CENPQ	0.02007	88	1.76616
ATXN10	0.02007	88	1.76616
OR2B2	0.02007	88	1.76616
ENPEP	0.02007	88	1.76616
ABL1	0.02007	88	1.76616
PAPOLA	0.02007	88	1.76616
HUNK	0.02007	88	1.76616
MYOG	0.02007	88	1.76616
C20orf195	0.02007	88	1.76616
ZDHHC15	0.02007	88	1.76616
ARRDC3	0.02007	88	1.76616
C5orf44	0.02007	88	1.76616

Molm13

GeneSymbol	P(wZ)	Rank	E value
GIMAP4	0.0008161	77	0.0628359
TMCC3	0.0008161	77	0.0628359
LONP2	0.0008161	77	0.0628359
GPR125	0.0008184	80	0.0654752
CISH	0.0008244	81	0.0667764
ZFYVE1	0.0008255	82	0.067691
TPK1	0.0008255	82	0.067691
ZDHHC5	0.0008412	84	0.0706591
APOBEC3F	0.0008418	85	0.0715513
CLPTM1L	0.0008418	85	0.0715513
SPEF1	0.0008418	85	0.0715513
APOBEC3G	0.0008418	85	0.0715513
ATG10	0.0008418	85	0.0715513
LYZ	0.0008418	85	0.0715513
KIAA1432	0.000842	91	0.0766247
PDE7A	0.0008438	92	0.0776333
NCOA7	0.000845	93	0.0785822
SF3A1	0.0008486	94	0.0797684
HNRNPK	0.0008505	95	0.0807985
CDC25C	0.0008507	96	0.081671
PARP15	0.0008537	97	0.0828079
OR5L1	0.000858	98	0.084085
OR5L2	0.000858	98	0.084085
HLA-DRA	0.0008601	100	0.086006
SGCD	0.0008616	101	0.0870206
FUCA2	0.0008727	102	0.0890164
AASDHPPT	0.0008727	102	0.0890164
MAD2L1	0.0008796	104	0.0914732
MAGEB6	0.0008836	105	0.092777
WNT16	0.0008836	105	0.092777
ZNF763	0.0008836	105	0.092777
ARID4B	0.0008836	105	0.092777
PCGF3	0.0008836	105	0.092777
TC2N	0.0008836	105	0.092777
EIF4B	0.0008836	105	0.092777
MDH1B	0.0008836	105	0.092777
OSGIN2	0.000891	113	0.1006864
PTPN21	0.000891	113	0.1006864
TRAPPC9	0.0009038	115	0.1039382
COL29A1	0.0009038	115	0.1039382
FAM167B	0.0009038	115	0.1039382
PGLYRP4	0.0009038	115	0.1039382
LOC90379	0.0009038	115	0.1039382
TRIM36	0.0009038	115	0.1039382
C6orf224	0.0009038	115	0.1039382
C4orf17	0.0009139	122	0.1114934
TMTC4	0.0009139	122	0.1114934
C6orf162	0.0009263	124	0.1148562
C4orf16	0.0009348	125	0.1168513
POSTN	0.0009405	126	0.118498
SPIC	0.000949	127	0.120523
RMND1	0.000949	127	0.120523
MAGT1	0.000949	127	0.120523
MVP	0.000949	127	0.120523
DAAM1	0.000949	127	0.120523
C4orf37	0.0009513	132	0.1255769
DNAH11	0.0009563	133	0.1271852
TRIM6-TRIM34	0.0009563	133	0.1271852
PSMC3IP	0.0009563	133	0.1271852
TRIM34	0.0009563	133	0.1271852
MLX	0.0009563	133	0.1271852
UBA5	0.0009652	138	0.1332004
TBL1XR1	0.000969	139	0.1346924
KTI12	0.000969	139	0.1346924
TRIM62	0.000969	139	0.1346924
CPS1	0.000969	139	0.1346924
ENOX2	0.0009703	143	0.1387458
AQP4	0.0009738	144	0.1402286
ZNF207	0.0009742	145	0.1412518
IFNGR1	0.0009826	146	0.1434581
SEZ6L	0.0009826	146	0.1434581
NEO1	0.0009909	148	0.1466562
KIAA0467	0.0009909	148	0.1466562
SEMA5B	0.0009909	148	0.1466562
PCDHB6	0.0009909	148	0.1466562
EFCAB2	0.0009909	148	0.1466562
C12orf54	0.0009909	148	0.1466562

Supplemental Table 1 - Genes Identified by BINGS as mediators of AML cell fate in cytarabine

MV4-11				Molm13			
GeneSymbol	P(wZ)	Rank	E value	GeneSymbol	P(wZ)	Rank	E value
				KLF12	0.0009999	154	0.1539831
				KPNA1	0.0010008	155	0.155124
				WDFY3	0.001004	156	0.156624
				KIAA0100	0.0010047	157	0.1577379
				RBBP6	0.0010047	157	0.1577379
				MUS81	0.0010047	157	0.1577379
				TCHP	0.0010047	157	0.1577379
				MRPS21	0.0010047	157	0.1577379
				FYB	0.0010047	157	0.1577379
				SARM1	0.0010047	157	0.1577379
				SLC46A1	0.0010047	157	0.1577379
				INTS2	0.0010204	165	0.168366
				FGFR2	0.0010375	166	0.172225
				TXNDC12	0.0010423	167	0.1740641
				SMAD7	0.0010423	167	0.1740641
				FKBP11	0.0010502	169	0.1774838
				CADM4	0.0010565	170	0.179605
				FANCG	0.0010572	171	0.1807812
				DLX6	0.0010608	172	0.1824576
				HMGCLL1	0.0010722	173	0.1854906
				QRSL1	0.0010722	173	0.1854906
				ZC3H13	0.0010722	173	0.1854906
				PKD2L1	0.0010751	176	0.1892176
				IMPG1	0.0010791	177	0.1910007
				OR2F2	0.0010974	178	0.1953372
				GPATCH8	0.0010987	179	0.1966673
				C10orf11	0.001101	180	0.19818
				FAM117B	0.001101	180	0.19818
				CCNE2	0.0011271	182	0.2051322
				FERMT3	0.0011328	183	0.2073024
				LYRM4	0.0011328	183	0.2073024
				PLDN	0.0011328	183	0.2073024
				TMEM71	0.0011328	183	0.2073024
				LPGAT1	0.0011533	187	0.2156671
				LAMA2	0.0011666	188	0.2193208
				SH2D1A	0.0011666	188	0.2193208
				MTIF3	0.0011666	188	0.2193208
				FAM131A	0.0011666	188	0.2193208
				SSX3	0.0011787	192	0.2263104
				KLK2	0.0011816	193	0.2280488
				EPHA3	0.0011842	194	0.2297348
				TBC1D8B	0.0012015	195	0.2342925
				MED23	0.0012024	196	0.2356704
				VCAN	0.001203	197	0.236991
				OIP5	0.0012073	198	0.2390454
				C2orf67	0.0012073	198	0.2390454
				RPE	0.0012073	198	0.2390454
				TLR10	0.0012073	198	0.2390454
				FASTKD5	0.0012073	198	0.2390454
				GPAM	0.0012073	198	0.2390454
				C19orf66	0.0012073	198	0.2390454
				TMEM177	0.0012073	198	0.2390454
				CCT5	0.0012073	198	0.2390454
				C1orf25	0.0012204	207	0.2526228
				CALU	0.0012268	208	0.2551744
				LRRC48	0.0012287	209	0.2567983
				RTP4	0.0012287	209	0.2567983
				SOX4	0.0012373	211	0.2610703
				IGF2BP3	0.0012373	211	0.2610703
				PAK7	0.0012407	213	0.2642691
				GK	0.0012449	214	0.2664086
				KIAA1219	0.0012506	215	0.268879
				FOXN3	0.0012506	215	0.268879
				CPT1A	0.0012506	215	0.268879
				ZCCHC9	0.0012506	215	0.268879
				LILRA5	0.0012506	215	0.268879
				TAF6L	0.0012506	215	0.268879
				ZNF562	0.0012506	215	0.268879
				CENPK	0.0012555	222	0.278721
				MTERFD2	0.0012555	222	0.278721
				FHL1	0.0012559	224	0.2813216
				PRPF38B	0.0012687	225	0.2854575
				C14orf4	0.0012813	226	0.2895738
				ARL5B	0.0012838	227	0.2914226
				C21orf66	0.0012877	228	0.2935956
				FAR1	0.0012879	229	0.2949291
				RBM4	0.0012932	230	0.297436

Supplemental Table 1 - Genes Identified by BINGS as mediators of AML cell fate in cytarabine

MV4-11				Molm13			
GeneSymbol	**P(wZ)**	**Rank**	**E value**	**GeneSymbol**	**P(wZ)**	**Rank**	**E value**
				GALNT3	0.0012943	231	0.2989833
				GPR34	0.0012943	231	0.2989833
				FAM115A	0.0012943	231	0.2989833
				DTX3	0.0012943	231	0.2989833
				PBRM1	0.0012943	231	0.2989833
				TTK	0.0012943	231	0.2989833
				MMP24	0.001313	237	0.311181
				KIAA0907	0.0013143	238	0.3128034
				WDR75	0.0013153	239	0.3143567
				ANGPTL6	0.0013186	240	0.316464
				SYNE2	0.0013318	241	0.3209638
				GNPTAB	0.0013402	242	0.3243284
				NOP14	0.0013471	243	0.3273453
				NCSTN	0.0013565	244	0.330986
				ZNF2	0.0013565	244	0.330986
				ZNF280D	0.0013565	244	0.330986
				SCO1	0.0013565	244	0.330986
				ANGPTL2	0.0013565	244	0.330986
				CD44	0.0013683	249	0.3407067
				PON2	0.001386	250	0.3465
				PSORS1C1	0.0013896	251	0.3487896
				KIAA1024	0.0013896	251	0.3487896
				LUC7L	0.0013896	251	0.3487896
				AADAT	0.0013896	251	0.3487896
				XPO5	0.0013896	251	0.3487896
				IDUA	0.001405	256	0.35968
				ENSA	0.0014185	257	0.3645545
				NUMA1	0.0014243	258	0.3674694
				C9orf4	0.0014261	259	0.3693599
				SLC22A11	0.0014276	260	0.371176
				JMJD1C	0.0014342	261	0.3743262
				FOXD4L1	0.0014373	262	0.3765726
				TMED7	0.0014373	262	0.3765726
				FOXD4	0.0014373	262	0.3765726
				GANAB	0.0014373	262	0.3765726
				PDE7B	0.0014373	262	0.3765726
				RHPN2	0.0014373	262	0.3765726
				SMYD2	0.0014373	262	0.3765726
				ANP32E	0.0014494	269	0.3898886
				LPHN1	0.00145	270	0.3915
				MED14	0.0014637	271	0.3966627
				FCGR2C	0.0014904	272	0.4053888
				HDX	0.0014939	273	0.4078347
				CANT1	0.001528	274	0.418672
				SKIL	0.001528	274	0.418672
				DNAJA2	0.001528	274	0.418672
				MGAT2	0.001528	274	0.418672
				SYCP3	0.001528	274	0.418672
				STIP1	0.001528	274	0.418672
				HTATSF1	0.001528	274	0.418672
				MEA1	0.001528	274	0.418672
				PPP2R2C	0.001528	274	0.418672
				CBL	0.001528	274	0.418672
				EEA1	0.001537	284	0.436508
				PSME4	0.0015453	285	0.4404105
				HSF1	0.00161	286	0.46046
				GYPC	0.0016435	287	0.4716845
				RTN4IP1	0.0016435	287	0.4716845
				API5	0.0016435	287	0.4716845
				OVOL1	0.0016435	287	0.4716845
				MRPL4	0.0016435	287	0.4716845
				HCN3	0.0016435	287	0.4716845
				TH1L	0.0016435	287	0.4716845
				YAF2	0.0016435	287	0.4716845
				FGFBP3	0.0016435	287	0.4716845
				SNAPC4	0.0016435	287	0.4716845
				OBFC2B	0.0016435	287	0.4716845
				GABARAPL1	0.0016435	287	0.4716845
				ZDHHC15	0.0016435	287	0.4716845
				KLHL22	0.0016435	287	0.4716845
				ADAT3	0.0016435	287	0.4716845
				ADSL	0.0016435	287	0.4716845
				FAM60A	0.0016442	303	0.4981926
				CCDC22	0.0016505	304	0.501752
				PEX5L	0.0016526	305	0.504043
				NADK	0.0016778	306	0.5134068
				TUB	0.0016778	306	0.5134068

Supplemental Table 1 - Genes Identified by BINGS as mediators of AML cell fate in cytarabine

MV4-11				Molm13			
GeneSymbol	**P(wZ)**	**Rank**	**E value**	**GeneSymbol**	**P(wZ)**	**Rank**	**E value**
				ESR1	0.0016885	308	0.520058
				LILRA2	0.0016963	309	0.5241567
				WBP4	0.0017357	310	0.538067
				NFIX	0.0017439	311	0.5423529
				OSBPL7	0.0017448	312	0.5443776
				ALDH5A1	0.0017536	313	0.5488768
				YTHDF3	0.0017564	314	0.5515096
				SLMO2	0.0017697	315	0.5574555
				DEPDC1	0.0017697	315	0.5574555
				TEKT5	0.0017697	315	0.5574555
				PEX14	0.0017697	315	0.5574555
				FOSL1	0.0017697	315	0.5574555
				NEBL	0.0017697	315	0.5574555
				ALG10B	0.0017697	315	0.5574555
				SLC35E1	0.0017697	315	0.5574555
				C2CD2L	0.0017697	315	0.5574555
				YWHAE	0.0017697	315	0.5574555
				C3AR1	0.0017697	315	0.5574555
				AMACR	0.0017697	315	0.5574555
				LYN	0.0017759	327	0.5807193
				HNRNPD	0.0018093	328	0.5934504
				ATP6V0D1	0.0018109	329	0.5957861
				MRPS30	0.0018173	330	0.599709
				DTNA	0.001818	331	0.601758
				LILRA4	0.0019084	332	0.6335888
				CYP1B1	0.001914	333	0.637362
				POF1B	0.0019232	334	0.6423488
				SDCCAG10	0.0019232	334	0.6423488
				EEF1D	0.0019232	334	0.6423488
				RND2	0.0019232	334	0.6423488
				ABCA13	0.0019232	334	0.6423488
				EIF6	0.0019232	334	0.6423488
				ZNF609	0.0019232	334	0.6423488
				GPR172A	0.0019232	334	0.6423488
				MIOS	0.0019232	334	0.6423488
				PPFIA4	0.0019232	334	0.6423488
				DSCC1	0.0019232	334	0.6423488
				ZNF484	0.0019232	334	0.6423488
				OR3A1	0.0019232	334	0.6423488
				TRNT1	0.0019232	334	0.6423488
				REV1	0.0019232	334	0.6423488
				ARFIP1	0.0019574	349	0.6831326
				HLA-DOA	0.0019587	350	0.685545
				CCND3	0.0019703	351	0.6915753
				MFSD4	0.0019703	351	0.6915753
				MKI67	0.0019728	353	0.6963984
				OPALIN	0.0019827	354	0.7018758
				CMTM6	0.0019849	355	0.7046395
				GRLF1	0.0019929	356	0.7094724
				EML4	0.0019996	357	0.7138572
				PABPC4	0.0020036	358	0.7172888
				GTF2I	0.0020036	358	0.7172888
				PPAP2A	0.0020036	358	0.7172888
				ERCC8	0.0020079	361	0.7248519
				DPM2	0.0020258	362	0.7333396
				WAC	0.002027	363	0.735801
				ZBTB7C	0.002036	364	0.741104
				RASGRP3	0.0020601	365	0.7519365
				OLFM2	0.0020601	365	0.7519365
				NARG2	0.002064	367	0.757488
				FAM120A	0.002064	367	0.757488
				TMLHE	0.002064	367	0.757488
				FAM65A	0.002064	367	0.757488
				TUBE1	0.002064	367	0.757488
				MRPS23	0.002064	367	0.757488
				RABEP1	0.002064	367	0.757488
				ST3GAL3	0.002064	367	0.757488
				CYorf15B	0.002064	367	0.757488
				INO80D	0.002064	367	0.757488
				ARL6IP6	0.002064	367	0.757488
				NECAP1	0.002064	367	0.757488
				ZSCAN18	0.002064	367	0.757488
				EVC2	0.002064	367	0.757488
				DOT1L	0.002064	367	0.757488
				GNAI3	0.0020654	382	0.7889828
				LAMA4	0.0020654	382	0.7889828
				CEP350	0.0020847	384	0.8005248

Supplemental Table 1 - Genes Identified by BINGS as mediators of AML cell fate in cytarabine

MV4-11				Molm13			
GeneSymbol	**P(wZ)**	**Rank**	**E value**	**GeneSymbol**	**P(wZ)**	**Rank**	**E value**
				MGC29506	0.0020974	385	0.807499
				RHOQ	0.0021001	386	0.8106386
				CPNE3	0.0021168	387	0.8192016
				CRAMP1L	0.0021615	388	0.838662
				DCUN1D4	0.0021755	389	0.8462695
				SRPRB	0.0021787	390	0.849693
				ADAP2	0.0022023	391	0.8610993
				ZBTB33	0.0022023	391	0.8610993
				GRID1	0.0022072	393	0.8674296
				BAX	0.0022109	394	0.8710946
				TMEM48	0.0022281	395	0.8800995
				GPR89B	0.0022372	396	0.8859312
				CORO1C	0.0022659	397	0.8995623
				SLC30A2	0.0022997	398	0.9152806
				LOC153364	0.0022997	398	0.9152806
				TNFSF8	0.0022997	398	0.9152806
				PRKAA1	0.0022997	398	0.9152806
				TCTN2	0.0022997	398	0.9152806
				OAZ1	0.0022997	398	0.9152806
				KCNE3	0.0022997	398	0.9152806
				POU6F1	0.0022997	398	0.9152806
				UFSP2	0.0022997	398	0.9152806
				TSHR	0.0022997	398	0.9152806
				ZDHHC16	0.0022997	398	0.9152806
				AICDA	0.0022997	398	0.9152806
				PHOX2A	0.0023166	410	0.949806
				RPRD1A	0.0023253	411	0.9556983
				EEF2	0.0023323	412	0.9609076
				TNFRSF25	0.0023429	413	0.9676177
				NUP93	0.0023927	414	0.9905778
				SSBP3	0.002405	415	0.998075
				KMO	0.0024292	416	1.0105472
				FOLH1	0.0024806	417	1.0344102
				ARHGAP21	0.0024822	418	1.0375596
				MMP13	0.0024903	419	1.0434357
				CXorf21	0.0024903	419	1.0434357
				EMX2	0.0025065	421	1.0552365
				VANGL1	0.0025066	422	1.0577852
				ARSA	0.0025088	423	1.0612224
				SPRY2	0.0025537	424	1.0827688
				OPA3	0.0025537	424	1.0827688
				NBEA	0.0025537	424	1.0827688
				FAM9A	0.0025537	424	1.0827688
				PHEX	0.0025537	424	1.0827688
				C2orf68	0.0025537	424	1.0827688
				MTCP1	0.0025537	424	1.0827688
				JAM3	0.0025537	424	1.0827688
				HISPPD1	0.0025537	424	1.0827688
				FAM55A	0.0025537	424	1.0827688
				ERMP1	0.0025537	424	1.0827688
				ALDH1A2	0.0025537	424	1.0827688
				PRPF4	0.0025537	424	1.0827688
				ZNF575	0.0025537	424	1.0827688
				AP4E1	0.0025537	424	1.0827688
				RPL32	0.0025537	424	1.0827688
				SOX10	0.0025537	424	1.0827688
				LMX1A	0.0025537	424	1.0827688
				CHD1L	0.0025537	424	1.0827688
				TRIP6	0.0025537	424	1.0827688
				DNAJB2	0.0025537	424	1.0827688
				GABRG2	0.0025537	424	1.0827688
				HMX2	0.0025537	424	1.0827688
				RAMP1	0.0025537	424	1.0827688
				SNRPD1	0.0025537	424	1.0827688
				CYP24A1	0.0025537	424	1.0827688
				GRSF1	0.002586	450	1.1637
				MFNG	0.0025903	451	1.1682253
				MRAP	0.0026068	452	1.1782736
				COL2A1	0.0026442	453	1.1978226
				ZFP64	0.0026609	454	1.2080486
				C1QTNF5	0.0027038	455	1.230229
				APBA3	0.0027342	456	1.2467952
				USP1	0.0027356	457	1.2501692
				NFYB	0.0027405	458	1.255149
				ABCC9	0.0027405	458	1.255149
				NAPEPLD	0.0027442	460	1.262332
				CAND1	0.002756	461	1.270516

Supplemental Table 1 - Genes Identified by BINGS as mediators of AML cell fate in cytarabine

MV4-11				Molm13			
GeneSymbol	P(wZ)	Rank	E value	GeneSymbol	P(wZ)	Rank	E value
				DHX57	0.0027713	462	1.2803406
				MAF	0.0027816	463	1.2878808
				TWF2	0.0027883	464	1.2937712
				BHLHE40	0.0028456	465	1.323204
				NCBP1	0.0028615	466	1.333459
				USP48	0.0028668	467	1.3387956
				NCOA1	0.0028783	468	1.3470444
				WAPAL	0.0029825	469	1.3987925
				TREM1	0.0030029	470	1.411363
				TCL6	0.0030029	470	1.411363
				MMP11	0.0030029	470	1.411363
				SLCO2B1	0.003013	473	1.425149
				KIAA0329	0.00304	474	1.44096
				PKP2	0.003071	475	1.458725
				BCL9	0.003071	475	1.458725
				WDR17	0.003071	475	1.458725
				WDR18	0.003071	475	1.458725
				CYP39A1	0.003071	475	1.458725
				NPPA	0.003071	475	1.458725
				SLC2A14	0.003071	475	1.458725
				CEACAM4	0.003071	475	1.458725
				HTRA2	0.003071	475	1.458725
				RAG2	0.003071	475	1.458725
				TM2D3	0.0030804	485	1.493994
				FADS1	0.0030804	485	1.493994
				RNF148	0.0030804	485	1.493994
				PRKAR1A	0.0031281	488	1.5265128
				APH1A	0.0031748	489	1.5524772
				ACVR1B	0.003206	490	1.57094
				DOC2B	0.0032698	491	1.6054718
				BFAR	0.0032698	491	1.6054718
				RGS18	0.0032928	493	1.6233504
				PRUNE	0.0033881	494	1.6737214
				TRIM68	0.0034376	495	1.701612
				RBM22	0.0034495	496	1.710952
				FAS	0.0034499	497	1.7146003
				MRPL1	0.0036776	498	1.8314448
				CBLL1	0.0036776	498	1.8314448
				COL18A1	0.0036776	498	1.8314448
				FGF1	0.0036776	498	1.8314448
				PDAP1	0.0036776	498	1.8314448
				TBC1D15	0.0036776	498	1.8314448
				SFMBT1	0.0036776	498	1.8314448
				CYB5A	0.0036776	498	1.8314448
				NEUROD1	0.0036776	498	1.8314448
				NQO1	0.0036776	498	1.8314448
				DPP10	0.0036776	498	1.8314448
				CRTAM	0.0036776	498	1.8314448
				EP400	0.0036776	498	1.8314448
				LIAS	0.0036776	498	1.8314448
				MPP5	0.0036776	498	1.8314448
				LOX	0.0036776	498	1.8314448
				NSUN7	0.0036776	498	1.8314448
				TIMM8B	0.0036776	498	1.8314448
				TM4SF5	0.0036776	498	1.8314448
				RPS27	0.0036776	498	1.8314448
				TLR4	0.003697	518	1.915046
				POLDIP3	0.0038295	519	1.9875105
				H2AFV	0.0038295	519	1.9875105
				AFG3L2	0.0038295	519	1.9875105

Supplemental Table 2 - Genes Identified by RFC as mediators of AML cell fate in cytarabine

MV4-11

GeneSymbol	log2nFC
DLX4	-4.597072929
WEE1	-3.862507006
TUBB1	-3.590536218
RAD52	-3.326683677
SKP1	-3.27614601
VCL	-3.258145204
POLR3E	-3.229308243
HSBP1	-3.14403938
FUSIP1	-3.137320823
HIST1H2BK	-3.117291165
FHL1	-3.078975163
REEP1	-3.011378432
DCLRE1B	-2.944227192
ACVR1B	-2.771340776
FN1	-2.674823875
ABCE1	-2.662331699
RAD17	-2.620217591
BRCC3	-2.601738851
ANKRD28	-2.601671488
UBE3A	-2.596832638
PIP5K3	-2.56722358
NBN	-2.553856542
NBS	-2.553856542
PHYH	-2.525330448
TMEM87A	-2.476952135
SAFB	-2.427593194
CHAF1A	-2.392818475
PRKCA	-2.369836031
KRT33B	-2.292377061
CPE	-2.287604788
MAT2A	-2.263768024
ANAPC5	-2.241611108
EFR3A	-2.223958722
ATP2B4	-2.197839318
DTNA	-2.196057539
KIAA1033	-2.187653543
SACM1L	-2.16038101
PTGER3	-2.159490107
PRND	-2.150833672
FGA	-2.146677492
CREBZF	-2.140521303
LRRC8E	-2.129029302
TRPC1	-2.125354734
IDH3A	-2.111197735
YWHAQ	-2.106524734
PTBP1	-2.027059636
CDH12	-2.004248972
PPAT	-1.956212221
FDX1	-1.947227859
SPA17	-1.927482493
CDH19	-1.917120285
RPL24	-1.913178121
STAMBP	-1.911063016
DSCR6	-1.896878563
SLC39A2	-1.896389084
H3F3B	-1.887780954
NPIPL1	-1.886636672
ATP6V1A	-1.880320201
SHANK2	-1.870381895
KIR3DL1	-1.82984297
ZNF415	-1.828673713
SLTM	-1.825023916
CSPG4	-1.808950335
RPS6KA5	-1.801747911
SYCP1	-1.789187072
ACADL	-1.767335013
AQP6	-1.764862522

Molm13

GeneSymbol	log2nFC
CACNG6	-3.800313111
ATF5	-3.438648166
SPRED2	-3.343078485
SMPD1	-3.241508867
CLDN20	-3.170573749
PTPRR	-3.081981786
ZFP42	-2.966281693
STC1	-2.91353524
FKBP1A	-2.896983553
MED21	-2.887918034
ZBTB7A	-2.83997411
MFF	-2.789096131
EIF5B	-2.7724533
RWDD2A	-2.755673891
POLR2C	-2.720398184
PAQR6	-2.699524076
SCRN3	-2.689748953
MAPK8IP3	-2.6662447
PPP3CA	-2.643453047
MDGA2	-2.639315061
SLC1A2	-2.637359306
RAD18	-2.623569122
LRRC25	-2.608830509
TMEM97	-2.583393865
ARHGAP11A	-2.560433311
FHL1	-2.557424088
C4orf18	-2.550018539
CPNE4	-2.521213374
ARSD	-2.515967465
RUNX2	-2.50997655
TIMP3	-2.496327011
TUBB3	-2.490457878
RRAGA	-2.483684238
C9orf5	-2.483631245
KIAA1012	-2.48229368
NCOA2	-2.479487227
UBA5	-2.478426746
SMOX	-2.473555181
SFRP1	-2.459378966
CLIC5	-2.439639351
NPAS2	-2.434485065
HSP90AA1	-2.426951764
UBE3A	-2.422398664
ITGB3	-2.420817832
DOCK9	-2.418694242
MLL	-2.412009909
TEAD4	-2.409161464
SNTB2	-2.398903091
ITGB8	-2.398839629
MAP3K8	-2.396959088
CCHCR1	-2.39096079
NEK3	-2.389243275
AR	-2.386921115
RBBP6	-2.385583937
GOLGA2	-2.383838537
GSTA4	-2.378936928
OR4D2	-2.371391748
COX15	-2.370107333
SULT1A2	-2.340875305
NDE1	-2.337137234
FUT6	-2.322258708
BBS9	-2.318381204
GTF2I	-2.31001486
IFIT5	-2.309785377
PTBP1	-2.306433807
MYO7A	-2.301360731
ASPH	-2.29845644

Supplemental Table 2 - Genes Identified by RFC as mediators of AML cell fate in cytarabine

MV4-11

GeneSymbol	log2nFC
ZNF22	-1.750987869
NRAP	-1.724330538
CD209	-1.696619592
ECSIT	-1.671098503
NDUFB4	-1.671098503
NCAPD2	-1.67099462
PRSS21	-1.659148272
CX3CL1	-1.643824492
STX2	-1.625220553
PNLIP	-1.602237648
PPP6C	1.652676636
NFYC	1.679225913
FAM98A	1.690146697
KIR3DL1	1.710647368
FZD7	1.746074802
SHROOM2	1.813529598
CYB5A	1.81467233
CHN2	1.814703352
TRIOBP	1.818140028
GTF2H1	1.820731721
CPNE3	1.843777728
KCTD12	1.844263115
PKDREJ	1.855767128
OR7A17	1.869855903
FYB	1.874571455
SP110	1.878816771
GART	1.916587107
CHRNE	1.931417974
ACTC1	1.946580049
SENP3	1.94723346
UGDH	1.967321587
NCR1	1.969719783
NASP	1.98244456
ASMT	2.030945573
SEMA4F	2.039157386
CDC14A	2.04726106
TRAF5	2.054596837
NDRG3	2.059112157
BUB3	2.066192058
KARS	2.068193319
TPSAB1	2.070665653
TPSB2	2.070665653
GBP1	2.070889673
AZGP1	2.07924661
EDNRB	2.081711689
APBA2	2.088801627
CLIP1	2.094791902
SLAMF8	2.103841415
MED20	2.107930469
EFEMP1	2.113024194
ATP2A2	2.119843652
GULP1	2.135808276
HSBP1	2.165809972
VTI1B	2.167209049
C1orf115	2.16724852
TOP2A	2.167256451
USP34	2.175545389
CLASP2	2.186967719
CTH	2.193290042
PSG9	2.194407556
TFB1M	2.195917549
STAT1	2.196634055
UGDH	2.199266594
ZC3H11A	2.204359337
HMGN4	2.205204996
CPLX2	2.20954929
MCM4	2.214491183

Molm13

GeneSymbol	log2nFC
ABCC4	-2.295025045
ADAMTS5	-2.293091915
UPF3A	-2.289585896
SETDB1	-2.28291541
ACVR1B	-2.279540272
CDC42EP4	-2.279354044
RPS6KB1	-2.27761968
ZNF396	-2.274564456
POT1	-2.268629314
XPA	-2.26228205
TRIM7	-2.255919396
PDE4DIP	-2.253930816
SBF1	-2.253865911
KIR2DL1	-2.248336973
KIR2DL2	-2.248336973
PBX2	-2.240512748
KCNJ15	-2.2351404
RIC3	-2.226061897
NADK	-2.223981508
GGA2	-2.214347826
TMEM51	-2.20534268
TUBB2A	-2.204364033
TUBB2B	-2.204364033
RAG1AP1	-2.189433391
VAC14	-2.187950164
C12orf35	-2.186489174
C1orf149	-2.183977451
DCP2	-2.183835871
SEPT6	-2.178409205
IGF2R	-2.176481522
CPLX3	-2.174969675
CXCR7	-2.17052744
RICS	-2.169074036
RHOJ	-2.168988669
PPFIBP1	-2.164223803
RMND1	-2.163085072
NRG1	-2.161100087
SLC26A1	-2.160389677
MT3	-2.1569296
ZNF644	-2.155855408
KLC1	-2.150637393
LYRM7	-2.147389293
ADAMTS19	-2.143155133
MAP4K2	-2.14216245
UBE2D2	-2.140594333
DNAL1	-2.139132669
ATP11A	-2.128898791
FOXO3	-2.119121081
MBNL1	-2.104776178
SLA	-2.102938666
SMARCA2	-2.102007079
ADK	-2.097510135
CDC2L6	-2.094970211
THOC1	-2.092972408
NMT1	-2.08977291
CALM1	-2.087609815
KYNU	-2.081977635
TAF4	-2.064908496
CDH19	-2.053223085
NTSR2	-2.053223085
RAB18	-2.053003459
PTGER3	-2.052916509
DIDO1	-2.045997773
TUBG1	-2.043771234
ZC3HAV1L	-2.043771234
GLS	-2.04199351
CAST	-2.03775107

Supplemental Table 2 - Genes Identified by RFC as mediators of AML cell fate in cytarabine

MV4-11

GeneSymbol	log2nFC
SPON1	2.229431676
DOC2A	2.231413716
PDCD4	2.242448747
PSG1	2.256958738
PSG6	2.256958738
PSG8	2.256958738
MAFB	2.26642233
POLE3	2.271738557
CD24	2.274761954
PIK3R1	2.283173965
MBD2	2.294428651
ME2	2.31491343
UBE3A	2.329271843
SAA1	2.335288641
TUBB	2.347819708
MARS	2.351453724
AGFG1	2.360906108
PRKCB	2.364044764
CREBZF	2.369003474
BUB3	2.369790932
STAU1	2.376769931
QKI	2.402762988
TPI1	2.412213491
PIP4K2A	2.417765869
SAA2	2.434380014
NFX1	2.438210367
CD93	2.442401192
PIAS2	2.454697212
RAB5A	2.465798625
RPL39	2.478910025
SRPK2	2.499503184
SPON1	2.513328371
CLEC1A	2.515853836
SLC6A6	2.530975098
NNMT	2.531689525
FAM21A	2.539534738
FAM21C	2.539534738
PPP6C	2.540991525
C6orf106	2.55251939
RCHY1	2.560075995
DHPS	2.561257172
MAP4	2.564673525
ACTR3	2.566686822
NDFIP1	2.567836015
BID	2.568057277
SYPL1	2.570029281
MTRR	2.577921658
PCDHGA11	2.579058853
SELENBP1	2.583607437
RRS1	2.611194151
HNRNPH1	2.623504236
PKP4	2.629677234
DPT	2.631147038
STX6	2.643736233
40244	2.652651895
WARS	2.66493734
SLC2A3	2.669175155
PTPN11	2.673518038
GALC	2.682328119
CD58	2.73750339
RECQL	2.752685932
G3BP1	2.780268474
ABAT	2.78670547
TSR1	2.822777229
UBL3	2.823008284
SLC1A7	2.836304945
AGPAT3	2.843665413

Molm13

GeneSymbol	log2nFC
GRTP1	-2.036565989
CACYBP	-2.032165387
C1S	-2.027044678
RLIM	-2.019371101
SPAM1	-2.018097768
EIF2S1	-2.006057926
NTRK1	-2.005843758
IGFBP5	-2.001449718
CELSR1	-1.998695871
WAC	-1.996031934
CSRNP3	-1.99255082
RNASET2	-1.984373872
MRPS25	-1.978030308
BAALC	-1.97696829
HNRNPM	-1.97554906
ESR1	-1.974719044
STAT5B	-1.963000077
RETNLB	-1.959455313
PAFAH1B3	-1.958610782
ADAM28	-1.95786646
FEN1	-1.957588676
LUC7L	-1.957584594
RAC2	-1.956357805
ZNF250	-1.956175995
H1F0	-1.950008637
TXNIP	-1.946073233
NCAPD2	-1.944429334
EPHB4	-1.940398202
MTSS1	-1.932714644
GBP1	-1.931096917
SLC16A5	-1.92297251
ZNF609	-1.922521712
IL25	-1.91909093
FOXC2	-1.917912711
BLVRA	-1.916297199
PDLIM4	-1.915767958
FARSA	-1.912890182
IL17A	-1.910642976
GRK6	-1.910492253
WNT16	-1.902191646
NRP2	-1.901515909
CR1	-1.90120914
SF3B1	-1.897010737
NRF1	-1.892559285
CC2D1A	-1.891757477
PPP1R7	-1.88979526
HLA-DQB1	-1.884767555
CDC27	-1.883357407
FCER1G	-1.881170546
N4BP2L1	-1.877161037
ZNF749	-1.87704689
RFC3	-1.872968043
FGF5	-1.869457071
OSBPL3	-1.868379461
C22orf9	-1.86573247
BRAP	-1.859789718
LGALS8	-1.85409034
DDX11	-1.85255313
MARK4	-1.843159506
GGCX	-1.84262695
TWF1	-1.84262695
HLA-DRB1	-1.834673223
TNKS	-1.828295101
TYRO3	-1.826103461
MEA1	-1.817924919
SYDE1	-1.817017726
NF1	-1.814092922

Supplemental Table 2 - Genes Identified by RFC as mediators of AML cell fate in cytarabine

MV4-11

GeneSymbol	log2nFC
RCVRN	2.855496609
PCBP2	2.863963168
DUS4L	2.876403572
SDC2	2.905502467
TFPI	2.912247936
STAG2	2.919861811
RDX	2.935675181
IKBKB	2.959238887
TMX1	2.967268971
ZFYVE9	2.983857633
ARG2	3.05656463
CD46	3.066688332
GNRHR	3.071330204
PPP3CA	3.087919793
NF1	3.111420549
DAZ1	3.193781499
DAZ2	3.193781499
DAZ3	3.193781499
DAZ4	3.193781499
PTAFR	3.226803109
BBS10	3.353364643
BLVRA	3.376738098
PPARGC1B	3.387845626
PLXNC1	3.436268401
RALA	3.544785987
DST	3.552210257
BANK1	3.558656576
PAFAH1B1	3.56408249
NUP107	3.697902402
TLE1	3.73414682
MAGEB4	3.819826588
CUL5	3.939217845
GATAD1	4.369497396
ITSN1	4.41709597
AFF1	4.680787332
NFATC2IP	4.781172419
OLFML1	4.781172419
MAPK9	4.943302066
STRN3	5.03175276
SMC3	6.227046921

Molm13

GeneSymbol	log2nFC
UQCRH	-1.813783252
MYOF	-1.804025852
PIK3CG	-1.800557767
C10orf28	-1.79877187
BCORL1	-1.7949129
MLL2	-1.789765809
DDX3X	-1.780497247
SLC35D2	-1.773470637
STK19	-1.768718488
MYO1B	-1.767697609
MON1B	-1.762955417
COL4A3	-1.762708644
AP1S1	-1.757370335
ISG20	-1.747813624
NAT8B	-1.743502326
MAP3K7	-1.738901379
B2M	-1.735466483
POMGNT1	-1.734983511
C20orf7	-1.730017709
ELL3	-1.725556888
GMDS	-1.725099644
G6PD	-1.720408241
PPAP2B	-1.71896314
IDS	-1.714783342
COX4I1	-1.714376901
VBP1	-1.712950045
HS6ST1	-1.709001983
PRB3	-1.709001983
PRB4	-1.709001983
SNAP23	-1.707851986
CES2	-1.706466956
CREB1	-1.703763625
MAK10	-1.700644681
SLC13A3	-1.700581863
CBLB	-1.699517743
BAD	-1.685263033
DCUN1D4	-1.685029889
CNTNAP2	-1.677663061
FAM21A	-1.669318817
PPP1R10	-1.668780789
PDE4D	-1.66224714
DBT	-1.656288868
STS	-1.655798653
GSK3B	-1.64925125
DLX6	-1.646842671
SUMO2	-1.645346639
DUS4L	-1.633718524
H3F3B	-1.63102055
WARS2	-1.629755632
PCDHGA11	-1.629283084
RPL13	-1.627907294
SOCS1	-1.617193927
SLC26A2	-1.5958358
ARSF	-1.577347338
HMGA2	1.606109773
RINT1	1.640837441
PRKCI	1.649832121
NUCB1	1.670521381
ZFPL1	1.674995596
HGF	1.676575717
MAP2K2	1.680986497
ME2	1.69151394
COL4A3	1.697608231
C3orf1	1.701451674
H2AFZ	1.722095155
DDX17	1.750206458
RAB3GAP1	1.767386127

Supplemental Table 2 - Genes Identified by RFC as mediators of AML cell fate in cytarabine

MV4-11

GeneSymbol	log2nFC

Molm13

GeneSymbol	log2nFC
COMMD10	1.767629811
MLLT4	1.778082499
PLCB1	1.811205235
TCL6	1.826255127
MED31	1.833778995
EIF1AY	1.836843383
EPHB4	1.837216866
MED13L	1.838738836
EIF5B	1.843468122
ZNF238	1.859106134
RANBP9	1.861146532
C1orf89	1.870854634
RPL13	1.875640889
IKBKB	1.876090065
CLN5	1.880024803
ATRX	1.883138935
TBC1D22B	1.891930483
SOX9	1.894011444
AKAP13	1.904457404
CYP2B6	1.904468591
IL1RN	1.906069966
MMP11	1.909074003
SULF1	1.911712113
SYNCRIP	1.917529446
FTSJD1	1.919516003
PATZ1	1.923790603
GRSF1	1.926416563
ZFP64	1.92752836
TPD52L1	1.930699138
DERL1	1.937787411
SEPT10	1.941527829
FTSJD2	1.970546057
CPVL	1.977931966
USP11	1.979904654
SUSD4	1.982859173
DHRS7	1.983862805
RPRD1A	1.986139591
TREM1	1.991406075
CAND1	1.99152933
MAP4	1.994333375
GCOM1	2.003832829
GRINL1A	2.003832829
C16orf35	2.01139864
NOP14	2.012802216
ADAM7	2.016476564
POU3F1	2.029394796
RTF1	2.03102785
RPN2	2.03402226
C6orf62	2.035045813
FMR1	2.035687828
DHX57	2.036098513
ACN9	2.036585508
HLA-DRA	2.042952145
SLCO2B1	2.047044776
PEX6	2.0473455
EBP	2.053173863
BHLHE40	2.053887145
LRP8	2.054027209
OTUD6B	2.059907975
PLD1	2.062083729
FGFR2	2.078234487
ITCH	2.080608739
TNFRSF19	2.089802745
NFYB	2.103668006
RNF160	2.113198978
GPR89B	2.120335841
CD44	2.122502308

Supplemental Table 2 - Genes Identified by RFC as mediators of AML cell fate in cytarabine

MV4-11

GeneSymbol	log2nFC

Molm13

GeneSymbol	log2nFC
RPLP2	2.125936835
HNRNPD	2.132078101
TANK	2.13627489
LPHN1	2.149581483
TMEM48	2.154289221
TNFRSF25	2.165016485
CADM4	2.179779482
GPLD1	2.183531008
TRIOBP	2.187225089
UBE2L3	2.219415876
RBM22	2.238682309
SGCD	2.239344189
FAR1	2.240249654
RER1	2.249819075
ABCC9	2.254987046
WAPAL	2.265463816
NADK	2.276124168
CREBZF	2.277408356
UBE3A	2.302957826
FCRL4	2.305523389
GNPTAB	2.328799298
COL3A1	2.332862892
FREQ	2.336747119
HNRNPK	2.342843778
TRAPPC4	2.34427559
PURA	2.345551794
SYNE2	2.356826357
CEP170	2.357337237
DR1	2.374353033
C4orf16	2.377492898
ARFIP1	2.380052401
EPHB2	2.381489602
AQP1	2.390193508
SLC6A8	2.400024611
ENOX2	2.400818231
KSR1	2.403579407
GTSE1	2.415325113
PAX8	2.422600595
SLC2A3	2.424558981
AXL	2.424879443
IMPG1	2.431027346
CCNL1	2.435580695
PLEKHA3	2.437517468
TBX5	2.451990333
CACYBP	2.461556488
LPIN1	2.514485282
DNAJB12	2.528961359
PDLIM5	2.536805398
CSTF2T	2.540662879
EDA	2.544368556
RYK	2.547665621
U2AF2	2.547665621
INTS12	2.579635281
PIAS2	2.585688797
C12orf49	2.606351566
TPT1	2.616700081
KPNA1	2.622478109
AFF3	2.622724101
NEB	2.651192457
RUNX1	2.65171588
DNAJC12	2.68493713
DIAPH1	2.69343259
HNRPDL	2.695843243
LPGAT1	2.705950151
OSBPL9	2.721378373
SSX3	2.725390067
UNC5C	2.733526006

Supplemental Table 2 - Genes Identified by RFC as mediators of AML cell fate in cytarabine

MV4-11

GeneSymbol	log2nFC

Molm13

GeneSymbol	log2nFC
YTHDF3	2.738263888
PSMC1	2.738702526
FMN2	2.769729142
TTC22	2.788525847
HSFY1	2.793589809
MEF2C	2.887627652
USP25	2.904563497
PIGR	2.905724599
CCDC25	2.918516712
LPCAT2	2.94098671
SKI	2.960191516
CYBB	2.982527054
TRIM33	3.146404622
TPM4	3.148437705
RPS6	3.152577679
RSBN1	3.259271686
ZSCAN5A	3.277551555
ANXA4	3.33773027
ABHD6	3.404412763
FANCA	3.439807984
FBXO11	3.44885006
HNRNPH1	3.698962083
ALS2CR11	3.886941873
GPR125	3.95567872

Supplemental Table 3 - Mediators of AML cell fate in cytarabine (BINGS RFC overlap)

Genes which confer Chemosensitivity when knocked down

ABCC4
ABCE1
ACVR1B
ADAMTS5
ANAPC5
ANKRD28
ARHGAP11A
ARSD
ATF5
ATP6V1A
BBS9
C1orf149
C1S
C4orf18
C9orf5
CACNG6
CACYBP
CAST
CCHCR1
CDH12
CHAF1A
CLDN20
CLIC5
CNTNAP2
COX15
CPE
CPNE4
CREBZF
DCLRE1B
DCP2
DLX4
DOCK9
DTNA
EFR3A
FGA
FHL1
FKBP1A
FN1
FUSIP1
FUT6
GOLGA2
GTF2I
H3F3B
HSBP1
HSP90AA1
IDH3A
IFIT5
ITGB3
ITGB8
KCNJ15
KIAA1012
KIAA1033
KIR2DL1
KIR2DL2
KRT33B
LRRC25
LRRC8E
LYRM7
MAP3K8
MAPK8IP3
MAT2A
MDGA2
MED21
MFF
MLL
MTSS1
MYO7A
NBN
NBS
NCOA2
NDE1
NEK3
NPAS2
NRG1
OR4D2
PAFAH1B3
PAQR6
PBX2
PDE4D
PHYH
PIP5K3
POLR2C
PPP3CA
PRKCA
PTBP1
PTPRR
RAD17
RAD18
RAD52
RBBP6
REEP1
RIC3
RICS
RMND1
RRAGA
RUNX2
RWDD2A
SAFB
SCRN3
SETDB1
SFRP1
SKP1
SLC1A2
SLC26A1
SMOX
SMPD1
SNTB2
SPRED2
STC1
SULT1A2
TAF4
TIMP3
TMEM87A
TMEM97
TRPC1
TUBB1
UBA5
UBE3A
VCL
WAC
WEE1
XPA
ZBTB7A
ZFP42
ZNF396

Supplemental Table 3 - Mediators of AML cell fate in cytarabine (BINGS RFC overlap)

Genes which confer Chemoresistance when knocked down

ABAT
ABCC9
ABHD6
ACTR3
AFF1
AFF3
AGPAT3
ALS2CR11
ANXA4
AQP1
ARFIP1
ARG2
AXL
BANK1
BBS10
BHLHE40
BLVRA
C4orf16
C6orf106
CACYBP
CADM4
CAND1
CCDC25
CCNL1
CD44
CD46
CD58
CD93
CEP170
CLASP2
CLEC1A
CPNE3
CREBZF
CSTF2T
CUL5
CYB5A
CYBB
DAZ1
DAZ2
DAZ3
DAZ4
DHPS
DHX57
DIAPH1
DNAJB12
DNAJC12
DPT
DR1
DST
DUS4L
EDA
ENOX2
EPHB2
FANCA
FAR1
FBXO11
FCRL4
FGFR2
FMN2
FYB
G3BP1
GATAD1
GNPTAB
GNRHR
GPR125
GPR89B
GRSF1
GTSE1
HLA-DRA
HNRNPD
HNRNPH1
HNRNPK
HNRPDL
HSFY1
IKBKB
IMPG1
INTS12
ITSN1
KPNA1
KSR1
LPCAT2
LPGAT1
LPHN1
LPIN1
MAGEB4
MAP4
MAPK9
MEF2C
MMP11
NADK
NDFIP1
NEB
NF1
NFATC2IP
NFYB
NOP14
NUP107
OLFML1
OSBPL9
PAFAH1B1
PAX8
PCDHGA11
PDLIM5
PIAS2
PIGR
PIP4K2A
PKP4
PLEKHA3
PLXNC1
PPARGC1B
PPP3CA
PSMC1
PTPN11
PURA
RALA
RBM22
RCHY1
RDX
RECQL
RNF160
RPL13
RPRD1A
RPS6
RRS1
RSBN1
RUNX1
RYK
SDC2
SELENBP1
SGCD
SKI
SLC2A3
SLC6A6
SLC6A8
SLCO2B1
SMC3
SPON1
SRPK2
SSX3
STAG2
STRN3
SYNE2
SYPL1
TBX5
TCL6
TFPI
TLE1
TMEM48
TMX1
TNFRSF19
TNFRSF25
TPM4
TPT1
TRAPPC4
TREM1
TRIM33
TRIOBP
TSR1
TTC22
TUBB
U2AF2
UBE2L3
UBL3
UNC5C
USP25
WAPAL
YTHDF3
ZC3H11A
ZFP64
ZSCAN5A

Supplemental Table 4 - Top Molecular and Cellular Function from Functional Genetic Screening- Cell cycle

Category	Functions Annotation	p-Value	Molecules	# Molecules
Cell Cycle	entry into G2 phase of eukaryotic cells	7.16E-06	MAP3K8, RUNX2, WEE1	3
Cell Cycle	cell division process	2.74E-05	ACVR1B, ANAPC5, ATF5, CAST, CHAF1A, DCLRE1B, FKBP1A, FN1, GOLGA2, GTF2I, HSP90AA1, MAP3K8, MLL, NBN, NDE1, NRG1, PIKFYVE, PPP3CA, PRKCA, RAD17, RAD18, RAD52, RUNX2, TUBB1, WEE1, XPA	26
Cell Cycle	entry into interphase of endothelial cells	5.14E-05	FN1, RUNX2	2
Cell Cycle	G2 phase	6.42E-05	ANAPC5, ATF5, MAP3K8, NBN, NRG1, RAD17, RUNX2, WEE1	8
Cell Cycle	interphase	9.31E-05	ACVR1B, ANAPC5, ATF5, FN1, GTF2I, MAP3K8, NBN, NRG1, PPP3CA, PRKCA, RAD17, RAD18, RUNX2, WEE1	14
Cell Cycle	entry into G2/M phase of eukaryotic cells	1.53E-04	RUNX2, WEE1	2
Cell Cycle	entry into interphase of cell lines	1.58E-04	FN1, GTF2I, MAP3K8, NRG1, WEE1	5
Cell Cycle	entry into interphase of eukaryotic cells	2.00E-04	FN1, GTF2I, MAP3K8, NRG1, RUNX2, WEE1	6
Cell Cycle	entry into G2 phase of cell lines	3.06E-04	MAP3K8, WEE1	2
Cell Cycle	cell stage	3.64E-04	ACVR1B, ANAPC5, ATF5, FN1, GOLGA2, GTF2I, HSP90AA1, MAP3K8, NBN, NDE1, NRG1, PPP3CA, PRKCA, RAD17, RAD18, RUNX2, TUBB1, WEE1	18
Cell Cycle	cell division process of eukaryotic cells	6.26E-04	ATF5, CAST, FN1, GOLGA2, GTF2I, MAP3K8, MLL, NBN, NDE1, NRG1, PIKFYVE, PRKCA, RAD17, RAD18, RUNX2, WEE1, XPA	17
Cell Cycle	arrest in cell division process	6.55E-04	ATF5, FKBP1A, FN1, GOLGA2, GTF2I, HSP90AA1, MLL, NBN, NRG1, PRKCA, RAD18, WEE1	12
Cell Cycle	G2 phase of eukaryotic cells	7.81E-04	ATF5, MAP3K8, NRG1, RAD17, RUNX2, WEE1	6
Cell Cycle	interphase of cell lines	8.14E-04	ATF5, FN1, GTF2I, MAP3K8, NRG1, PRKCA, RAD17, RAD18, RUNX2, WEE1	10
Cell Cycle	interphase of eukaryotic cells	8.86E-04	ATF5, FN1, GTF2I, MAP3K8, NBN, NRG1, PRKCA, RAD17, RAD18, RUNX2, WEE1	11
Cell Cycle	cell division process of cell lines	9.60E-04	ATF5, CAST, FN1, GOLGA2, GTF2I, MAP3K8, MLL, NRG1, PIKFYVE, PRKCA, RAD17, RAD18, RUNX2, WEE1	14
Cell Cycle	arrest in cell stage of eukaryotic cells	1.00E-03	ATF5, FN1, GOLGA2, GTF2I, NBN, NRG1, PRKCA, RAD18, WEE1	9
Cell Cycle	G2/M phase of colon cancer cell lines	1.05E-03	RAD17, WEE1	2
Cell Cycle	cell stage of eukaryotic cells	1.06E-03	ATF5, FN1, GOLGA2, GTF2I, MAP3K8, NBN, NDE1, NRG1, PRKCA, RAD17, RAD18, RUNX2, WEE1	13
Cell Cycle	checkpoint control	1.23E-03	DCLRE1B, NBN, RAD17, RAD18	4
Cell Cycle	entry into S phase of cell lines	1.30E-03	FN1, GTF2I, MAP3K8, NRG1	4
Cell Cycle	cell stage of cell lines	1.36E-03	ATF5, FN1, GOLGA2, GTF2I, MAP3K8, NRG1, PRKCA, RAD17, RAD18, RUNX2, WEE1	11
Cell Cycle	arrest in S phase of eukaryotic cells	1.55E-03	GTF2I, NBN, RAD18	3
Cell Cycle	arrest in cell division process of eukaryotic cells	1.76E-03	ATF5, FN1, GOLGA2, GTF2I, MLL, NBN, NRG1, PRKCA, RAD18, WEE1	10
Cell Cycle	G2 phase of cell lines	1.82E-03	ATF5, MAP3K8, NRG1, RAD17, WEE1	5
Cell Cycle	G2/M phase transition	1.89E-03	ANAPC5, ATF5, MAP3K8, NRG1	4
Cell Cycle	arrest in interphase of eukaryotic cells	2.16E-03	ATF5, FN1, GTF2I, NBN, NRG1, PRKCA, RAD18, WEE1	8
Cell Cycle	G2/M phase transition of cell lines	2.55E-03	ATF5, MAP3K8, NRG1	3
Cell Cycle	S phase checkpoint control of cell lines	2.71E-03	RAD17, RAD18	2
Cell Cycle	S phase of eukaryotic cells	2.87E-03	FN1, GTF2I, MAP3K8, NBN, NRG1, RAD18	6
Cell Cycle	G2/M phase	3.03E-03	NBN, RAD17, RUNX2, WEE1	4
Cell Cycle	S phase of cell lines	3.42E-03	FN1, GTF2I, MAP3K8, NRG1, RAD18	5
Cell Cycle	exit from cell division process of eukaryotic cells	3.64E-03	GTF2I, PRKCA, RUNX2	3
Cell Cycle	G2 phase of tumor cell lines	4.05E-03	ATF5, NRG1, RAD17, WEE1	4
Cell Cycle	arrest in G2 phase of breast cancer cell lines	4.42E-03	NRG1, WEE1	2
Cell Cycle	exit from interphase of eukaryotic cells	5.08E-03	GTF2I, RUNX2	2
Cell Cycle	arrest in cell stage of cell lines	6.22E-03	ATF5, GOLGA2, GTF2I, NRG1, PRKCA, RAD18, WEE1	7
Cell Cycle	arrest in cell division process of cell lines	6.49E-03	ATF5, GOLGA2, GTF2I, MLL, NRG1, PRKCA, RAD18, WEE1	8
Cell Cycle	arrest in G0/G1 phase transition of breast cell lines	7.20E-03	PRKCA	1

Supplemental Table 4 - Top Molecular and Cellular Function from Functional Genetic Screening- Cell cycle

Category	Functions Annotation	p-Value	Molecules	# Molecules
Cell Cycle	arrest in G0/G1 phase transition of epithelial cell lines	7.20E-03	PRKCA	1
Cell Cycle	arrest in G2/M phase transition of hepatoma cell lines	7.20E-03	ATF5	1
Cell Cycle	arrest in cell cycle progression of intestinal cell lines	7.20E-03	PRKCA	1
Cell Cycle	arrest in mid-G1 phase of microvascular endothelial cells	7.20E-03	FN1	1
Cell Cycle	delay in G1 phase of bone cell lines	7.20E-03	RUNX2	1
Cell Cycle	delay in G2 phase of breast cancer cell lines	7.20E-03	NRG1	1
Cell Cycle	entry into G1/S phase transition of microvascular endothelial cells	7.20E-03	FN1	1
Cell Cycle	entry into G2/M phase of colon cancer cell lines	7.20E-03	WEE1	1
Cell Cycle	entry into G2/M phase of endothelial cells	7.20E-03	RUNX2	1
Cell Cycle	entry into G2/M phase transition of leukocyte cell lines	7.20E-03	MAP3K8	1
Cell Cycle	exit from G2/M phase of endothelial cells	7.20E-03	RUNX2	1
Cell Cycle	exit from cell cycle progression of enterocytes	7.20E-03	PRKCA	1
Cell Cycle	propagation of mitosis of neurons	7.20E-03	NDE1	1
Cell Cycle	re-entry into cell division process	8.82E-03	CAST, FN1, NRG1	3
Cell Cycle	exit from cell division process of normal cells	8.97E-03	PRKCA, RUNX2	2
Cell Cycle	G2/M phase of eukaryotic cells	9.67E-03	RAD17, RUNX2, WEE1	3
Cell Cycle	cell cycle progression	9.86E-03	CAST, CHAF1A, FKBP1A, GOLGA2, HSP90AA1, MLL, NBN, NDE1, NRG1, PIKFYVE, PRKCA, TUBB1, WEE1, XPA	14
Cell Cycle	G1/S phase transition	1.14E-02	ACVR1B, FN1, NBN, NRG1, PPP3CA	5
Cell Cycle	arrest in S phase of cell lines	1.38E-02	GTF2I, RAD18	2
Cell Cycle	assembly of mitotic spindle	1.38E-02	NDE1, TUBB1	2
Cell Cycle	mitosis	1.42E-02	GOLGA2, HSP90AA1, NBN, NDE1, NRG1, PRKCA, TUBB1, WEE1	8
Cell Cycle	S phase checkpoint control of carcinoma cell lines	1.44E-02	RAD17	1
Cell Cycle	S phase checkpoint control of lung cancer cell lines	1.44E-02	RAD17	1
Cell Cycle	arrest in G2/M phase transition of ovarian cancer cell lines	1.44E-02	NRG1	1
Cell Cycle	arrest in S phase of fibroblasts	1.44E-02	NBN	1
Cell Cycle	arrest in metaphase of cervical cancer cell lines	1.44E-02	GOLGA2	1
Cell Cycle	cell cycle progression of bladder cancer cell lines	1.44E-02	PIKFYVE	1
Cell Cycle	entry into mitosis of breast cancer cell lines	1.44E-02	NRG1	1
Cell Cycle	exit from S phase of fibroblast cell lines	1.44E-02	GTF2I	1

Supplemental Table 5 - Differentially expressed genes in AML cells exposed to cytarabine

GENE	FC
DPYD	1.358273
ENST00000258817	1.191148
SNX4	1.225983
SLC35F1	1.289602
ATAD1	1.163746
HGSNAT	1.381167
ATP10D	1.361045
RPN1	1.106393
ZMYM4	1.153256
GOLGA2	1.314267
RAB3GAP1	1.133477
PUM1	1.086046
C2ORF30	1.300421
ENST00000390915	1.042245
AGTPBP1	1.235211
MIB1	1.209681
DRAM	1.347038
AIM1	1.153657
INTS6	1.30663
GYPE	1.164174
CCR2	1.336057
TPMT	1.376244
DNAJC3	1.342187
JARID1B	1.117541
CRKRS	1.155387
DYNLT1	1.366088
USP32	1.210017
SUPT6H	1.183724
RWDD3	1.251011
PTPRM	1.194227
C20ORF197	1.462025
ARCN1	1.109042
ANXA7	1.20709
C10ORF118	1.25692
UBE2D1	1.380564
OSBPL8	1.241062
CHMP5	1.226297
CFTR	1.160325
MNDA	1.493508
LMO7	1.529543
TXNDC4	1.195619
SNX14	1.396174
FTHL3P	1.282283
RP1-19N1.1	1.230345
ZNF548	1.161692
BAZ2A	1.149296
FAM127A	1.336858
LRMP	1.200475
TMEM131	1.224066
CAB39	1.192618
ENST00000408656	1.108001
N4BP2L1	1.389736
C3ORF23	1.440722
TRAF3IP3	1.310977
TMEM63A	1.32937
PIGT	1.106553
MPZ	1.315408
IL1RAP	1.23008
ATP2B1	1.140538
PPM2C	1.237652
CALR	1.106744
DNAJC13	1.230565
CASP3	1.148132
UBE4A	1.122076
ARHGAP18	1.330156
YPEL2	1.449161
SNORA46	1.430257
IRF2	1.167137
FAM129A	1.24597
ARSB	1.239435
AKAP13	1.353334
SEC61B	1.104038
GPR124	1.130809
SIL1	1.321855
HERPUD2	1.285087
SKAP2	1.265124
ZNF799	1.374353
FMO4	1.168018
C6ORF115	1.157281
FBXO11	1.163853
NPHP3	1.212585
CCDC126	1.097249
UTRN	1.338133
NFXL1	1.297365
PCNXL2	1.328678
FAM124B	1.051543
ZYG11B	1.357676
C2ORF63	1.270345
RP5-1022P6.2	1.227
ICAM2	1.232856
FAM45A	1.187698
DDX42	1.109429
FNIP1	1.227512
XRN1	1.178814
GIT2	1.24266
LPCAT2	1.328392
INPP4A	1.271118
NLRC4	1.251696
CDC42SE2	1.153746
RPN2	1.105772

Supplemental Table 5 - Differentially expressed genes in AML cells exposed to cytarabine

GENE	FC
ENST00000362636	-1.13475
ENST00000385944	-1.12626
RNPS1	-1.06068
TIAM2	-1.13552
ENST00000331219	-1.245
ENST00000364831	-1.14721
SNORA10	-1.25469
C19ORF10	-1.11474
HSD17B10	-1.12804
CCL20	-1.14375
LOC646836	-1.21386
EBPL	-1.31061
RPS6KA2	-1.60061
GNB2L1	-1.06905
RNF187	-1.16734
EFNA3	-1.14972
MCF2	-1.1182
C1ORF93	-1.19723
OGDHL	-1.14137
TMEM141	-1.22434
ENST00000384125	-1.12412
EIF5A	-1.13455
WDR46	-1.43366
LOC348262	-1.21018
RP1-21O18.1	-1.07893
ASS1	-1.26679
EIF4B	-1.11369
LOC347292	-1.1179
HIST1H2BJ	-1.31954
COBRA1	-1.17225
ENST00000384310	-1.06278
LEMD1	-1.15709
GTPBP3	-1.20888
UNC93B1	-1.09493
FGFBP1	-1.29991
BAT1	-1.05838
ENST00000410312	-1.23272
SPATA19	-1.13955
LOXL3	-1.09815
ENST00000410573	-1.30833
GOLGA2LY1	-1.12243
WBP11P1	-1.11569
MGC45800	-1.14776
C2ORF16	-1.1914
OR5AN1	-1.25685
C1ORF189	-1.2505
AARSD1	-1.20428
ENST00000324144	-1.35362
C9ORF150	-1.11251
PRPF6	-1.06923
TNS1	-1.07962
SP2	-1.2117
ZNF793	-1.14818
DYDC1	-1.08689
ACO2	-1.05768
GEMIN7	-1.08616
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FXN	-1.39065
COX7A2	-1.10059
LOC441795	-1.26149
SCGB3A2	-1.17102
EIF4A1	-1.18645
DTD1	-1.26756
SLITRK3	-1.08219
DPY19L2P1	-1.45233
SLC41A3	-1.24233
HSPBP1	-1.2272
AADACL2	-1.15228
ARS2	-1.21838
MRPL53	-1.15498
CLEC6A	-1.22012
GBL	-1.33276
SF3A1	-1.07026
TLR8	-1.06182
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NPHP4	-1.13279
R3HCC1	-1.18594
MAP1S	-1.06937
ENST00000385400	-1.11491
STC2	-1.3506
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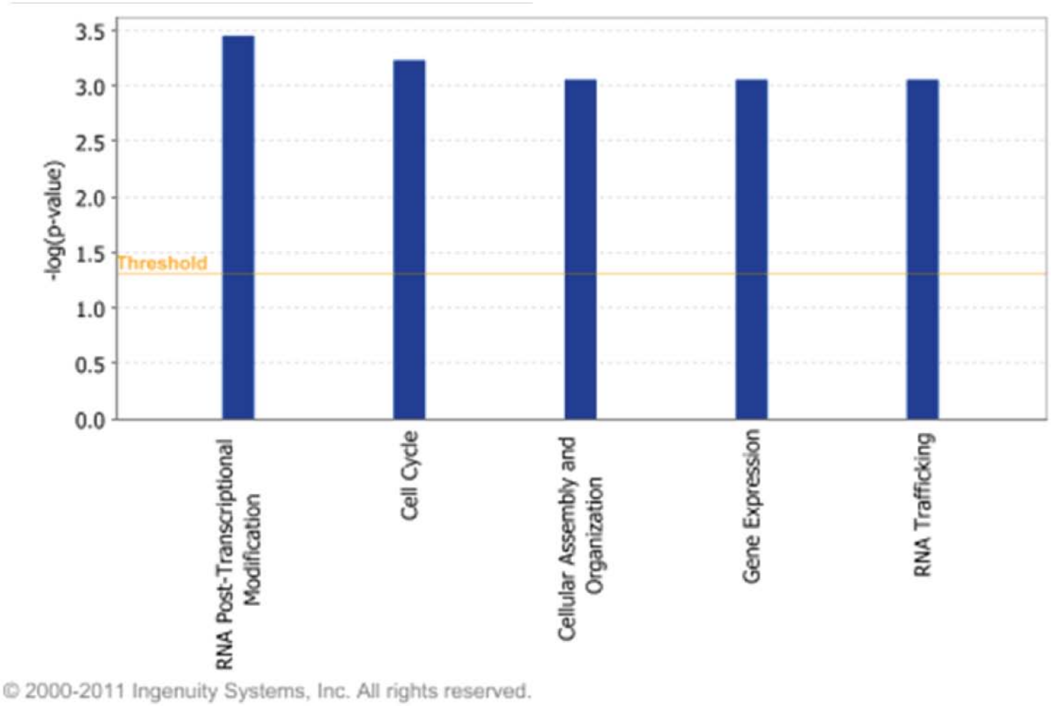
COASY	-1.27545
NSUN5	-1.29376
CCND2	-1.2975
TFIP11	-1.15037
TRAF2	-1.20673
TBRG4	-1.26301
ENST00000387204	-1.2244
TMEM143	-1.39955
ENST00000386940	-1.18842
CHAC1	-1.34119
MPI	-1.25002
RNF43	-1.19427
ENST00000407306	-1.31086
ACTBL2	-1.18539
UQCRQ	-1.17492
SLC35A4	-1.0681
WIT1	-1.1546
ENST00000384322	-1.1253
FLJ00290	-1.09461

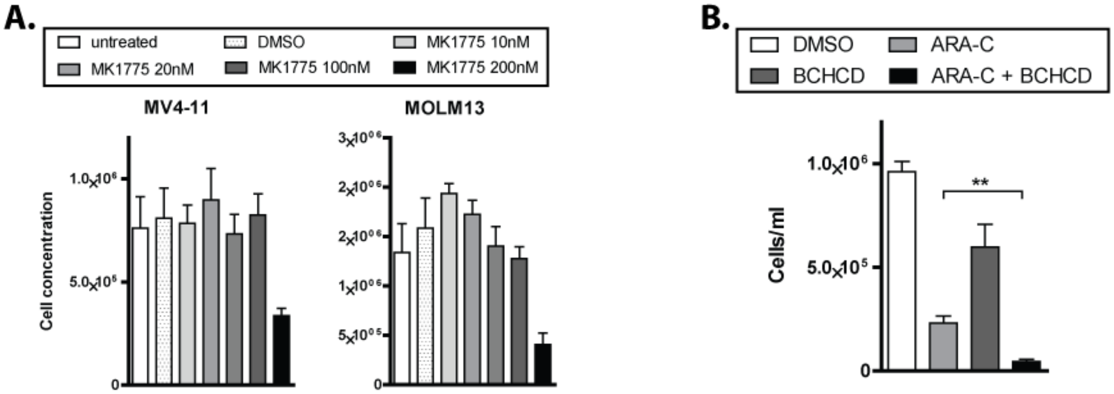
Supplemental Figure 1.Top Molecular and biological functions represented by top differentially expressed genes exposed to ARA-C. The top differentially expressed genes were subject to analysis by Ingenuity Pathways Analysis.



Supplemental Figure 2. Pharmacologic inhibition of WEE1

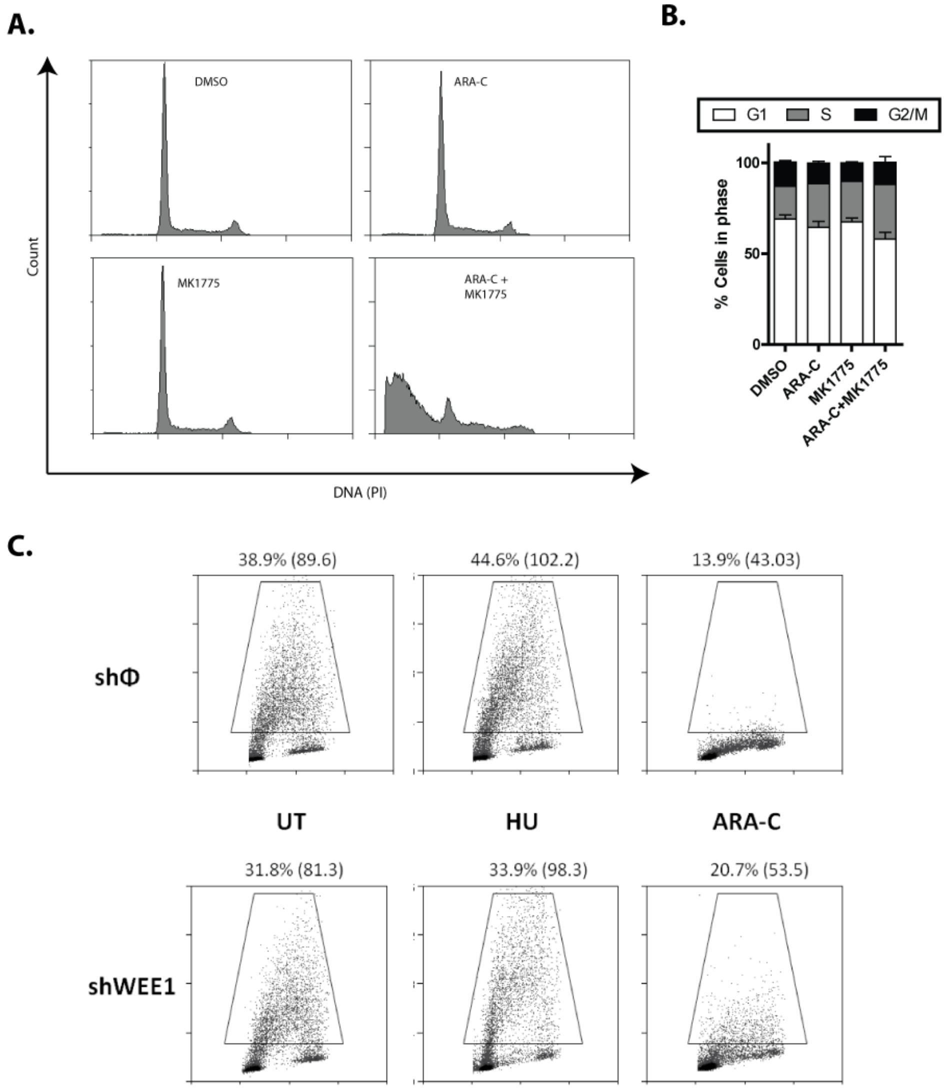
A. MK1775 alone has little effect on AML cell proliferation at concentrations below 100nM. MV4-11 and Molm13 cells were seeded at $2x10^5$ cells/ml and treated with a WEE1 inhibitor, MK1775, at the indicated doses for 72 hours and counted by flow cytometry and propidium iodide exclusion. The concentration of live cells is depicted graphically. MK1775 has little effect on cellular proliferation at doses under 100nM.

B. Inhibition of WEE1 with a small molecule unrelated to MK1775 sensitizes AML cells to cytarabine. MV4-11 cells were treated with cytarabine and/or BCHCD for 72 hours and then counted by propidium iodide exclusion and flow cytometry. The number of live cells is depicted.



Supplemental Figure 3. Cell cycle analyses.

A & B. Assessment of cell cycle by DNA content shows large sub-G1 population, but little change with cytarabine and MK1775 among live cells. MV4-11 cells were treated with DMSO, cytarabine 800nM, MK1775 200nM, or both for 72 hours, fixed and stained with propidium iodide and analyzed by flow cytometry. **A.** Representative histograms are shown. Note dramatic increase in Sub-G1. **B.** The live cell population was analyzed for DNA content after exclusion of the Sub-G1 population. **C. BrdU incorporation in cells in which WEE1 has been knocked down.** Molm13 cells transduced with a non-silencing sequence (shΦ) or an shRNA against WEE1 (shWEE1; as in Figure 5) were treated with cytarabine (12.5 nM), hydroxyurea (50μM) or left untreated for 48 hours, followed by exposure to BrdU for 1 hour. Cells were harvested, fixed and analyzed by flow cytometry as in Figure 6. While the effects of HU and ARA-C were different at the doses tested, the S phase effects induced by cytarabine and HU are abrogated in cells in which WEE1 is knocked down. The percentage of BrdU$^+$ cells is shown (with mean fluorescence intensity).



Supplemental Figure 4. Inhibition of WEE1 sensitizes primary AML cells to cytarabine.

A. Two additional primary AML samples treated and analyzed as in Figure 7C.

B. Inhibition of WEE1 abrogates inhibitory phosphorylation of CDK2 induced by cytarabine. Cells from primary AML sample number 7379 were subject to western blotting 72 hours after treatment with cytarabine (250nM) and/or MK1775 (250nM).