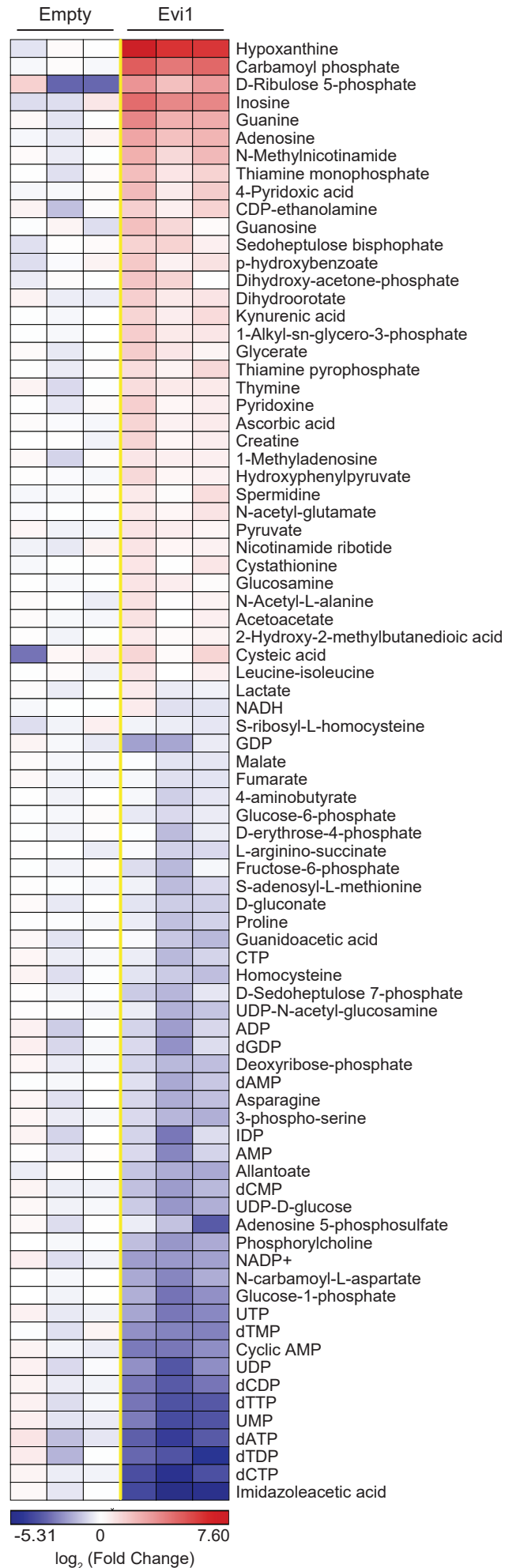
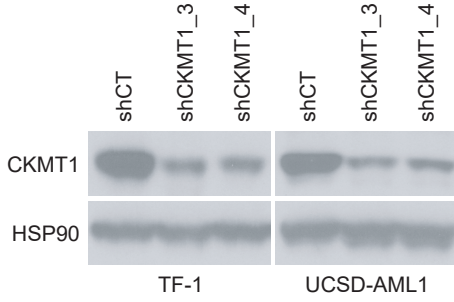


Supplementary Figure S1

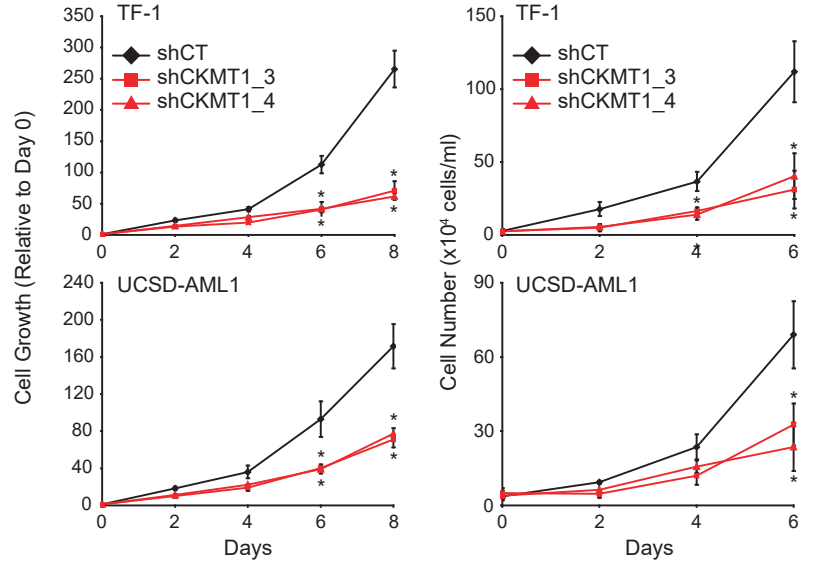


Supplementary Figure S2

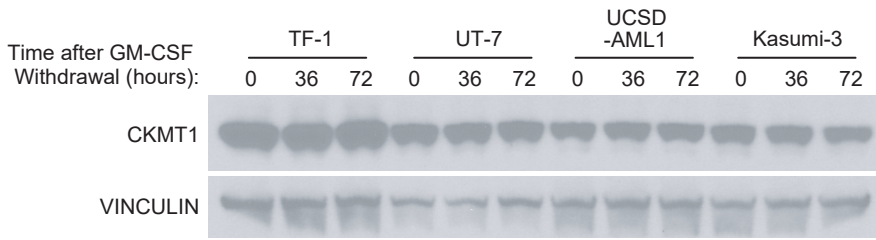
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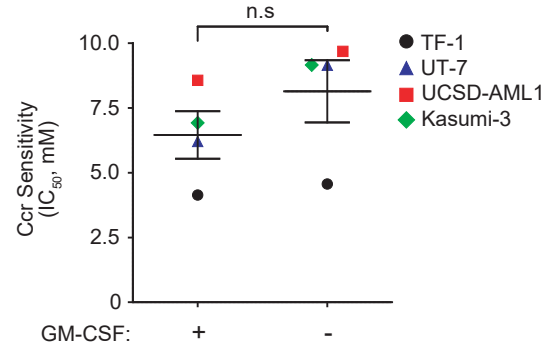
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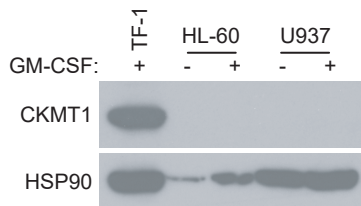
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D.

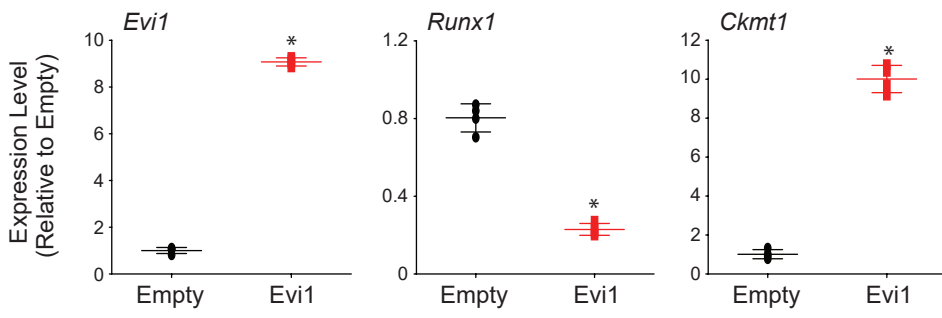


E.

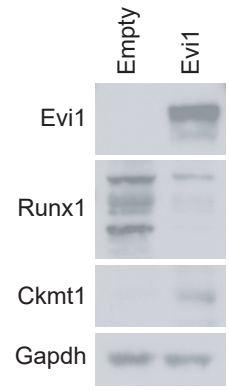


Supplementary Figure S3

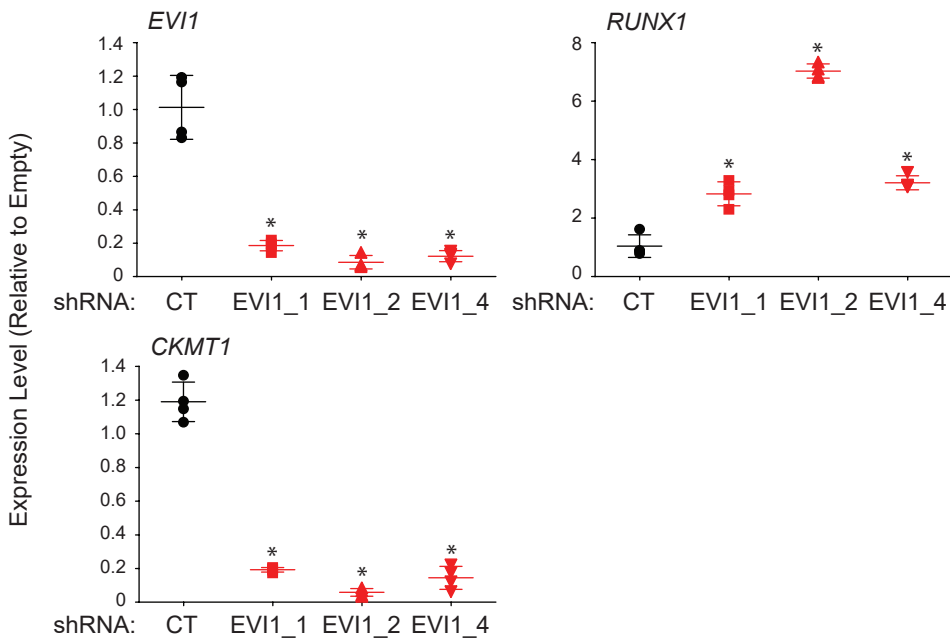
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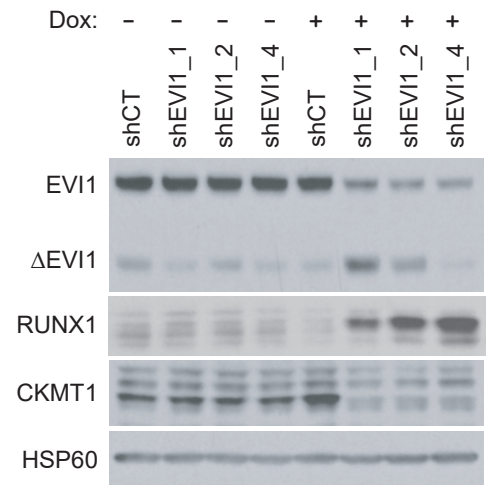
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C.

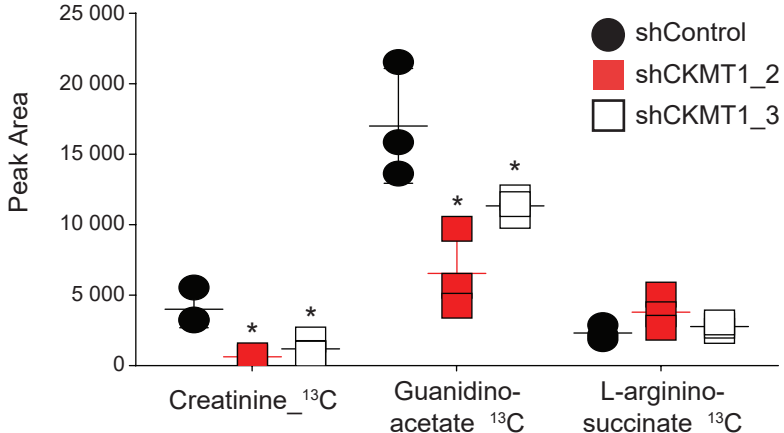


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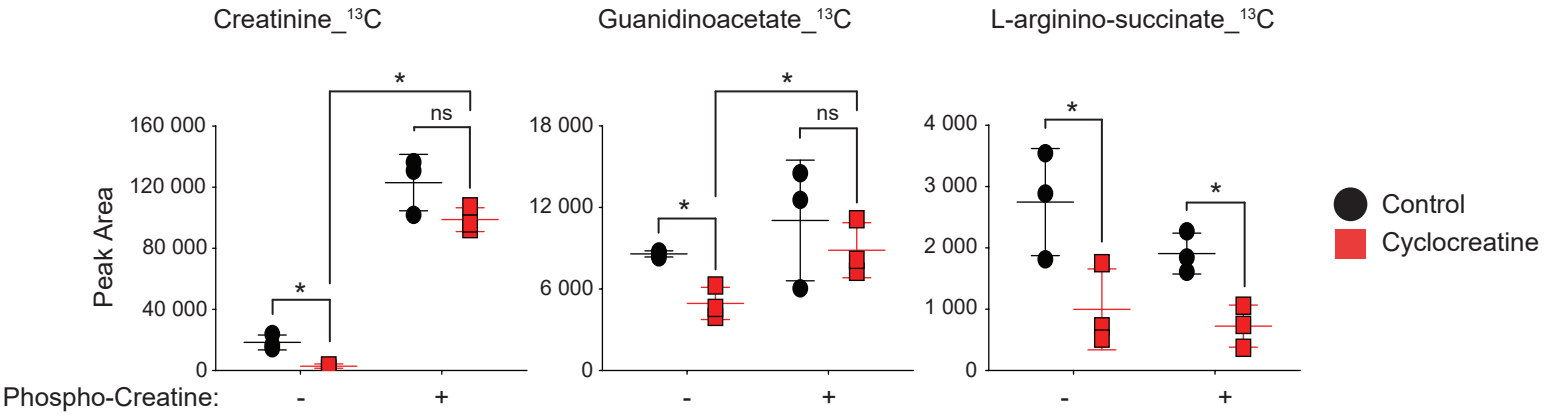


Supplementary Figure S4

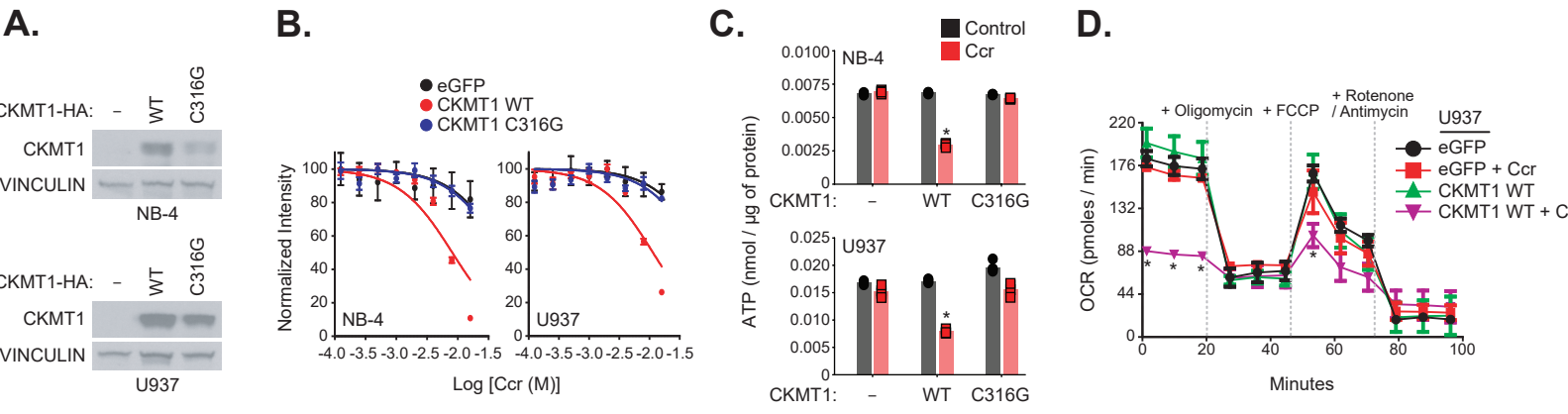
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B.

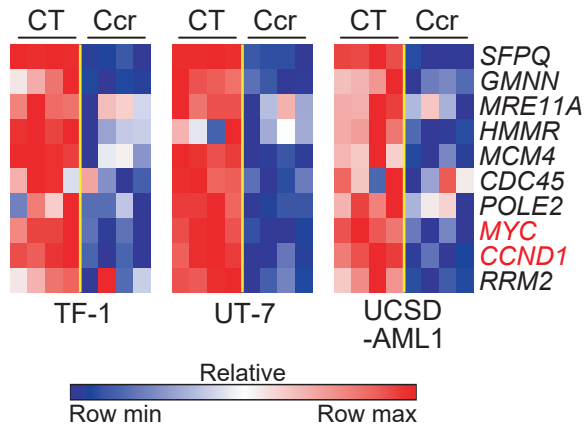


Supplementary Figure S5

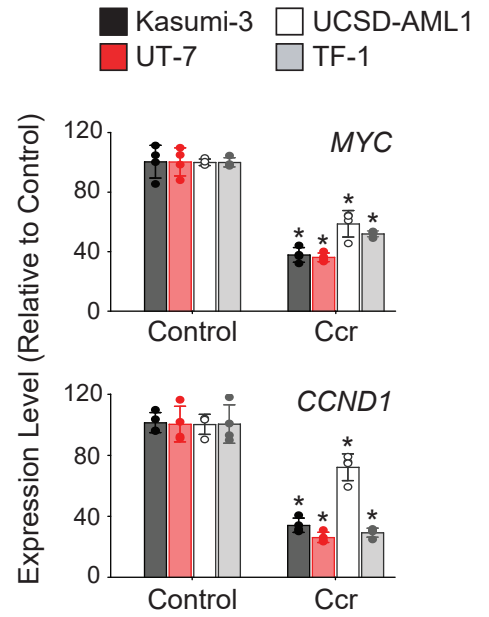


Supplementary Figure S6

A.

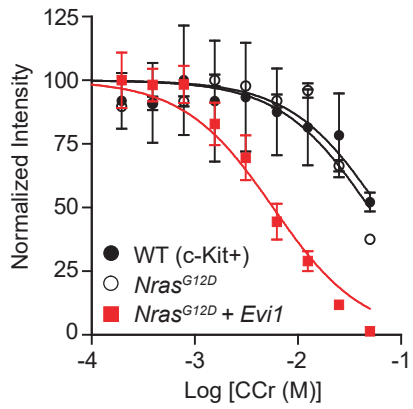


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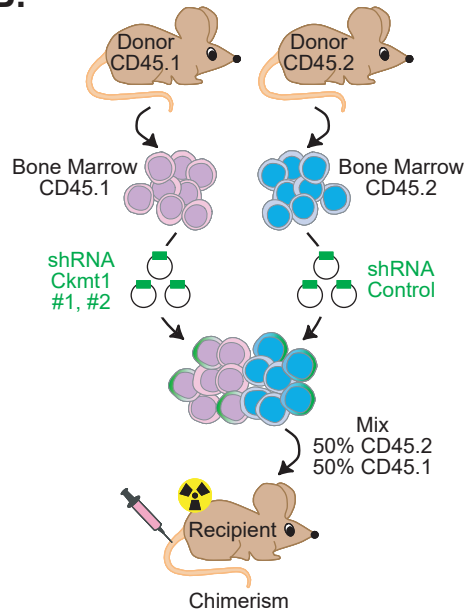


Supplementary Figure S7

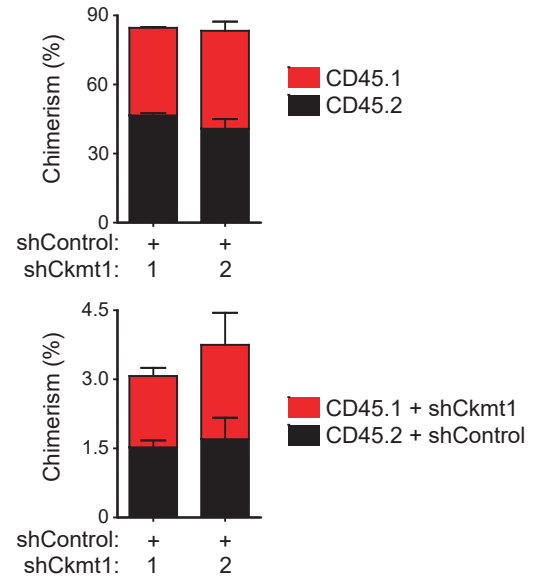
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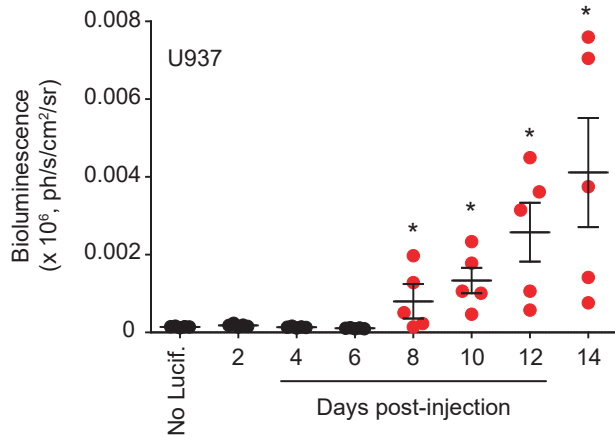
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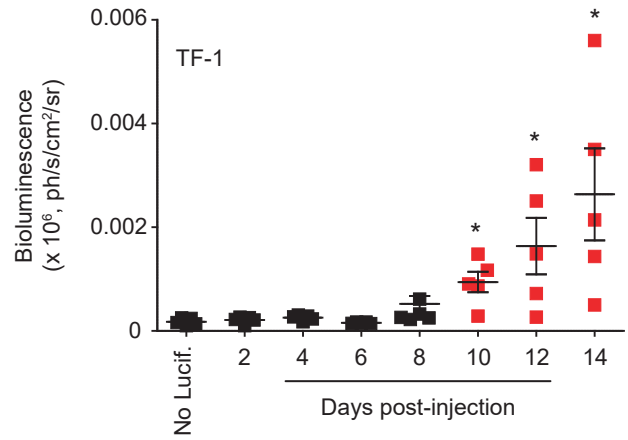
C.



D.



E.



Supplementary Table S1

Gene	Category	NES UCSD-AML1	Log10 (P Value) UCSD-AML1	NES TF-1	Log10 (P Value) TF-1
DLD	Core_Depletion	-2.94	1.80	-4.11	2.64
RPIA	Core_Depletion	-1.44	1.24	-2.91	2.40
OGDH	Core_Depletion	-3.57	2.51	-2.33	1.81
SDHA	Core_Depletion	-2.13	1.38	-1.99	1.29
CS	Core_Depletion	-1.32	1.05	-1.50	1.15
ALDOC	Core_Depletion	-1.97	1.42	-1.41	1.46
CKMT1	Core_Depletion	-1.75	1.31	-1.32	1.04
GAPDH	Core_Depletion	-3.20	2.20	-1.16	1.07
ACO2	Core_Depletion	-2.72	2.00	-0.47	0.90
DLST	TF-1_Depletion	0.91	0.25	-4.21	2.92
PDK2	TF-1_Depletion	-0.74	0.64	-1.85	1.22
FBP1	TF-1_Depletion	-0.05	0.33	-1.46	0.99
PDK3	TF-1_Depletion	-0.53	0.72	-1.19	1.09
IDH2	TF-1_Depletion	-0.59	0.75	-1.07	1.24
PGLS	TF-1_Depletion	-0.44	0.68	-1.05	1.01
PRPS1	TF-1_Depletion	-0.47	0.69	-0.82	1.11
SLC2A1	UCSD-AML1_Depletion	-1.59	1.07	0.17	1.37
MDH1B	0	-1.00	0.87	-1.20	0.98
PCK1	0	-0.49	0.70	-0.89	0.92
PKM2	0	-1.35	0.96	-0.82	0.71
TKT	0	-0.90	0.68	-0.70	0.61
PGM2	0	-0.57	0.58	-0.49	0.60
SUCLG2	0	0.84	0.27	-0.39	0.55
PGAM1	0	-0.02	0.38	-0.36	0.54
PDP2	0	0.80	0.17	-0.18	0.45
PDPR	0	0.46	0.23	-0.14	0.37
PDK1	0	0.82	0.70	-0.12	0.51
PDK4	0	0.80	0.18	-0.07	0.34
PKLR	0	1.24	0.24	0.15	1.25
TALDO1	0	0.61	0.50	0.24	0.28
ACLY	0	0.42	0.31	0.30	0.42
BPGM	0	-0.20	0.45	0.30	0.49
PGK2	0	0.06	0.66	0.35	0.45
IDH3A	0	0.77	0.36	0.39	0.77
PFKL	0	0.92	0.38	0.41	0.27
SLC2A3	0	0.41	0.51	0.44	0.29
PDHB	0	0.70	0.17	0.46	0.37
PDHA1	0	0.75	0.72	0.50	0.44
TPI1	0	0.59	0.42	0.52	0.49
IDH1	0	0.59	0.39	0.52	0.38
G6PD	0	0.95	0.66	0.53	0.40
LDHC	0	0.93	0.35	0.55	0.21
PC	0	0.57	0.23	0.56	0.24
PGM1	0	0.98	0.70	0.58	0.37
PGK1	0	-0.72	0.60	0.61	0.47
DLAT	0	0.40	0.28	0.61	0.37
PRPS2	0	0.67	0.23	0.62	0.14
H6PD	0	0.69	0.64	0.65	0.46
SUCLA2	0	0.97	0.61	0.65	0.34
HK2	0	-0.72	0.64	0.85	0.73
SLC2A2	0	0.99	0.49	0.89	0.15
GCK	0	0.71	0.13	0.91	0.07
HK3	0	0.37	0.40	1.02	0.64
SUCLG1	0	0.55	0.26	1.02	0.96
ENO1	0	-0.81	0.62	1.15	0.28
LDHB	0	0.20	0.30	1.39	0.20
MDH1	0	0.70	0.59	1.33	0.75
ALDOB	UCSD-AML1_Enrichment	1.03	1.29	0.69	0.67
MDH2	UCSD-AML1_Enrichment	0.45	1.05	1.00	0.78
GPI	TF-1_Enrichment	0.98	0.13	0.97	1.13
GALM	TF-1_Enrichment	0.87	0.57	0.97	1.01
PTEN	Core_Enrichment	1.56	2.17	1.33	1.52
PCK2	Core_Enrichment	1.15	1.26	0.92	0.85
RPE	Core_Enrichment	1.28	2.40	1.02	0.90
GPD2	Core_Enrichment	1.07	1.18	1.34	1.58
TP53	Core_Enrichment	1.06	1.60	1.44	2.06
RB1	Core_Enrichment	1.79	2.24	1.73	1.32

Supplementary Table S2

# ID	Age	Sex	Diagnosis	WHO subtype	Disease Status	FLT3	NPM1	Cytogenetics	Molecular Characteristics
1	62	F	AML	Without Maturation	relapsed/refractory	WT	unknown	46XY, t(3;3)	CEBPa negative
2	73	F	AML		relapsed	mutant	WT	karyotype failed	IDH1 mutation
3	82	M	AML		relapsed/refractory	FLT3-ITD	unknown	46XY	
4	77	M	AML		refractory	FLT3 D835	WT	46XY	
5	42	F	AML	Monoblastic Differentiation	relapsed	WT	WT	Complex Karyotype	TP53 mutation
6	67	M	AML	Monocytic Differentiation	relapsed	WT	mutant	48XY, +1; +8	
7	58	F	AML		new	WT	WT	47XX, +8	
8	n/a	M	AML		n/a	n/a	n/a	n/a	
9	72	M	AML	With MDS Related Changes	relapsed	WT	WT	45Y, t(Y;13), -20, add(3)(q11.2), del5q, add(17)(p11.2)	
10	11	M	AML		new	FLT3-ITD	unknown	46XY, add(6)(q21), add(9)(p24)	
11	59	F	AML		relapsed/refractory	FLT3-ITD	mutant	46XX, t(4;11)	
12	73	F	AML	Myelomonocytic Features	refractory	WT	WT	46XX	
13	70	M	AML	Monocytic Differentiation	new	WT	WT	47XY, +11	
14	60	F	AML		new	WT	WT	46 XX, inv16	
15	67	F	AML	Monocytic Differentiation	new	WT	mutant	46XX	
16	58	M	AML	Monocytic Differentiation	new	WT	WT	46XY, del9q	
17	38	M	AML		relapsed	WT	unknown	Complex Karyotype	
18	71	F	AML	Without Maturation	new	WT	WT	complex karyotype, del 5q, del7q	
19	60	F	AML		relapsed	WT	unknown	47XX, +13	
20	30	M	AML	Monocytic Features	new	WT	WT	n/a	MLL-AF9
21	48	F	AML		new	WT	WT	46X, idic(X)(q13)	CEBPa single mutation
22	66,0	F	AML		new	WT	WT	Complex Karyotype	
23	71	F	AML		new	FLT3-ITD	WT	46XX, del7q	DNMT3A and IDH1 mutation
24	89	M	AML		relapsed/refractory	WT	WT	46XY, del5q	
25	58	F	AML		relapsed	FLT3-ITD	WT	46XX	
26	69	F	AML	Myelofibrosis Background	relapsed	WT	WT	unknown	JAK2V617F, IDH1, and TP53 mutations
27	25	M	AML		new	WT	WT	46XY	WT1 mutation
28	47	F	AML		new	WT	WT	Complex Karyotype	
29	n/a	n/a	AML		n/a	FLT3-ITD	n/a	n/a	
30	n/a	F	AML		refractory	n/a	n/a	n/a	
31	67	F	AML		relapsed	FLT3-ITD	mutant	46XX, t(10;12)	
32	63	M	AML		refractory	WT	WT	45XY, -7	
33	64	F	AML	Monocytic Features	new	WT	WT	complex karyotype, -5/del5q	
34	69	M	Acute Undifferentiated Leukemia		new	FLT3-ITD	WT	47XY, +13	IDH2 mutation
35	53	F	AML		relapsed	WT	WT	n/a	
36	72	M	MDS	RAEB-2	new	WT	WT	46XY	
37	52	M	AML		new	WT	WT	Complex Karyotype	TET2 and BCORL1 mutations
38	54	M	B-ALL		new	WT	WT	46XY, t3;11, 19;22	
39	44	F	AML		relapsed	WT	WT	normal karyotype at initial diagnosis	
40	60	M	AML		new	WT	WT	Complex Karyotype	
41	75	M	AML		new	WT	WT	46XY, t(8;21)	
42	44	F	AML		relapsed	FLT3-ITD, FLT3 D835	mutant	n/a	
43	49	M	AML	Monocytic	new	FLT3-ITD	mutant	46XY	
44	64	F	AML		new	WT	WT	46XX	
45	63	F	MDS	RAEB	new	WT	WT	Complex Karyotype	
46	37	M	AML		new	n/a	n/a	n/a	
47	65	F	AML	Therapy Related	relapsed	FLT3-ITD	unknown	46XX	
48	66	M	AML	Myelomonocytic Differentiation	new	FLT3 D835	mutant	46XY	
49	60	M	AML		new	WT	WT	46XY, t(15;17)	
50	63	F	AML		relapsed	FLT3 D835	mutant	46XX, del7q	
51	61	M	AML		relapsed	FLT3-ITD, FLT3 D835Y	mutant	47X, -Y, del6q, +8, +14, del15q	
52	58	M	AML		new	WT	WT	48XY, +11, +22	
53	67	M	AML		refractory	WT	unknown	Complex Karyotype	
54	66	F	AML		new	FLT3-ITD	unknown	46XX	
55	63	M	AML		new	WT	WT	46XY, del20q	
56	41	M	AML		relapsed	WT	WT	45XY, -7	
57	74	M	AML	MDS Changes	new AML	WT	WT	46XY	
58	83	M	AML		refractory	FLT3-ITD	unknown	46XY	
59	75	M	AML		relapsed	unknown	WT	46X, -Y, +11, t1;22	
60	80	M	MDS		new	WT	WT	46XY, del 20q	CEBPA negative
61	75	M	AML	MDS Related Changes	new	WT	WT	n/a	
62	48	M	AML		refractory	WT	WT	Complex Karyotype	TP53 mutations
63	58	M	AML		new	FLT3-ITD	mutant	n/a	
64	65	F	AML		relapsed	WT	WT	46XX, del7q	DNMT3A and IDH2 mutations
65	57	F	AML		new	WT	WT	Complex Karyotype	TP53 mutant
66	55	M	AML	Monocytic Differentiation	new	WT	mutant	47XY, +8	
67	74	M	AML		relapsed	WT	mutant	46XY, del15q	IDH1 mutation
68	52	M	AML		new	FLT3-ITD	WT	46XY, t(15;17)	

Supplementary Table S5

#	Functional Group	Geneset ID	NES	Adjusted P value	Ccr vs ctl
1		BIOCARTA_CELLCYCLE_PATHWAY	-1,530	0,012	DOWN
2		REGULATION_OF_MITOSIS	-1,696	0,014	DOWN
3		WHITFIELD_CELL_CYCLE_G2_M	-1,716	0,014	DOWN
4		CELL_CYCLE_CHECKPOINT_GO_0000075	-1,490	0,021	DOWN
5		CHANG_CYCLING_GENES	-1,756	0,022	DOWN
6		PUJANA_CHEK2_PCC_NETWORK	-1,747	0,033	DOWN
7		REGULATION_OF_CELL_CYCLE	-1,305	0,036	DOWN
8	Cell Cycle	CELL_CYCLE_GO_0007049	-1,312	0,038	DOWN
9		MITOTIC_CELL_CYCLE_CHECKPOINT	-1,609	0,045	DOWN
10		MITOTIC_CELL_CYCLE	-1,422	0,046	DOWN
11		MITOSIS	-1,506	0,048	DOWN
12		KEGG_CELL_CYCLE	-1,458	0,053	DOWN
13		REACTOME_MITOTIC_G1_G1_S_PHASES	-1,638	0,055	DOWN
14		REACTOME_RNA_POL_III_TRANSCRIPTION_INITIATION_FROM_TYPE_2_PROMOTER	-1,633	0,062	DOWN
15		LAMB_CCND1_TARGETS	-1,432	0,062	DOWN
16		MOLENAAR_TARGETS_OF_CCND1_AND_CDK4_UP	-1,634	0,020	DOWN
17		KEGG_FRUCTOSE_AND_MANNOSE_METABOLISM	-1,848	0,010	DOWN
18		REACTOME_GLUCOSE_METABOLISM	-1,662	0,024	DOWN
19		REACTOME_GLUCOSE_TRANSPORT	-1,615	0,039	DOWN
20	Energy Metabolism	MOOTHA_GLYCOLYSIS	-1,559	0,026	DOWN
21		GLUCOSE_METABOLIC_PROCESS	-1,554	0,021	DOWN
22		BIOCARTA_MITOCHONDRIA_PATHWAY	-1,536	0,028	DOWN
23		REACTOME_GLYCOLYSIS	-1,521	0,048	DOWN
24		PID_MYC_ACTIV_PATHWAY	-1,856	0,001	DOWN
25		IVANOVA_HEMATOPOIESIS_LATE_PROGENITOR	-1,533	0,001	DOWN
26		WEI_MYCN_TARGETS_WITH_E_BOX	-1,979	0,004	DOWN
27		BENPORATH_ES_1	-1,610	0,010	DOWN
28		KIM_MYCN_AMPLIFICATION_TARGETS_UP	-1,415	0,015	DOWN
29		IVANOVA_HEMATOPOIESIS_EARLY_PROGENITOR	-1,507	0,017	DOWN
30	Cell Stemness	BENPORATH_NANOG_TARGETS	-1,445	0,018	DOWN
31		KEGG_ACUTE_MYELOID_LEUKEMIA	-1,747	0,018	DOWN
32		GAZDA_DIAMOND_BLACKFAN_ANEMIA_PROGENITOR_UP	-1,675	0,023	DOWN
33		BENPORATH_ES_2	-1,494	0,049	DOWN
34		RAMALHO_STEMNESS_UP	-1,638	0,034	DOWN
35		BILD_MYC_ONCOGENIC_SIGNATURE	-1,362	0,032	DOWN
36		DMAP_MONO.VS.HSC	1,623	0,001	UP
37		KRIGE_RESPONSE_TO_TOSEDOSTAT_6HR	1,705	0,012	UP
38		ZUBER_JQ1_DIFFERENTIATION	1,950	0,012	UP
39	Cell Differentiation	DIFFERENTIATION_DOT1L	1,387	0,038	UP
40		STEGMAIER_DIFFERENTIATION_PMA	1,459	0,042	UP
41		STEGMAIER_DIFFERENTIATION_VITD	1,442	0,061	UP
42		DIFFERENTIATION_ZUBER	1,499	0,013	UP
43		KEGG_TYROSINE_METABOLISM	1,459	0,018	UP
44	Amino Acid Metabolism	KEGG_BETA_ALANINE_METABOLISM	1,548	0,022	UP
45		KEGG_GLYCINE_SERINE_AND_THREONINE_METABOLISM	1,746	0,001	UP

Extended Data. Uncropped images from immunoblot experiments presented in main and supplementary figures.

Figure 1F

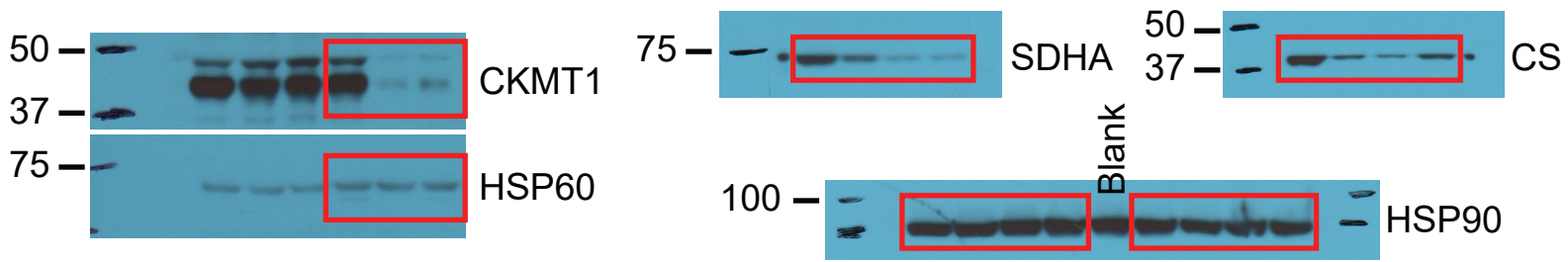


Figure 2A

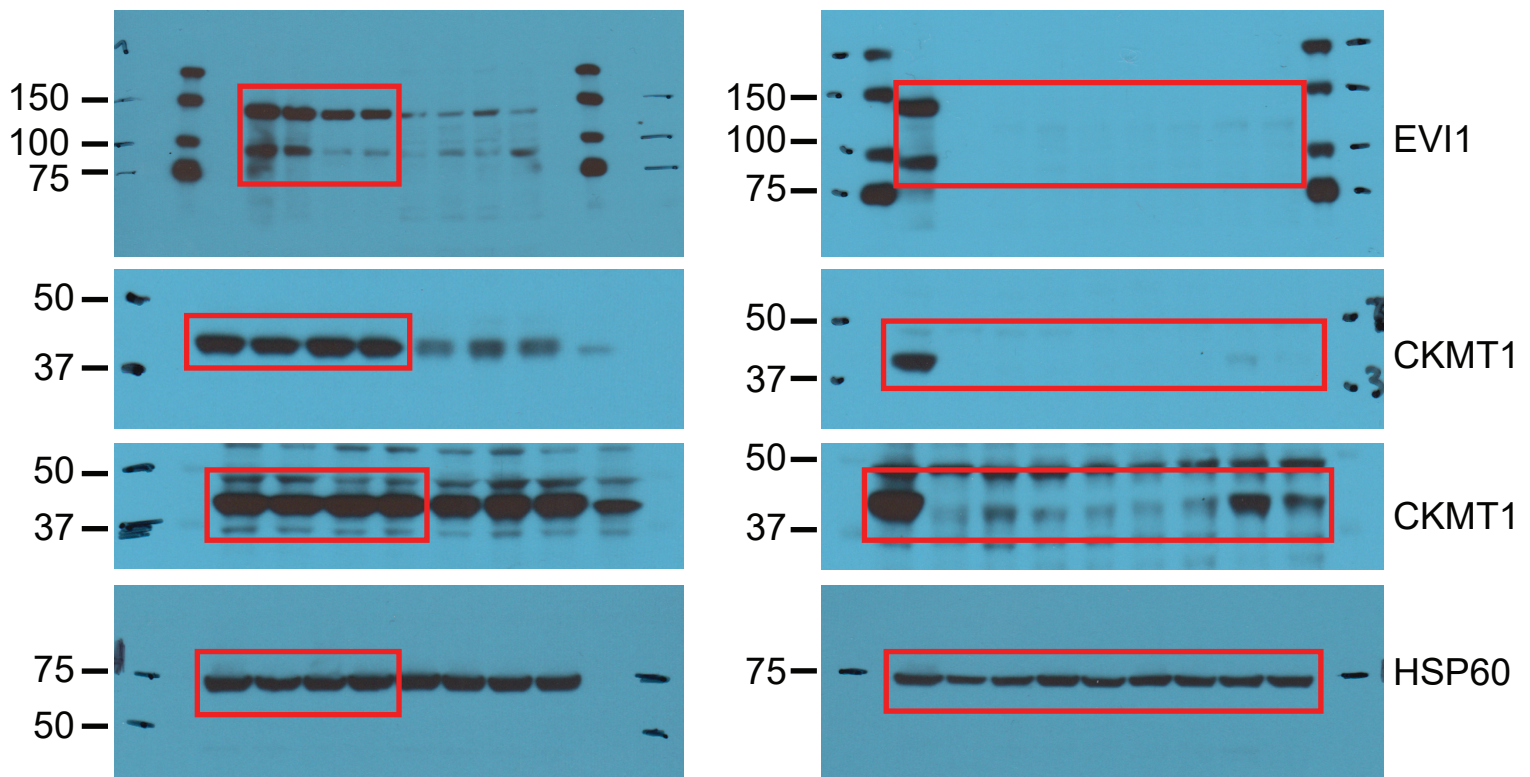
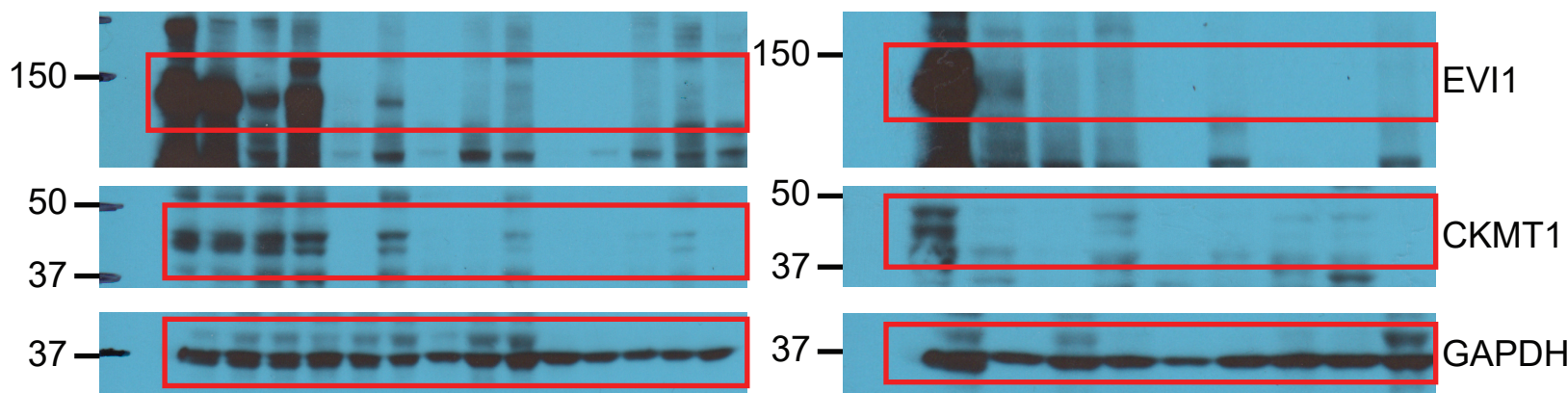


Figure 2F



Extended Data (cont'd)

Figure 3A

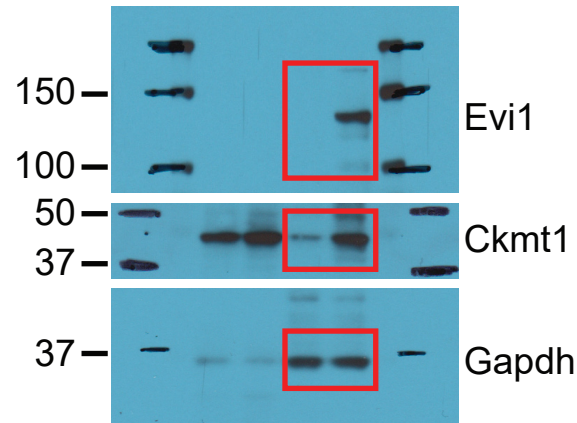


Figure 3G

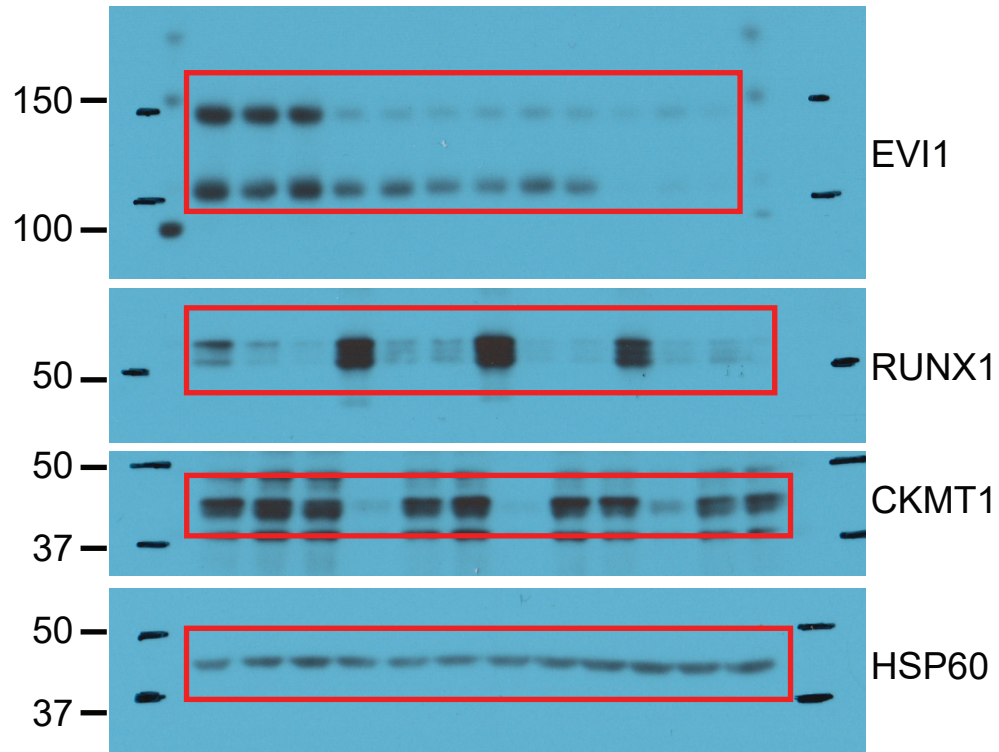


Figure 6A

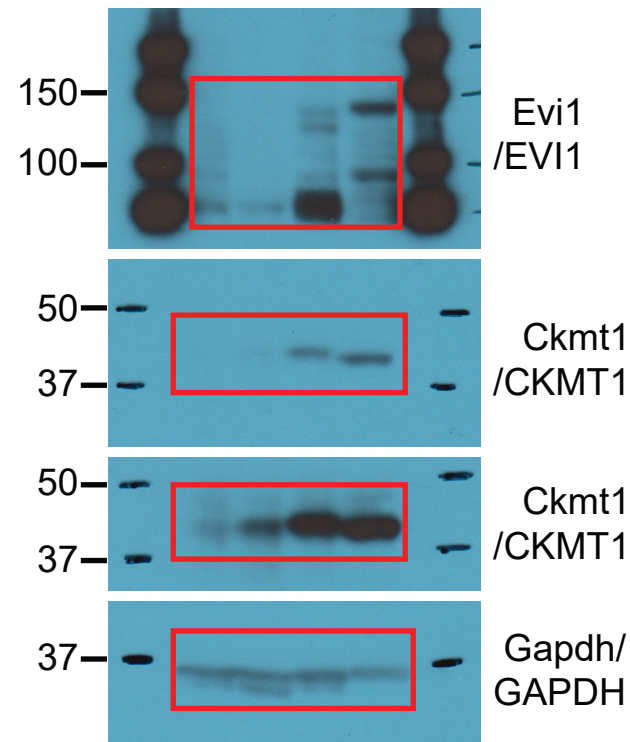
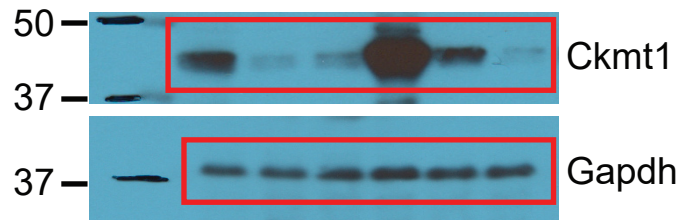
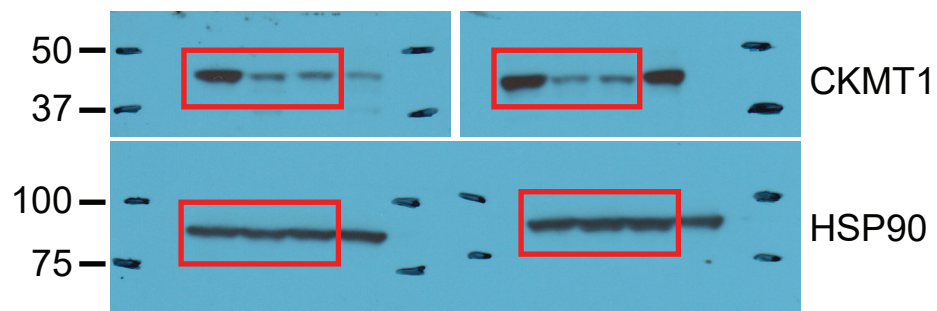


Figure 6C

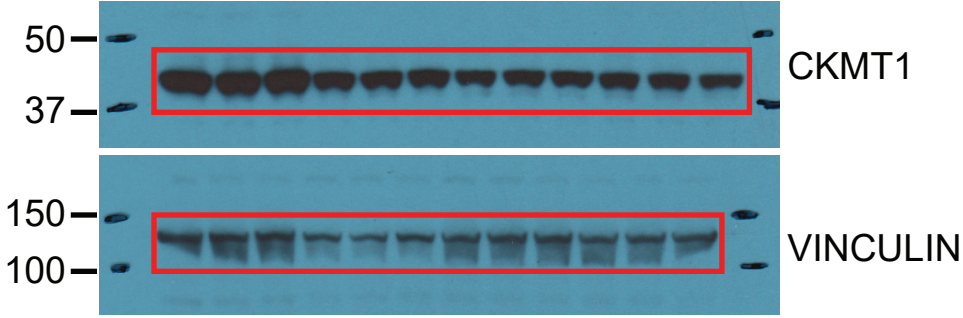


Supplementary Figure S2A

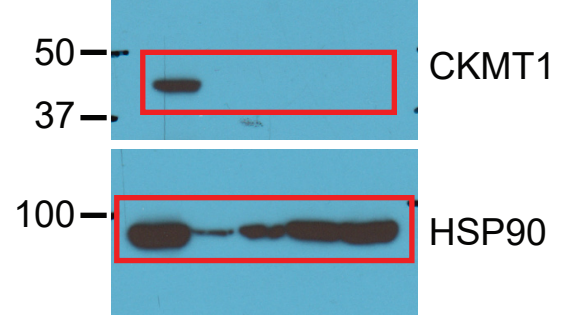


Extended Data (cont'd)

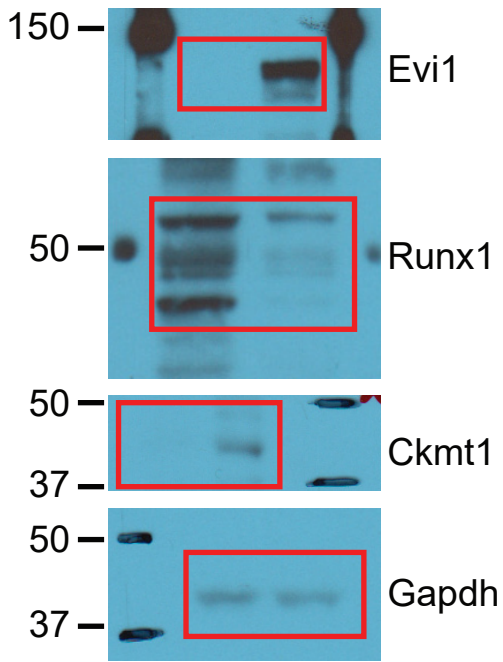
Supplementary Figure S2C



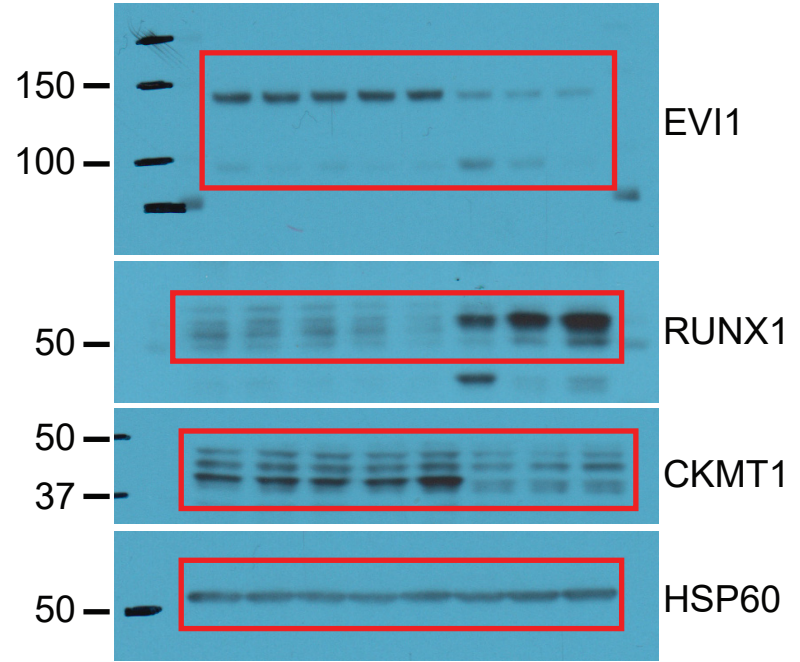
Supplementary Figure S2E



Supplementary Figure S3B



Supplementary Figure S3D



Supplementary S5A

