Supplementary Information Inventory

Metabolic gatekeeper function of B-lymphoid transcription factors

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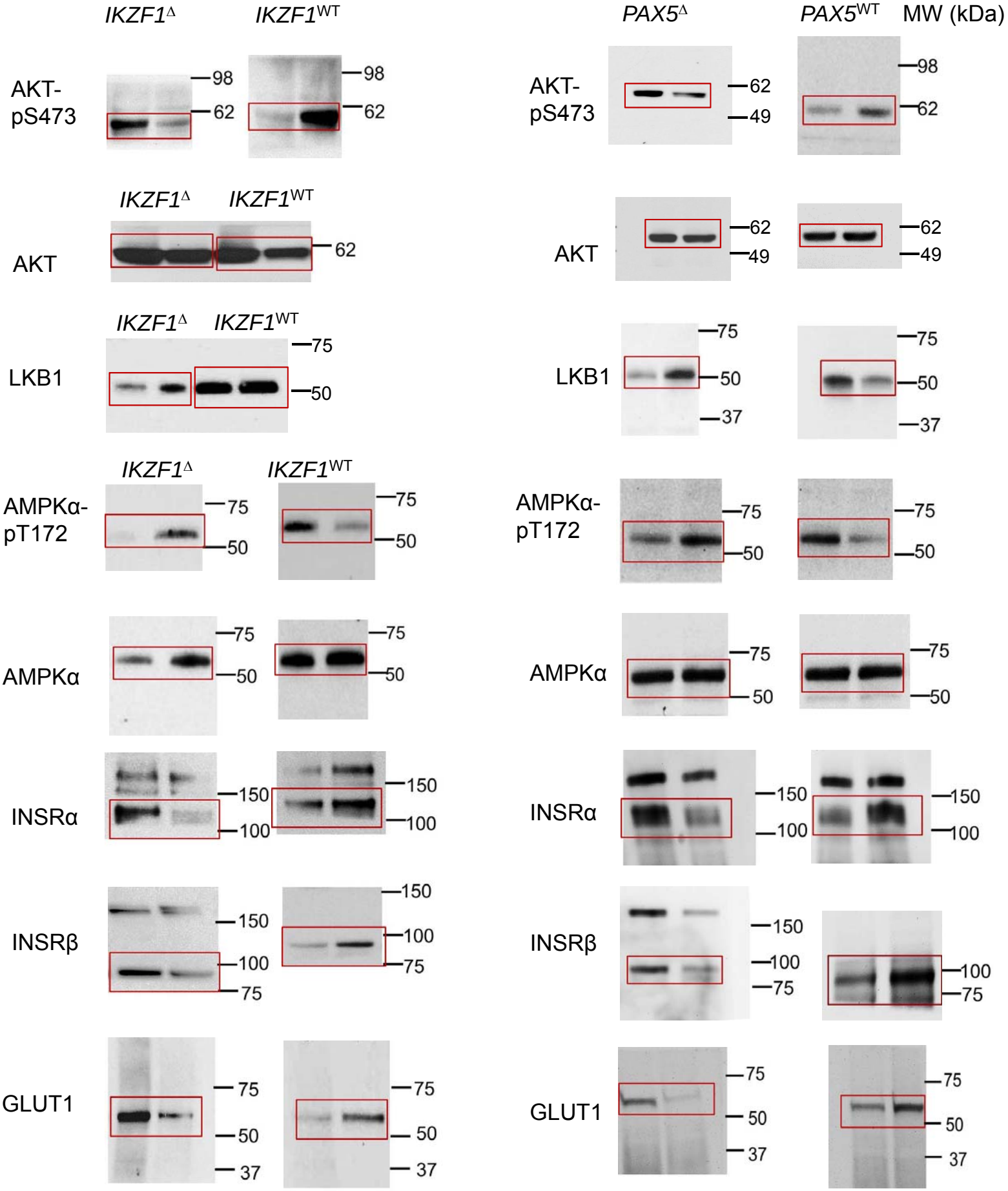
- Supplementary Figure 1 (Gel Scans)
- Supplemental Tables S1-S10

Figure 1a


IKZF1Δ
IKZF1WT
PAX5Δ
PAX5WT
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AKT-pS473
AKT
LKB1
AMPKα-pT172
AMPKα
INSRα
INSRβ
GLUT1
98
62
49
75
50
37
150
100

Figure 1a, continued

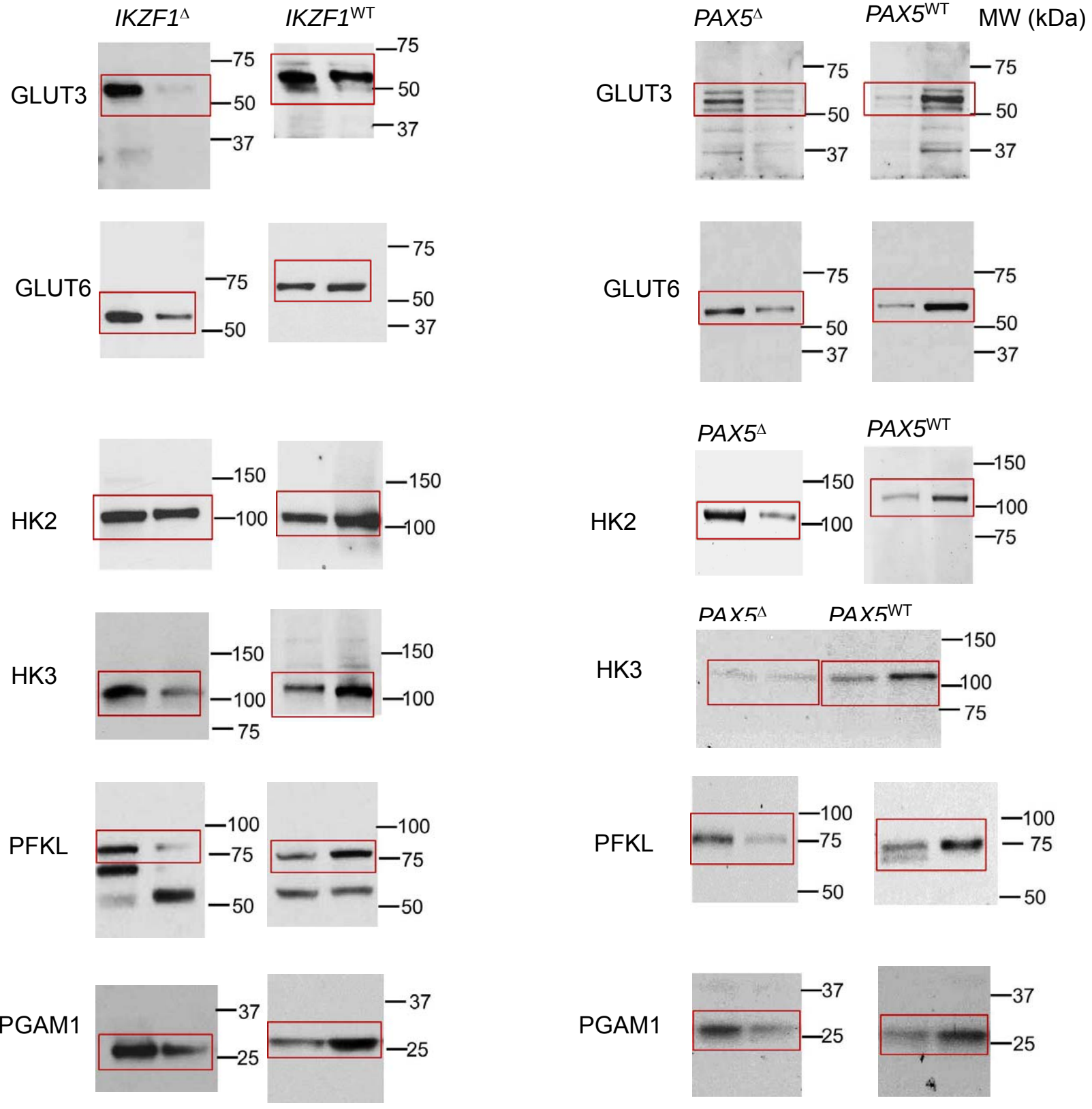


Figure 1a, continued

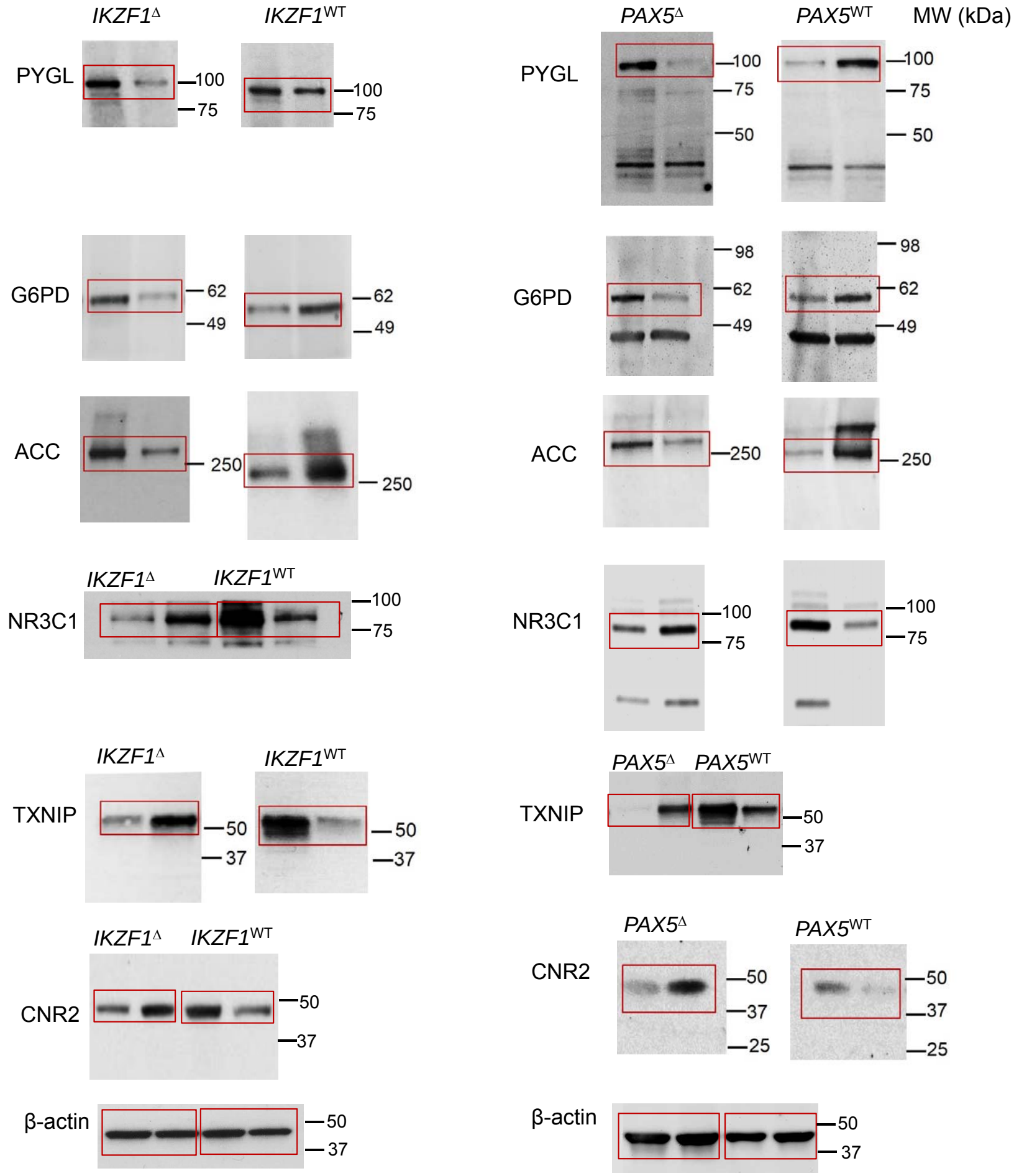
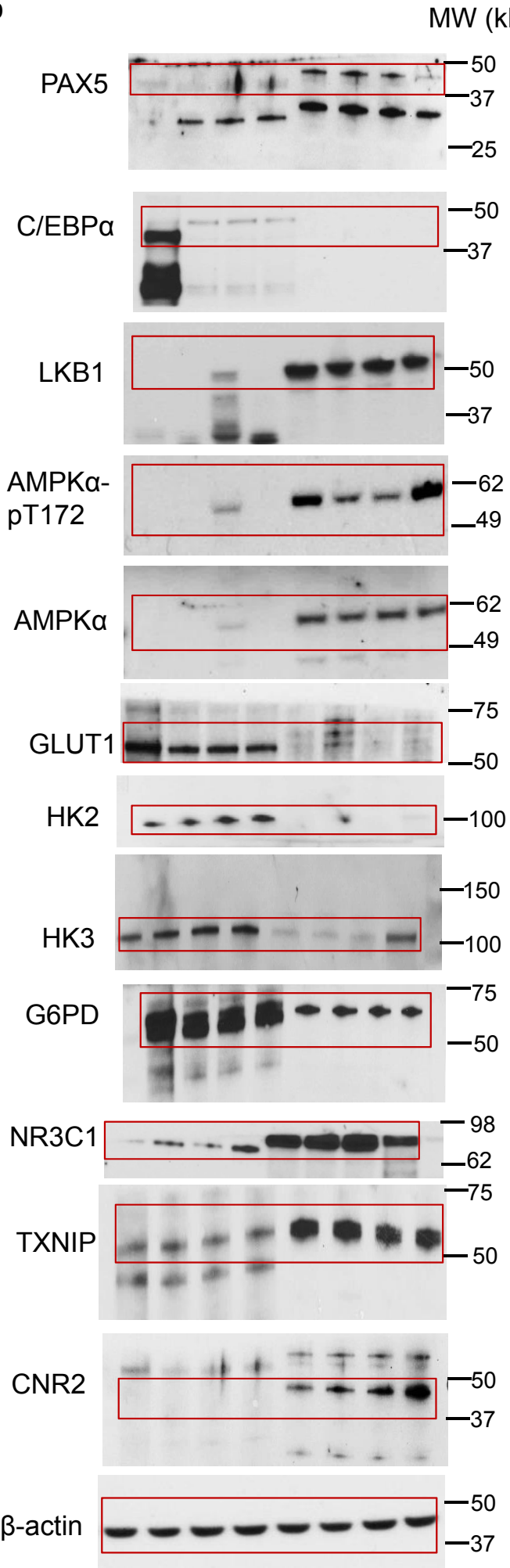


Figure 2b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PAX5
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37
25
C/EBPα
50
37
LKB1
50
37
AMPKα-
pT172
62
49
AMPKα
62
49
GLUT1
75
50
HK2
100
HK3
150
100
G6PD
75
50
NR3C1
98
62
TXNIP
75
50
CNR2
50
37
β-actin
50
37

Figure 3c

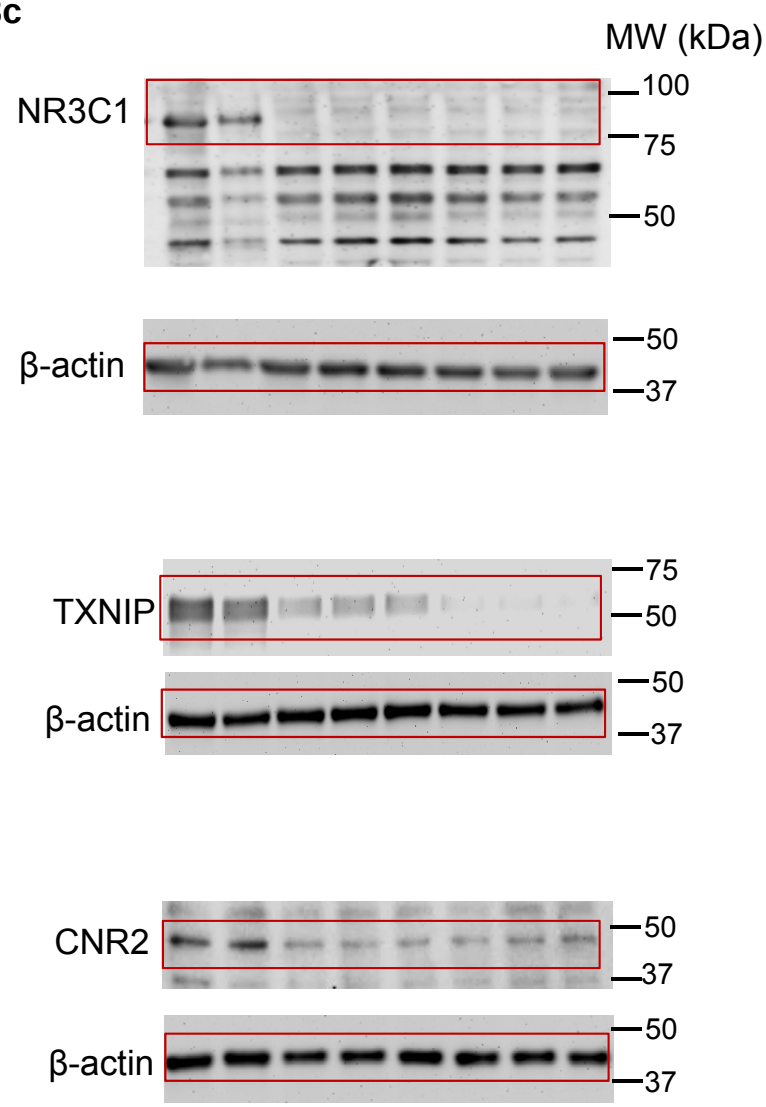
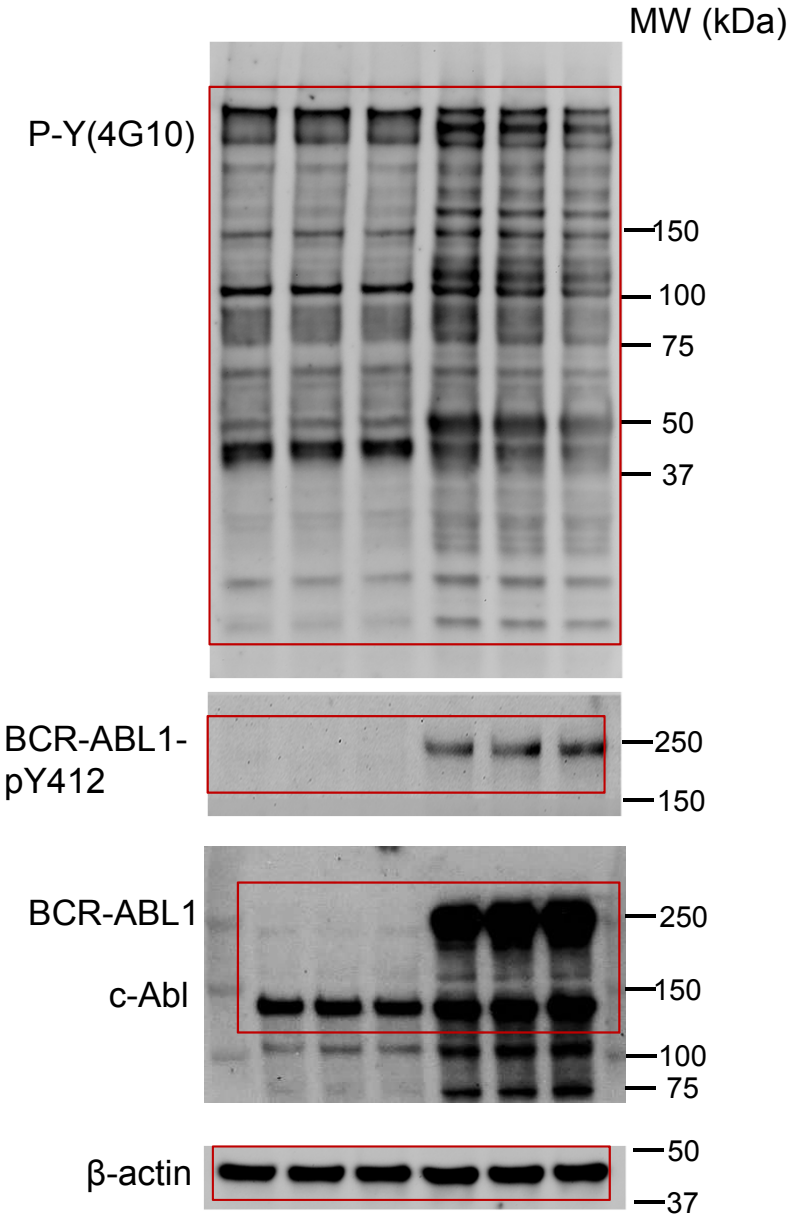
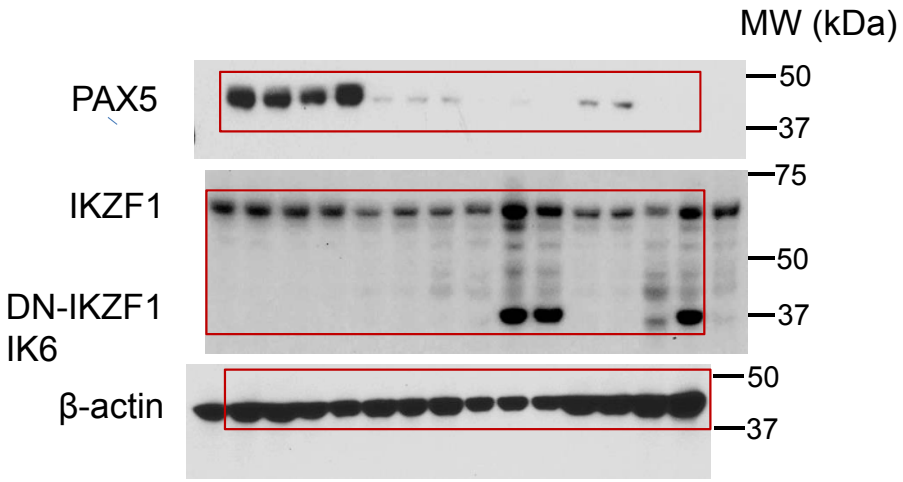

MW (kDa)
NR3C1
100
75
50
β-actin
50
37
TXNIP
75
50
β-actin
50
37
CNR2
50
37
β-actin
50
37

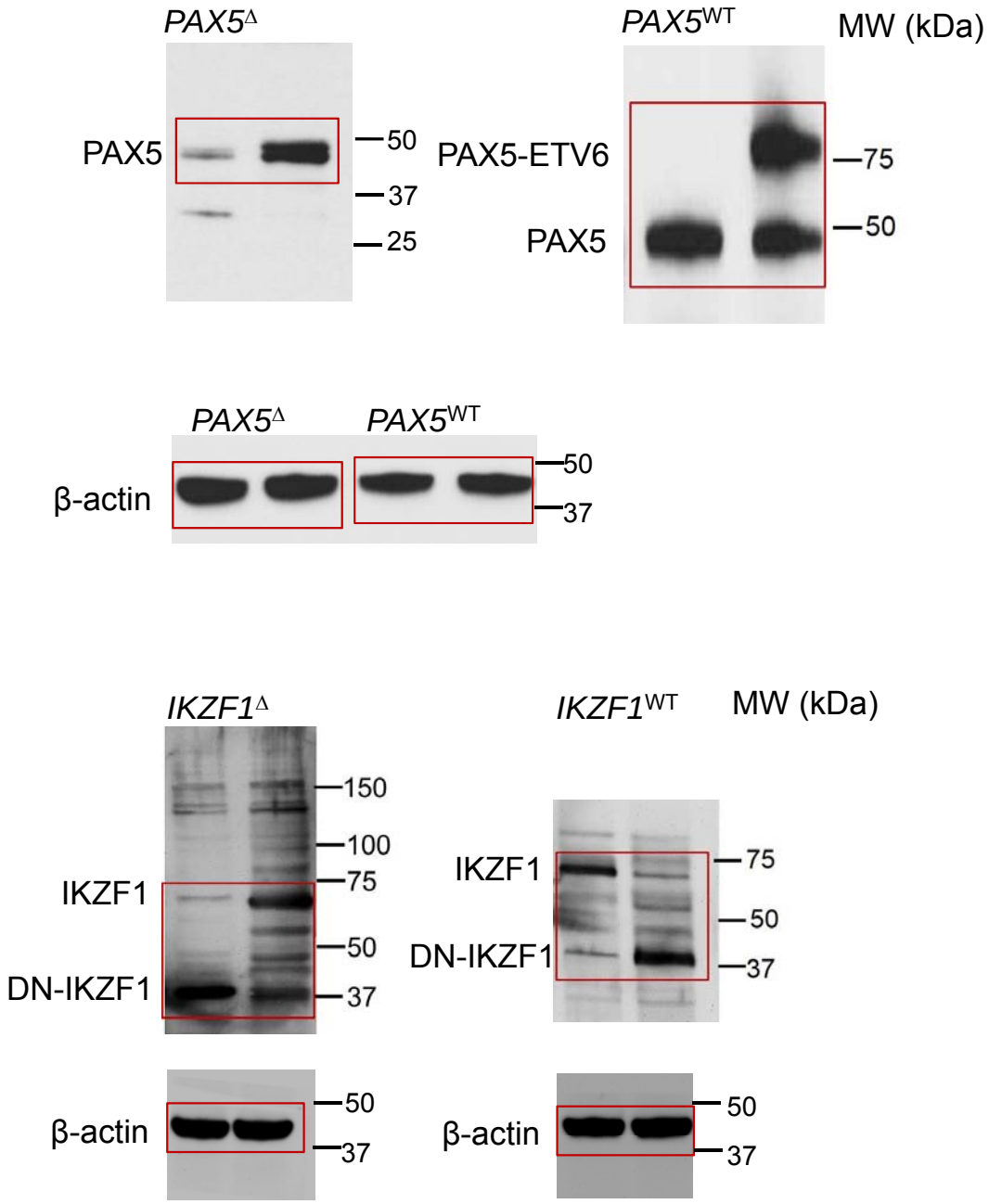
Figure 4c.


MW (kDa)
P-Y(4G10)
150
100
75
50
37
BCR-ABL1-
pY412
250
150
BCR-ABL1
c-Abl
250
150
100
75
β-actin
50
37

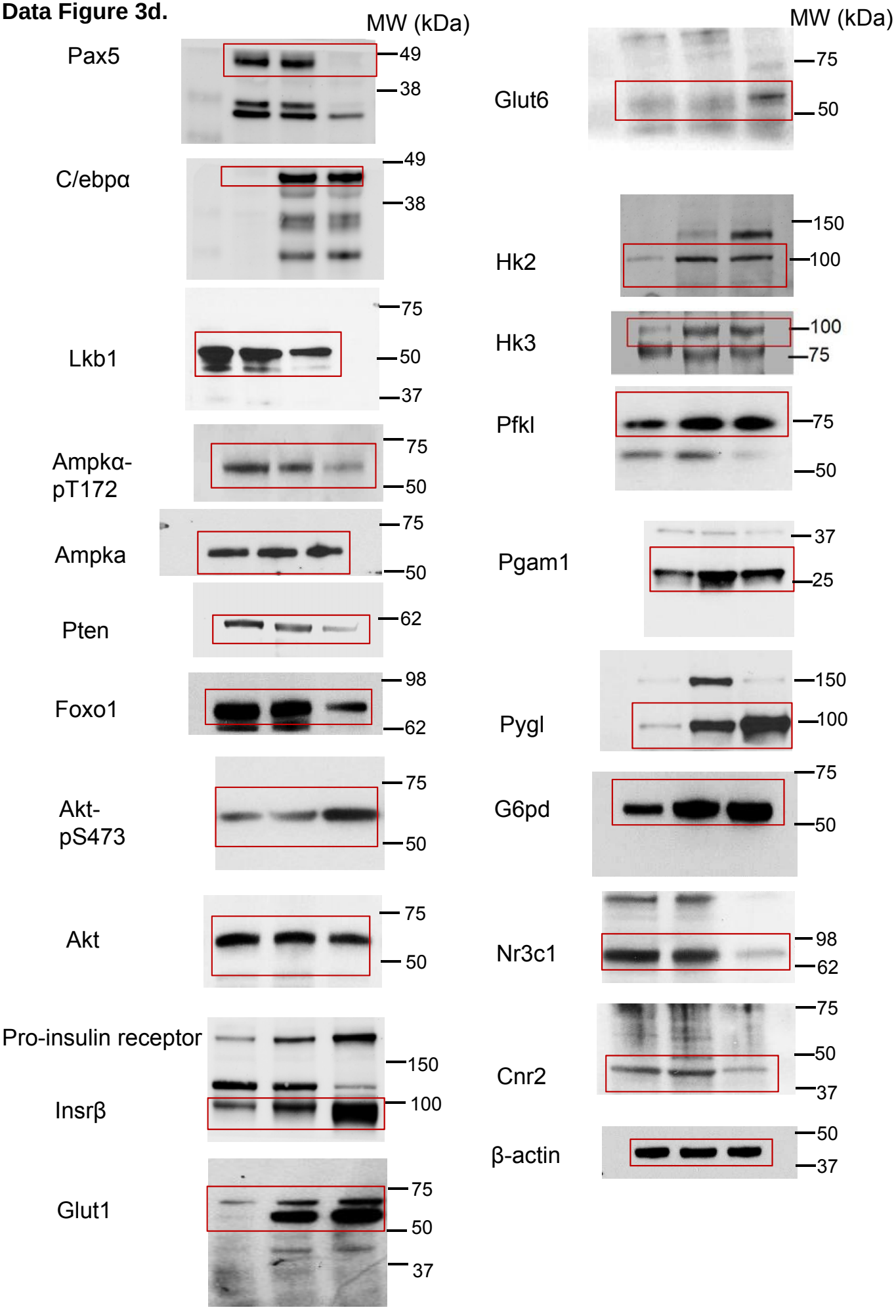
Extended Data Figure 1c



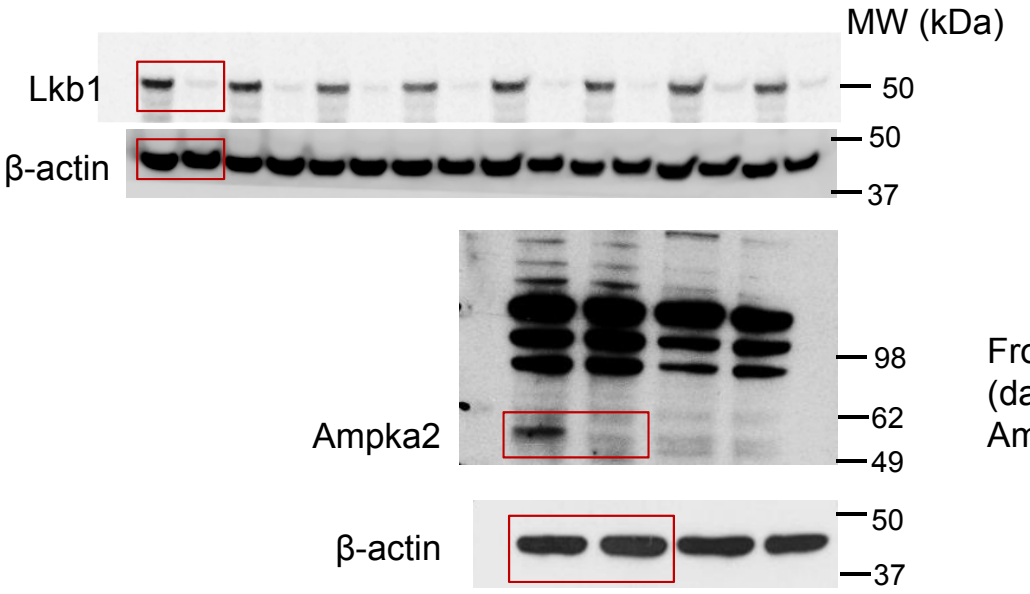
Extended Data Figure 2a



Extended Data Figure 3d.



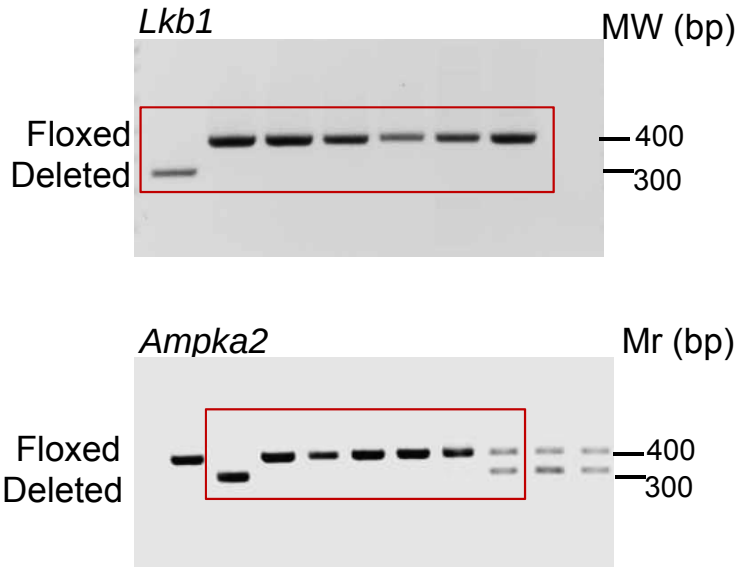
Extended Data Figure 4b.



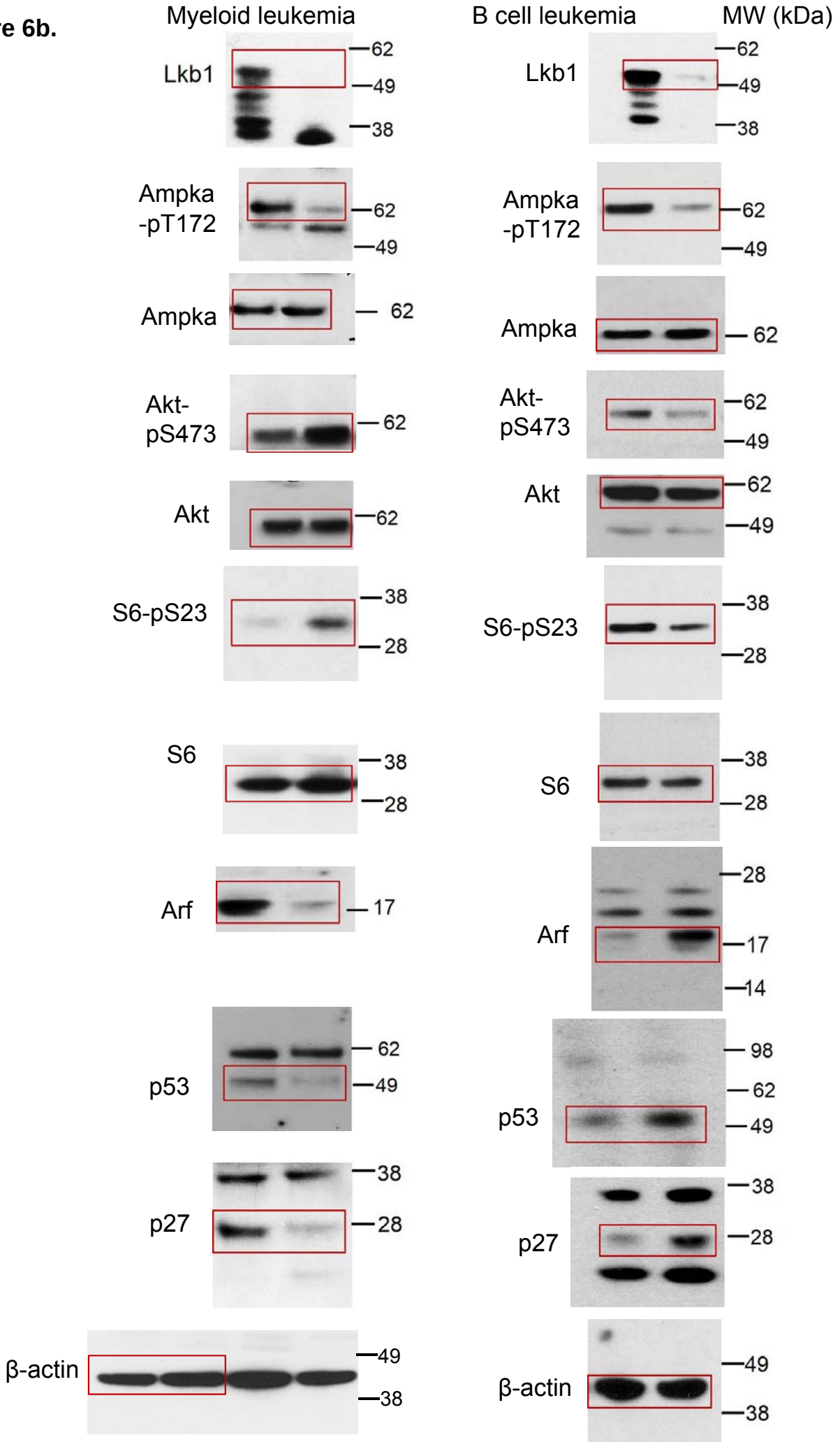
Protein levels of Lkb1 following 4OHT induction at different time points (EV vs. Cre)

From left to right: EV, Cre (day 2, day 3, day 4); Ampka2 levels

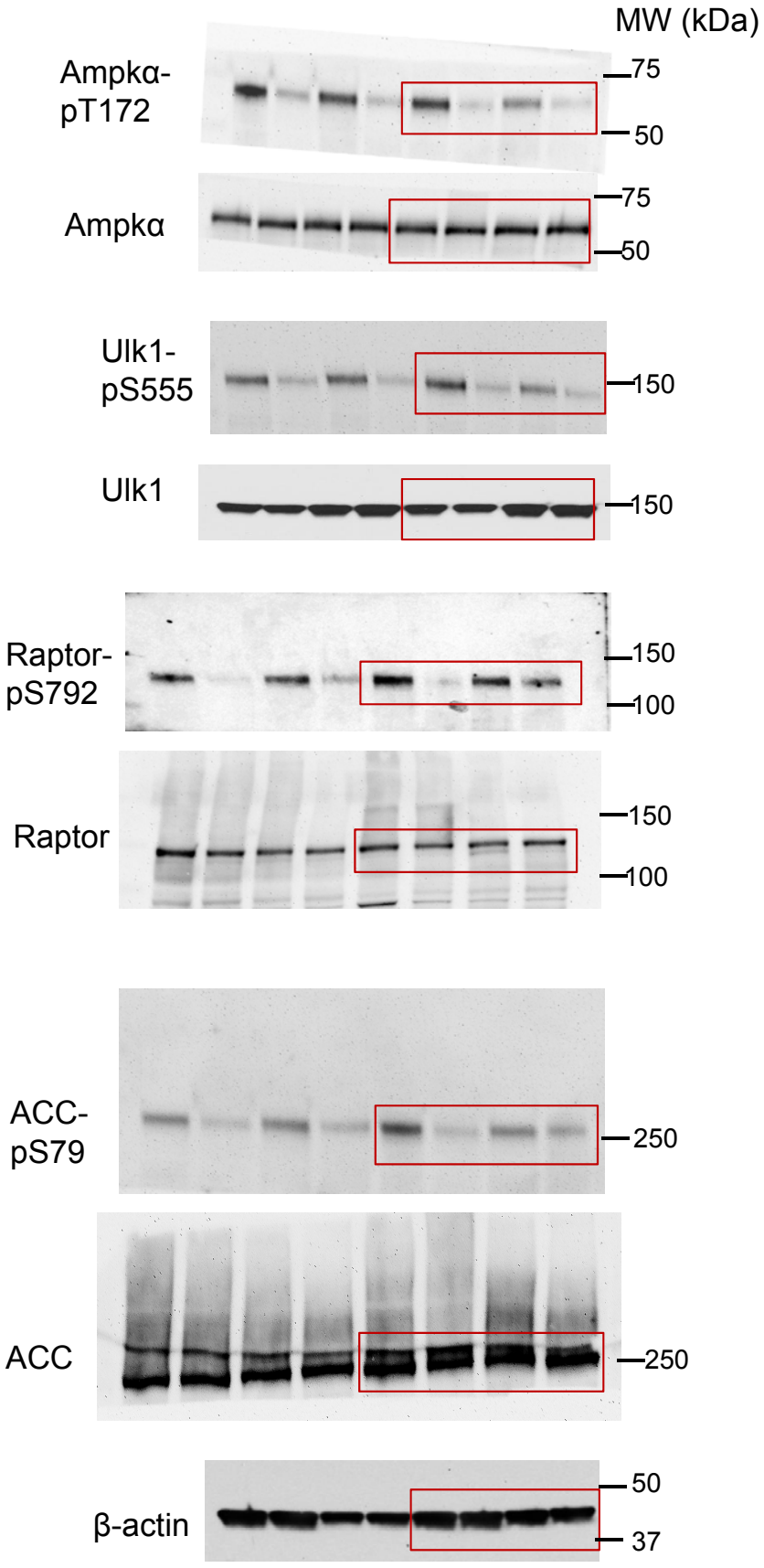
Extended Data Figure 4i.



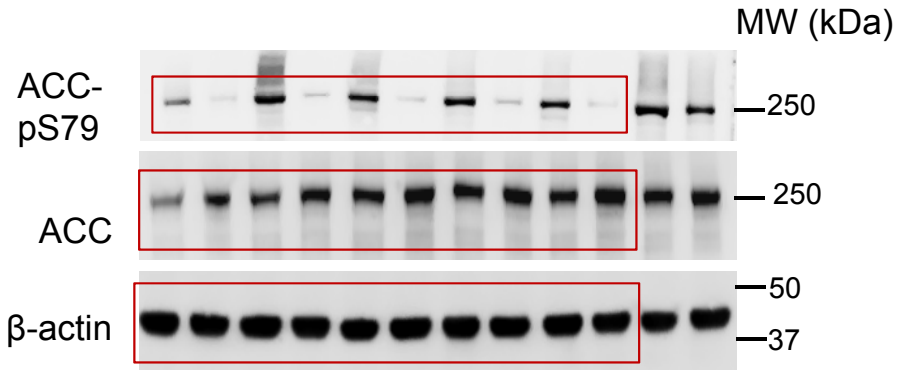
Extended Data Figure 6b.



Extended Data Figure 7d.



Extended Data Figure 8c.



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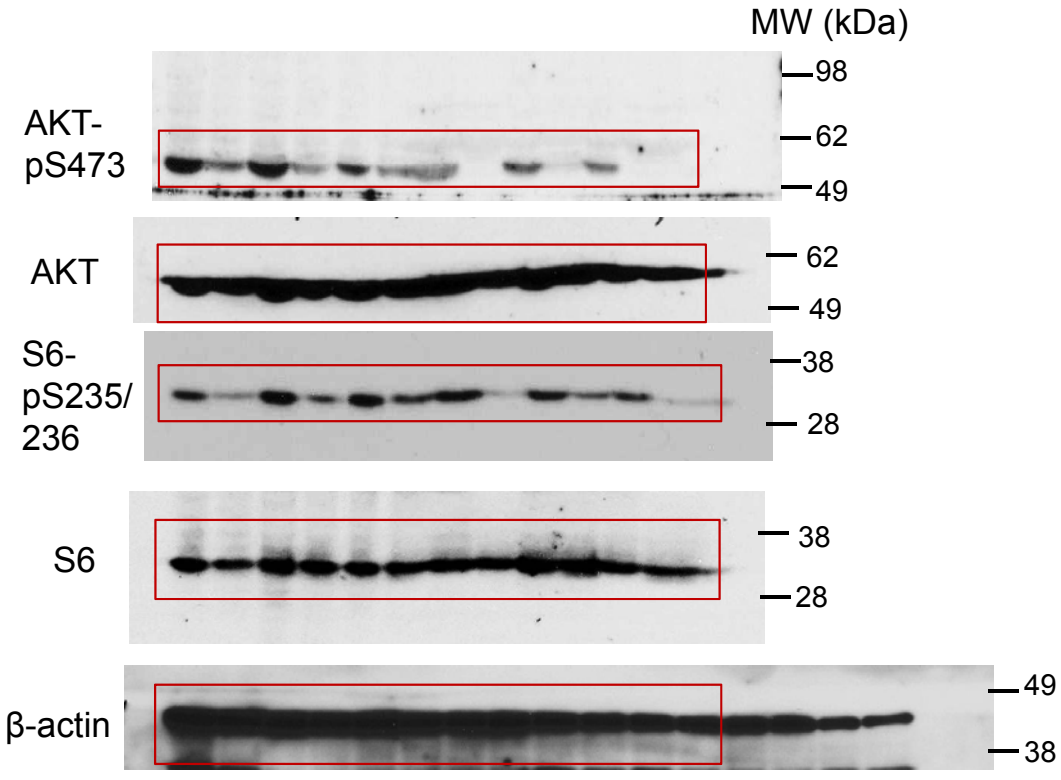
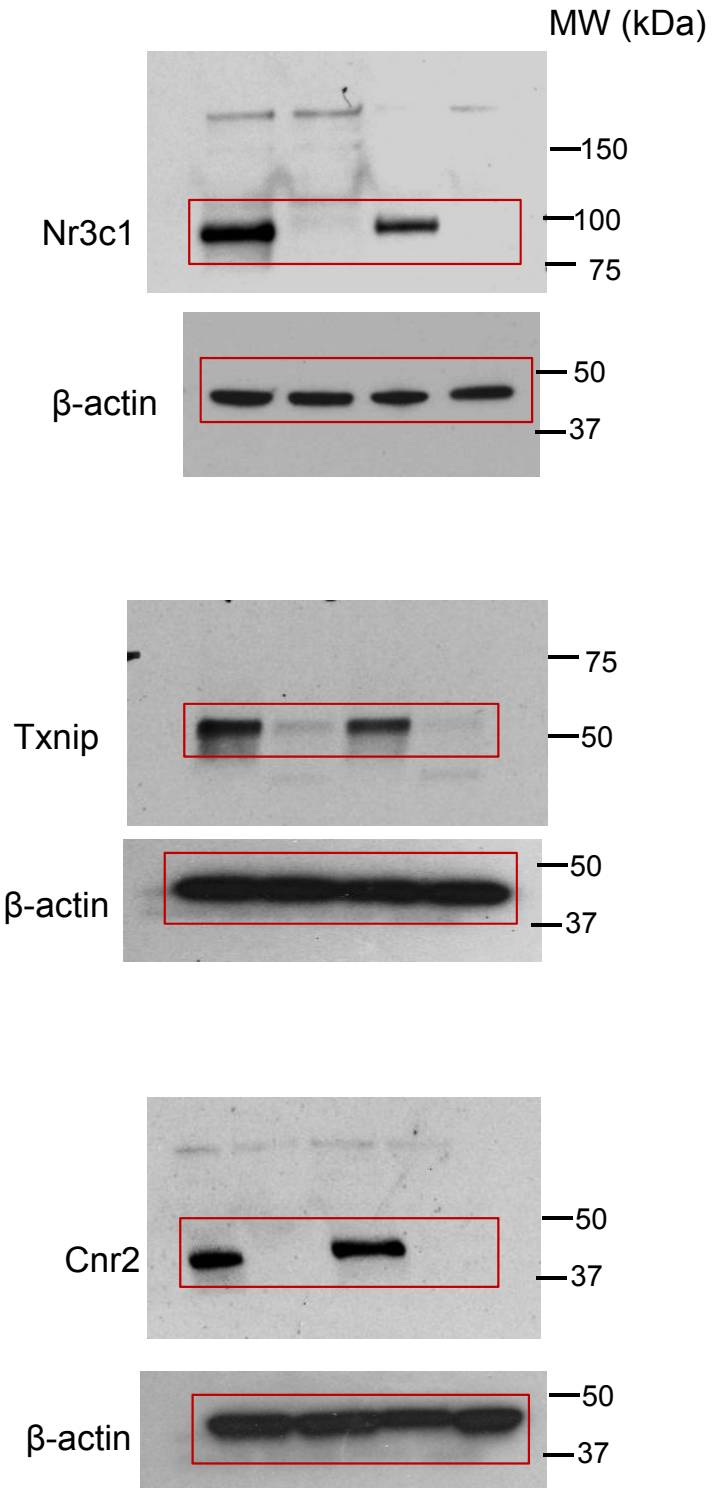


Extended Data Figure 9d.



SUPPLEMENTARY TABLES

Table S1: *Combination index values obtained from combination drug treatments in patient-derived samples*

		Combination Index (CI) values at			
pre-B ALL cases	**Drug Combination**	**ED_{50}**	**ED_{75}**	**ED_{90}**	**Average CI**
PDX2	BML275+Prednisolone	0.501	0.251	0.125	0.292
LAX7	BML275+Prednisolone	0.169	0.405	0.971	0.515
MXP4	BML275+Prednisolone	0.178	0.166	0.180	0.175
LAX9	BML275+Prednisolone	0.866	0.127	0.128	0.374
MXP2	BML275+Prednisolone	0.0915	0.0313	0.0146	0.0458
PDX2	BML275+Dex	0.572	0.382	0.346	0.433
LAX7	BML275+Dex	0.351	0.401	0.458	0.403
MXP4	BML275+Dex	0.264	0.407	0.806	0.492
LAX9	BML275+Dex	0.0231	0.0179	0.0202	0.0204
MXP2	BML275+Dex	0.362	0.470	0.620	0.484
PDX2	HU308+Prednisolone	0.597	0.677	0.669	0.648
LAX7	HU308+Prednisolone	0.475	0.643	0.946	0.688
MXP2	HU308+Prednisolone	0.732	0.779	0.863	0.791
PDX2	D-allose+Prednisolone	0.520	0.504	0.490	0.505
LAX7	D-allose+Prednisolone	0.483	0.530	0.609	0.541
MXP2	D-allose+Prednisolone	0.578	0.523	0.492	0.531
PDX2	3-O-MG+Prednisolone	0.407	0.423	0.454	0.428
LAX7	3-O-MG+Prednisolone	0.385	0.267	0.190	0.281
MXP2	3-O-MG+Prednisolone	0.739	0.844	0.971	0.851

Notes: Patient-derived pre-B ALL cells were treated with the indicated drug combination for 72 hr. Relative viability was measured by CCK-8 assays. Combination index (CI) values were calculated using the CalcuSyn software.

Table S2: *Overview of patient-derived pre-B ALL samples studied*

Case	Cytogenetics	Oncogene	Clinical course	Gener/Age
LAX2	t(9;22)(q34;q11)	*BCR-ABL1;* p210, T315I	Relapse (Imatinib)	m/38
BLQ5	FISH der(9),der(22)	*BCR-ABL1;* p190, T315I	Relapse (Imatinib)	f
LAX9	t(9;22)(q34;q11)	*BCR-ABL1;* p190	at diagnosis	m
ICN1	t(9;22)(q34;q11)	*BCR-ABL1;* p210	at diagnosis	
PDX2	der(9)(q10)t(9;22)(q34;q11)	*BCR-ABL1*	at diagnosis	f/52
MXP2	t(9;22)(q34;q11)	*BCR-ABL1*; p190; *PAX5* deletion	at diagnosis	6
MXP4	t(9;22)(q34;q11)	*BCR-ABL1;* p210*; PAX5* deletion	at diagnosis	14
MXP9		*PAX5* deletion (exons 2-6)	at diagnosis	f/2
MXP5	t(9;22)(q34;q11)	*BCR-ABL1*; p190; *PAX5* deletion (exons 2-6)	at diagnosis	m/5
LAX7			at diagnosis	m
LAX7R		$KRAS^{G12V}$	Relapse	m
BLQ1	FISH der(9), der(22)	*BCR-ABL1;* p210, T315I	Relapse (Imatinib	
BLQ11	FISH der(9), der(22)	*BCR-ABL1;* p210, T315I	Relapse (Imatinib	m
PDX59	46,XY, t(9;22)(q34;q11.2)	*BCR-ABL1*		m/6

Notes: All primary samples are bone marrow biopsies, blast content >80%; LAX, Los Angeles; BLQ, Bologna; TXL, Berlin; ICN, Seoul; PDX, Portland; MXP, Milan; f, female; m, male. All cells were mycoplasma-free.

Cell line	Type	Genetic lesion
MHH-PREB-1	Burkitt lymphoma	t(8;14) *MYC-IGH* alteration, hyperdiploidy
L1236	Hodgkin's lymphoma	Hypotriploid karyotype with 17% polyploidy; *BCL6* mutation
KM-H2	Hodgkin's lymphoma	Amplifications*: CCND2*, *FGFR3/MMSET*, *JAK2*; *BCL6* mutation
JEKO-1	Mantle cell lymphoma	*MYC* amplication, *P16INK4A* deletion

Notes: All cells were mycoplasma-free.

Table S3: *Overview of patient-derived chronic myeloid leukemia cases studied*

Patient	Age at Dx	Phase	BCR-ABL1 Transcript	Cytogenetics	BCR-ABL1% (IS) at Dx	Prior therapy
CML1	55 (CP)	Newly diagnosed			250	None
CML2	29 (CP)	Newly diagnosed			170	None
CML3	60 (CP)	Newly diagnosed	b2a2			None
CML4	21 (CP)	Newly diagnosed			51	None
CML5	63 (CP)	Newly diagnosed	b3a2	46,XY,t(9;22)(q34;q11),inv(1)(p13q21)		None
CML6	57 (CP)	Newly diagnosed	b2a2			None
CML7	59 (CP)	Newly diagnosed	b2a2	46,XY,t(9;22)(q34;q11)		None
CML8	42 (CP)	After TKI	b3a2			Nilotinib
CML10	37 (CP)	After TKI	b3a2			Nilotinib

Notes: CP, chronic phase; Dx, diagnosis; IS, Minimal residual disease quantitative PCR results. All cells were mycoplasma-free.

Table S4: *Overview of genetic mouse models studied*

Mouse strain	Investigator	Purpose
[a] *Stk11(Lkb1)*$^{fl/fl}$	Sean Morrison, Dallas, TX	Genetic loss-of-function experiments
[b] *Prkaa2 (AMPKα2)*$^{fl/fl}$	Sean Morrison, Dallas, TX	Genetic loss-of-function experiments
[c] *Nr3c1*$^{fl/fl}$	Jonathan D. Ashwell, NCI	Genetic loss-of-function experiments
[d] *Txnip*$^{fl/fl}$	Richard T. Lee, Boston, MA	Genetic loss-of-function experiments
[e] *Cnr2 (Cb2)* KO	Deltagen, Inc	Genetic loss-of-function experiments
[f] Vav-tTA x Tet^{off}-sh*Pax5*	Ross A. Dickins, Melbourne, AU	Tet^{OFF}-sh*Pax5* transgenic mouse model
NOD/SCID	Jackson Laboratories	Transplant recipient mice
NSG	Jackson Laboratories	Transplant recipient mice
[g] *Bcr*$^{+/LSL\text{-}BCR/ABL}$	Theodora S. Ross, Dallas, TX	Metabolite priming experiments
[h] *Mb1*-Cre	Michael Reth, Freiburg, Germany	Genetic loss-of-function experiments
[i] *Cd21*-Cre	Klaus Rajewsky, Berlin, Germany	Genetic loss-of-function experiments

References:

a. Nakada, D., Saunders, T.L., and Morrison, S.J. (2010) Lkb1 regulates cell cycle and energy metabolism in haematopoietic stem cells. *Nature 468*, 653-658.

b. Saito, Y., Chapple, R.H., Lin, A., Kitano, A., and Nakada, D. (2015) AMPK protects leukemia-initiating cells in myeloid leukemias from metabolic stress in the bone marrow. *Cell Stem Cell* 17, 585-596.

c. Mittelstadt, P.R., Monteiro, J.P., and Ashwell, J.D. (2012) Thymocyte responsiveness to endogenous glucocorticoids is required for immunological fitness. *J Clin. Invest*. *122*, 2384-2394.

d. Yoshioka, J., Imahashi, K., Gabel, S.A., Chutkow, W.A., Burds, A.A., Gannon, J., Schulze, P.C., MacGillivray, C., London, R.E., Murphy, E., and Lee, R.T. (2007) Targeted deletion of thioredoxin-interacting protein regulates cardiac dysfunction in response to pressure overload. *Circ. Res*. *101*, 1328-1338.

e. Pereira, J.P., An, J., Xu, Y., Huang, Y., and Cyster, J.S. (2009) Cannabinoid receptor 2 mediates the retention of immature B cells in bone marrow sinusoids. *Nat. Immunol*. *10*, 403-411.

f. Liu GJ, Cimmino L, Jude JG, Hu Y, Witkowski MT, McKenzie MD, Kartal-Kaess M, Best SA, Tuohey L, Liao Y, Shi W, Farrar MA, Nutt SL, Smyth GK, Zuber J, Dickins RA. (2014) Pax5 loss imposes a reversible differentiation block in B-progenitor acute lymphoblastic leukemia. *Genes Dev. 28*, 1337-1350.

g. Foley, S.B., Hildenbrand, Z.L., Soyombo, A.A., Magee, J.A., Wu, Y., Oravecz-Wilson, K.I., and Ross. T.S. (2013) Expression of BCR/ABL p210 from a knockin allele enhances bone marrow engraftment without inducing neoplasia. *Cell Rep*. 17, 51-60.

h. Hobeika, E., Thiemann, S., Storch, B., Jumaa, H., Nielsen, P.J., Pelanda, R., and Reth, M. (2006). Testing gene function early in the B cell lineage in mb1-cre mice. *Proc. Natl. Acad. Sci. U.S.A. 103,* 13789-13794.

i. Kraus M., Alimzhanov, M.B., Rajewsky, N., and Rajewsky, K. (2004). Survival of resting mature B lymphocytes depends on BCR signaling via the Igalpha/beta heterodimer. *Cell 117*, 787-800.

Table S5: *Retroviral vector and lentiviral vector systems used*

Construct	Overexpression of	Purpose
Constitutive expression		
MSCV BCR-ABL1 (p210)-Neo	BCR-ABL1	Leukemic transformation (*Ph*$^+$ ALL, CML)
pQCXI-LUC-BLAST (retroviral)	Firefly-Luciferase	Luciferase bioimaging
pMIG	GFP	Empty vector control
pMIG-Cre-GFP	Cre; GFP	Cre-mediated deletion of target genes
[a]pCLIP-hCMV-gRNA-RFP	gRNA for target gene; RFP	CRISPR/Cas9-mediated deletion of target gene
[a]pCLIP-hCMV-Cas9-Nuclease-Blast	Cas9 nuclease	CRISPR/Cas9-mediated deletion of target gene
pCL6-hCMV-dCas9-VPR-Blast	dCas9-VPR	CRISPR/dCas9-mediated transcriptional activation
pCL6-hCMV-gRNA-dsRed	RNA for target gene; dsRed	CRISPR/dCas9-mediated transcriptional activation
Inducible expression		
MSCV - ER^{T2}-IRES-Puro	Puromycin resistance	Empty vector control
MSCV - ER^{T2}-IRES-GFP	GFP	Empty vector control
pRetroX-Tet3G	Tet-On	Regulator vector
MSCV - Cre-ER^{T2}-IRES-Puro	Cre; Puromycin resistance	Inducible activation of Cre
MSCV - Cre-ER^{T2}-IRES-GFP	Cre; GFP	Inducible activation of Cre
pRetroX-TRE3G-Puro	Tet-On	Empty vector control
pRetroX-TRE3G-C/EBPα-Puro	Tet-On; *Cebpa*	Inducible expression of C/EBPα
pRetroX-TRE3G-PAX5-Puro	Tet-On; *PAX5*	Inducible expression of PAX5
pCL6-ER^{T2}-IRES-GFP	GFP	Empty vector control
pCL6-PAX5-ER^{T2}-IRES-GFP	PAX5; GFP	Inducible activation of PAX5
pCL6-PAX5-ETV6-ER^{T2}-IRES-GFP	PAX5-ETV6; GFP	Inducible activation of PAX5-ETV6
pLVX-EF1a-Tet3G	Tet-On	Regulator vector
pLVX-TRE3G-GFP	Tet-On	Empty vector control
pLVX-TRE3G-IKZF1-GFP	Tet-On; IKZF1	Inducible expression of IKZF1 and GFP
pLVX-TRE3G-IK6-GFP	Tet-On; IK6	Inducible expression of IK6 and GFP

Notes: a. Vectors were purchased from Transomic Technologies Inc.

Table S6: *gRNA sequences for CRISPR-mediated gene editing*

gRNA sequences for CRISPR/Cas9-mediated deletion

TXNIP:
g-08:GCATGTTCATTCCTGATGGG g-50:CCTTTGAAGGATGTTCCCAG g-92:TTACTCGTGTCAAAGCCGTT
NR3C1:
g-11:CTTTAAGTCTGTTTCCCCCG g-53:TTAGTGTCCGGTAAAATGAG g-95:GTCATTCCACCAATTCCCGT
CNR2:
g-37:GCAGAGGTATCGGTCAATGG g-79:GAGCACAGCCACGTTCTCCA g-21:GCTAAGTGCCCTGGAGAACG
Non-targeting (NT):
GGAGCGCACCATCTTCTTCA

Table S6, continued: *gRNA sequences for CRISPR/dCas9-mediated activation*

GLUT1:
AGTGCACCGAAGTCACCCAG TAGTAACAGTACCACCTCGT TTAGAACAGCGTCTACTGCA
GLUT3:
TGTCTGTGGGGCGGGGGCGG ATTAGAAGAGGGAAGGAGTA GTGGAGAGAGTGGAAGGATG
GLUT6:
GGATGCGGACCCGGCTTCCC TCCCAGGGCGGAGCCCCTGC TCTTGGGGCGTGACCTTCGG
INSR:
CGCCAGCTACAAATACTGAG GGCCCCGAGATCCTGGGACG GGTCGGGGCCACCACCGCAA
HK2:
ACTTCAGCGTCCCAAATAGC TGGGAGGACTGCTTGAGCCC TTGAGGACGTGCATTTAGAA
HK3:
ACTCTTAGGGCAGGCTTGGA ATTAGCTGATGTTTGGTAAG GCAAGATGATTACCGCGAAG
PFKL:
CCTCGAGACCACCGGGGTGG GGGGGGGGTCTCACTGCTCA TAAACCTGTGCAATGTCACG
PGAM1:
AGCGCGCCCCCTCCTGTCGG CAGAGCGAGTGGAAAGATTT TGCGCTGCATCCTGGCGCTG
FBP1:
TTCCGTTTTATGATTTTGG CTCCACCCGCACTGTGGAG CCTCCACCCGCACTGTGGAG
PYGL:
CTCTGGGGCCGCAGTGGGCT GGCGAGACCCCTGCCAGCCC GGGAGACGAGGTCCAAGCGC
G6PD:
ACCCGTGCCCGCCGGAATTG GGCGGGGAAACCGGACAGTA GGGGATTCGGGAGCACTACG
INSRR:
CACTGTCAGCTGGCGCTGGG CCGCGCGCCCGGAGGGATCC CTCCGCAGGGAGAGTCTCCC
IGF2BP2:
ACTCGGCGCGGCTGCCTCCT CTCCGCCTCTGCCCCCGGGC GGGCAGAGTCCCGGGCCGGG
ACC (NM_198836):
CTCCATGAGGTGACTACGTC GCGCGGGCCCGAGGGCTCAG TGAACGGCCTGGAGTAACCC
ACC (NM_198837):
ATACCAATTATCAGACTGCA CCAGAGGGAGGAGCACAGCT GTGGGGAAAAGCAGGTCAGG
ACC (NM_198839):
CGGAGCGCGAGCCCCTCTAG GGTGAGGCGCCAGGCAGCGC TGGCGCGGATTAGGGGGTCT
Non-tageting:
AAGATGAAAGGAAAGGCGTT

Table S7: *Antibodies used in this study*

Mouse cells, flow cytometry

Surface antigen	Manufacturer
CD19-APC	Biolegend
CD19-FITC	BD Biosciences
CD19-PerCP-Cy5.5	Biolegend
CD19-PE	Biolegend
B220-PE	BD Biosciences
B220-PEcy7	Biolegend
B220-AF700	Biolegend
CD13-PE	BD Biosciences
CD43-APC	Biolegend
c-Kit-FITC	BD Biosciences
CD11b (Mac1)-PE	BD Biosciences
CD127 (IL-7Ra)-PE	eBioscience
CD2-PE	Biolegend
Sca-1-PE	BD Biosciences
Sca-1-FITC	BD Biosciences
IgM-PerCP-Cy5.5	Biolegend
IgD-APCcy7	Biolegend
Ig κ light chain-PE	BC Biosciences
TruStain fcX Fc block	Biolegend

Human cells, flow cytometry

Surface antigen	Manufacturer
CD19-PerCP-Cy5.5	Biolegend
CD22-PE	BD Biosciences
CD33-PE	BD Biosciences
CD11b (Mac1)-PE	Biolegend
CD10-PE	BD Biosciences
TruStain fcX Fc block	Biolegend

Table S7, continued *Antibodies used for Western blots*

Antigen	Clone	Manufacturer
β-actin	Monoclonal (sc-47778)	Santa Cruz Biotechnology
LKB1	Monoclonal (3047)	Cell Signaling Technology
p-LKB1-S^{428}	Monoclonal (3482)	Cell Signaling Technology
AMPKα	Polyclonal (2532)	Cell Signaling Technology
AMPKα2	Polyclonal (2757)	Cell Signaling Technology
p-AMPKα (T^{172})	Monoclonal (2535)	Cell Signaling Technology
ACC	Monoclonal (3676)	Cell Signaling Technology
p-ACC (S^{79})	Monoclonal (11818)	Cell Signaling Technology
S6	Monoclonal (2217)	Cell Signaling Technology
p-S6 (S235/236)	Monoclonal (4856)	Cell Signaling Technology
p70 S6 kinase	Polyclonal (9202)	Cell Signaling Technology
p-p70 S6 kinase (T389)	Polyclonal (9205)	Cell Signaling Technology
p27	Polyclonal (sc-528)	Santa Cruz Biotechnology

p53	Monoclonal (2524)	Cell Signaling Technology
p19ARF (mouse)	Polyclonal (ab80)	Abcam
PTEN	Monoclonal (sc-393186)	Santa Cruz Biotechnology
Akt	Polyclonal (9272)	Cell Signaling Technology
p-Akt (S473)	Polyclonal (9271)	Cell Signaling Technology
Pax5	Monoclonal (8970)	Cell Signaling Technology
Pax5	Polyclonal (AB4227)	EMD Millipore
C/EBPα	Monoclonal (8178)	Cell Signaling Technology
Glut1	Monoclonal (12939)	Cell Signaling Technology
Glut3	Monoclonal (sc-74399)	Santa Cruz Biotechnology
Glut6 (mouse)	Polyclonal (sc-134538)	Santa Cruz Biotechnology
Glut6 (human)	Polyclonal (SAB2102200)	Sigma-Aldrich
PFKL	Polyclonal (8175)	Cell Signaling Technology
PGAM1	Monoclonal (12098)	Cell Signaling Technology
PYGL	Polyclonal (SAB1411168)	Sigma-Aldrich
PYGL	Polyclonal (15851-1-AP)	Proteintech
G6PD	Polyclonal (8866)	Cell Signaling Technology
Insulin receptor β	Monoclonal (3025)	Cell Signaling Technology
FoxO1	Monoclonal (2880)	Cell Signaling Technology
Hexokinase III (HK3)	Polyclonal (sc-28890)	Santa Cruz Biotechnology
Glucocorticoid receptor, NR3C1	Polyclonal (sc-1004)	Santa Cruz Biotechnology
TXNIP	Monoclonal (14715)	Cell Signaling Technology
CB2 (CNR2)	Polyclonal (sc-25494)	Santa Cruz Biotechnology
Insulin receptor α	Polyclonal (sc-710)	Santa Cruz Biotechnology
Hexokinase II (HK2)	Polyclonal (2867)	Cell Signaling Technology
ULK1	Monoclonal (8054)	Cell Signaling Technology
p-ULK1 (S555)	Monoclonal (5869)	Cell Signaling Technology
Raptor	Monoclonal (2280)	Cell Signaling Technology
p-Raptor (S792)	Polyclonal (2083)	Cell Signaling Technology
IKAROS (IKZF1)	Polyclonal (sc-13039)	Santa Cruz Biotechnology
Phospho-tyrosine (P-Tyr-100)	Monoclonal (9411)	Cell Signaling Technology
c-Abl (Ab-3)	Monoclonal (OP 20)	Calbiochem
p-c-Abl1 (Y412)	Monoclonal (2865)	Cell Signaling Technology

Table S7, continued *Antibodies used for single-locus quantitative ChIP*

Antigen	Clone ID	Manufacturer
Pax-5 (C-20)	Polyclonal (sc-1974)	Santa Cruz Biotechnology
Normal goat IgG	sc-2028	Santa Cruz Biotechnology

Table S8: *Sequences of oligonucleotide primers used*

PCR primers for qChIP

GLUT1 promoter:
5'-ACTCCCACTGCGACTCTGAC-3' 5'-AGGCAAGAGGTAGCAACAGC-3'

G6PD promoter:
5'-ACAGCTATGACACCGGAAGC-3' 5'-AAAGGACCACACCTGTCAGC-3'

INSR promoter:
5'-CTCGGGCCCGTAAACAAC-3' 5'-AAGCTTTCCCTCCCTCTCCT-3'

CEBPA promoter:
5'-TATAAAAGCTGGGCCGGCGC-3' 5'-TAGAGTTCTCCCGGCATGGC-3'

TXNIP promoter:
5'-CCCCTCTTTTTCTCCAAAGG-3' 5'-ACGCCGCTGGTTACACTAAG-3'

NR3C1 promoter:
5'-AGAAGCGTGTTGCAATTTCC-3' 5'- GCTTTCACCCCATTCAAAAG-3'

CNR2 promoter:
5'-CCACTCAGAGCACCTGTTGA-3' 5'-ACCTGGAGGGGAAGTGGTAA-3'

LKB1 promoter:
5'-GTCTCCGAGGACCAATGAGC-3' 5'-CTGACGATTGGAGCGTTTG-3'

CD19 promoter:
5'-ACCACCGCCTTCCTCTCTG-3' 5'-TGGCATGGTGGTCAGACTCT-3'

ACTA1 promoter:
5'-AGAGTCAGAGCAGCAGGTAG3' 5'-CAAGGCTCAATAGCTTTCTT-3'

PCR primers for genotyping

Cd21-Cre
5'-GCGGTCTGGCAGTAAAAACTATC-3' 5'-GTGAAACAGCATTGCTGTCACTT-3'

Mb1 wild-type
5'-TTCAGCCTTCAGTCTAACATC-3' 5'-ATCTGTGAAGACAGGGTGC-3'

Mb1-Cre
5'-CCCTGTGGATGCCACCTC-3' 5'-GTCCTGGCATCTGTCAGAG-3'

Lkb1$^{fl/fl}$
5'-ATCGGAATGTGATCCAGCTT-3'
5'-ACGTAGGCTGTGCAACCTCT-3'
5'-CTGTGCTGCCTAATCTGTCG-3'

Ampkα2$^{fl/fl}$
5'-GCAGGCGAATTTCTGAGTTC-3'
5'-ACCACCTGCCTAGTGCTGAC-3'
5'-ACACCCGAGAGGAAACACAC-3'

Table S9: *Summary of accession numbers for gene expression data*

GEO ID	Description	Figure
GSE32330	Gene expression from C/EBPα-induced transdifferentiation of pre-B cells into macrophages (the myeloid lineage); Data from DiTullio et al., 2011.	Extended Data Fig. 3
GSE52870	Expression profiling of Pax5 restoration in murine B-progenitor ALL by high throughput sequencing; Data from Liu et al., 2014.	Extended Data Fig. 1a
GSE38463	Expression profiling of wild-type mouse B cell precursor populations from common lymphoid progenitor through to Hardy fraction F; Data from Holmfeldt et al., 2013. Gene expression data revealed that while expression of the α1-form peaked at later stages of B cell development, expression of both Lkb1 and the α2-form of Ampk shared similar patterns and was higher in pre-B cells compared to to later stages.	Extended Data Fig. 4b (stated in legends)

Table S10: *Summary of clinical trial data used in this study*

Clinical trial	Malignancy	N=	GEO ID	Publication
COG P9906	ALL	207	GSE11877	Kang et al., 2010; Harvey et al., 2010

References:

Harvey, R.C., Mullighan, C.G., Wang, X., Dobbin, K.K., Davidson, G.S., Bedrick, E.J. et al. Identification of novel cluster groups in pediatric high-risk B-precursor acute lymphoblastic leukemia with gene expression profiling: correlation with genome-wide DNA copy number alterations, clinical characteristics, and outcome. *Blood* **116,** 4874-4884 (2010).

Kang, H., Chen, I.M., Wilson, C.S., Bedrick, E.J., Harvey, R.C., Atlas S.R., et al. Gene expression classifiers for relapse-free survival and minimal residual disease improve risk classification and outcome prediction in pediatric B-precursor acute lymphoblastic leukemia. *Blood* **115,** 1394-1405 (2010).