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Supplementary information

IFITM3 functions as a PIP3 scaffold to amplify PI3K signalling in B cells

In the format provided by the authors and unedited

Supplementary Tables

Supplementary Table S1: *List of differentially expressed surface receptors between Ifitm3$^{-/-}$ B-ALL cells and wildtype counterparts.* Biotin labeled cell surface proteins were enriched with streptavidin affinity pull-down followed by on-bead trypsin digestion. Digested peptides were analyzed on a Thermo Q-Exactive Plus Mass spectrometer and quantified with Label-Free Quantification (LFQ) values (n=3 biologically independent samples; Welch's two-sided *t*-test).

Protein	Log2 LFQ ratio	-Log10 [*P*-value]	FACS validation	Lipid raft-associated
Thy1	-9.19	4.11	Low expression	Yes
Slamf7	-8.59	3.5	Yes	Yes
Siglec10	-5.56	2.67		Yes
Slc4a8	-4.97	3.11		Yes
Plxdc1	-4.76	2.73		
Thbd	-4.56	2.82		Yes
Cd22	-4.3	1.67	Yes	Yes
Itgb1	-4.06	1.1	Yes	Yes
Slc2a3	-3.68	2	Yes	Yes
Slamf6	-3.12	2.33		Yes
Crlf2	-3.08	0.67	Yes	Yes
Sell	-3.03	2.599	Yes	Yes
Fcgr2	-2.97	2.48	Yes	Yes
Cd79b	-2.92	1.84	Yes	Yes
Cd2	-2.88	1.43	Yes	Yes
Il2ra	-2.86	1.47	Yes	Yes
Cip2a	-2.67	1.63	Yes	Yes
Cxcr4	-2.67	2.73	Yes	Yes
Itgb2	-2.63	2.35	Yes	
Cd48	-2.32	2.77	Yes	Yes
Itga6	-2.29	1.7	Yes	Yes
Cxcr5	-2.28	1.43		Yes
Cd44	-2.27	2.05	Yes	Yes
Cd79a	-2.19	2.22	Yes	Yes
Cd19	-2.16	1.38	Yes	Yes
Pecam1	-1.84	2.05	Yes	Yes
Tlr4	-1.81	1.33	Low expression	Yes
B3GNT2	-1.5	1.44		
Kcna3	-1.4	1.45		
Adam17	-1.38	1.66		
Cd72	-1.35	1.6	Yes	Yes
Ptprs	-1.31	0.92		
Sdc1	-1.27	1.69		
Tmed1	-1.2	0.82		
Cd1d1	-1.19	1.05		Yes
B4galt1	-1.18	0.99		
Clptm1l	-1.17	1.28		
Mtnd5	-1.15	1		
Tmem132e	-1.1	1.18		
Slc38a2	-1.1	1.32		Yes

Protein	Log2 LFQ ratio	-Log10 [*P*-value]	FACS validation	Lipid raft-associated
Cers2	-1.06	0.55		
Cpm	-0.99	1.84		
Unc93b1	-0.96	1.46		
Dll4	-0.92	1.36		Yes
Tgfbr2	-0.89	1.01		Yes
Slc1a5	-0.88	1.2		Yes
Kirrel1	-0.88	1.05		Yes
Sema6d	-0.86	0.67		Yes
Tmem119	-0.86	0.252		
Srprb	-0.86	0.58		
Gfra2	-0.83	0.91		Yes
Igf2r	-0.81	1.09		Yes
Atl2	-0.81	0.5		
Chst3	-0.78	0.96		Yes
Tm9sf2	-0.78	1.02		Yes
Ceacam1	-0.77	1.21	Low expression	Yes
Ifngr1	-0.71	0.99		Yes
Tmem106b	-0.7	0.39		
Cd93	-0.69	1.14	Yes	Yes
Ugt3a2	-0.69	0.34		
Tnfrsf21	-0.65	1.03		Yes
Ly9	-0.57	0.74		Yes
Il7r	-0.56	0.82	Low expression	Yes
Cd84	-0.31	0.24	Yes	Yes
Cd5	1.44	4.1	Yes	Yes
Ifitm2	2.35	0.73		Yes
Cd28	2.4	3.49	Low expression	Yes
Insr	3.98	2.966	Low expression	Yes
Nt5e	5.47	3.04	Low expression	Yes

Table S1: *List of differentially expressed surface receptors between Ifitm3$^{-/-}$ B-ALL cells and wildtype counterparts (continued)*

Supplementary Table S2: *Statistical analysis of IFITM3 mRNA levels in normal and malignant hematopoiesis.*

IFITM3 mRNA levels across human normal and malignant lymphoid samples collected from http://amazonia.transcriptome.eu/ are summarized and assessed by two-tailed *t*-test. Total values are provided as Excel file appended to this manuscript, related to **Extended Data Figure 1f.**

	Mean *IFITM3* mRNA level	***P*-value (Normal vs Malignant)**
Pre-B (n=14)	81.3	
Pre-B ALL (n=121)	617.5	7.59E-06
Naïve (n=10)	168.9	
CLL (n=124)	499.9	0.044267
MCL (n=13)	620.3	0.004678
GCB (n=10)	433	
Follicular (n=20)	1047.2	5.59E-05
Memory (n=10)	188.8	
DLBCL (n=216)	1107.3	9.62E-05
Plasma cell (n=5)	101.7	
Myeloma (n=30)	758.4	0.152484

Supplementary Table S3: *Median survival, in vivo leukemia initiation assay for BCR-ABL1 and NRAS^{G12D} B-ALL.*

To identify a potential contribution of Ifitm3 to leukemogenesis, indicated numbers of *Ifitm3*$^{+/+}$ and *Ifitm3*$^{-/-}$ *BCR-ABL1* (**Figure 2d, left;** n=5 per group) or *NRAS*^{G12D} (**Figure 2d, right,** n=7 per group) B-ALL cells were injected to sublethally irradiated NSG mice via tail vain. Mantel-Cox log-rank test was used to compare differences groups.

	BCR-ABL1					
	Ifitm3$^{+/+}$			*Ifitm3*$^{-/-}$		
Injected cell number	1×10^6	1×10^5	1×10^4	1×10^6	1×10^5	1×10^4
Median survival [Day]	14	15	22	44	>200	>200
P-value (vs *Ifitm3*$^{+/+}$)				0.0041	0.0038	0.0168

	***NRAS*^{G12D}**	
	Ifitm3$^{+/+}$	*Ifitm3*$^{-/-}$
Injected cell number	3×10^6	3×10^6
Median survival [Day]	41	>200
P-value (vs *Ifitm3*$^{+/+}$)		0.0005

Supplementary Table S4: *Statistical analysis of median survival, in vivo oncogenic priming assay with Mb1-Cre; LSL-Bcr$^{+/BCR\text{-}ABL1}$ B-cell precursors*

This LSL-*Bcr*$^{+/BCR\text{-}ABL1}$ knockin model expressing a single copy of the BCR-ABL1 from the *BCR* promoter in B-lineage does not develop leukemia. Given that BCR-ABL1 expression alone is insufficient to induce disease, we tested reconstitution of IFITM3 can overcome suppressive barrier to leukemia progression (n=7 per group). Mantel-Cox log-rank test was used to compare the difference to EV control with GraphPad Prism 7.

	EV	**IFITM3**	**IFITM3^{Y20E}**
Injected cell number	1×10^7	1×10^7	1×10^7
Median survival [Days]	undefined	224.5	196
P-value (vs EV)		0.0143	0.0012

Supplementary Table S5: *Recombinant human IFITM3 proteins for lipid binding assay, related to Figure 4*

Name	Sequence	Source
GST-IFITM3	GST-MNHTVQTFFSPVNSGQPPNYEMLKEEHEVAVLGAPHNPAPPTSTVIHIRSETSVPDHVVWSLFNTLFMNPCCLGFIAFAYSVKSRDRKMVGDVTGAQAYASTAKCLNIWALILGILMTILLIVIPVLIFQAYG	Abnova
^{1}N-term^{57}	MNHTVQTFFSPVNSGQPPNYEMLKEEHEVAVLGAPHNPAPPTSTVIHIRSETSVPDH-Biotin	Life Tein
^{58}TM1^{70}	VVWSLFNTLFMNPCC-Biotin	Life Tein
^{71}CIL^{105}	CCLGFIAFAYSVKSRDRKMVGDVTGAQAYASTAKC-Biotin	New England peptide
^{71}CIL^{87}	CCLGFIAFAYSVKSRDR-Biotin	Life Tein
^{89}CIL^{105}	MVGDVTGAQAYASTAKC-Biotin	Life Tein
^{71}R85A^{105}	CCLGFIAFAYSVKSADRKMVGDVTGAQAYASTAKC-Biotin	New England peptide
^{71}K83A/K104A^{105}	CCLGFIAFAYSVASRDRKMVGDVTGAQAYASTAAC-Biotin	New England peptide
^{71}R85A/R87A/K88A^{105}	CCLGFIAFAYSVKSADAAMVGDVTGAQAYASTAKC-Biotin	New England peptide

Supplementary Table S6: *Calculated average interaction energy of IFITM3 (residues 57-128) with PIP2 or PIP3, related to Extended Data Figure 9.*

We calculated the interaction energy of PIP2 or PIP2 to IFITM3 with MD simulation. The one residue contact (1 basic aa) indicates conformations of PIP2 or PIP3 contact with only one basic residue in the patch KSRDRK. '2 basic aa' refers to the binding conformations of PIP2 or PIP3 with two basic residues. *p*-values were determined by two-tailed *t*-test.

	Binding to	**Average Interaction energy [-kJ/mol]**	**Error [-kJ/mol]**	**# of events**
$PI(4,5)P_2$	1 basic aa	213	44	18,324
	2 basic aa	453.6	37.9	268
	3 basic aa			0
$PI(3,4,5)P_3$	1 basic aa	224.47	26 (*P*=0.848)	10,477
	2 basic aa	704	33 (*P*=0.0008)	8,875
	3 basic aa			13

Supplementary Table S7: *Overview of patient-derived B-ALL cell samples examined in this study*

Case	B-ALL	Lesion	Disease Stage	Cytogenetics/Karyotype	Gender/age
ICN1	*Ph*$^+$ ALL	*BCR-ABL1*	Diagnosis	t(9;22)(q34;q11)	
LAX2	*Ph*$^+$ ALL	*BCR-ABL1*	T315I, Relapse	t(9;22)(q34;q11)	m/38
LAX9	*Ph*$^+$ ALL	*BCR-ABL1*	Diagnosis	t(9;22)(q34;q11)	m
PDX2	*Ph*$^+$ ALL	*BCR-ABL1*	Diagnosis	t(9;22)(q34;q11)	f/52
ICN12	B-ALL	*TCF3-PBX1*	Diagnosis	t(1;19)(q23;p13)	f/8
SFO2	*Ph*$^+$ ALL	*BCR-ABL1*	Diagnosis	t(9;22)(q34;q11)	m/7

Notes: All primary samples are bone marrow biopsies, blast content >80%; ICN, Seoul, KR; LAX, Los Angeles, US; PDX, Portland, US; SFO, San Francisco, US; f, female; m, male

Supplementary Table S8: *Overview of leukemia and lymphoma cell lines used in this study*

Cell line	Malignancy	Transforming lesions	Source
BV-173	*Ph*$^+$ ALL	*BCR-ABL1; MAP3K14; IKZF1*	DSMZ
JEKO1	Mantle cell lymphoma	*IGH-CCND1; ITK; MAP2K1; TP53*	ATCC
Jurkat	T-ALL	*PTEN; LCK; CD4*	ATCC

Supplementary Table S9: *Overview of genetic mouse models used in this study*

Mouse strain	Name	Investigator	Purpose
Ifitm3^{tm1Masu}	*Ifitm3*$^{-/-}$	Dr. Michael S. Diamond	Loss-of-function experiments
NOD.Cg-*Prkdc*^{scid} *Il2rg*^{tm1Wjl}/SzJ	NSG	Leonard D. Shultz, The Jackson Laboratory	Transplant recipient mice
B6.C(Cg)-*Cd79a*$^{tm1(cre)Reth}$/EhobJ	Mb1-Cre	Dr. Michael Reth, Freiburg	Expression of Cre in B-lineage
B6.129S2-*Ighm*^{tm1Cgn}/J	μMT mice	Dr. Klaus Rajewsky, Berlin	Immunization, adoptive transfer experiments
Mb1-Cre; LSL-Bcr$^{+/BCR-ABL1}$	Mb1-Cre; BCR-ABL1	Theodora Ross, UT Southwestern, Dallas	Conditional expression of BCR-ABL1 in B-cell lineage
C;129S4-*Pten*^{tm1Hwu}/J	*Pten*$^{fl/fl}$	Dr. Hong Wu, UCLA	Inducible PI3K-activation

Supplementary Table S10: *List of antibodies used in this study*

Antibodies for Western blot

Polyclonal anti-STAT1-pY701	Cell Signaling Technology	9172
Polyclonal anti-STAT1	Cell Signaling Technology	5605
Polyclonal anti-STAT5-pY694	Cell Signaling Technology	9351
Polyclonal anti-STAT5	Cell Signaling Technology	9363
Polyclonal anti-IFITM3	Cell Signaling Technology	9037
Polyclonal anti-AKT-pS473	Cell Signaling Technology	9271
Polyclonal anti-AKT	Cell Signaling Technology	9272
Polyclonal anti-ERK-pT202/Y204	Cell Signaling Technology	4370
Polyclonal anti-ERK	Cell Signaling Technology	9102
Polyclonal (D8E8G) anti-IFITM3	Cell Signaling Technology	59212
Polyclonal (D84C12) anti-c-Myc	Cell Signaling Technology	5605
Polyclonal anti-c-Abl-pY412	Cell Signaling Technology	2865
Polyclonal anti-c-Abl	Santa Cruz Biotechnology	sc-131
Polyclonal anti-Src-pY416	Cell Signaling Technology	6943
Polyclonal anti-Lyn	Cell Signaling Technology	2796
Polyclonal anti-Syk-pY352	Cell Signaling Technology	2717
Polyclonal anti-Syk	Cell Signaling Technology	2712
Polyclonal (C-2) anti-Bcl-2	Santa Cruz Biotechnology	sc-7382
Polyclonal anti-p21 (C-19)	Santa Cruz Biotechnology	sc-397
Polyclonal anti-CD19-pY531	Cell Signaling Technology	3571
Monoclonal (D4V4B) anti-CD19	Cell Signaling Technology	90176
Polyclonal anti-VAP-A	Novus Biologicals	NBP1-31237
Monoclonal (1C12) anti-p53	Cell Signaling Technology	2524
Polyclonal anti-p19/Arf	ABCAM	ab80
Monoclonal (4G10) anti-Phosphotyrosine	EMD Millipore	05-321
Polyclonal anti-HA tag	ABCAM	ab9110
Polyclonal (D6N9Y) anti-IKZF1	Cell Signaling Technology	14859
Polyclonal anti-PIK3CD; p110δ	ABCAM	ab109006
Monoclonal (M2) anti-FLAG	Sigma-Aldrich	F1804
Polyclonal anti-eIF4E	Santa Cruz Biotechnology	sc-13963
Polyclonal anti-LYN-pY397	Cell Signaling Technology	70926
Monoclonal (108D2) anti-p70 S6K-pT389	Cell Signaling Technology	9234
Polyclonal anti-p70 S6K-pT421/S424	Cell Signaling Technology	9204
Monoclonal (49D7) anti-p70 S6 Kinase	Cell Signaling Technology	2708
Monoclonal (D30A3) anti-RICTOR-pT1135	Cell Signaling Technology	3806
Monoclonal (53A2) anti-RICTOR	Cell Signaling Technology	2114
Polyclonal anti-CXCR4-pS339	Cell Signaling Technology	59028
Polyclonal anti-CXCR4	Novus Biologicals	74396
Polyclonal anti-FAK-pY397	Cell Signaling Technology	3283
Polyclonal anti-FAK-pY575/577	Cell Signaling Technology	3281
Monoclonal (D2R2E) anti-FAK	Cell Signaling Technology	13009
Polyclonal anti-PAK1-pS199/204	Cell Signaling Technology	2605
Polyclonal anti-PAK1	Cell Signaling Technology	2602
Polyclonal anti-ITGB1-pY783	ABCAM	ab62337
Polyclonal anti-ITGB1-pT788/789	Thermo Fisher Scientific	44-872G
Polyclonal anti-ITGB1	Cell Signaling Technology	4706
Monoclonal (C4) anti-β-actin	Santa Cruz Biotechnology	sc-47778

Supplementary Table S10, continued: *Antibodies used in this study*

Antibodies for Flow Cytometry

Monoclonal (HIB19) anti-human CD19	Biolegend	302254
Monoclonal (M2) anti-FLAG	Columbia Biosciences	M2
Polyclonal anti-HA tag	Columbia Biosciences	D5-1718
Monoclonal (OKT4) anti-human CD4	Biolegend	317418
Monoclonal (UCHT1) anti-human CD3	Biolegend	555335
Monoclonal (G20-127) anti-human IgM	BD Biosciences	561285
Monoclonal (6D5) anti-mouse CD19	Biolegend	115508
Monoclonal (RA3-6B2) anti-B220 (CD45R)	Biolegend	103224
Monoclonal (HM79-12) anti-CD79b	Biolegend	132804
Monoclonal (RB6-8C5) anti-mouse Gr-1 (Ly-6GC)	Biolegend	108422
Monoclonal (PK136) anti-mouse NK-1.1	Biolegend	108730
Monoclonal (2B8) anti-CD117 (c-kit)	Biolegend	105808
Monoclonal (D7) anti-Sca-1 (Ly-6A/E)	Biolegend	108102
Monoclonal (S11) anti-mouse CD43	Biolegend	143208
Monoclonal (6C3) anti-mouse BP-1 (Ly-51)	Biolegend	108308
Monoclonal (M1/69) anti-mouse CD24	Biolegend	101822
Monoclonal (R6-60.2) anti-mouse IgM	BD Biosciences	553408
Monoclonal (11-26c.2a) anti-mouse IgD	Biolegend	405716
Monoclonal (B3B4) anti-mouse CD23	BD Biosciences	561773
Monoclonal (7E9) anti-mouse CD21/CD35	Biolegend	123412
Monoclonal (M1/70) anti-mouse Mac-1 (CD11b)	Biolegend	101206
Monoclonal (53-7.3) anti-mouse CD5	Biolegend	100612
Monoclonal (17A2) anti-mouse CD3	Biolegend	100204
Monoclonal (RM4-5) anti-mouse CD4	BD Biosciences	553051
Monoclonal (Jo2) anti-mouse CD95	BD Biosciences	562499
Monoclonal (GL7) anti-mouse GL7	Affymetrix eBioscience	13-5902-82
Monoclonal (L276F12) anti-mouse CXCR4	Biolegend	146508
Monoclonal (GL-1) anti-mouse CD86	Biolegend	105016
Monoclonal (A7R34) anti-mouse CD127 (IL-7R)	eBioscience	135012
Monoclonal (OX-7) anti-mouse Thy1 (CD90)	BD Biosciences	551401
Monoclonal (RM2-5) anti-mouse CD2	Biolegend	100108
Monoclonal (HM48-1) anti-mouse CD48	Biolegend	103415
Monoclonal (IM7) anti-mouse CD44	Biolegend	103012
Monoclonal (MEC13.3) anti-mouse Pecam1	Biolegend	102508
Monoclonal (TY/23) anti-mouse CD73 (5NTD)	BD Biosciences	550741
Monoclonal (37.51) anti-mouse CD28	BD Biosciences	553297
Monoclonal (4G2) anti-mouse CD319	Biolegend	152004
Monoclonal (OX-97) anti-mouse CD22	Biolegend	126112
Polyclonal anti-GLUT3	Alomone labs	AGT-023
Monoclonal (93) anti-mouse CD16/32	Biolegend	101314
Monoclonal (2G10) anti-CIP2A	Novus Biologicals	59722APC
Monoclonal (SA15-21) anti-mouse TLR4 (CD284)	Biolegend	145404
Polyclonal anti-KV1.3 (KCNA3)	Alomone labs	APC-101
Polyclonal anti-Insulin R/CD220	R&D Systems	FAB1544A
Monoclonal (P84) anti-mouse CD172a (SIRPα)	Biolegend	144014
Polyclonal anti-ABCG1	Invitrogen	PA5-72939

Supplementary Table S10, continued: *Antibodies used in this study*

monoclonal (EPR13130) anti-TMEM173	ABCAM	ab208874
Polyclonal anti-ORP8 (OSBPL8)	Biorbyt	orb496769
Polyclonal anti-OSBPL5	Biorbyt	orb189989
Polyclonal anti-Squalene Epoxidase	Biorbyt	orb7410
Monoclonal (22H9) anti-mouse TSLPR (TSLP-R)	Biolegend	151806
Monoclonal (MAb-CC1) anti-mouse Ceacam1 (CD66a)	Biolegend	134524
Monoclonal (AA4.1) anti-mouse CD93	Biolegend	136504
Monoclonal (L276F12) anti-mouse CD184 (CXCR4)	Biolegend	146508
Monoclonal (A7R34) anti-mouse CD127 (IL-7Rα)	Biolegend	135012
Monoclonal (PC61) anti-CD25	Biolegend	102008
Monoclonal (K10.6) anti-mouse CD72 a, b and d	BD Biosciences	550966
Monoclonal (mCD44.7) anti-mouse CD84	Biolegend	122806
Brilliant Violet 421™ Streptavidin	Biolegend	405225
Monoclonal (5H10-27(MFR5)) anti-mouse CD49e (Integrin α5)	Biolegend	103805
Monoclonal (GoH3) anti-mouse CD49f (Integrin α6)	Biolegend	313612
Monoclonal (MEL-14) anti-mouse CD62L (L-selectin)	Biolegend	104408
Monoclonal (HM β1-1) anti-mouse CD29 (Integrin β1)	Biolegend	102216
Monoclonal (37.51) anti-mouse CD28	BD Biosciences	553297
Monoclonal (SA275A11) anti-mouse CD20	Biolegend	150410
Anti Ct-B (Cholera toxin subunit B) antibody	Thermo Fisher Scientific	V34405

Antibodies for Proximity Ligation Assay

Polyclonal anti-human IgM	OriGene	AP10433PU-N
Polyclonal anti-human LAMP1	R & D Systems	IC7985G
Polyclonal (D8E8G) anti-IFITM3	Cell Signaling Technology	59212
Monoclonal (CB3-1) anti-CD79B	Thermo Fisher Scientific	14-0793-82

Antibodies for immunofluorescence, Immunization

Biotinylated Peanut Agglutinin (PNA)	Vector Laboratories	B-1075
Alexa Fluor® 647 Streptavidin	Biolegend	405237
Polyclonal (RA3-6B2) anti-B220	BD Biosciences	553089
Monoclonal (17A2) anti-mouse CD3	Biolegend	100214

Antibodies for lipid strip analysis

Polyclonal anti-GST tag	Thermo Fisher Scientific	CAB4169
Monoclonal (D5A7) anti-Biotin	Cell Signaling Technology	5597

Antibodies for cell stimulation

Polyclonal anti-HA tag	ABCAM	ab9110

Supplementary Table S10, continued: *Antibodies used in this study*

Monoclonal (1D3) purified NA/LE anti-mouse CD19	BD Biosciences	553782
Polyclonal anti-mouse IgM	Southern Biotech	1020-01
Polyclonal F(ab')$_2$ anti-human μ chain	Jackson Immunoresearch	109-006-129
Monoclonal (OKT3) purified LE/AF anti-human CD3	Biolegend	317304

Supplementary Table S11, *Overview of reagents used in this study*

Chemicals, Peptides, and Recombinant Proteins

Recombinant mouse IL-7	Peprotech	217-17
Recombinant GST-tag protein	Sigma-Aldrich	SRP5348
Recombinant human GST-IFITM3 protein	Abnova	H00010410
Recombinant human IFITM3 N-terminal protein	Life Tein	Custom peptide
Recombinant human IFITM3 TM1 protein	Life Tein	Custom peptide
Recombinant human IFITM3 ^{71}CIL^{105} protein	Life Tein	Custom peptide
Recombinant human IFITM3 ^{71}CIL^{87} protein	Life Tein	Custom peptide
Recombinant human IFITM3 ^{89}CIL^{105} protein	Life Tein	Custom peptide
Imatinib	LC Laboratories	I-5577
Dasatinib	SelleckChem	S1021
Resazurin	R & D Systems	AR002
4-Hydroxytamoxifen	Sigma-Aldrich	94873
Doxycycline	Clontech Laboratories	631311
Fixation and Permeabilization Solution	BD Biosciences	554722
Fixation Buffer	Biolegend	420801
Perm/Wash Buffer	BD Biosciences	554723
Filipin III from Streptomyces filipinensis	Sigma-Aldrich	F4767
Methyl-β-cyclodextrin	Sigma-Aldrich	M7439
Fluo-4, AM	Thermo Fisher Scientific	F14217
Rhod-2, AM	Thermo Fisher Scientific	R1244
Wheat Germ Agglutinin, Alexa Fluor 488 Conjugate	Thermo Fisher Scientific	W11261
Sigma Adjuvant System	Sigma-Aldrich	S6322
NP-KLH (Keyhole Limpet Hemocyanin)	Biosearch Technologies	N-5060-25
NP-PE (Phycoerythrin)	Biosearch Technologies	N-5070-1
Phosphatidylinositol 3,4,5-trisphosphate diC16 (PI(3,4,5)P3 diC16)	Echelon Biosciences	P-3916
Unlabeled Shuttle PIP Carrier 2 (Histone H1)	Echelon Biosciences	P-9C2
ProLong™ Diamond Antifade Mountant	ThermoFisher Scientific	P36961
Sodium metaperiodate	VWR	13798-22
Biocytin hydrazide	Biotium	90060
Aniline	Sigma-Aldrich	242284
RIPA buffer	Millipore	20-188
HALT protease inhibitors	Pierce	78442
Neutravidin agarose resin	Thermo Fisher Scientific	29200
Trypsin protease	Pierce	90057
Trifluoroacetic acid	Sigma-Aldrich	T6508-10AMP
Acetonitrile	Sigma-Aldrich	34998-4L
LC/MS grade water	Fisher Scientific	W64
Formic acid	Honeywell	94318
Dynabeads® MyOne™ Streptavidin C1	Thermo Fisher Scientific	65002
Duolink *in situ* PLA	Sigma-Aldrich	DUO92101
BrdU Flow Kit	BD Biosciences	552598
CellTiter-Glo® Luminescent Cell Viability Assay	Promega	G7570
Pierce Crosslink Magnetic IP/Co-IP kit	Thermo Fisher Scientific	88805

Supplementary Table S11, continued: *Overview of reagents used in this study*

Vybrant™ Lipid Raft Labeling Kit	Thermo Fisher Scientific	V34405
Annexin V Apoptosis Detection Kit with 7-AAD	Biolegend	640930
Membrane Lipid Strips	Echelon Biosciences	P-6002
Colony forming assay	STEMCELL Technologies	M3231
PI(3,4,5)P3 Mass ELISA	Echelon Biosciences	K-2500S
PI(4,5)P2 Mass ELISA	Echelon Biosciences	K-4500
Ig Isotyping Mouse Instant ELISA Kit	Invitrogen	88-50660
Mouse IgE ELISA Kit	Invitrogen	EMIGHE
Pierce™ Fab Preparation Kit	Thermo Fisher Scientific	44985

Supplementary Table S12: *Accession numbers and publicly deposited data from this study*

Description	Source	Accession #
RNA sequencing (RNA-Seq) data with *Ifitm3*$^{+/+}$ and *Ifitm3*$^{-/-}$ *BCR-ABL1* or *NRAS*^{G12D} B-ALL cells	This study	GSE155305
RNA sequencing (RNA-Seq) data with *Pten*$^{fl/fl}$ pre-B cells carrying 4-OHT-inducible Cre-ER^{T2} or ER^{T2}	This study	GSE155618
Phosphorylated protein levels in PDX2 B-ALL cells transduced with HA-tagged IFITM3^{Y20E} or empty vector (EV) control	This study	PXD020696
Bio-ID, BirA-IFITM3 interactomes	This study	PXD020697
Cell surface proteome	This study	PXD014691
Gene expression profiles of pre-treatment specimens from 207 patients from the COG P9906 study	Kang H. et al., 2010; Harvey, R.C. et al., 2010	GSE11877
37 BCR-ABL positive and 17 BCR-ABL negative adult ALL specimens from the ECOG/MRC intergroup study E2993	Juric D. et al., 2007	GSE5314
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IFITM3 mRNA levels across human normal and malignant B-lymphoid samples	AmaZonia http://amazonia.transcriptome.eu/	http://amazonia.transcriptome.eu/
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