Supplement

Supplemental Tables

Table S1. *α6 expression and karyotype of ALL*

ALL	Status	Cytogenetics	% α6
LAX53	Relapse	Unknown	99.8
ICN24	Diagnosis	Normal	100
ICN3	Diagnosis	MLL-AF4	100
LAX56	Relapse	t(Y;7)(p1.3;p13)	99.9
LAX7R	Relapse	$KRAS^{G12V}$	100
TXL3	Diagnosis	BCR-ABL1	98.0
ICN1	Diagnosis	BCR-ABL1	99.6
PDX2	Diagnosis	BCR-ABL1	100
SFO2	Relapse	BCR-ABL1	100
LAX2	Relapse	BCR-ABL1 (T315I)	98.5
BLQ1	Diagnosis	BCR-ABL1 (T315I)	100
Kasumi-2	Diagnosis	TCF3-PBX1	99.5
BEL-1	Relapse	t(4; 11) (q21; q23) MLL-AFF1	92.6

Table S2 *Sequences of oligonucleotide primers*

Genomic PCR	
Murine α6-floxed_Fw	5'-GCCGCATTACCGGTCGATGCAAGA-3'
Murine α6-floxed_Rv	5'-GTGGVAGATGGCGCGGCAAC-3'
Murine HPRT_Fw	5'- TTGACCCGACTGATGGTTCC-3'
Murine HPRT_Rv	5' –AAGACTCCTTCCTGCCTCCA-3'
Quantitative RT- PCR	
Murine BCR-ABL1_Fw	5'-ATCGTGGGCGTCCGCAAGAC-3'
Murine BCR-ABL1_Rv	5'-GCTCAAAGTCAGATGCTACTG -3'
Murine HPRT_Fw	5'- GGGGGCTATAAGTTCTTTGC -3'
Murine HPRT_Rv	5'- TCCAACACTTCGAGAGGTCC -3'

Table S3. *Antibodies used for flow cytometry, Western blotting and Histochemistry*

Antibody	Clone ID	Company
Murine CD19 (FITC)	1D3	eBioscience
Human CD19 (FITC)	HIB19	BD Biosciences
Murine CD45 (FITC)	30-F11	BD Biosciences
Human CD45 (APC)	HI30	BD Biosciences
Human/mouse CD49f (PE)	G_0H3	BD Biosciences
Human CD49f (Purified)	G_0H3	eBioscience
Murine CD45.1 (FITC)	A20	eBioscience
Murine CD45.2 (FITC)	104	eBioscience
B220 (PE)	RA2-6B2	Biolegend
Human CD20 (FITC)	2H7	Biolegend
Human CD10 (PE)	HI10a	Biolegend
Human IgM (APC)	MHM-88	Biolegend
Human CD19 (PE/cyanine7)	HIB19	Biolegend
Human/mouse CD49f (APC/cyanine7)	G_0H3	Biolegend
Human CD45 (Pacific Blue)	2D1	Biolegend
Human CD34 (PerCP/cyanine5.5)	8G12	Biolegend
PARP	-	Cell Signaling
Caspase 3	-	Cell Signaling
Caspase 7	-	Cell Signaling
Caspase 8	-	Cell Signaling
Caspase 9	-	Cell Signaling
p-Lyn^{Tyr507}	-	Cell Signaling
Lyn	-	Cell Signaling
p-Fyn^{Tyr530}	-	Cell Signaling
Fyn	-	Cell Signaling
p-Src^{Tyr418}	-	Cell Signaling
Src	-	Cell Signaling
ITGA6 (α6)	-	Cell Signaling
p53	-	Cell Signaling
β-Actin	AC-15	Santa Cruz Biotechnology
CD79a	11E3	Leica Biosystems
CD49f	Polyconal	Abcam
Mouse IgG2a	MG2a-53	Abcam
Rabbit IgG	EPR25A	Abcam

Supplemental Methods

Phosphoproteomic profiling

Phosphoproteomics sample preparation was performed as described previously [24]. Briefly, cell pellets on ice were resuspended in fresh sonication buffer supplemented with 8M urea (Sigma), 50 mM Tris pH7.5 (Invitrogen), protease inhibitor (Sigma), 1 mM Na3VO4 (Sigma), 100 mM β-Glycerophosphate disodium (Sigma) and 1 mM NaF (Sigma) prior to sonication. Cell suspension was homogenized by 50% duty cycle (pulse) for 2 minutes using Qsonica Sonicator Q500 (Thermo Fisher Scientific). The homogenized lysates were centrifuged at 3,500g at 15°C for 5 minutes and supernatant was filtered with 0.45 μm syringe filter first, followed by 0.2 μm syringe filter. Protein concentration was measured with Bradford assay prior to store at -80°C for later use.

4.7 mg urea cell lysate was reduced with DTT, then alkylated with IAA, diluted 4-fold to 2 M urea, and digested with trypsin overnight. After purification of the tryptic peptides over a C18 column, pTyr-containing peptides were enriched by immunoprecipitation using pY (4G10) antibody beads. After an overnight incubation, the beads were washed and peptides were eluted with 0.1% TFA, desalted using C18 Ziptips, vacuum dried, and resuspended in 2% ACN, 0.1% formic Acid. Samples were submitted for two replicate LC-MS/MS analyses.

Using an Ultimate 3000 HPLC (Dionex), peptides were loaded on an Acclaim PepMap Nanotrap column (Thermo Scientific) and separated over a 15 cm x 75 um Acclaim PepMap RSLC 2 μm C18 column (Thermo Scientific) utilizing a 60 min gradient of 3-40% ACN, 0.1% FA. Eluted peptides were analyzed on a QE Plus mass spectrometer (Thermo Scientific). Full MS was

performed with 70K resolution. Top 12 ions fragmented by HCD were analyzed with 17.5K resolution. Raw data files were processed with Proteome Discoverer 1.4 (Thermo Scientific) using the SwissProt mouse proteome (downloaded October 2014), with pY, pS, and pT as dynamic modifications and a decoy database search with target FDR of 0.01.

Peptides were quantified using Skyline (MacLean et al., 2010) (MacCoss Lab Software). After filtration for pY-containing peptides, the peptide peak boundaries were manually curated. Intensities of peptides from replicate runs were averaged.

In vitro and *in vivo* model for BCR-ABL1-transformed *alpha6*$^{fl/fl}$ ALL and bioluminescence imaging

Whole bone marrow cells from alpha6$^{fl/fl}$ mice[33] were harvested and mononuclear cells (MNCs) isolated by red blood cell lysis using BD lysis Buffer. MNCs were retrovirally transformed by BCR-ABL1[25] in the presence of 10 ng/mL murine IL7 (Peprotech, Rocky Hill, NJ) in Retronectin- (Takara Bio USA, Mountain View, CA) coated plates. All BCR-ABL1-transformed ALL cells derived from bone marrow of mice were maintained in Iscove's modified Dulbecco's medium (IMDM) (Invitrogen) with GlutaMAX (Invitrogen) containing 20% fetal bovine serum (Invitrogen), 100 IU/ml penicillin, 100 µg/ml streptomycin (Invitrogen), and 50 µM 2-mercaptoethanol (Sigma-Aldrich) at 37 °C in a humidified incubator with 5% CO_2. After cytokine-independent proliferation, BCR-ABL1 transformed alpha6$^{fl/fl}$ cells were transduced retrovirally with EmptyER^{T2} or CreER^{T2} followed by puromycin (1 µg/ml) (Invitrogen) selection. For bioluminescent imaging, these cells were then transduced with a lentiviral vector (pCCL-MNDU3-LUC) encoding firefly luciferase and with a neomycin selection marker in 24 well

plates coated with retronectin (Takara Bio USA) for 48 hours as described previously [6]. After 1 µg/ml puromycin selection, α6 deletion was induced *in vitro* by addition of 1.5 µM tamoxifen (Sigma-Aldrich). For *in vivo* deletion of alpha6, 0.5 x 10^6 luciferase-labeled alpha6$^{fl/fl}$ BCR-ABL1$^+$ EmptyER^{T2} or CreER^{T2} ALL cells were injected via tail vein into sublethally irradiated (250 cGy) NOD/SCID mice. α6 in vivo deletion was induced by daily administration of 100 mg/kg~150 mg/kg Tamoxifen per oral gavage on day 3-8 and day 16-20 after leukemia cell transfer. Serial monitoring of leukemia progression in mice was performed as described earlier [25,26] at indicated time points using an *in vivo* IVIS 100 bioluminescence/optical imaging system (Xenogen). D-Luciferin (Promega) dissolved in PBS was injected intraperitoneally at a dose of 2.5 mg per mouse 15 minutes before measuring the luminescence signal. General anesthesia was induced with 5% isoflurane and continued during the procedure with 2% isoflurane introduced via a nose cone. Mice were monitored for weight loss and other leukemia symptoms. Moribund mice were sacrificed and tissues were analyzed for leukemia cell infiltration to confirm leukemia as the cause of death. All mouse experiments were subject to institutional approval by Children's Hospital Los Angeles IACUC (Institutional Animal Care and Use Committee).

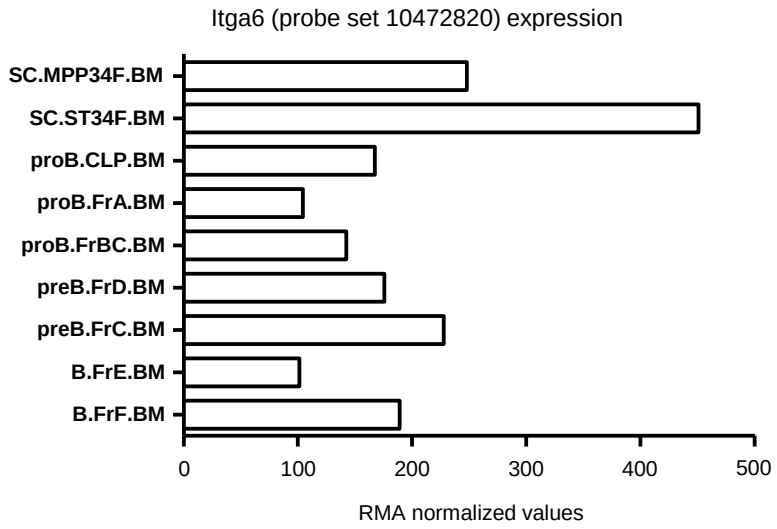
Immunohistochemistry

BM biopsies from the patients were paraffin-embedded after fixation in 4% paraformaldehyde (Sigma) followed by 5 µm sections mounted on Apex superior adhesive slides (Leica Microsystems) and stained on a Ventana BenchMark automated IHC stainer (Leica Microsystems, Tucson, Arizona). The Bond Rx^m Autostainer (Leica Biosystems, Newcastle, UK) was used and the antigen-antibody reaction were detected and visualized by Bond polymer Refine Detection kit (Leica Microsystems) (CD79a) and Bond polymer Refine Red Detection kit

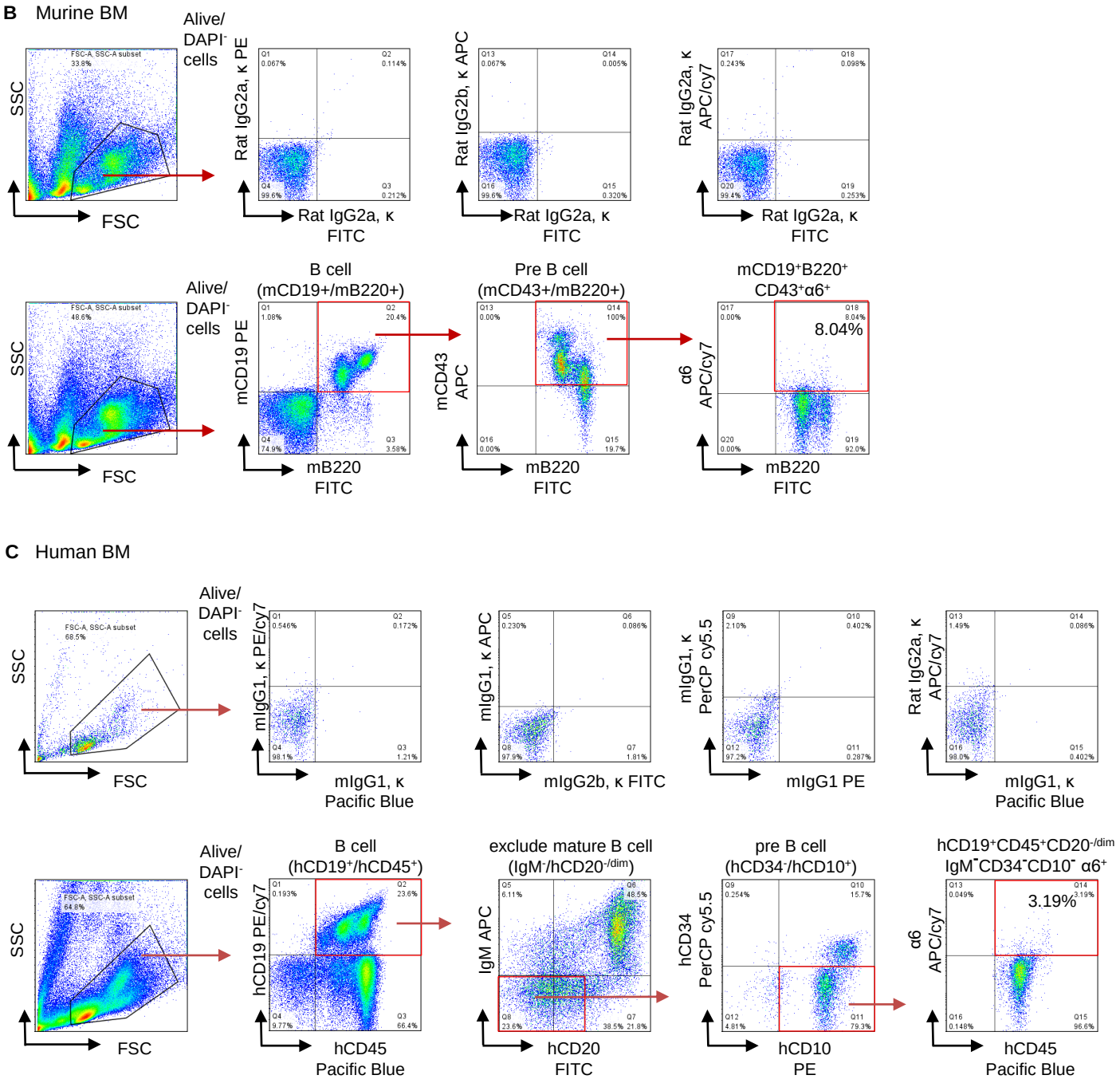
(Leica Microsystems) (α6). Slides were also counterstained with routine hematoxylin for cell nuclei. Mounting medium (Pro-Long Gold Antifade Reagent; Invitrogen) was applied and coverslips sealed, prior to acquisition of fluorescent images at room temperature on a Zeiss Axiovert 200M inverted confocal microscope with a 40 Plan Neofluor objective using IP Lab 4.0 software (Scanalytics). Photomicrographs were acquired using a Hamamatsu ORCAER HAL100 digital camera (Bridgewater, NJ) (400x magnification) and brightness was enhanced using Adobe Photoshop 6.0.

Supplementary Figure 1.

A



Population name	Long name	Description
SC.MPP34F.BM	Multipotent Progenitor	CD34+ Flk2+ Lin- c- kit+ Sca1+
SC.ST34F.BM	Multipotent Progenitor	CD34+ Flk2- Lin- c- kit+ Sca1+
proB.CLP.BM	Common Lymphoid Progenitor	LIN- AA4+ Kit+ IL7Ra+ B220-
proB.FrA.BM	Fr. A (Pre-Pro-B)	LIN- AA4+ Kit+ IL7Ra+ B220+
proB.FrBC.BM	pro-B stage cell population, Fr. B & Fr. C	IgM- CD19+ CD43+ CD24+
preB.FrD.BM	small pre-B population, Fr. D	CD19+ IgM- CD45R+ CD43-
preB.FrC.BM	Fr. Cprime (Cycling Pre-B)	AA4+ IgM- CD19+ CD43+ HSA++
B.FrE.BM	newly-formed B cell population, Fr. E	CD19+ IgM+ AA4.1+ CD24+
B.FrF.BM	Bone Marrow Fraction F	CD19+ IgM+ AA4.1- CD24-


B Murine BM
Alive/ DAPI- cells
SSC
FSC
Rat IgG2a, κ PE
Rat IgG2a, κ FITC
Rat IgG2b, κ APC
Rat IgG2a, κ FITC
Rat IgG2a, κ APC/cy7
Rat IgG2a, κ FITC
B cell (mCD19+/mB220+)
mCD19 PE
mB220 FITC
Pre B cell (mCD43+/mB220+)
mCD43 APC
mB220 FITC
mCD19+B220+ CD43+α6+
8.04%
α6 APC/cy7
mB220 FITC
C Human BM
Alive/ DAPI- cells
SSC
FSC
mIgG1, κ PE/cy7
mIgG1, κ Pacific Blue
mIgG1, κ APC
mIgG2b, κ FITC
mIgG1, κ PerCP cy5.5
mIgG1 PE
Rat IgG2a, κ APC/cy7
mIgG1, κ Pacific Blue
B cell (hCD19+/hCD45+)
hCD19 PE/cy7
hCD45 Pacific Blue
exclude mature B cell (IgM-/hCD20-/dim)
IgM APC
hCD20 FITC
pre B cell (hCD34-/hCD10+)
hCD34 PerCP cy5.5
hCD10 PE
hCD19+CD45+CD20-/dim IgM-CD34-CD10- α6+
3.19%
α6 APC/cy7
hCD45 Pacific Blue

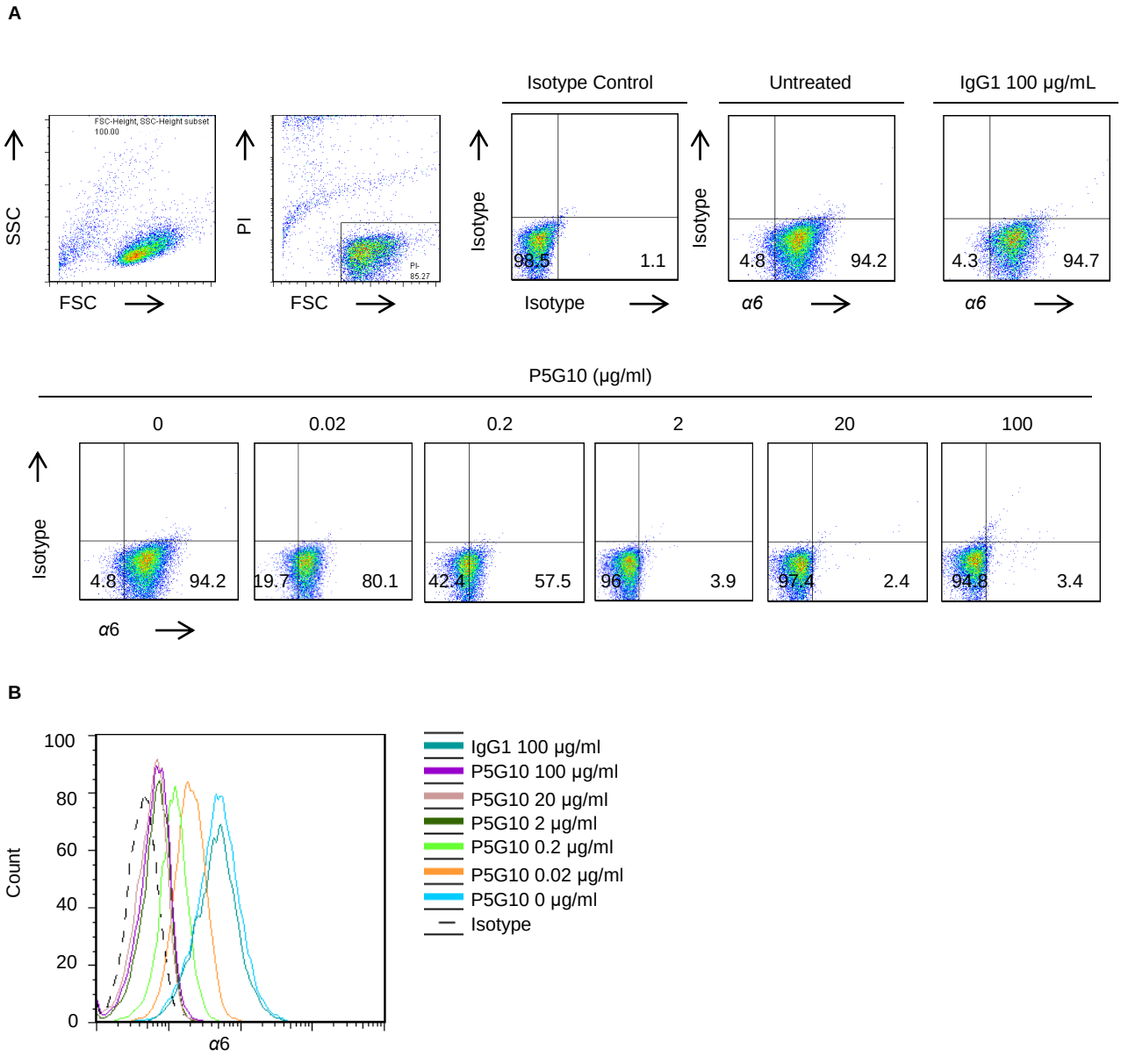
D

Integrin α6 expression in normal BM Pre-B cells of healthy human donors and healthy mice (C57Bl6/J)

Samples	α6 (%)
Murine (C57Bl6/J) BM-Pre-B cells (n=2)	8.17±0.18
Human healthy donor BM- Pre-B cells (n=3)	3.24±1.21

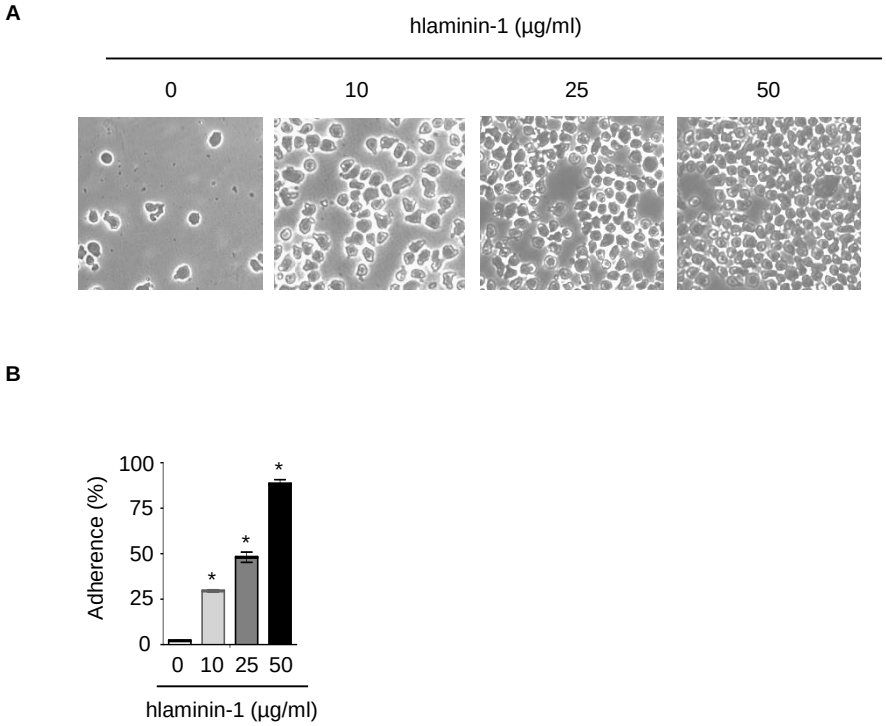
Legend. ***Expression of integrin α6 in normal murine and human Pre-B cells.***
(**A**) Itga6 (probe ID: 10472820) expression in stem cells and different stages of B cells from 6 to 10 weeks old C57BL/6J were analyzed by using microarray data from ImmGen Skyline (http://rstats.immgen.org/Skyline/skyline.html) and shown with RMA (Robust multi-array average) on the x-axis. Lineage marker expression for each group is shown in the table. Lineage marker expression for each group is shown in the table.
(**B**) 8-weeks old C57BL6/J mice (Jackson Laboratory) were sacrificed and the whole femoral bone marrow were treated with ACK lysis buffer to lyse red blood cells and subsequently stained for indicated antibodies and appropriate isotype controls. α6 (CD49f)-expressing pre-B cells were identified as $mCD19^{+}B220^{+}CD43^{+}$[28]. Representative flow plots are shown.
(**C**) Bone marrow aspirates of healthy human donors were treated with ACK lysis buffer for red blood cells lysis and subsequently stained for indicated antibodies and appropriate isotype controls. α6-expressing pre-B cells were identified as $hCD19^{+}CD45^{+}CD20^{-/dim}IgM^{-}CD34^{-}CD10^{+}$[29]. Representative flow plots are shown.
(**D**) Summary of the mean percentages and standard deviation of α6 expression in normal bone marrow pre-B cells. Two independent experiments for the murine immunocompetent (C57Bl6/J) BM (n=2) and the human BM (n=3).

Supplementary Figure 2



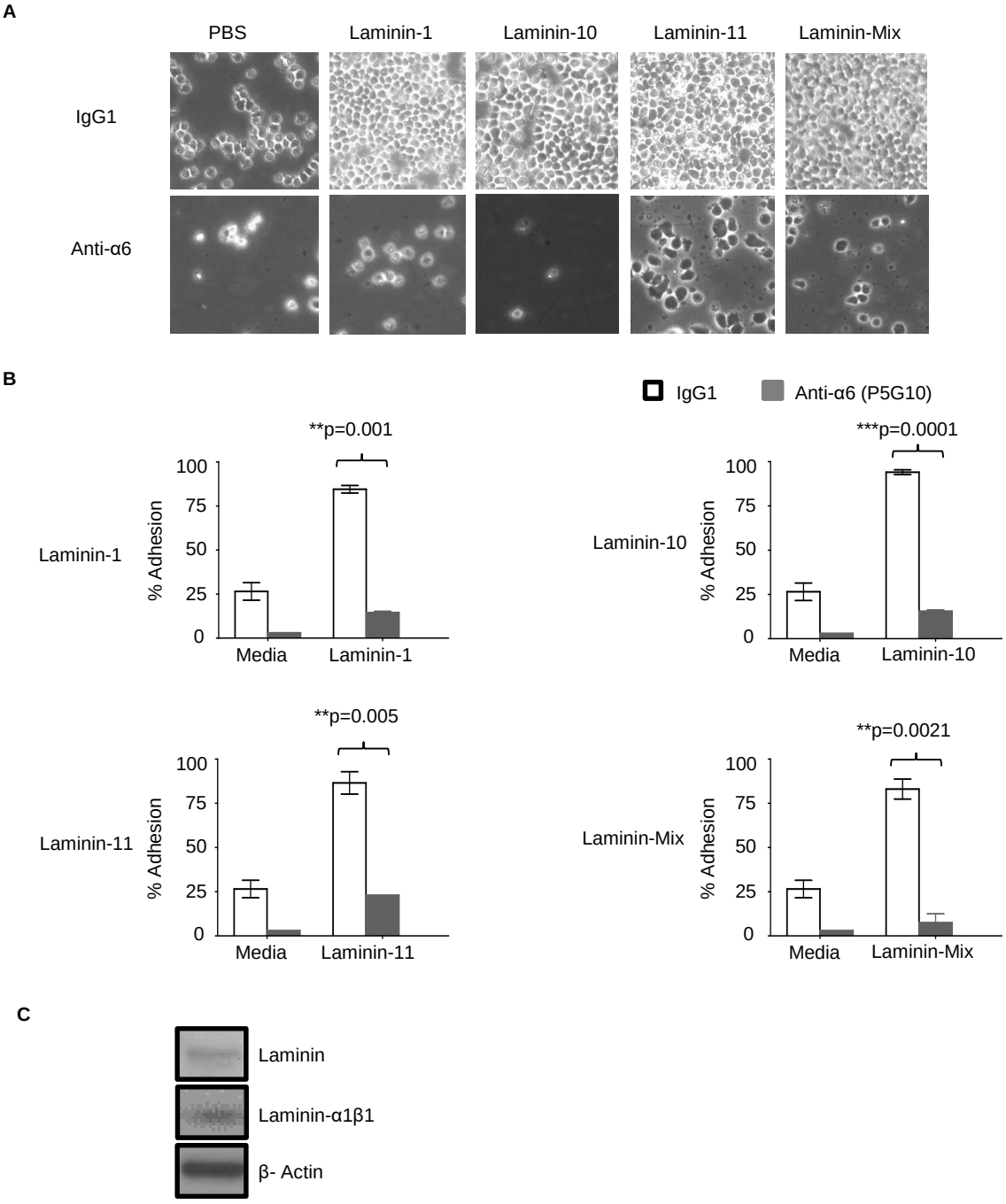
Legend. ***Dose escalation of anti integrin α6 antibody to saturate binding of α6 in primary ALL (ICN1).*** Pre B ALL ICN1 cells were plated onto human Laminin-1-coated plates (tissue culture) overnight and then treated with indicated concentrations of anti-α6 (P5G10) (0-100 µg/ml) for 60 min. Cells were stained with Alexa Fluor 488-conjugated P5G10 Ab prior to flow cytometric analysis. (**A**) Dot plots and (**B**) histograms of one representative flow cytometric staining are shown. The numbers in the quadrants indicate % of the cells. One of two experiments in triplicates.

Supplementary Figure 3



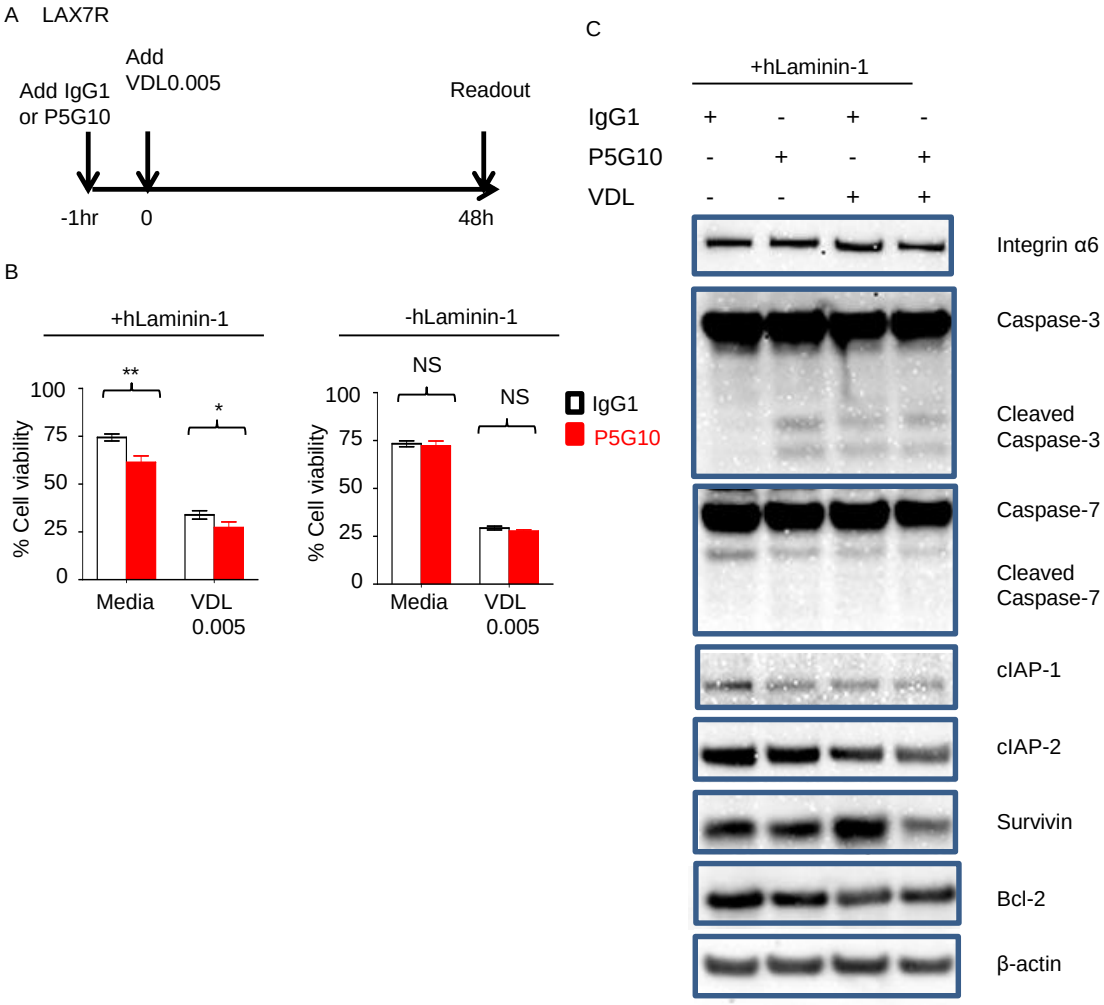
Legend. ***Dose determination of human Laminin-1.*** Human Pre-B ALL LAX7R cells were plated onto tissue culture plate coated with human (h) Laminin-1 at different doses (0, 10, 25, 50 µg/ml) as indicated and incubated overnight. (**A**) Microscopic pictures for adhering cells on different doses of hLaminin-1. The original magnification was 200x. (**B**) % of adherence was calculated as adherent live cell numbers divided by total cells plated and then x100%. *p<0.05 when compared with control (hLaminin 0µg/ml). One of two experiments in triplicates.

Supplementary Figure 4



Legend: ***Integrin α6 blockade de-adheres primary ALL from human laminin-1, 10, 11-coated plates.*** ICN1 cells were incubated overnight on plates coated with human Laminin-1, Laminin-10, Laminin-11, or mixed Laminin1, 10 and 11- coated tissue culture plates for 4 hours prior to antibody addition. (**A**) Representative images of ALL cells treated as indicated with anti-α6 (P5G10) antibodies used for de-adhesion assessed post overnight incubation. The original magnification was 200x. (**B**) % adhesion by P5G10 antibody. (**C**) Murine Laminin and Laminin-α1β1 expression in OP9 cells assessed by Western blot analysis.

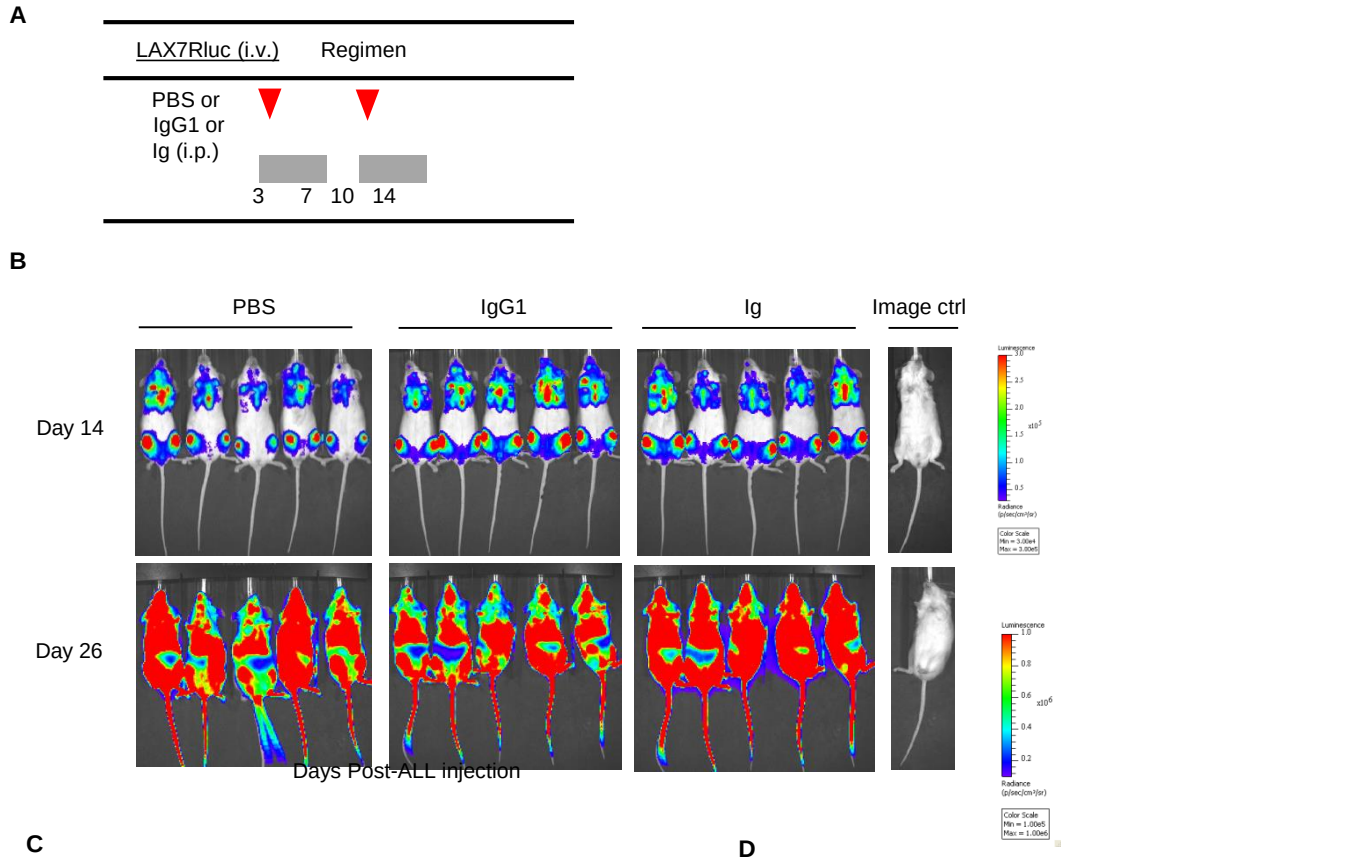
Supplementary Figure 5.



Legend. ***α6 antibody P5G10 sensitizes primary B-ALL cells to chemotherapy and induces apoptosis.***

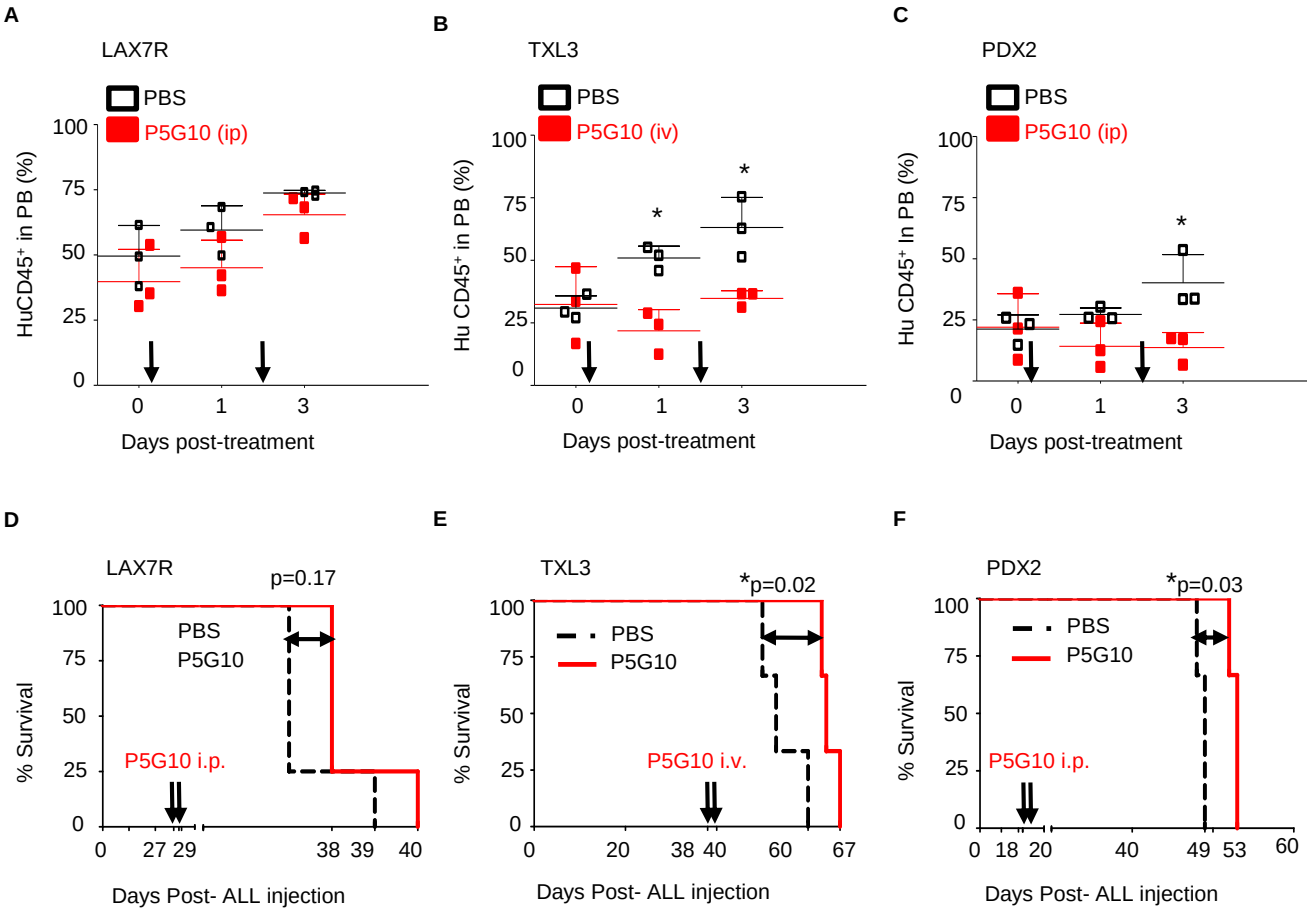
(**A**) Schematic of the experiments. (**B**) Cell viability was measured using Annexin V/7-AAD staining analyzed on FACSCalibur. P5G10 induced more apoptosis in the presence of chemotherapeutical agents (VDL). (**C**) Western blot analysis was performed. β-actin was used as a loading control. One of two experiments shown. ANOVA followed by Tukey's Multiple Comparison test. *p<0.05,**p<0.01; NS: not significant.

Supplementary Figure 6.



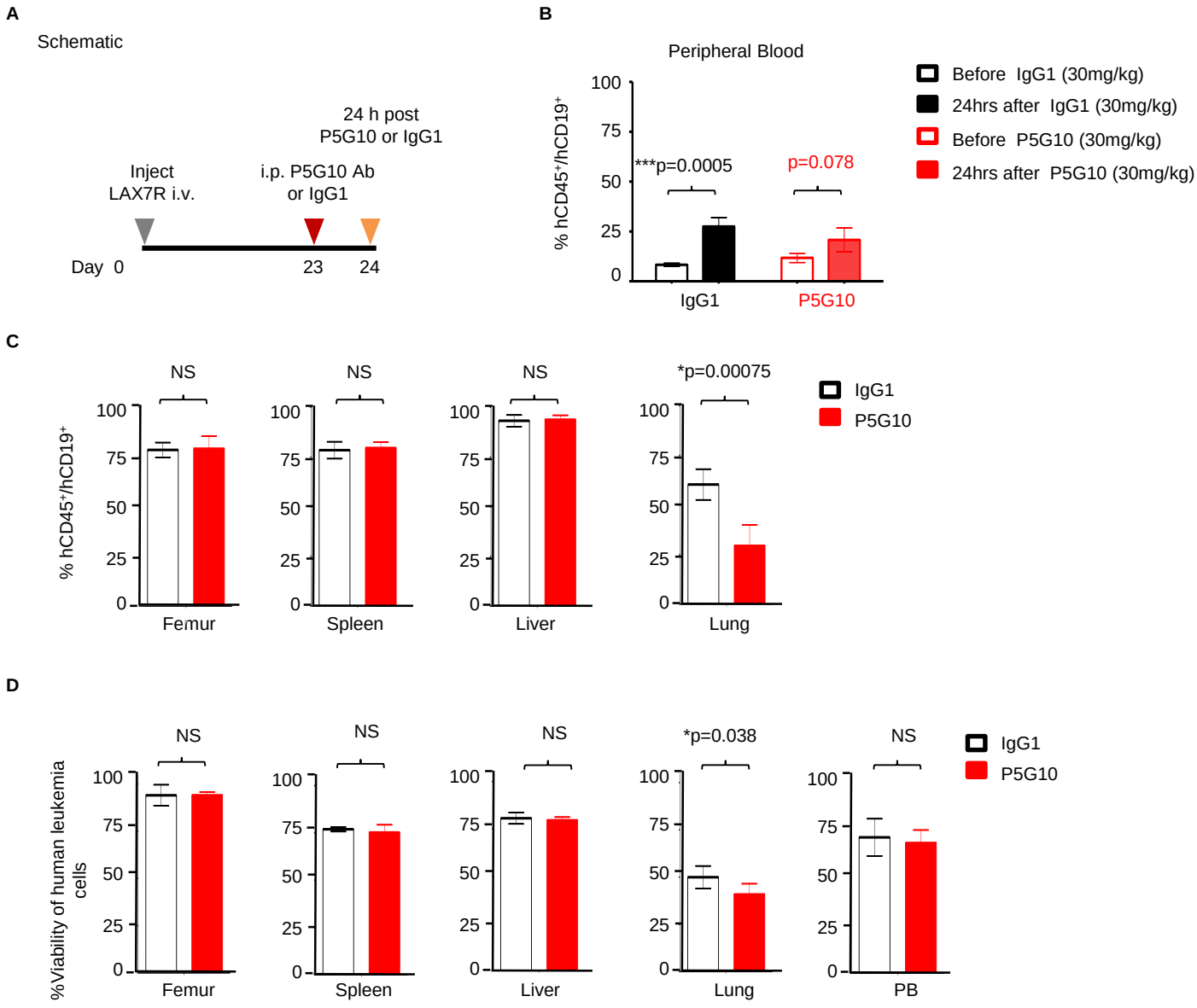
Legend. ***Survival analysis after treatment with control treatments PBS, IgG1 and IgG.***
(**A**) Schematic of the experimental treatment. B-ALL cells (LAX7R) were labeled with firefly luciferase (LAX7Rluc) prior to intravenous (i.v.) injection into female NSG mice. On Day 3 post- ALL injection, mice were injected with PBS (Thermofisher) (n=5); IgG1 (30mg/kg) (BioLegend) (n=5) and Ig (30mg/kg) (CSL Behring LLC) (n=5) intraperitoneally (i.p.). (**B**) Bioimaging of mice on Day 14 and Day 26 post B-ALL injection. (**C**) Weight changes compared to initial weights at beginning of experiment. (**D**) Survival curve. There was no statistical difference in survival or weights between any treatment groups by Log-rank (Mantel-Cox) Test. One experiment.

Supplementary Figure 7



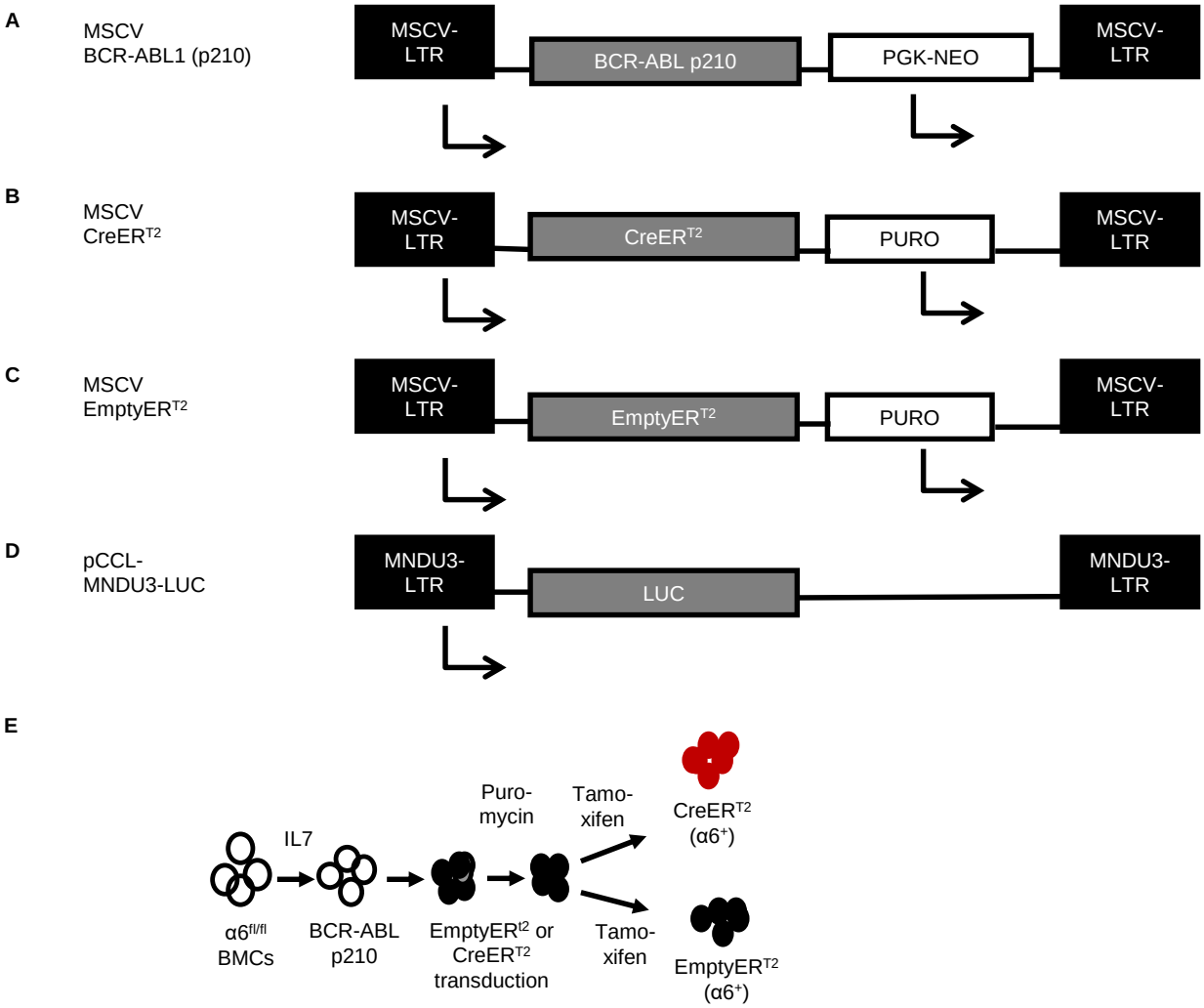
Legend. ***Blockade of α6 does not mobilize leukemia cells into the peripheral blood of recipient mice.*** Primary ALL cells TXL3, PDX2 (both BCR-ABL1$^+$) or LAX7R (BCR-ABL1$^-$) were injected into NSG mice (2.5x10^6 cells/mouse). Mice were injected intraperitoneally with 30 mg/kg P5G10 or PBS control. The % of human CD45$^+$ and CD19$^+$ in peripheral blood (PB) was analyzed by flow cytometry before, and 1 and 3 days after treatment (**A-C**). The arrows indicated the day when P5G10 was injected. *p<0.05 using Student t test. (**D-F**) Kaplan-Meier survival curve was analyzed and median survival time (MST) for each group (n=3/group) was determined. One experiment per leukemia case. P values (Log-rank test) are shown on the graphs. *p<0.05 indicates a significant difference.

Supplementary Figure 8



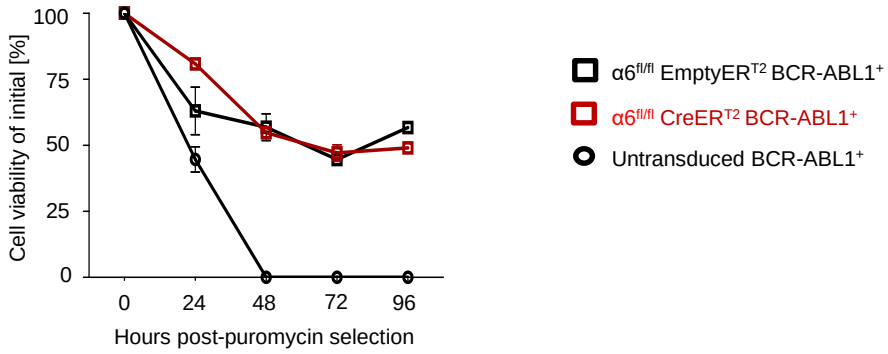
Legend. ***Effect of P5G10 on mobilization of primary Pre-B ALL LAX7R cells.*** (**A**), Schematic of the experiments. LAX7R ALL cells were intravenously (tail vein) injected into NSG mice (n=5 each group). Percentages of human CD45$^+$/CD19$^+$ cells were determined by flow cytometry in peripheral blood (**B**), and different tissue and organs on day 24 (24h post P5G10 or IgG1 intraperitoneal injection). (**C**) Viability was counted using Trypan blue exclusion of dead cells except PB which was by PI (Propidium Iodide) flow cytometry (**D**). One experiment. Viability of ALL cells determined by Trypan blue count exclusion of dead cells except PB, which was determined by Propidium iodide (PI) staining and flow cytometry. NS, not significant.

Supplementary Figure 9



Legend. ***Retroviral and lentiviral vectors and transduction methods.*** Schematic of the MSCV-based retroviral vectors used for oncogenetic transduction of (**A**) BCR-ABL1 p210^{+}; (**B**) CreER^{T2} for conditional deletion of CD49f (integrin alpha6) and (**C**) EmptyER^{T2} (Control) transduction. (**D**) Lentiviral pCCL backbone vectors were used for firefly luciferase transduction. Transfections of the HEK 293Tcells with above MSCV-based retroviral constructs encoding BCR-ABL1, EmptyERT2 and Cre-ERT2 were performed using Lipofectamine 2000 (Invitrogen, Carlsbad, CA) with Opti-MEM media (Invitrogen). Retroviral supernatant was produced as described. (**E**) Schematic for mouse leukemia model with inducible alpha6 deletion*:* α6$^{fl/fl}$ whole bone marrow cells were harvested and primed with IL-7 followed by oncogenetic transduction of BCR-ABL1 p210^{+} and then EmptyER^{T2} or CreER^{T2}. For conditional deletion of α6 tamoxifen was used in vitro and in vivo.

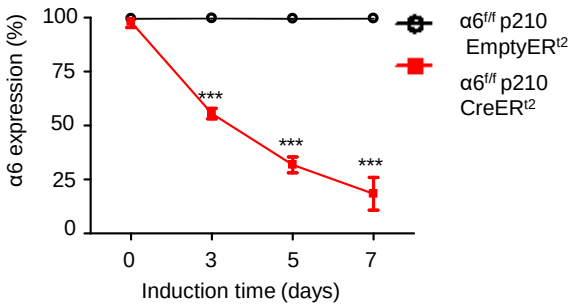
Supplementary Figure 10



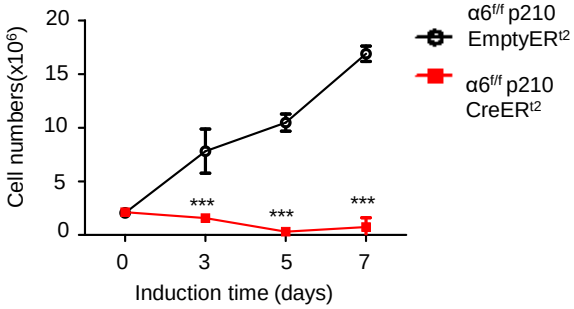
Legend. ***Puromycin selection post EmptyER^{T2} and CreER^{T2} transduction of α6 $^{fl/fl}$ in murine (BCR-ABL1^{+}) leukemia.*** α6$^{fl/fl}$ EmptyER^{T2} BCR-ABL1^{+} (black squares) and CreER^{T2} BCR-ABL1^{+} (red squares) cells were selected by puromycin (1µg/ml) for 96 hours. Viability of selected cells was assessed by trypan blue exclusion of dead cells. Control cells not transduced BCR-ABL1^{+} cells were killed by the puromycin treatment as expected (black circles).

Supplementary Figure 11

A

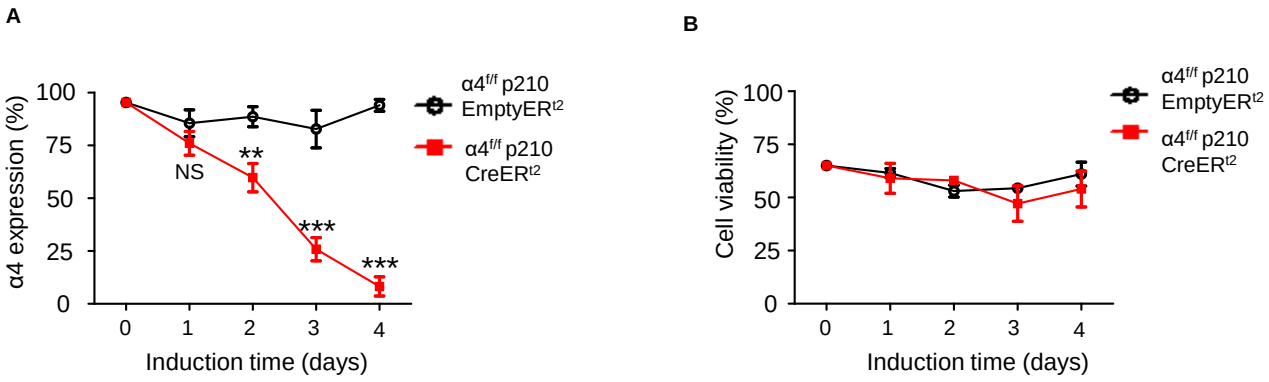


B



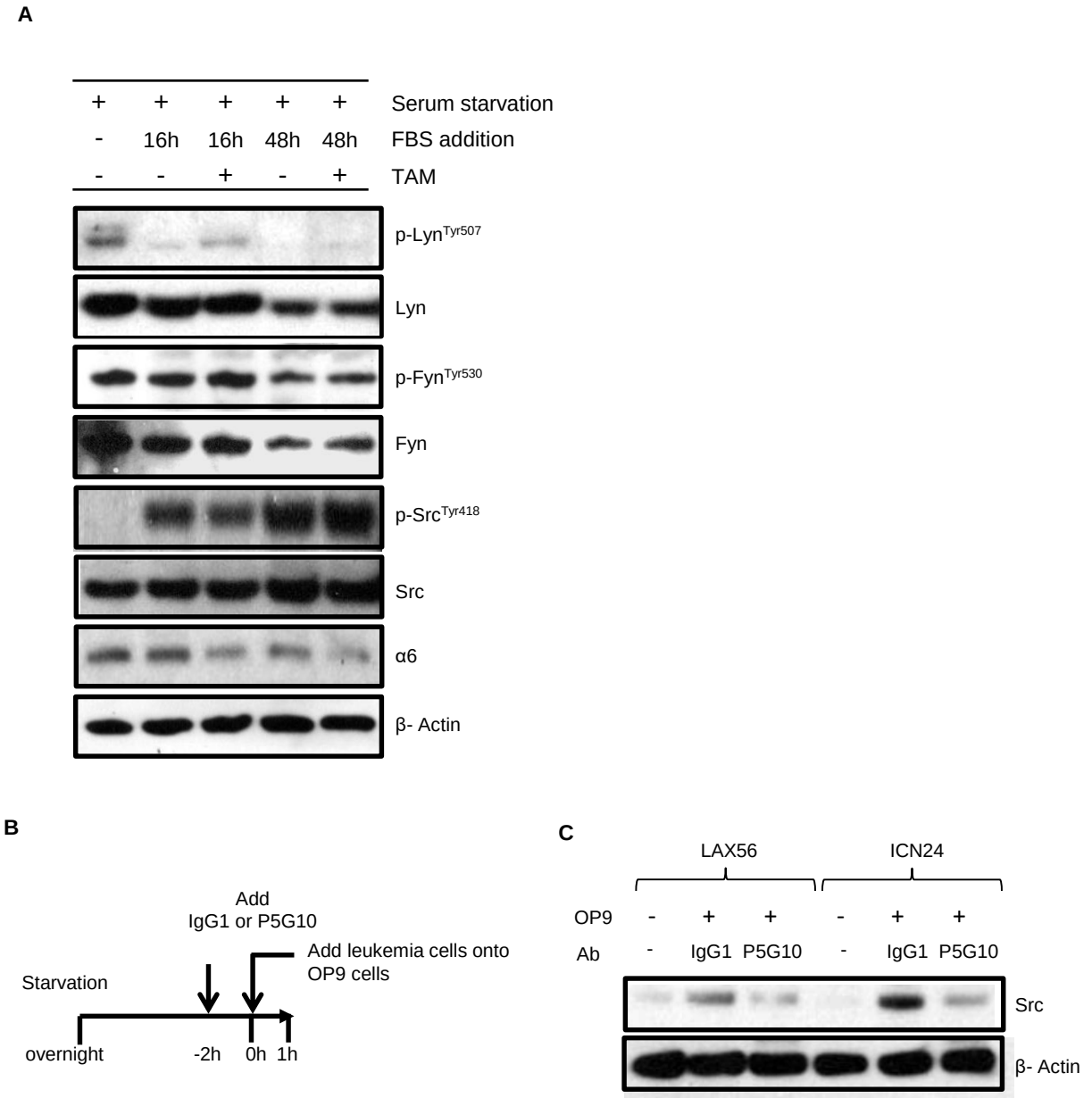
Legend. ***Inhibition of cell proliferation by integrin α6 deletion.***
(**A**) Murine $\alpha6^{f/f}$ p210 $EmptyER^{t2}$ and $CreER^{t2}$ cells were treated with tamoxifen (1.5μM) for 7 days to induce α6 deletion. α6 expression was determined by flow cytometry. (**B**) Cell proliferation was assayed using Trypan blue exclusion of dead cells. ANOVA followed by Tukey's Multiple Comparison test was used for statistical difference. ***p<0.001: Tamoxifen versus media control. One of three experiments. Each experiment was performed in triplicates.

Supplementary Figure 12



Legend. ***Cell viability is not decreased by integrin*** α4 ***deletion.***
(**A**) Murine α4$^{f/f}$ p210 EmptyER^{t2} and CreER^{t2} cells were incubated with Tamoxifen (1.5μM) for 4 days to induce α4 deletion. α4 expression was determined by flow cytometry. (**B**) Cell viability was measured by Trypan blue exclusion of dead cells. One of three experiments. Each experiment was performed in triplicates. **p<0.01 and ***p<0.001 when compared with the corresponding groups by ANOVA and post Tukey's test.. NS, not significant.

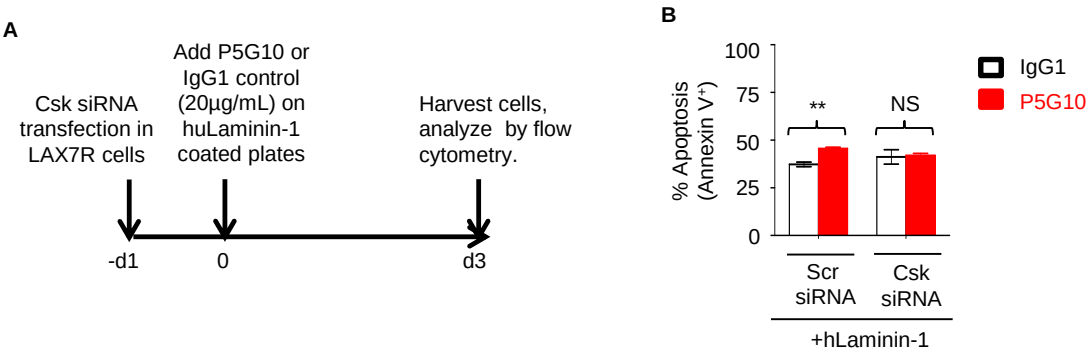
Supplementary Figure 13.



Legend. ***Downregulation of Src signaling by integrin α6 deletion or antibody against α6 in B-ALL cells.***

(A) Western blot analysis detecting phosphorylated Lyn or Fyn protein in murine $\alpha6^{fx/fx}$ BCR-ABL1^{+} (CreER^{T2}) cells starved for 4 hours (serum starvation) followed by 16hrs or 48 hrs FBS stimulation (FBS addition) and tamoxifen addition (+), or not (-), as indicated above the figure. β-Actin served as loading control. (**B**) Schematic for the treatment of primary ALL cells LAX56 and ICN24 (diagnosis samples with normal karyotype) with P5G10 or IgG1 (20 μg/ml) for 2 h prior to co-culture of the leukemia cells with OP9 stromal cells for 1 h. **(C)** Western blot of cell lysates of (Supplemental Fig. 13B) for Src . β-actin, loading control.

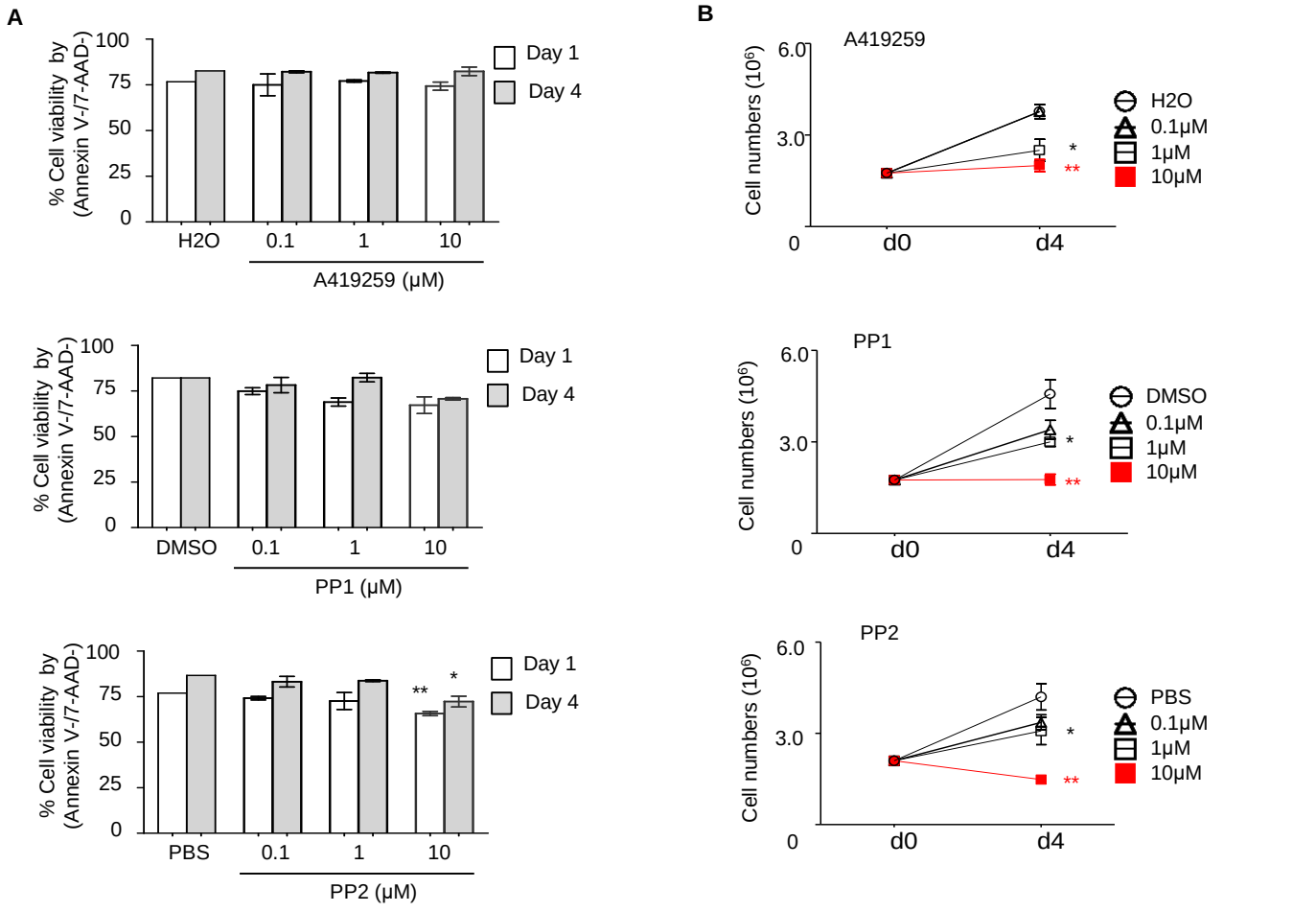
Supplementary Figure 14.



Legend. ***Inhibition of Csk using siRNA rescues the apoptosis induced by anti-α6 antibody P5G10.***

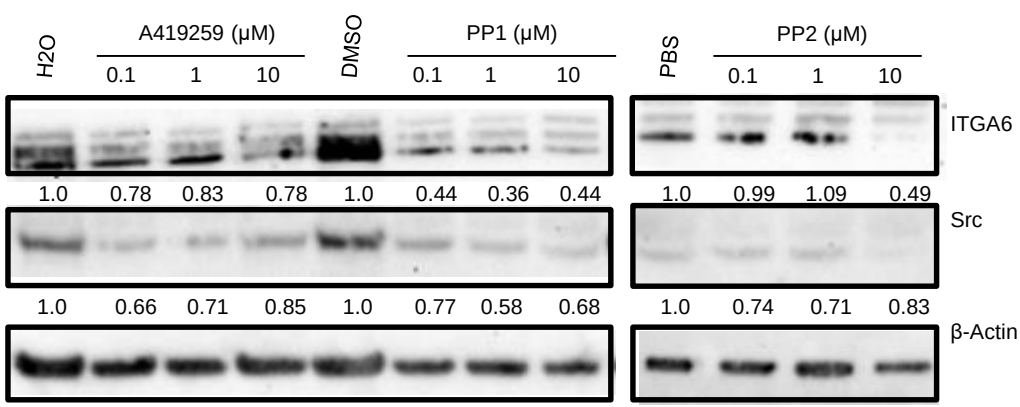
(**A**) LAX7R cells were transfected with CSK siRNA and one day later treated with either P5G10 or IgG1 control. After 3 days, ALL cells were harvested and analyzed by flow cytometry. **(B)** Apoptosis of ALL cells was measured using Annexin V/7-AAD staining and analyzed using FACSCalibur. P5G10 induced apoptosis which was rescued by Csk siRNA (NS between Scr siRNA-P5G10 and Csk siRNA-P5G10 groups. One way ANOVA with Tukey post test was performed. **p<0.01. Scr: Scrambled. One of three experiments. Each experiment was performed in triplicates.

Supplementary Figure 15.



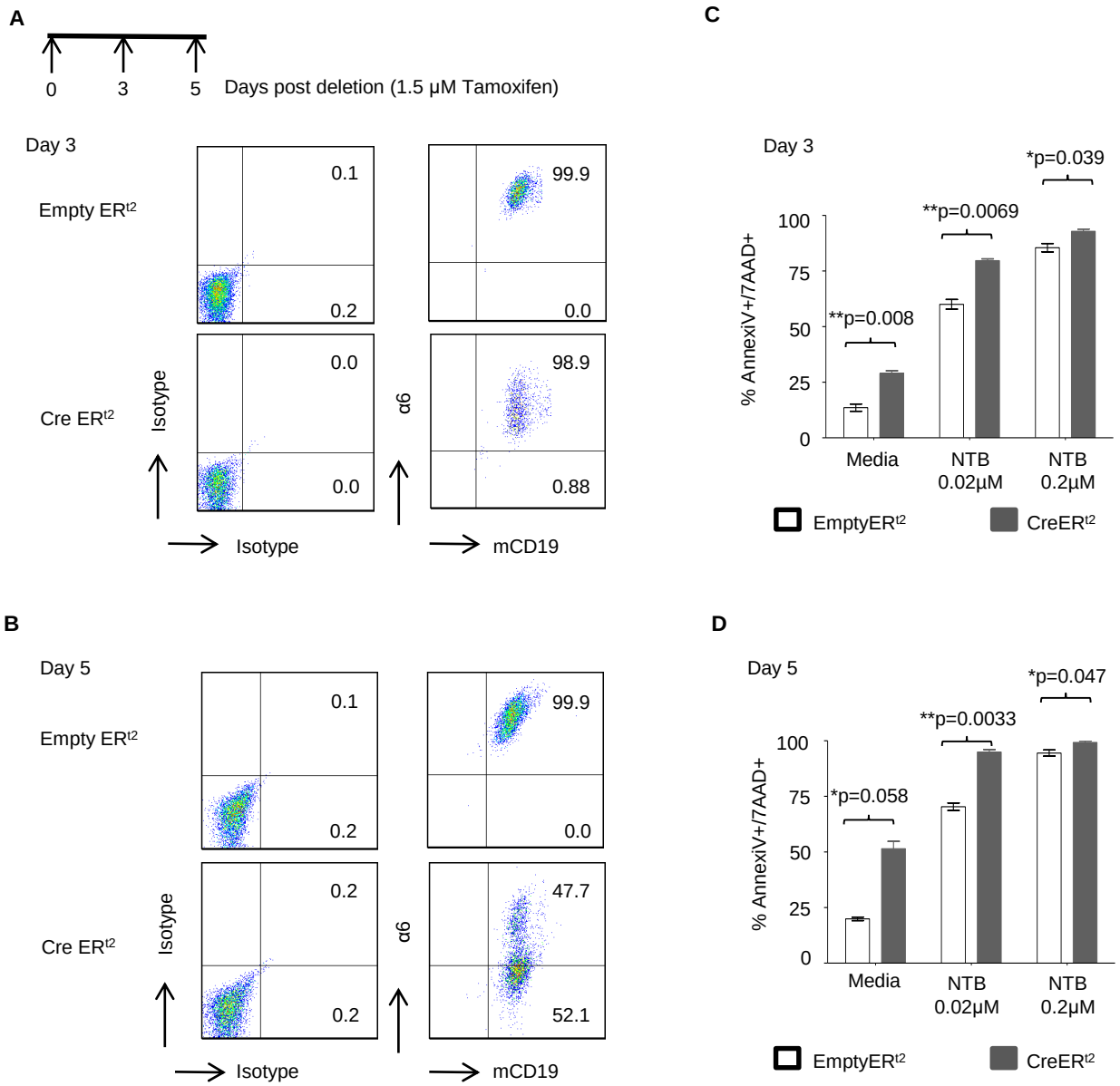
C

Src inhi-bitor	Treat ment (days)	GR50 (μM)
A 419259	4	0.31
PP1	4	4.30
PP2	4	13.1



Legend. ***Src inhibitors do not decrease cell viability but inhibit proliferation.*** Primary B-ALL ICN24 cells were plated on OP9 cells and treated with indicated doses of Src inhibitors up to 4 days: A419259 (as described in [44]); PP1: 4-amino-5-(4-methylphenyl)-7-(t-butyl)pyrazolo[3,4-d]-pyrimidine (as described in [45]); PP2 (4-amino-5-(4-chloro-phenyl)-7-(t-butyl)pyrazolo[3,4-d]pyrimidine) (as described in [46]); (all from Sigma). (**A**) Cell viability was determined by flow cytometry (Annexin V^-/7-AAD^- staining). *p<0.05 and **p<0.01 when compared with vehicle (H2O, DMSO or PBS) control. (**B**) Cell proliferation was determined by cell counting using Trypan blue exclusion of dead cells. *p<0.05 and **p<0.01 when compared with vehicle control. (**C**) GR50 (50% Growth retardation) was calculated based on apoptosis determined in (B) after 4 days incubation with respective Src inhibitors by cell counting using Trypan blue exclusion of dead cells. (**D**) Western blot for ITGA6 and Src expression. β-Actin was used as loading control. Densitometry was performed using Image J and shown below the bands. One of three experiments. Each experiment was performed in triplicates.

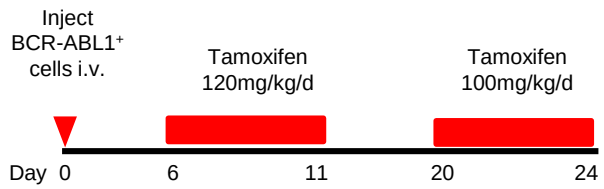
Supplementary Figure 16



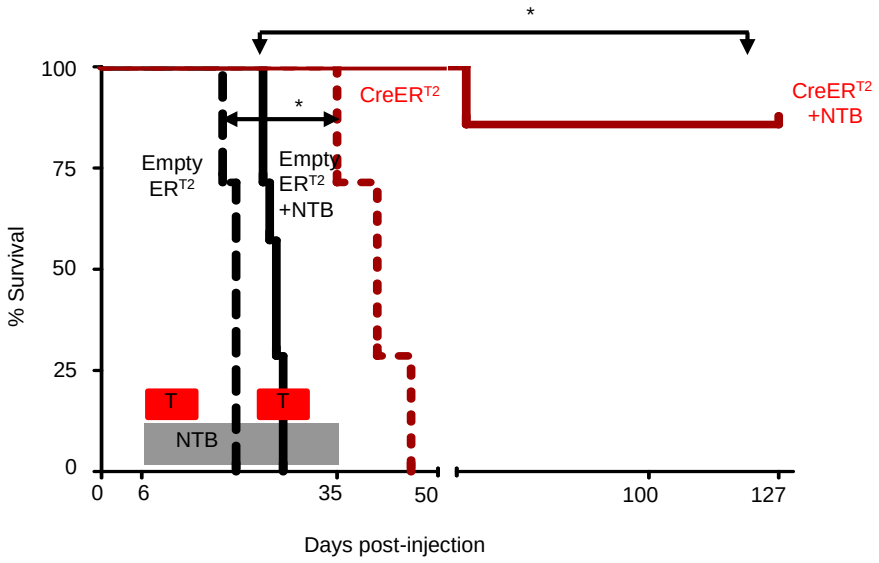
Legend. ***Alpha6 deletion sensitizes murine leukemia to tyrosine kinase inhibition.*** $\alpha6^{fl/f}$ p210 EmptyER^{T2} or CreER^{T2} cells were treated with tamoxifen to delete α6 and treated with Nilotinib (NTB) at the same time for 5 days in vitro. Drugs were changed once on day 3 post-treatment. (**A, B**) α6 expression by flow cytometry. The numbers indicated % of positive cells in each quadrant. (**C, D**) % apoptosis was determined by Annexin V/7-AAD staining followed by flow cytometric acquisition and analysis.

Supplementary Figure 17

A



B



Legend. ***α6 deletion in vivo in murine leukemia.*** (**A**) Schematic for α6 *in vivo* deletion induced by Tamoxifen treatment (100 and 120 mg/kg/day). $\alpha6^{fl/fl}$ BCR-ABL1^{+} p210 EmptyER^{T2} or CreER^{T2} mouse cells were intravenously (i.v.) injected into NOD/SCID mice. (**B**) Kaplan-Meier survival curve. Mice were treated with Tamoxifen (T) and 50mg/kg Nilotinib (NTB). MST was calculated for each group by Log-rank Test (MST for EmptyER^{T2} = 20 days; MST for CreER^{T2} = 41 days; MST for EmptyER^{T2} +NTB = 26 days MST for CreER^{T2} +NTB = undefined). * $p<0.05$, n=7/group.