Supplemental Data

Supplemental Material and Methods

Super-enhancer Identification

Super-enhancers were identified using RANK ORDERING OF SUPER-ENHANCERS (ROSE) (https://bitbucket.org/youngcomputation/rose)(Hnisz et al. 2013; Loven et al. 2013; Whyte et al. 2013). H3k27ac peaks within 12.5 kb of each other, except for those that were fully contained within +/- 2 kb of a transcriptional start site (TSS), were ranked along the x axis based on their H3K27ac enrichment and plotted on the y axis. Super-enhancers were subsequently identified as regions which are to the right of the inflection point based on the resulting curve. Both enhancers and super-enhancers were assigned to the nearest RefSeq genes.

CRISPR/Cas9 Gene Knockout

For genetic knockout experiments, single guide RNA (sgRNA) was designed using the CRISPR Design Tool (http://crispr.mit.edu/) and cloned into lentiCRISPv2 (Addgene plasmid # 52961) or FgH1tUTG (Addgene plasmid # 70183) using BsmB1 enzyme sites. Lentiviruses were produced using the same protocol for shRNA knockdown analysis. Jurkat cells infected with the virus were selected by 0.7 µg/ml of puromycin (Sigma) from day 3 to day 7. To identify genetic deletion, we isolated genomic DNA using the QIAamp DNA Blood Mini Kit (Qiagen) followed by PCR amplification using specific primers flanking the -135 kb element, as follows: forward, 5'-CGT CAA CCA CCA CTG CTT TT-3'; reverse, 5'-TTC CAG TAA CGT GGC AGT CC-3'.

shRNA Sequences

shRNA	Sequence
shGFP	ACA ACA GCC ACA ACG TCT ATA
shLUC	CTT CGA AAT GTC CGT TCG GTT
shARID5B #3	CTA CAC CTG TAG GAA GTT CAT
shARID5B #7	GCC TTC AAA GAG AAC CAT TTA
shTAL1	GCT CAG CAA GAA TGA GAT CCT
shHEB	CCA TCC CAT AAT GCA CCA ATT
shE2A	CCC GGA TCA CTC AAG CAA TAA
shGATA3	GCC TAC ATG CTT TGT GAA CAA
shRUNX1	CAG AGT CAG ATG CAG GAT ACA
shMYB	CCA GAT TGT AAA TGC TCA TTT
shLMO1	CGC GAC TAC CTG AGG CTC TTT

qRT-PCR Primers

Genes	Species	Forward	Reverse
TAL1	Human	TTC CCT ATG TTC	AAG ATA CGC CGC ACA
		ACC ACC AA	ACT TT
GATA3	Human	TTC AGT TGG CCT	CGC CGG ACT CTT AGA
		AAG GTG GT	AGC TA
RUNX1	Human	GTG TCT TCA GCC	CGA CTG TGT ACC GTG
		AGA TG	GAC TG

MYB	Human	TGT TGC ATG GAT	AGT TCA GTG CTG GCC
		CCT GTG TT	ATC TT
ARID5B	Human	CAG AAG AAT GCT	TGG GAA ACT ATT GGC
		GAG CCA AC	ACG TA
MYC	Human	TCA TTG GAA AAT	GTC GTT TCC GCA ACA
		TGA CAG CAT AGT	AGT CCT CTT C
ALDH1A2	Human	AGG CCC TCA	ACA TCT TGA ATC CCC
		CAGTGTCTT CT	CAA AG
MAX	Human	TTC CTC CCT CAT	GCT CTT CAG GCT CAG
		GGA AGA TG	ACT CC
EGR1	Human	CTT CAA CCC TCA	GGA AAA GCG GCC AGT
		GGC GGA CA	ATA GGT
EGR2	Human	GCA TAA GCC CTT	TGC TTT TCC GCT CTT
		CCA GTG TC	TCT GT
CDKN1A	Human	AGG TGG ACC TGG	TCC TCT TGG AGA AGA
		AGA CTC TCA G	TCA GCC G
HnRNPH3	Human	CGA CCG GGA CCA	TGA ACT TGC ATC ACC
		TAT GAT AG	AGC TC
Exon 7 of	Human	AAG AGG CCT TTA	GAA ACA AAC AAA ACC
C10orf107		ATG CAC GA	AGC CA
GAPDH	Human	CTC CTC TGA CTT	TGC TGT AGC CAA ATT
		CAA CAG CGA CAC	CGT TGT CAT
Arid5b	Mouse	GGC CAA CTA CAT	GGG ACA TGA TAC CAG
		TGC CAA CT	GGT TG
Мус	Mouse	AGC TGT TTG AAG	AAT AGG GCT GTA CGG
		GCT GGA TT	AGT CG

β-Actin	Mouse	GGC TGT ATT CCC	CCA GTT GGT AAC AAT
		CTC CAT CG	GCC ATG T
туса	Zebrafish	CGC GCT ACG GGA	GCA GGG GGT GGG
		TGA GAT CCC T	AGT TCT TGG A
mycb	Zebrafish	AAG CGG CCA AAG	CAC TAC TTT GCC ACA
		TGG TGA TCC	CCC TCG C
ef1a	Zebrafish	CTG GAG GCC AGC	ATC AAG AAG AGT AGT
		TCA AAC AT	ACC GCT AGC ATT AC
cd4	Zebrafish	TTT ACG CAC AGG	CTC TGC GGG TTC CTG
		TAG GAG GGA	TTG AT
cd8	Zebrafish	AAT CGC AAA GCA	AGT CCG CTG TCT GTC
		GAC GGA AG	СТТ ТТ
tcra	Zebrafish	ACC AAG TGG GAA	TGC CCA GTG ACA AGA
		ACT CAT GC	AGT TG
lck	Zebrafish	GCC TCC AGT CAG	TTG TAT ATG GCC ACC
		TCA GAA TTT	ACC AG
E130	Synthesized	GCT TGA GGA GCT	GCG GTC GGT ATA AAA
(ERCC	RNA	TGA AGC AG	TCA GG
spike-in)			

ChIP-PCR Primers

Primers for the analysis of transcription factor binding

Targets	Forward	Reverse
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N-Me (1)	ATG GGG TTC CCA TGG	GCC CTG CTG TTT CAT GAT TT
	TAT TT	
TAL1 (1)	CCT CTC ACC ACT TGC	CCC CAC CCC ATT CCT ATT AC
	тст сс	
GATA3 (1)	CGC ACG GTA AGC AGG	AGC TCA GCA TGT TTC TGC
	AAG	AA
RUNX1 (1)	CCT GTG GTT TTC TCG	TGC ACC TGC AGA GTT TTC
	CTC TC	AC
INIYB (1)	ATA ATG TET CEG EGA	GUITIG GITTCA GUI GUI UT
	TGG AT	
IGFBP3	AGT ACT CTG CAC TTA	TCT TCT CAC TGG AGA TAA
(control	GAG AAT CGA G	TAT GTG G
locus)		
,		

Primers for the analysis of H3K27ac

Targets	Forward	Reverse
N-Me (2)	CTT AGG TTG GAG GCA	CAT GTC CAA GCA GGA AGG
	CGA AA	ТТ
TAL1 (2)	CTG TCA CCA CTC CCA	ATG CAG AAA GTT CCC TGT
	GCT AA	GC
GATA3 (2)	TTG TTC AGC AGA GGA	GCC CTT CTC AAC AGT TCC
	TGC AG	TG
RUNX1 (2)	GGG GGT CAA ATC TTT	AGA GAG TTG ACC TGG CCT
	TGG TT	GA

MYB (2)	GAT ATG GCA GTG GCT	ATG GAG GTC TGG CTT TGT
	GCA C	TG

CRISPR/CAS9 sgRNA Sequences

sgRNA	Sequence
EGFP	CAA GTT CAG CGT GTC CGG CG
sgRNA #1	AGG TTT TGT GAT TGC CGA GG
sgRNA #2	AGG CCT AAG GAC TTG GTA CA
sgARID5B Exon 6	GAA AAA CCA AAG GTT GCC AT

Cell Cycle Analysis

Cells transduced with lentivirus expressing shRNA were harvested after 3 days, washed with PBS and fixed overnight using 70% ethanol. The cells were subsequently incubated with propidium iodide and analyzed with a BD[™] LSR II flow cytometer using BD FACSDiva[™] software.

Immunoprecipitation

Cells were lysed using IP lysis buffer containing 150 mM NaCl, 20 mM Tris pH 7.5, 1 mM EDTA, 0.5% NP40, 10% glycerol and 1x protease inhibitor (Roche). One microgram of a primary antibody, IgG (Santa Cruz) or ARID5B (Bethyl Laboratories), TAL1 (Santa Cruz) was added to 1 mg of protein. The protein lysate and antibody were incubated overnight at 4°C. The immune complex was precipitated using Dynabeads[®] Protein G (Thermo

Fisher Scientific), and this was followed by Western blot analysis with specific antibodies against ARID5B (Bethyl Laboratories) and PHF2, HDAC1, HDAC2, HDAC3 and HDAC4 (Cell Signaling Technology).

HDAC Inhibitor Treatment

Jurkat cells were treated with either DMSO or SAHA (2µM) (Sigma Aldrich) in RPMI-1640 medium. At 24 hours after drug treatment, cells were harvested for qPCR analysis as described in RNA Extraction and Gene Expression Analysis.

Western Blot Analysis for H3K27Ac

Jurkat cells were infected with shLUC (Control), shARID5B #3 and #7 lentivirus in the presence of polybrene (8 µg/ml; Millipore) by centrifugation at 1,300 rcf for 1.5 hr. The infected cells were selected with 0.7 µg/ml of puromycin (Sigma) in RPMI-1640 medium for at least 36 hr after infection. At day 3 after infection, cells were harvested for protein extraction using radioimmunoprecipitation assay (RIPA) buffer. Twenty microgram of protein lysate was used for western blot analysis with antibodies specific to H3K27ac and H3 (Cell Signalling Technology).

Overexpression of ARID5B and PHF2 in 293T Cells

Six microgram of pCS2+ mammalian expression constructs for expression of human *ARID5B* and *PHF*2 cDNAs were transfected into 293T cells grown in 10 cm Petri dish

using FuGENE® 6 Transfection Reagent (Promega). At 48 hours after transfection, cells were harvested for immunoprecipitation.

Inducible shRNA Knockdown

The shRNA sequences targeting the *ARID5B* mRNA were designed according to the RNA Consortium's recommendation (http://www.broadinstitute.org/mai/trc) and cloned into the inducible lentivirus expression vector Tet-pLKO-puro. Lentiviruses were produced by cotransfecting individual shRNA constructs with the packaging plasmids pMDLg/pRRE and pRSV-Rev and the envelope plasmid pMD2.G into 293T cells by using FuGENE 6 transfection reagent (Promega). Supernatants containing lentivirus particles were collected and filtered through a 0.45 μ m filter (Thermo). Jurkat cells expressing doxcycyline dependent shRNA were established through lentiviral infection in the presence of polybrene (8 μ g/ml; Millipore) by centrifugation at 1,300 rcf for 1.5 hr. The infected cells were selected with 0.7 μ g/ml of puromycin (Sigma) in RPMI-1640 medium for at least 36 hrs after infection. shRNA knockdown was induced by culturing the cells with 1 μ g/mL of Doxycycline in RPMI-1640 media for at least 24 hrs followed by Western blot analysis.

Overexpression of BCL2 and MYC in T-ALL Cells

Retrovirus were produced by co-transfecting the retrovirus vector, MSCV-IRES-GFP containing the *BCL2* or *MYC* cDNA with packaging plasmids, pMD-MLV and the envelope plasmid pCMV-VSV-G into 293T cells by using FuGENE 6 transfection reagent

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(Promega). Supernatants containing retrovirus particles were collected and filtered through a 0.45 µm filter (Thermo). Jurkat cells were infected in the presence of polybrene (8 µg/ml; Millipore) by centrifugation at 1,300 rcf for 1.5 hr. After 3 days, infected cells were analyzed with a BD[™] LSR II flow cytometer using BD FACSDiva[™] software. Successfully infected cells that express GFP were sorted using FACS Aria Flow Cytometer (BD Biosciences).

Inducible CRISPR/Cas9 Knockout

Cas9-expressing Jurkat cells was established using lentiviruses produced through cotransfecting of FUCas9Cherry (Addgene plasmid #70182) with the packaging plasmids pMDLg/pRRE and pRSV-Rev and the envelope plasmid pMD2.G into 293T cells. after infection, cells were analyzed with a BD[™] LSR II flow cytometer using BD FACSDiva[™] software. Successfully infected cells that express mCherry were sorted using FACS Aria Flow Cytometer (BD Biosciences). The single guide RNA (sgRNA) sequences targeting the ARID5B genomic DNA were designed using the CRISPR Design Tool (http://crispr.mit.edu/) and cloned into the inducible lentivirus expression vector FgH1tUTG (Addgene plasmid # 70183) using BsMB1 enzyme sites. Lentivirus was produced using the same protocol as described for shRNA knockdown and infected into Jurkat cells that stably expresses Cas9. After 3 days, cells were analyzed with a BD™ LSR II flow cytometer. Dual-positive eGFP and mCherry cells were sorted using FACS Aria Flow Cytometer (BD Biosciences). sgRNA expression was induced by culturing cells with 1 µg/mL of Doxycycline in RPMI-1640 media for 6 days and protein expression was analyzed using Western blot.

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Zebrafish Genotyping

Zebrafish were selected based on the presence of mCherry fluorescence and subsequently genotyped using primers targeting the human *ARID5B* gene. The primers used for sequencing were as follows: rag2, forward, 5'-AAA TGG AAG GCC TGG AAG CAT CGG-3'; ARID5B, reverse, 5'-GTC CTC TCT TCC CAC AAC AGC-3'.

Supplemental Figure Legend

Supplemental Figure S1. ARID5B is regulated under the -135kb enhancer in T-ALL

(A) Gene expression changes of 13 target genes of the TAL1 transcriptional complex after TAL1 knockdown. See Figure 1A legend for details. (B) Schematic diagram indicating the sgRNA target sites (blue arrows), PCR primers (gray arrows) and the size of the deleted region (green arrows). (C) The sgRNAs (#1 and 2) targeting the 5' and 3' ends of the -135 kb element, respectively, or a control sgRNA targeting EGFP were transduced into Jurkat cells by lentiviral infection. Genomic DNA was harvested at day 6 after lentivirus infection and amplified using specific primers by PCR. (D) Sanger sequence chromatogram in the knockout cells. The black arrowheads indicate the genomic DNA cleavage site targeted by the sgRNA (#1 or #2). (E) The mRNA expression of exon 7 of the C10orf107 gene, which is located under the -135 kb element, was measured by qRT-PCR analysis in control and knockout samples. *p<0.05 by two-sample, two-tailed t-test. (F) Gene Expression Commons database showing mouse Arid5b mRNA expression in hematopoietic cell subpopulations. (G) Expression of human ARID5B gene in different stage of human hematopoietic cells were analyzed using an RNA-seq dataset reported by Casero et al. (Casero et al. 2015). Two samples were included for each fraction in the original dataset. Expressions are shown by FPKM values. Hematopoietic stem cells (HSC), CD34⁺CD38^{neg}lin^{neg}; lymphoid-primed multipotent progenitors (LMPP), CD34⁺CD38⁺CD10^{neg}CD45RA⁺CD62L^{high}lin^{neg}; common lymphoid progenitor (CLP), CD34⁺CD38⁺CD10⁺CD45RA⁺lin^{neg}; Thy1, CD34⁺CD7^{neg}CD1a^{neg}CD4^{neg}CD8^{neg}; Thy2, CD34+CD7+CD1a^{neg}CD4^{neg}CD8^{neg}; Thy3, CD34+CD7+CD1a+CD4^{neg}CD8^{neg}; Thy4, CD4⁺CD8⁺; Thy5, CD3⁺CD4⁺CD8^{neg}; and Thy6, CD3⁺CD4^{neg}CD8⁺. Thy1-3, Thy4, Thy5

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and Thy6 represent double-negative (DN), double-positive (DP), CD4 single-positive (SP) and CD8 SP cells, respectively.

Supplemental Figure S2. ARID5B overexpression supports the survival of TAL1positive T-ALL cells

(A) Cell viability of Jurkat cells overexpressing BCL2 was measured by CellTiter Glo assay at days 3, 5 and 7 post-infection with lentivirus expressing shLUC, (control), shARID5B-3 or shARID5B-7. Cell growth rates (fold-change compared to day 3) are shown as the mean \pm standard deviation (SD) of duplicate samples. (B) Western blot analysis for protein expressions of ARID5B, PARP and α -tubulin (loading control) in Jurkat cells on day 3 after shRNA-expressing lentivirus infection. (C) Cell cycle distribution of Jurkat cells on day 3 after shRNA-expressing lentivirus infection was measured by flow cytometry using propidium iodide DNA staining. The data represent the mean \pm SD of duplicate samples. (D) Detection of apoptosis by Annexin V staining in CCRF-CEM, PF-382, MOLT-4 and LOUCY cells on day 3 after transduction with shRNA-expressing lentivirus. The data represent the mean of duplicate samples. See Figure 2B legend for details.

Supplemental Figure S3: ARID5B-bound regions are predominantly associated with active histone marks. (A) Immunoprecipitation assay performed in Jurkat cells with IgG, ARID5B or TAL1-specific antibodies. The whole-cell lysate (WCL), immunoprecipitate (IP) and flow-through (FT) were analyzed by immunoblotting (IB) with HDAC1-, HDAC2-, HDAC3- and HDAC4-specific antibodies. Of note, TAL1 did not interact with any of HDAC proteins in this analysis. (B) mRNA expression of EGR1, EGR2 and CDKN1A in Jurkat cells on day 3 after infection with shGFP and shARID5B-3 was analyzed by qRT-PCR. The relative gene expression was normalized to the ERCC Spikein exogenous control (*E130*). The data represent the mean \pm SD of duplicate samples. *p<0.05 by two-sample, two-tailed t-test. (C) mRNA expression of EGR1, EGR2 and CDKN1A. Jurkat cells treated for 24 hrs with DMSO or a small-molecule HDAC inhibitor (SAHA) at a concentration of 2 μ M were analyzed by qRT-PCR. The relative gene expression was normalized to the ERCC Spike-in exogenous control (E130). The data represent the mean ± SD of duplicate samples. *p<0.05, **p<0.01 by two-sample, twotailed t-test. (D) "Active" genes in Jurkat were defined as those bound by RNA polymerase II and H3K4me3 within +/- 2.5 kb of the TSS and also bound by H3K79me2 in the first 5 kb of the gene. All selected genes were then ranked by the ARID5B signals. Top 500 genes with the highest ARID5B signals (ARID5B targets). Bottom 500 genes with the lowest ARID5B signals (non-ARID5B targets). (E) Jurkat cells were transduced with shLUC (control), shARID5B-3 or shARID5B-7 for 3 days. Protein expression of ARID5B, H3K27ac and total H3 (loading control) were analysed by Western blot. (F) WCL was subjected to immunoprecipitation using an anti-ARID5B antibody or control IgG followed by immunoblotting (IB) analysis with an anti-ARID5B or PHF2 antibody. IP, immunoprecipitant; FT, flowthrough. (G) 293T cells were transfected with constructs for expression of human ARID5B and PHF2 cDNAs. At 48 hours after transfection, WCL were subjected to immunoprecipitation using an anti-ARID5B antibody followed by immunoblotting (IB) with an anti-ARID5B or PHF2 antibody.

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Supplemental Figure S4. ARID5B transcriptionally activates *MYC* oncogene in T-ALL cells

(A) ChIP enrichment analysis (ChEA) and Gene ontology (GO) analysis were performed in the Enricher program by using genes that were significantly downregulated after knockdown of each of transcription factors (TAL1, GATA3, RUNX1, MYB) (with an adjusted p-value<0.05 and a log2 fold-change<-0.5 between 2 control and 2 knockdown samples). The top 10 terms ranked by the combined score are shown. (B) Western blot analysis for protein expression of MYC in Jurkat cells overexpressing BCL2 on day 3 after the transduction of lentivirus expressing shLUC, shARID5B-3 or shARID5B-7. (C) The sgRNA targeting exon 6 of ARID5B gene was induced using a doxycycline-induced system in Jurkat cells expressing Cas9 protein to knock out ARID5B protein. Protein expression of MYC was analyzed by Western blot in control and knockout samples. (D) ChIP analysis was performed using an anti-ARID5B antibody or control IgG in Jurkat, CCRF-CEM, RPMI-8042 and LOUCY cells. Fold enrichment of ChIP samples compared to input (whole cell lysate) at the NOTCH1-driven MYC enhancer region was measured by PCR. Negative control (IGFBP3 genomic region) that is not bound by TAL1 or ARID5B and is not associated with active histone marks was used for normalization. The error bars represent the SD of the fold enrichment. *p<0.05, ***p<0.001 by two-sample, twotailed t-test. (E) Jurkat cells were transduced with a doxycycline-inducible shRNA targeting ARID5B. The cells were treated with or without doxycycline for 48 hours. ChIP analysis was performed using an anti-H3K27ac antibody or control IgG in control and knockdown samples. Fold enrichment of ChIP samples compared to input (whole cell

Iysate) around the NOTCH1-driven *MYC* enhancer region was measured by PCR. (**F**) Cell viability of Jurkat cells overexpressing *MYC* was measured by CellTiter Glo assay at days 3, 5 and 7 post-infection with lentivirus expressing shLUC (control), shARID5B-3 or shARID5B-7. Cell growth rates (fold-change compared to day 3) are shown as the mean \pm SD of duplicate samples. (**G**) mRNA expression of *MYC* in T-ALL cell lines was determined by microarray analysis. (**H**) Relative expression of mouse *Myc* in DN1, DN2 and DN3 populations harvested from the thymus of 8 to 10 weeks old *NOD-Rag1^{null} IL2rg^{null}*(*NRG*) mice. See Figure 1H legend for details. *p<0.05, **p<0.01 by two-sample, two-tailed t-test.

Supplemental Figure S5. ARID5B coordinately regulates the expression of TAL1 targets in T-ALL cells

Heatmap image representing the expression levels of TAL1 target genes in shGFP (control) and shARID5B knockdown samples.

Supplemental Figure S6. ARID5B positively regulates the expression of the TAL1 complex in T-ALL cells

(A-D) Occupancy of ARID5B at the *TAL1* (A), *GATA3* (B), *RUNX1* (C) and *MYB* (D) enhancer regions in Jurkat, CCRF-CEM, RPMI-8042 and LOUCY cells was analyzed by ChIP-PCR. See Supplemental Figure S4D legend for details. *p<0.05, ***p<0.001 by two-sample, two-tailed t-test. (E-H) H3K27ac signals at the *TAL1* (E), *GATA3* (F), *RUNX1* (G) and *MYB* (H) enhancer regions in Jurkat. See Supplemental Figure S4E legend for details.

*p<0.05, **p<0.01 by two-sample, two-tailed t-test. **(I)** Protein expression of ARID5B, TAL1, GATA3, RUNX1, MYB and α-tubulin on day 6 after the doxycycline-induced expression of sgRNA targeting ARID5B. See Supplemental Figure S4C legend for details. **(J)** Western blot analysis for protein expression of TAL1 in Jurkat cells overexpressing BCL2 on day 3 after the transduction of lentivirus expressing shLUC, shARID5B-3 or shARID5B-7

Supplemental Figure S7. Overexpression of ARID5B leads to thymus retention and the development of T-cell lymphoma in zebrafish

(A) Clustal Omega protein sequence alignment of the full-length human *ARID5B* and zebrafish *arid5b* proteins. (B) Schematic diagram of the plasmids that were co-injected into one-cell-stage embryos. Meganuclease I-Scel was used to digest and insert the zebrafish *rag2* promoter into the target gene sequences of the zebrafish genomic DNA. (C) Genotype of *rag2-ARID5B* transgenic zebrafish. Genomic DNA extracted from the zebrafish fin was subjected to PCR using *rag2* forward, *ARID5B* forward and *ARID5B* reverse primers.

Supplemental Tables, provided as Excel files

Supplemental Table 1. Genes significantly downregulated or upregulated by ARID5B knockdown

Supplemental Table 2. ChEA and gene ontology analysis for genes differentiallyregulated by transcription factors

Supplemental Table 3. Genes significantly downregulated after TAL1 knockdown

Supplemental References

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Supplemental Figure 1

Leong_FigS2



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Supplemental Figure 2



Supplemental Figure 3

Leong_FigS3

А ChEA ΤΔΙ 1

IALI	p-value	
RUNX_20019798_ChIP-Seq_JUKART_Human	9.27E-09	leukocyte activation (GO:0045321)
NOTCH1_21737748_ChIP-Seq_TLL_Human	5.29E-07	leukocyte differentiation (GO:0002521)
RUNX1_17652178_ChIP-ChIP_JURKAT_Human	8.40E-07	lymphocyte differentiation (GO:0030098)
TRIM28_21343339_ChIP-Seq_HEK293_Human	7.77E-05	positive regulation of alpha-beta 1 cell activati
SOX2_20726797_ChIP-Seq_SW620_Human	4.58E-06	lymphocyte activation (GO:0046649)
ZNF217 24962896 ChIP-Seq_MCF-7_Human	2.98E-06	B cell activation (GO:0042113)
PRDM14 20953172 ChIP-Seq ESCs Human	3.8E-06	tissue morphogenesis (GO:0048729)
CLOCK 20551151 ChIP-Seg 293T Human	0.000215	positive regulation of T cell activation (GO:005
GATA3 27048872 Chip-Seg THYMUS Human	4.26E-06	regulation of response to wounding (GO:1903
MYB 26560356 Chip-Seq_TH1_Human	8.27E-06	B cell differentiation (GO:0030183)
CATA3		
	p-value	regulation of response to wounding (GO:19030
RUNX_20019798_ChIP-Seq_JUKAR1_Human	3.34E-21	leukocyte activation (GO:0045321)
SOX2_20/26/97_ChIP-Seq_SW620_Human	1.18E-12	regulation of cell activation (GO:0050865)
SUZ12_20075857_ChIP-Seq_MESCs_Mouse	4.45E-17	regulation of immune effector process (GO:000
MTF2_20144788_ChIP-Seq_MESCs_Mouse	3.14E-12	positive regulation of cell activation (GO:00508
MYB_21317192_ChIP-Seq_ERMYB_Mouse	3.29E-08	regulation of leukocyte activation (GO:0002694
ZNF217_24962896_ChIP-Seq_MCF-7_Human	3.54E-08	response to virus (GO:0009615)
KDM2B_26808549_Chip-Seq_K562_Human	3.91E-08	loukopute differentiation (CO:0002521)
SUZ12_18692474_ChIP-Seq_MEFs_Mouse	2.19E-06	regulation of loukoouto modiated immunity (GC
SCL_21571218_ChIP-Seq_MEGAKARYOCYTES_Human	1.17E-07	regulation of leukocyte mediated minutity (GC
SCL_19346495_ChIP-Seq_HPC-7_Human	0.000187	positive regulation of defense response (GO.0
RUNX1		
RUNX 20019798 ChIP-Seg JUKART Human	p-value	T cell differentiation (GO:0030217)
ZNF217 24962896 ChIP-Seg MCF-7 Human	9.03E-18	positive regulation of secretion (GO:0051047)
CTNNB1 20460455 ChIP-Seg HCT116 Human	1.91E-09	leukocyte activation (GO:0045321)
SOX2 20726797 ChIP-Seq SW620 Human	1.44E-07	myeloid cell activation involved in immune resp
SMAD4 21799915 ChIP-Seg A2780 Human	1.02E-07	positive regulation of secretion by cell (GO:190
SMAD4_21799915_ChIP-Seq_A2780_Human	2.93E-09	positive regulation of secretion by cell (GO:190 T cell activation (GO:0042110)
SMAD4_21799915_ChIP-Seq_A2780_Human GATA3_27048872_Chip-Seq_THYMUS_Human	2.93E-09 2.22E-07	positive regulation of secretion by cell (GO:190 T cell activation (GO:0042110) lymphocyte differentiation (GO:0030098)
SMAD4_21799915_ChIP-Seq_A2780_Human GATA3_27048872_Chip-Seq_THYMUS_Human PAX3-FKHR_20663909_ChIP-Seq_RHABDOMYOSARCOMA_Human	2.93E-07 2.22E-07 6.03E-06	positive regulation of secretion by cell (GO:190 T cell activation (GO:0042110) lymphocyte differentiation (GO:0030098) alpha-beta T cell activation (GO:0046631)
SMAD4_21799915_ChIP-Seq_A2780_Human GATA3_27048872_Chip-Seq_THYMUS_Human PAX3-FMHR_20663909_ChIP-Seq_RHABDOMYOSARCOMA_Human FOXA2_19822575_ChIP-Seq_HepG2_Human	1.82E-07 2.93E-09 2.22E-07 6.03E-06 5.16E-08	positive regulation of secretion by cell (GO:190 T cell activation (GO:0042110) lymphocyte differentiation (GO:0030098) alpha-beta T cell activation (GO:0046631) positive regulation of lymphocyte differentiation
SMAD4_21799915_ChIP-Seq_A2780_Human GATA3_27048872_Chip-Seq_THYMUS_Human PAX3-FKHR_20663909_ChIP-Seq_RHABDOMYOSARCOMA_Human FOXA2_19822575_ChIP-Seq_HepG2_Human PRDM14_20953172_ChIP-Seq_ESCs_Human	2.93E-07 2.93E-09 2.22E-07 6.03E-06 5.16E-08 5.54E-06	positive regulation of secretion by cell (GO:190 T cell activation (GO:0042110) lymphocyte differentiation (GO:0030098) alpha-beta T cell activation (GO:0046631) positive regulation of lymphocyte differentiation regulation of lymphocyte differentiation (GO:00
SMAD4_21799915_ChIP-Seq_A2780_Human GATA3_27048872_Chip-Seq_THYMUS_Human PAX3-FKHR_20663909_ChIP-Seq_RHABDOMYOSARCOMA_Human FOXA2_19822575_ChIP-Seq_HepG2_Human PRDM14_20953172_ChIP-Seq_ESCs_Human AR_22383394_ChIP-Seq_PROSTATE_CANCER_Human	2.93E-07 2.93E-09 2.22E-07 6.03E-06 5.16E-08 5.54E-06 3.42E-06	positive regulation of secretion by cell (GO:190 T cell activation (GO:0042110) lymphocyte differentiation (GO:0030098) alpha-beta T cell activation (GO:0046631) positive regulation of lymphocyte differentiation regulation of lymphocyte differentiation (GO:00
SMAD4_21799915_ChIP-Seq_A2780_Human GATA3_27048872_Chip-Seq_THYMUS_Human PAX3-FKHR_20663909_ChIP-Seq_RHABDOMYOSARCOMA_Human FOXA2_19822575_ChIP-Seq_HepG2_Human PRDM14_20953172_ChIP-Seq_ESCs_Human AR_22383394_ChIP-Seq_PROSTATE_CANCER_Human MYB	2.93E-09 2.22E-07 6.03E-06 5.16E-08 5.54E-06 3.42E-06	positive regulation of secretion by cell (GO:190 T cell activation (GO:0042110) lymphocyte differentiation (GO:0030098) alpha-beta T cell activation (GO:0046631) positive regulation of lymphocyte differentiation regulation of lymphocyte differentiation (GO:00
SMAD4_21799915_ChIP-Seq_A2780_Human GATA3_27048872_Chip-Seq_THYMUS_Human PAX3-FKIHR_20663909_ChIP-Seq_RHABDOMYOSARCOMA_Human FOXA2_19822575_ChIP-Seq_HepG2_Human PRDM14_20953172_ChIP-Seq_ESCs_Human AR_22383394_ChIP-Seq_PROSTATE_CANCER_Human MYB RUNX_20019798_ChIP-Seq_JUKART_Human	2.93E-09 2.22E-07 6.03E-06 5.16E-08 5.54E-06 3.42E-06 p-value 3.79E-12	positive regulation of secretion by cell (GO:190 T cell activation (GO:0042110) lymphocyte differentiation (GO:0030098) alpha-beta T cell activation (GO:0046631) positive regulation of lymphocyte differentiation regulation of lymphocyte differentiation (GO:00 ncRNA metabolic process (GO:0034660)
SMAD4_21799915_ChIP-Seq_A2780_Human GATA3_27048872_Chip-Seq_THYMUS_Human PAX3-FKIHR_20663909_ChIP-Seq_RHABDOMYOSARCOMA_Human FOXA2_19822575_ChIP-Seq_HepG2_Human PRDM14_20953172_ChIP-Seq_ESCs_Human AR_22383394_ChIP-Seq_PROSTATE_CANCER_Human MYB RUNX_20019798_ChIP-Seq_JUKART_Human NOTCH1_21737748_ChIP-Seq_TLL_Human	1.52E-07 2.93E-09 2.22E-07 6.03E-06 5.16E-08 5.54E-06 3.42E-06 p-value 3.79E-12 1.05E-07	positive regulation of secretion by cell (GO:190 T cell activation (GO:0042110) lymphocyte differentiation (GO:0030098) alpha-beta T cell activation (GO:0046631) positive regulation of lymphocyte differentiation regulation of lymphocyte differentiation (GO:00 ncRNA metabolic process (GO:0034660) rRNA metabolic process (GO:0016072)
SMAD4_21799915_ChIP-Seq_A2780_Human GATA3_27048872_Chip-Seq_THYMUS_Human PAX3-FKIHR_20663909_ChIP-Seq_RHABDOMYOSARCOMA_Human FOXA2_19822575_ChIP-Seq_HepG2_Human PRDM14_20953172_ChIP-Seq_ESCs_Human AR_22383394_ChIP-Seq_PROSTATE_CANCER_Human MYB RUNX_20019798_ChIP-Seq_JUKART_Human NOTCH1_21737748_ChIP-Seq_TLL_Human EKLF_21900194_ChIP-Seq_ERYTHROCYTE_Mouse	1.52E-07 2.93E-09 2.22E-07 6.03E-06 5.16E-08 5.54E-06 3.42E-06 p-value 3.79E-12 1.05E-07 4.70E-10	positive regulation of secretion by cell (GO:190 T cell activation (GO:0042110) lymphocyte differentiation (GO:0030098) alpha-beta T cell activation (GO:0046631) positive regulation of lymphocyte differentiation regulation of lymphocyte differentiation (GO:00 ncRNA metabolic process (GO:0034660) rRNA metabolic process (GO:0016072) cholesterol biosynthetic process (GO:0006695
SMAD4_21799915_ChIP-Seq_A2780_Human GATA3_27048872_Chip-Seq_THYMUS_Human PAX3-FKIHR_20663909_ChIP-Seq_RHABDOMYOSARCOMA_Human FOXA2_19822575_ChIP-Seq_HepG2_Human PRDM14_20953172_ChIP-Seq_ESCs_Human AR_22383394_ChIP-Seq_PROSTATE_CANCER_Human MYB RUNX_20019798_ChIP-Seq_JUKART_Human NOTCH1_21737748_ChIP-Seq_TLL_Human EKLF_21900194_ChIP-Seq_ERYTHROCYTE_Mouse CLOCK_20551151_ChIP-Seq_293T_Human	1.52E-07 2.93E-09 2.22E-07 6.03E-06 5.16E-08 5.54E-06 3.42E-06 p-value 3.79E-12 1.05E-07 4.70E-10 3.53E-07	positive regulation of secretion by cell (GO:190 T cell activation (GO:0042110) lymphocyte differentiation (GO:0030098) alpha-beta T cell activation (GO:0046631) positive regulation of lymphocyte differentiation regulation of lymphocyte differentiation (GO:00 ncRNA metabolic process (GO:0034660) rRNA metabolic process (GO:0016072) cholesterol biosynthetic process (GO:0006695 rRNA processing (GO:0006364)
SMAD4_21799915_ChIP-Seq_A2780_Human GATA3_27048872_Chip-Seq_THYMUS_Human PAX3-FKIHR_20663909_ChIP-Seq_RHABDOMYOSARCOMA_Human FOXA2_19822575_ChIP-Seq_HepG2_Human PRDM14_20953172_ChIP-Seq_ESCs_Human AR_22383394_ChIP-Seq_PROSTATE_CANCER_Human MYB RUNX_20019798_ChIP-Seq_JUKART_Human NOTCH1_21737748_ChIP-Seq_JUKART_Human EKLF_21900194_ChIP-Seq_ERYTHROCYTE_Mouse CLOCK_20551151_ChIP-Seq_293T_Human MYC_19079543_ChIP-ChIP_MESCs_Mouse	2.93E-07 2.92E-07 6.03E-06 5.16E-08 5.54E-06 3.42E-06 p-value 3.79E-12 1.05E-07 4.70E-10 3.53E-07 5.59E-08	positive regulation of secretion by cell (GO:190 T cell activation (GO:0042110) lymphocyte differentiation (GO:0030098) alpha-beta T cell activation (GO:0046631) positive regulation of lymphocyte differentiation regulation of lymphocyte differentiation (GO:00 ncRNA metabolic process (GO:0034660) rRNA metabolic process (GO:0016072) cholesterol biosynthetic process (GO:0006695 rRNA processing (GO:0006364) small molecule biosynthetic process (GO:0044
SMAD4_21799915_ChIP-Seq_A2780_Human GATA3_27048872_Chip-Seq_THYMUS_Human PAX3-FKIHR_20663909_ChIP-Seq_RHABDOMYOSARCOMA_Human FOXA2_19822575_ChIP-Seq_HepG2_Human PRDM14_20953172_ChIP-Seq_ESCs_Human AR_22383394_ChIP-Seq_PROSTATE_CANCER_Human MYB RUNX_20019798_ChIP-Seq_PROSTATE_CANCER_Human NOTCH1_21737748_ChIP-Seq_JUKART_Human NOTCH1_21737748_ChIP-Seq_TLL_Human EKLF_21900194_ChIP-Seq_ERYTHROCYTE_Mouse CLOCK_20551151_ChIP-Seq_293T_Human MYC_19079543_ChIP-ChIP_MESCs_Mouse MYC_19030024_ChIP-ChIP_MESCs_Mouse	1.52E-07 2.93E-09 2.22E-07 6.03E-06 5.16E-08 5.54E-06 3.42E-06 p-value 3.79E-12 1.05E-07 4.70E-10 3.53E-07 5.59E-08 1.64E-12	positive regulation of secretion by cell (GO:190 T cell activation (GO:0042110) lymphocyte differentiation (GO:0030098) alpha-beta T cell activation (GO:0046631) positive regulation of lymphocyte differentiation regulation of lymphocyte differentiation (GO:00 ncRNA metabolic process (GO:0034660) rRNA metabolic process (GO:0016072) cholesterol biosynthetic process (GO:0006695 rRNA processing (GO:0006364) small molecule biosynthetic process (GO:0016126)
SMAD4_21799915_ChIP-Seq_A2780_Human GATA3_27048872_Chip-Seq_THYMUS_Human PAX3-FKIHR_20663909_ChIP-Seq_RHABDOMYOSARCOMA_Human FOXA2_19822575_ChIP-Seq_HepG2_Human PRDM14_20953172_ChIP-Seq_ESCs_Human AR_22383394_ChIP-Seq_PROSTATE_CANCER_Human MYB RUNX_20019798_ChIP-Seq_JUKART_Human NOTCH1_21737748_ChIP-Seq_JUKART_Human EKLF_21900194_ChIP-Seq_ERYTHROCYTE_Mouse CLOCK_20551151_ChIP-Seq_293T_Human MYC_19079543_ChIP-ChIP_MESCs_Mouse MYC_19030024_ChIP-ChIP_MESCs_Mouse MYC_19030024_ChIP-ChIP_MESCs_Mouse MYC_19030024_ChIP-ChIP_MESCs_Mouse	1.52E-07 2.93E-09 2.22E-07 6.03E-06 5.16E-08 5.54E-06 3.42E-06 p-value 3.79E-12 1.05E-07 4.70E-10 3.53E-07 5.59E-08 1.64E-12 2.52E 10	positive regulation of secretion by cell (GO:190 T cell activation (GO:0042110) lymphocyte differentiation (GO:0030098) alpha-beta T cell activation (GO:0046631) positive regulation of lymphocyte differentiation regulation of lymphocyte differentiation (GO:00 ncRNA metabolic process (GO:0034660) rRNA metabolic process (GO:0016072) cholesterol biosynthetic process (GO:0006695 rRNA processing (GO:0006364) small molecule biosynthetic process (GO:0016126) ncRNA propessing (GO:0034470)
SMAD4_21799915_ChIP-Seq_A2780_Human GATA3_27048872_Chip-Seq_THYMUS_Human PAX3-FKHR_20663909_ChIP-Seq_RHABDOMYOSARCOMA_Human FOXA2_19822575_ChIP-Seq_HepG2_Human PRDM14_20953172_ChIP-Seq_ESCs_Human AR_22383394_ChIP-Seq_PROSTATE_CANCER_Human MYB RUNX_20019798_ChIP-Seq_JUKART_Human NOTCH1_21737748_ChIP-Seq_TLL_Human EKLF_21900194_ChIP-Seq_ERYTHROCYTE_Mouse CLOCK_20551151_ChIP-Seq_293T_Human MYC_19079543_ChIP-ChIP_MESCs_Mouse MYC_19030024_ChIP-ChIP_MESCs_Mouse MYB_26560356_Chip-Seq_TH2_Human MYC_19555785_ChIP-Seq_MESCs_Mouse	1.52E-07 2.93E-09 2.22E-07 6.03E-06 5.16E-08 5.54E-06 3.42E-06 p-value 3.79E-12 1.05E-07 4.70E-10 3.53E-07 5.59E-08 1.64E-12 2.52E-10	positive regulation of secretion by cell (GO:190 T cell activation (GO:0042110) lymphocyte differentiation (GO:0030098) alpha-beta T cell activation (GO:0046631) positive regulation of lymphocyte differentiation regulation of lymphocyte differentiation (GO:00 ncRNA metabolic process (GO:0034660) rRNA metabolic process (GO:0016072) cholesterol biosynthetic process (GO:0006695 rRNA processing (GO:0006364) small molecule biosynthetic process (GO:0016126) ncRNA propessing (GO:0034470) cofactor metabolic process (GO:0051186)
SMAD4_21799915_ChIP-Seq_A2780_Human GATA3_27048872_ChiP-Seq_THYMUS_Human PAX3-FKHR_20663909_ChIP-Seq_RHABDOMYOSARCOMA_Human FOXA2_19822575_ChIP-Seq_HepG2_Human PRDM14_20953172_ChIP-Seq_ESCs_Human AR_22383394_ChIP-Seq_PROSTATE_CANCER_Human MYB RUNX_20019798_ChIP-Seq_UKART_Human NOTCH1_21737748_ChIP-Seq_UKART_Human EKLF_21900194_ChIP-Seq_ERYTHROCYTE_Mouse CLOCK_20551151_ChIP-Seq_293T_Human MYC_19079543_ChIP-ChIP_MESCs_Mouse MYC_19030024_ChIP-ChIP_MESCs_Mouse MYC_19030024_ChIP-ChIP_MESCs_Mouse MYB_26560356_ChIP-Seq_TH2_Human MYC_19030024_ChIP-Seq_TH2_Human MYC_19030024_ChIP-Seq_TH2_Human	1.52E-07 2.93E-09 2.22E-07 6.03E-06 5.16E-08 5.54E-06 3.42E-06 p-value 3.79E-12 1.05E-07 4.70E-10 3.53E-07 5.59E-08 1.64E-12 2.52E-10 2.95E-07 2.15E-07	positive regulation of secretion by cell (GO:190 T cell activation (GO:0042110) lymphocyte differentiation (GO:0030098) alpha-beta T cell activation (GO:0046631) positive regulation of lymphocyte differentiation regulation of lymphocyte differentiation (GO:00 ncRNA metabolic process (GO:0034660) rRNA metabolic process (GO:0016072) cholesterol biosynthetic process (GO:0006695 rRNA processing (GO:0006364) small molecule biosynthetic process (GO:0016126) ncRNA propessing (GO:0034470) cofactor metabolic process (GO:0051186) nucleob ase metabolic process (GO:0009112)
SMAD4_21799915_ChIP-Seq_A2780_Human GATA3_27048872_ChiP-Seq_THYMUS_Human PAX3-FKHR_20663909_ChIP-Seq_RHABDOMYOSARCOMA_Human FOXA2_19822575_ChIP-Seq_HepG2_Human PRDM14_20953172_ChIP-Seq_ESCs_Human AR_22383394_ChIP-Seq_PROSTATE_CANCER_Human MYB RUNX_20019798_ChIP-Seq_PROSTATE_CANCER_Human NOTCH1_21737748_ChIP-Seq_JUKART_Human EKLF_21900194_ChIP-Seq_JUKART_Human KUC_19079543_ChIP-Seq_ERYTHROCYTE_Mouse CLOCK_20551151_ChIP-Seq_293T_Human MYC_19079543_ChIP-ChIP_MESCs_Mouse MYB_26560356_ChIP-Seq_TH2_Human MYC_185557_85_ChIP-Seq_ERYTH2_Human MYC_185557_85_ChIP-Seq_ERYTB_Mouse	1.52E-07 2.93E-09 2.22E-07 6.03E-06 5.16E-08 5.54E-06 3.42E-06 p-value 3.79E-12 1.05E-07 4.70E-10 3.53E-07 5.59E-08 1.64E-12 2.52E-10 2.95E-07 3.15E-07	positive regulation of secretion by cell (GO:190 T cell activation (GO:0042110) lymphocyte differentiation (GO:0030098) alpha-beta T cell activation (GO:0046631) positive regulation of lymphocyte differentiation regulation of lymphocyte differentiation (GO:00 ncRNA metabolic process (GO:0034660) rRNA metabolic process (GO:0016072) cholesterol biosynthetic process (GO:0006695 rRNA processing (GO:0006364) small molecule biosynthetic process (GO:0016126) ncRNA propessing (GO:0034470) cofactor metabolic process (GO:0051186) nucleob ase metabolic process (GO:009112) cofactor biosynthetic process (GO:0051188)

GO Biological Process

0	
	p-value
leukocyte activation (GO:0045321)	1.46E-07
leukocyte differentiation (GO:0002521)	1.71E-07
lymphocyte differentiation (GO:0030098)	1.96E-06
positive regulation of alpha-beta T cell activation (GO:0046635)	4.39E-06
lymphocyte activation (GO:0046649)	1.26E-05
B cell activation (GO:0042113)	9.97E-06
tissue morphogenesis (GO:0048729)	3.76E-05
positive regulation of T cell activation (GO:0050870)	2.78E-05
regulation of response to wounding (GO:1903034)	7.65E-05
B cell differentiation (GO:0030183)	3.04E-05
()	

regulation of response to wounding (GO:1903034)	p-value 3.59E-09
leukocyte activation (GO:0045321)	3.57E-08
regulation of cell activation (GO:0050865)	2.05E-07
regulation of immune effector process (GO:0002697)	2.03E-07
positive regulation of cell activation (GO:0050867)	4.27E-07
regulation of leukocyte activation (GO:0002694)	8.73E-07
response to virus (GO:0009615)	4.69E-07
leukocyte differentiation (GO:0002521)	5.16E-07
regulation of leukocyte mediated immunity (GO:0002703)	3.18E-07
positive regulation of defense response (GO:0031349)	1.2E-06

	n value		p-value
		T cell differentiation (GO:0030217)	3.60E-06
	9.03E-10	positive regulation of secretion (GO:0051047)	3.08E-05
	1.91E-09	leukocyte activation (GO:0045321)	2.82E-05
	1.44E-07	myeloid cell activation involved in immune response (GO:0002275)	6 28E-05
	1.82E-07	positive regulation of secretion by cell (GO:1903532)	4 69E-05
	2.93E-09	T cell activation (GO:00/2110)	2 855 05
	2.22E-07	humphonite differentiation (CO:00220000)	2.00L-00
OSARCOMA_Human	6.03E-06	lymphocyte differentiation (GQ:0030098)	1.00E-05
	5.16E-08	alpha-beta I cell activation (GO:0046631)	5.92E-05
	5 54F-06	positive regulation of lymphocyte differentiation (GO:0045621)	1.92E-05
Human	3.42E-06	regulation of lymphocyte differentiation (GO:0045619)	4.21E-05
	0.422 00		
	n-value		p-value
	2 70E 12	ncRNA metabolic process (GO:0034660)	1 44F-11
	3.79E-1Z	rRNA metabolic process (GO:0016072)	2 53E-10
01100	1.05E-07	cholesterol biosynthetic process (GO:0006695)	1 20E 00
ouse	4.70E-10	rRNA processing (GO:0006364)	1.30E-09
	3.53E-07	small molecule biosynthetic process (GO:0044283)	1.96E-09
	5.59E-08	staral hissupthatic process (CO:0016126)	7.39E-09
	1.64E-12	Sterol biosynthetic process (GO:0010120)	1.09E-08
	2.52E-10	Incrina processing (GO:0034470)	2.18E-08
	2.95E-07	cofactor metabolic process (GO:0051186)	3.20E-08
	3 15E-07	nucleobase metabolic process (GO:0009112)	1.71E-08
	1 25E-07	cofactor biosynthetic process (GO:0051188)	3.10E-08
	1.200-07		



	Control ARID5B KD		Control	ARID5B KD
TRPC6 CX3CR1 LINC00892 GRB10 SIGLEC6 TNFRSF10D TPO		CCDC58 IQGAP2 CHST12 HHIP-AS1 CKLF-CMTM1 MYB TRIB1		
CAB39L INSIG1 PROX1-AS1 CCR2 PPM1H BTBD11 LYSMD2 SYPL1		ZNF429 EPSTI1 RNF168 ANXA3 MYCN TM7SF3 BICD2 GIMAP4		
ALDH1A2 RPL34-AS1 CTDSPL GCNT1 ARID5B BTBD3 TSHR PLCH1		CMIM1 SERINC5 PARP11 TCF7 TOP1 ZNF22 ISYNA1 LYL1		
STAT5A ZNF521 TRAM1 YBX3 PRKG2 PLCE1 ARL4C		CSTA TLE4 NEK7 ZNF652 ADCYAP1 ZNF792 TOMM20		
PAFAH2 UBE3C TSC22D3 TNFSF4 ITGA4 CPOX H6PD TAL1		DPF3 PRKCE REEP5 TEX30 TSPAN7 SIPA1L2 TULP4 FAM/6C		
ETV6 EARS2 TNFSF10 BCL9 STT3B SNTB1 TESPA1		MED12L SCML1 NKX3-1 ZFP91 FLT1 CR2 SAMSN1		
SELL ETV5 LEF1-AS1 RAB11FIP1 ARHGAP12 CD84 CEBPE		CD28 TGFBR2 ZBTB16 HHIP PREX2 MGAT4A CELF2		
CHCHD2 CHI3L2 RAD23A SVOPL TYW3 HES1 C9		ADAMTS19 STK17B NDST3 PI16 CYP4F2 PCDH9 FUT8 B4CALT6		
NIAAU125 SLC16A7 PLCL2 BNIP3L GZMA POLR2D		B4GAL16 ICOS NETO1 KSR2 CD69 EPAS1		



Supplemental Figure 5

Leong_FigS6



Supplemental Figure 6

CLUSTAL O(1.2.4) multiple sequence alignment

Hu Ze	ıman brafish	MEPNSLOWVGSPCGLHGPYI FYKAFQFHLEGKPRI LSLGDFFFVRCTPKDPI CI AELQLL		ladder IV	-W and					
		WEERTSRQLLSSSKLYFLPEDTPQGRNSDHGEDEVI AVSEKVI VKLEDLVKWHSDFSKW 		Hyper	rad2 F					
		RCGFHAGPVKTEALGRNGOKEALLKYROSTLNSGLNFKDVLKEKADLGEDEEETNVI KKGLOAVPLKPGVLKELGKNGOREALHKYRESTLNSGLNFKDVLKEKAELGEDADDKKVL	50	0bp —						
		VLSYPQYCRYRSMLKRI QDKPSSI LTDQFALALGGI AVVSRNPQI LYCRDTEDHPTLI EN VLSYPQYCRYRSI I ARLRERPSSLLTDHVVLALGGI ASLTNSTQI LYCRDTFEHPTLVEN	20	0bp —						
		ESI CDEFAPNLKGRPRKKKP- CPQRRDSFSGVKDSNNNSDGKAVAKVKCEARSALTKPKN ESVCDEFAPNLKGRPRKKKLSI SQRRDSQSGGARESNGVEGKTLVKMRADSKSGVSKPRN								
		NHNCKKVSNEEKPKVAI GEECRADEQAFLVALYKYMKERKTPI ERI PYLGFKQI NLWT PSTGSCKRVQSENKPKGDGGDECRTDEQAFLVALYKYMKERKTPI ERI PYLGFKQI NLWT								
		MFQAAQKLGGYETI TARRQWKHI YDELGGNPGSTSAATCTRRHYERLI LPYERFI KGEED MFQAAQKLGGYEVI TARRQWKNVYDELGGNPGSTSAATCTRRHYERLI LPYERFTKGEED	ARID Domain							
		KPLPPI KPRKOENSSOENENKTKVSGTKRI KHEI PKSKKEKENAPKPODAAEVSSEOEKE KPLPPAKPRKOEGSVOESI I KAKMPI KRPKDEOKTPRODKDASAKVLELGMEDM-								
	QETLI SOKSI PEPLPAADMKKKI EGYQEFSAKPLASRVDPEKD- NETDQGSNS EK - EELQ- EKQ NSQQLQA- PTQTDRDPNSPL TEDDEGVLVI KDEDQP									
	V AEEAGEKGPTPPLPSAPLAPEKDSALVPGASKOPLTSPSALVDSKQESKLCCFTES VLHNAYEHANGGLLPSLPODGAQL									
	PESEPGEASFPSFPTTOPPLANONETEDDKLPAMADYIANCTVKVDQLG EDCDAFPVAAVPLHHGHPLPNSHTSDQWKHGILEYKVPPSALANVEQSRPKEG 									
	SDDI HN ALKQTPKVLVVQSFDMFKDKDLTGPMNENHGLNYTPLLYSRGNPGI MSPLA QNQVVM/LPTLQQKPV TS- PEI PPERVEPLKKEESCFNFNPLLYPRGNPGI MSPLA : : : : : : : : : : : : : : : : :									
	KKKLLSQVSGASLSSSYPYGSPPPLISKKKLIARDDLCSSLSQTHHGQSTDHMAVSRP KKKMLSQVSGTQLLNNYPYGPPPLVSRRLSSSGTEVSSAGQSSSQVSSSVETSIVIRP									
	SVI QHVQSFRSKPSEERKTI NDI FKHEKLSRSDPHRCSFSKHHLNPLADSYVLKQEI QEG SVI QHAQSFKSRGSEDRRSSTEGSQKDQCSEGEPVHHSQTLI REPYLKRVDPHSS									
	KDKLLEKRALPHSHMPSFLADFYSSPHLHSLYRHTEHHLHNEQTSKYPSRDMYRESEN MEKSAEMPRPGQAPSFLSEFYSSPHLHNLCROTEHHLSKEQISKYLSRDVYTRDSETA									
		SSFPSHRHQEKLHVNYLTSLHLQDKKSAAAEAPTDDQPTDLSLPKNPHKPTGKVLG QGFPPSQHPDNVQLNFSARLSQKE-KGPPPERVTEEQPTDLSLPKSSPLKLPLSTSTLGG								
		LAFSTTGPQESKGI SQFQVL - GSQSRDCHPKACRVSPMTMSGPKKYPESLSRSGKP - H I PHAA- I QQDI KNSPHFQAGNSQSSSVDYHPRACRVPPMTVSASKKVTESHSKVLEKTPN : *:: *: *: *: *: *: *: *: *: *: *: *: *								
	HV- RLENFRKMEGM/HPILHRKMSPONIGAARPIKRSLEDLDLVIAGKKARAVSPLDPSK SRGEESMOFKIDEMSRPILSTKSSPONICTARPLKRNIEDLENGPTEKKIRAVTPLHCST									
	EVSGKEKASEQESEGSKAAH- GGHSGGGSEGHKLPLSSPI FPGLYSGSLCNSGLNSR QRDLPGKPRTPEADSESVKPAEPAVHI NSYTSEGHKI PLHSHLFGGLYPGTFVSQVQDMC									
		LPAGYSHSLQYLKNQTVLSPLMOPLAFHSLVMQRGIFTSPTNSQQL ESLGSHVTPS								
Pe AF AF	ercent Ide RID5B pro RID domai	ntity Matrix - created by Clustal2.1 otein: 48.69 in: 88.28								
В	Г									
	_	rag2 promoter ARID5B + Mega	nuclease I-Scel							
	_	rag2 promoter		Injection into cell stage en	one nbryo					

Meganuclease sequences



Hyperladder IV ARID5B FW and ARID5B RV ARID5B RV ARID5B RV

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