

Table 1: Experimental evidence for regulatory connections in the T-cell gene regulatory network. Confidence levels for regulatory interaction are given as follows: 1 – Evidence in non-T cells only; 2 – Evidence from gene perturbation in T-cell progenitors alone, or from cis-regulatory analysis in T-cell progenitors alone; 3 – Evidence from gene perturbation in T-cell progenitors and cis-regulatory analysis. P – post-transcriptional regulatory interaction. FL – fetal liver, BM – bone marrow. Cited references are given below.

Source	Sign	Target	Level	Experiment	Cell Type	Reference
Bcl11b	+	CD3e	2	Bcl11b over-expression + <i>in vitro</i> T-cell culture + mRNA analysis	Bcl11b-/ FL Lin-Sca1+Kit+ (LSK)	[1]
Bcl11b	-	CEBPa	2	Bcl11b over-expression + <i>in vitro</i> T-cell culture + mRNA analysis	Bcl11b-/ FL Lin-Sca1+Kit+ (LSK)	[1]
Bcl11b	-	Id2	1	mRNA expression profiling ChIP-seq using Bcl11b antibody	Bcl11b-/ double positive thymocytes	[2]
Bcl11b	-	Kit	2	Bcl11b over-expression + <i>in vitro</i> T-cell culture + surface expression analysis using flow cytometry	Bcl11b-/ FL Lin-Sca1+Kit+ (LSK)	[1]
Bcl11b	+	pTa	2	Bcl11b over-expression + <i>in vitro</i> T-cell culture + mRNA analysis	FL Lin-Sca1+Kit+ (LSK) cells	[1]
Bcl11b	-	PU.1	2	Bcl11b over-expression + <i>in vitro</i> T-cell culture + mRNA analysis	FL Lin-Sca1+Kit+ (LSK) cells	[1]
Deltex	-	Notch signaling	P	Deltex over-expression + Notch reporter measurements	Jurkat T-cell line	[3]
E protein activity	-	Gata3	2	<i>In vitro</i> T-cell culture + mRNA expression analysis mRNA expression analysis	HEB-/ Rag1-/ DN3 cells E47 ^{bm/bm} thymocytes (bm – DNA-binding site mutation)	[4] [5]
E protein activity	+	Gata3	1	Analysis of Gata3 cis-regulatory element (WT/mutated E-protein binding site)	Jurkat T-cell line	[6]
E protein activity	+	Gfi1	2	E47 over-expression + mRNA expression analysis	1F9 E2A-/ T-cell lymphoma line	[7]
E protein activity	+	Gfi1b	2	E47 over-expression + mRNA expression analysis / ChIP analysis using E2A antibody E47 over-expression + mRNA expression analysis	E2A-/ T-cell lymphoma E2A-/ Lin- BM cells (cultured)	[8] [9]
E protein activity	+	HEBAlt	2	Heb over-expression + mRNA expression analysis	P2C2 immature T-cell line	[10]
E protein activity	+	Hes1	2	E47 over-expression + mRNA expression analysis	E2A-/ Lin- BM cells (cultured)	[9]
E protein activity	+	IL-7R α	2	mRNA expression profiling E47 over-expression + mRNA expression analysis	E2A-/ Lin-Sca1+Kit+Flt3-hi (LMPP) E2A-/ Lin- BM cells (cultured)	[11] [9]
E protein activity	+	Lat	2	E47 over-expression + mRNA expression analysis	E2A-/ Lin- BM cells (cultured)	[9]
E protein activity	+	Notch1	3	mRNA expression profiling ChIP analysis using E2A antibody E47 over-expression + Notch1 promoter activity measurements	E2A-/ Lin-Sca1+Kit+Flt3-hi (LMPP) Rag2-/ DN3 thymocytes NIH-3T3 cell line	[11] [12]
E protein activity	+	Notch3	2	E47 over-expression + mRNA expression analysis	E2A-/ Lin- BM cells (cultured)	[9]
E protein	+	pTa	3	E47 over-expression + mRNA	E2A-/ Lin- BM cells	[9]

activity				expression analysis	(cultured)	
E protein activity	+	Rag-1	2	mRNA expression profiling	E2A-/ Lin-Sca1+Kit+Flt3-hi (LMPP)	[11]
Scl/Lyl1/E	+	Id3	1	Lyl1 over-expression + mRNA expression analysis	human AML cells	[13]
Scl/Lyl1/E	+	Hhex	1	Analysis of Hhex enhancer containing Scl sites ChIP-Seq using Scl antibody on putative enhancer	416B progenitor cell line HPC-7 progenitor cell line	[14] [15]
Scl/Lyl1/E	+	Kit	1	mRNA expression analysis	immature B-cells (B220+) from wildtype/SCL transgenic mice	[16]
Scl/Lyl1/E	-	pTa	2	mRNA expression analysis Scl over-expression + pTα enhancer activity analysis	Scl-Lmo1 transgenic mice AD10.1 immature T-cell line	[17]
Scl/Lyl1/E	+	Runx1	1	Scl over-expression + mRNA expression profiling ChIP analysis using Scl antibody	SCL-/ yolk sac cell line yolk sac / FL	[18]
Scl/Lyl1/E	+	Runx3	1	Scl over-expression + mRNA expression profiling ChIP analysis using Scl antibody	SCL-/ yolk sac cell line yolk sac / FL	[18]
Ets1	+	TCRβ	2	Ets1 over-expression + analysis of TCRβ enhancer activity	p19 cell line	[19]
Gata3	-	CEBPa	2	Gata3 over-expression + mRNA expression analysis	Bcl2-transgenic thymocytes	[20]
Gata3	+	Cpa3	3	Gata3 over-expression + mRNA expression analysis	Bcl2-transgenic thymocytes	[20]
Gata3	+	Deltex	1	Gata3 over-expression + mRNA expression analysis	adult DN1 thymocytes	[21]
Gata3	+	Gfi1b	2	Gata3 over-expression + mRNA expression analysis	Bcl2-transgenic thymocytes	[20]
Gata3	-	IL-7Rα	2	Gata3 over-expression + mRNA expression analysis	Bcl2-transgenic thymocytes	[20]
Gata3	+	Kit	2	Gata3 over-expression + mRNA expression analysis	Bcl2-transgenic thymocytes	[20]
Gata3	-	Lef1	2	Gata3 over-expression + mRNA expression analysis	Bcl2-transgenic thymocytes	[20]
Gata3	+	Notch3	2	Gata3 over-expression + mRNA expression analysis	Bcl2-transgenic thymocytes	[20]
Gata3	-	pTa	2	Gata3 over-expression + mRNA expression analysis	Bcl2-transgenic thymocytes	[20]
Gata3	-	PU.1	2	Gata3 over-expression + mRNA expression analysis	Bcl2-transgenic thymocytes	[20]
Gata3	-	Rag-1	2	Gata3 over-expression + mRNA expression analysis	Bcl2-transgenic thymocytes	[20]
Gata3	+	Scl/Tal1	2	Gata3 over-expression + mRNA expression analysis	Bcl2-transgenic thymocytes	[20]
Gata3	-	TCF-1	2	Gata3 over-expression + mRNA expression analysis	Bcl2-transgenic thymocytes	[20]
Gata3	+	TCRβ	2	Measurement of TCRβ enhancer activity (wildtype/mutated GATA binding site)	p5424 T-cell line	[22]
Gfi1	+	Lmo2	1	Gfi1 knockdown + <i>in situ</i> RNA hybridization	Zebrafish embryos	[23]
Gfi1	-	PU.1	3	mRNA expression analysis; ChIP analysis using Gfi1 antibody Gfi1 over-expression/knockdown + <i>in</i>	Gfi1-/ Lin-Sca1+Kit+ (LSK) cells Zebrafish embryos	[24] [23]

				<i>situ</i> RNA hybridization		
Gfi1	+	Rag-1	1	Gfi1 knockdown + <i>in situ</i> RNA hybridization	Zebrafish embryos	[23]
Gfi1	+	Scl/Tal1	1	Gfi1 knockdown + <i>in situ</i> RNA hybridization	Zebrafish embryos	[23]
Gfi1b	+	Bcl11b	1	Gfi1b knockdown + mRNA expression profiling	K562 myeloid leukemic line	[25]
Gfi1b	-	Gata3	2	Gfi1b over-expression + mRNA expression analysis	E2A-/ T-cell lymphoma	[8]
Gfi1b	-	Gfi1	2	Gfi1b over-expression + mRNA expression analysis mRNA expression analysis	E2A-/ T-cell lymphoma Gfi1b transgenic thymocytes	[8] [26]
Ikaros	-	Gfi1	2	Analysis of Gfi1-GFP reporter expression by flow cytometry	Ikaros-/ Lin-Sca1+Kit+ (LSK) cells with Gfi1-GFP reporter	[24]
Ikaros	-	PU.1	2	mRNA expression analysis	Ikaros-/ Lin-Sca1+Kit+ (LSK) cells	[24]
Ikaros	-	Runx1	2	mRNA expression analysis	Ikaros-/ adult DN thymocytes	[27]
IL-7R/Stat	-	Bcl11b	2	<i>In vitro</i> T-cell culture + IL7 drop + mRNA expression analysis	FL Lin-Sca1+Kit+ (LSK) cells	[1]
IL-7R/Stat	+	CEBPa	2	<i>In vitro</i> T-cell culture + IL7 drop + mRNA expression analysis	FL Lin-Sca1+Kit+ (LSK) cells	[1]
IL-7R/Stat	+	Ebf1	1	constitutive IL7 signaling activation + mRNA expression analysis	IL-7Ra -/ pre-pro B-cells	[28]
IL-7R/Stat	+	GATA3	1	Flow cytometry with intracellular staining using GATA3 antibody ChIP with Stat5 antibody	Stat5 -/ Th2 cells (n.b. cells were stimulated with IL-2 and IL-33)	[29]
IL-7R/Stat	+	Kit	2	<i>In vitro</i> T-cell culture + IL7 drop + mRNA expression analysis	FL Lin-Sca1+Kit+ (LSK) cells	[1]
IL-7R/Stat	-	Lck	2	<i>In vitro</i> T-cell culture + IL7 drop + analysis of Lck reporter	FL Lin-Sca1+Kit+ (LSK) cells	[1]
IL-7R/Stat	-	Lef1	2	IL-7 stimulation + mRNA expression analysis	IL-7Ra transgenic immature thymocytes	[30]
IL-7R/Stat	-	pTa	2	<i>In vitro</i> T-cell culture + IL7 drop + mRNA expression analysis	FL Lin-Sca1+Kit+ (LSK) cells	[1]
IL-7R/Stat	+	PU.1	2	<i>In vitro</i> T-cell culture + IL7 drop + mRNA expression analysis	FL Lin-Sca1+Kit+ (LSK) cells	[1]
IL-7R/Stat	-	TCF-1	2	<i>In vitro</i> T-cell culture + IL7 drop + mRNA expression analysis IL-7 stimulation + mRNA expression analysis	FL Lin-Sca1+Kit+ (LSK) cells IL-7Ra transgenic immature thymocytes	[1] [30]
Lmo2	+	E2A/Scl	P	EMSA assay using Lmo2 and Tal1 antibody	Lmo transgenic immature T-cell line	[31]
Lmo2	+	Hhex	2	mRNA expression analysis	Lmo transgenic DN3 leukemic cells	[32]
Lmo2	+	Kit	2	mRNA expression analysis	Lmo transgenic DN3 leukemic cells	[32]
Lmo2	+	Lyl1	2	mRNA expression analysis	Lmo transgenic DN3 leukemic cells	[32]
Myb	+	Gata3	1	dominant negative Myb over-expression + mRNA expression analysis	E16 cell line	[33]
Notch signaling	+	Bcl11b	3	<i>In vitro</i> culture (+/-DL1) + mRNA expression analysis ChIP analysis using CSL antibody	Thy1+ fetal thymocytes adult thymocytes	[34] [35]

Notch signaling	+	CD25	2	<i>In vitro</i> culture (+/-DL1) + surface expression analysis using flow cytometry surface expression analysis using flow cytometry	FL Lin-Kit+ cells DN3 thymocytes with inhibitor of Notch signaling (DNMAML)	[36] [37]
Notch signaling	+	CD3e	2	<i>In vitro</i> culture (+/-DL1) + mRNA expression analysis	Bcl2-transgenic thymocytes	[20]
Notch signaling	+	CD3g	2	<i>In vitro</i> culture (+/-DL1) + mRNA expression analysis	Bcl2-transgenic thymocytes	[20]
Notch signaling	-	CEBPa		<i>In vitro</i> culture (+/-DL1) + mRNA expression analysis	Thy1+ fetal thymocytes	[34]
Notch signaling	+	Deltex	3	<i>In vitro</i> culture (+/-DL1) + mRNA expression analysis <i>In vitro</i> culture (+/-DL1) + mRNA expression analysis <i>In vitro</i> culture (+/-DL1) + mRNA expression analysis	FL Lin-Kit+cells Thy1+ fetal thymocytes Bcl2-transgenic thymocytes	[36] [34] [20] many earlier references
Notch signaling	+	E2A (weak)	2	<i>In vitro</i> culture (+/-DL1) + mRNA expression analysis	Bcl2-transgenic thymocytes	[20]
Notch signaling	-	Ebf1	2	<i>In vitro</i> culture (+/-DL1) + mRNA expression analysis	FL Lin-Kit+ cells	[36]
Notch signaling	+	Gata3	2	<i>In vitro</i> culture (+/-DL1) + mRNA expression analysis (connection absent in humans)	FL Lin-Kit+ cells	[36] [38, 39]
Notch signaling	+	Gfi1b	2	<i>In vitro</i> culture (+/-DL1) + mRNA expression analysis	Bcl2-transgenic thymocytes	[20]
Notch signaling	+	HEBAlt	2	<i>In vitro</i> culture (+/-DL1) + mRNA expression analysis	Thy1+ fetal thymocytes	[34]
Notch signaling	+	Hes1	2	<i>In vitro</i> culture (+/-DL1) + mRNA expression analysis	FL Lin-Kit+ cells	[36] many earlier references
Notch signaling	-	Id3	2	<i>In vitro</i> culture (+/-DL1) + mRNA expression analysis <i>In vitro</i> culture (+/-DL1) + mRNA expression analysis	Thy1+ fetal thymocytes Bcl2-transgenic thymocytes	[34] [20]
Notch signaling	+	IL-7R α	3	Notch ICD over-expression + <i>in vitro</i> culture + surface expression analysis by flow Notch ICD over-expression + analysis of IL-7R α promoter activity	DN1 thymocytes 293T and Jurkat cell lines	[40]
Notch signaling	+	Lat	2	<i>In vitro</i> culture (+/-DL1) + mRNA expression analysis	Bcl2-transgenic thymocytes	[20]
Notch signaling	+	Lck	2	<i>In vitro</i> culture (+/-DL1) + mRNA expression analysis	Bcl2-transgenic thymocytes	[20]
Notch signaling	+	Lef1	2	<i>In vitro</i> culture (+/-DL1) + mRNA expression analysis	Bcl2-transgenic thymocytes	[20]
Notch signaling	+	Notch1	2	<i>In vitro</i> culture (+/-DL1) + mRNA expression analysis ChIP using CSL antibody Analysis of Notch 1 reporter construct	Bcl2-transgenic thymocytes Rag2-/ thymocytes NIH-3T3 cell line	[20] [12]
Notch signaling	+	Notch3	2	<i>In vitro</i> culture (+/-DL1) + mRNA expression analysis	Bcl2-transgenic thymocytes	[20]
Notch signaling	+	Nrarp	2	Notch IC over-expression + mRNA expression analysis Notch IC over-expression + analysis of Nrarp promoter activity	AKR1010 T-cell line 293T cells	[41] [42]
Notch signaling	+	pTa	3	Notch ICD over-expression + analysis of pTa enhancer activity <i>In vitro</i> culture (+/-DL1) + mRNA	293 cell line Thy1+ fetal thymocytes	[43] [34]

				expression analysis <i>In vitro</i> culture (+/-DL1) + mRNA expression analysis	Bcl2-transgenic thymocytes	[20]
Notch signaling	+	Rag-1	2	<i>In vitro</i> culture (+/-DL1) + mRNA expression analysis	Bcl2-transgenic thymocytes	[20]
Notch signaling	+	Runx1	3	<i>In vitro</i> culture (+/-DL1) + mRNA expression analysis <i>In vitro</i> culture (+/-DL1) + mRNA expression analysis Notch1 over-expression + mRNA expression analysis	Thy1+ fetal thymocytes Bcl2-transgenic thymocytes NIH-3T3 cell line	[34] [20] [44]
Notch signaling	+	TCF-1	2	<i>In vitro</i> culture (+/-DL1) + mRNA expression analysis	FL Lin-Kit+CD27+ progenitors Lin-cKit+Sca1+ (LSK) cells	[45] [46]
Nrarp	-	Notch signaling	P	Nrarp over-expression + mRNA expression analysis of Notch responsive genes	AKR1010 T-cell line	[47]
PU.1	+	Bcl11a	2	PU.1 over-expression + mRNA expression analysis	Thy1+ fetal thymocytes	[34]
PU.1	-	Bcl11b	2	PU.1 over-expression + mRNA expression analysis	Thy1+ fetal thymocytes	[34]
PU.1	-	CD3e	2	PU.1 over-expression + mRNA expression analysis	Thy1+ fetal thymocytes	[34]
PU.1	-	CD3g	2	PU.1 over-expression + mRNA expression analysis	Thy1+ fetal thymocytes	[34]
PU.1	-	E2A	2	PU.1 over-expression + mRNA expression analysis	Thy1+ fetal thymocytes	[34]
PU.1	-	Ets1	2	PU.1 over-expression + mRNA expression analysis	Thy1+ fetal thymocytes	[34]
PU.1	-	Gata3 activity	P	ChIP using Gata3 antibody	PU.1-/ CD4+ T-cells	[48]
PU.1	-	Gfi1	2	PU.1 over-expression + mRNA expression analysis	Thy1+ fetal thymocytes	[34]
PU.1	-	HEB	2	PU.1 over-expression + mRNA expression analysis	Thy1+ fetal thymocytes	[34]
PU.1	-	HEBAlt	2	PU.1 over-expression + mRNA expression analysis	Thy1+ fetal thymocytes	[34]
PU.1	-	Hes1	2	PU.1 over-expression + mRNA expression analysis	Thy1+ fetal thymocytes	[34]
PU.1	+	Id2	2	PU.1 over-expression + mRNA expression analysis	Thy1+ fetal thymocytes	[34]
PU.1	-	Id3	2	PU.1 over-expression + mRNA expression analysis	Thy1+ fetal thymocytes	[34]
PU.1	-	Ikaros	2	PU.1 over-expression + mRNA expression analysis	Thy1+ fetal thymocytes	[34]
PU.1	+	IL-7R α	2	mRNA expression analysis ChIP using PU.1 antibody	FL PU.1-/ FL cells FL-derived pro-B cells	[49]
PU.1	-	IL-7R α	2	PU.1 over-expression + mRNA expression analysis	Thy1+ fetal thymocytes	[34]
PU.1	-	Kit	2	PU.1 over-expression + surface expression analysis by flow cytometry	Thy1+ fetal thymocytes	[34]
PU.1	-	Lat	2	PU.1 over-expression + mRNA expression analysis	Thy1+ fetal thymocytes	[34]
PU.1	-	Lck	2	PU.1 over-expression + mRNA expression analysis	Thy1+ fetal thymocytes	[34]
PU.1	+	Lmo2	1	PU.1 over-expression + Lmo2 promoter activity measurements ChIP using PU.1 antibody	293T cell line 416B myeloid cell line	[50]
PU.1	+	Lyl1	1	ChIP using PU.1 antibody Lyl1 promoter activity measurements	416B myeloid cell line	[51]

				(WT/mutated PU.1 site)		
PU.1	-	Myb	2	PU.1 over-expression + mRNA expression analysis	Thy1+ fetal thymocytes	[34]
PU.1	+	PU.1	1	transfection with PU.1 regulatory element construct (+/- mutation to PU.1 binding site) + analysis of reporter expression / ChIP using PU.1 antibody	416B myeloid cell line	[52]
PU.1	-	Rag-1	2	PU.1 over-expression + mRNA expression analysis	Thy1+ fetal thymocytes	[34]
PU.1	-	Runx3	1	PU.1 over-expression + mRNA expression analysis	Thy1+ fetal thymocytes	[34]
PU.1	-	TCF-1	2	PU.1 over-expression + mRNA expression analysis	Thy1+ fetal thymocytes	[34]
PU.1	-	Zap70	2	PU.1 over-expression + mRNA expression analysis	Thy1+ fetal thymocytes	[34]
Runx1	-	PU.1	3	mRNA expression analysis Runx1/Runx1 dominant negative over-expression + analysis of PU.1 cis-regulatory element	Runx1-/ DN2, DN3 thymocytes P2C2 immature T-cell line + Raw264 myeloid cell line	[53] [54]
Runx1	-	Rag-1	2	Analysis of Rag1-GFP reporter expression by flow cytometry (wildtype/mutated Runx1 site)	Rag1 GFP-reporter transgenic DN thymocytes	[55]
Runx1	+	TCR β	1	Runx1 over-expression + analysis of TCR β enhancer activity	p19 cell line	[19]
TCF-1	-	PU.1	1	Analysis of PU.1 cis-regulatory element (WT/mutated Tcf site)	EL4 T-cell line	[56]
TCF-1	+	Lef1	2	Wnt pathway activation, ChiP using TCF antibody TCF-1 over-expression + mRNA expression analysis	DLD1 cancer cell line Lin-cKit+Sca1+ (LSK) cells	[57] [46]
TCF-1	+	TCF-1	3	TCF-1 over-expression + mRNA expression analysis ChiP analysis using TCF-1 antibody	Lin-cKit+Sca1+ (LSK) cells	[46]
TCF-1	+	Bcl11b	3	TCF-1 over-expression + mRNA expression analysis ChiP analysis using TCF-1 antibody	Lin-cKit+Sca1+ (LSK) cells	[46]
TCF-1	+	GATA3	3	TCF-1 over-expression + mRNA expression analysis ChiP analysis using TCF-1 antibody GATA3	Lin-cKit+Sca1+ (LSK) cells TCF-/ Th2 cells	[46] [58]
TCF-1	+	CD25	3	TCF-1 over-expression + mRNA expression analysis ChiP analysis using TCF-1 antibody	Lin-cKit+Sca1+ (LSK) cells	[46]

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