

Supplementary Table 1. Detailed parameters and statistics for the ChIP-seq libraries used in this study.

ChIP-seq library	Cell-type	Cytokines	Publication	Total number of sequence tags	That map to mm9	%	Multi-mapping reads (rejected)	%	mfold-value used	p-value	Number of peaks discovered	Estimated false positives	Estimated false positives %
STAT3	AfT-20 cells	LIF	Langlais et al., 2012	29,105,977	18,969,201	65.2%	8,844,683	30.4%	11,35	3.50E-06	7983	88	1.1%
IgG	AfT-20 cells PEC	LIF	Langlais et al., 2012	59,664,040	39,680,747	66.5%	17,927,704	30.0%	n.a.	n.a.	n.a.	n.a.	n.a.
STAT3	macrophages PEC	IL-10	Hutchins et al., 2012	5,099,637	4,028,627	79.0%	889,834	17.4%	16,35	1.00E-05	1724	1	0.1%
Input	macrophages	IL-10	Hutchins et al., 2012	4,832,537	3,662,036	75.8%	819,062	16.9%	n.a.	n.a.	n.a.	n.a.	n.a.
STAT3	CD4+ T cells	IL-21	Kwon et al., 2009	108,581,819	21,535,991	19.8%	12,405,640	11.4%	11,35	1.00E-06	5152	43	0.8%
Input	CD4+ T cells	IL-21	Kwon et al., 2009	76,954,817	15,237,894	19.8%	8,898,981	11.6%	n.a.	n.a.	n.a.	n.a.	n.a.
STAT3	ES cells	LIF	Chen et al., 2008	21,995,262	8,815,612	40.1%	5,585,494	25.4%	11,35	1.90E-07	2651	40	1.5%
GFP	ES cells	LIF	Chen et al., 2008	23,873,274	6,972,375	29.2%	4,168,346	17.5%	n.a.	n.a.	n.a.	n.a.	n.a.
c-MYC	ES cells	LIF	Chen et al., 2008	26,967,738	10,726,464	39.8%	6,067,557	22.5%	13,35	7.00E-07	3917	63	1.6%
n-MYC	ES cells	LIF	Chen et al., 2008	23,180,904	7,727,705	33.3%	4,107,895	17.7%	17,35	3.00E-06	11448	121	1.1%
CTCF	ES cells	LIF	Chen et al., 2008	24,300,222	3,440,101	14.2%	1,653,496	6.8%	32,50	1.00E-05	46934	39	0.1%
E2F1	ES cells	LIF	Chen et al., 2008	30,489,540	10,400,631	34.1%	5,236,397	17.2%	21,40	3.50E-06	22523	334	1.5%
ESRRB	ES cells	LIF	Chen et al., 2008	25,879,154	11,852,759	45.8%	4,840,122	18.7%	32,50	7.00E-06	56136	675	1.2%
KLF4	ES cells	LIF	Chen et al., 2008	22,126,359	6,703,974	30.3%	3,414,979	15.4%	19,35	1.00E-05	25734	105	0.4%
NANOG	ES cells	LIF	Chen et al., 2008	28,202,400	3,068,511	10.9%	1,920,771	6.8%	16,35	1.00E-05	10594	14	0.1%
OCT4	ES cells	LIF	Chen et al., 2008	24,021,520	8,071,104	33.6%	4,417,321	18.4%	12,35	1.70E-06	5611	74	1.3%
SOX2	ES cells	LIF	Chen et al., 2008	23,073,668	8,290,455	35.9%	4,197,831	18.2%	13,35	9.00E-07	5912	68	1.2%
ZFX	ES cells	LIF	Chen et al., 2008	17,968,940	7,419,724	41.3%	3,681,413	20.5%	23,40	1.00E-05	31637	173	0.5%
GATA3	Th17 cells	TGFb, IL-6, IL-1b	Wei et al., 2011	7,226,595	4,040,050	55.9%	2,443,773	33.8%	23,40	1.00E-05	2512	31	1.2%
Junb	Th17 cells	TGFb, IL-6, IL-1b											
GATA3	naive CD4+	None	Wei et al., 2011	9,147,587	4,264,960	46.6%	2,614,970	28.6%	23,40	1.00E-05	4685	42	0.9%

GATA3	Th2 cells	?	Wei et al., 2011	9,675,003	6,057,673	62.6%	3,329,879	34.4%	23,40	1.00E-09	5693	90	1.6%
IRF4	CD4+ T cells	IL-21	Kwon et al., 2009	44,641,032	11,775,280	26.4%	6,146,666	13.8%	23,40	1.00E-08	19708	188	1.0%
IRF4	CD4+ T cells	None	Kwon et al., 2009	48,730,424	12,555,258	25.8%	6,475,873	13.3%	23,40	2.00E-07	22298	222	1.0%
panJUN	CD4+ T cells	IL-21	Li et al., 2012							1.00E-09	2822	156	5.5%
panJUN	CD4+ T cells	None	Li et al., 2012							n.p.			
BATF	CD4+ T cells	IL-21	Li et al., 2012							1.00E-08	5171	105	2.0%

Supplementary Table 2. List of primers used in this study.

Name	Genomic location (mm9)	Forward	Reverse
Stat3	chr11:100800982-100801167	CTCCCTGAGTTGGCTGTTCT	GAGCCGTATCAGGGCATTTA
Socs3	chr11:117830790-117830997	CCCCCAACTTCTCATTACACA	TACATGAGGACCTCGGAGTG
Tcf4	chr18:69503838-69504238	CACACTGACAGGGACACTGC	GTGGGACTCACTCAGGTCGT
Ptpn1	chr2:167750629-167751029	ATGCTTCTCTGCAGCCTTTC	CCTCACTGGGCTCTTGAAAC
Junb	chr8:87500268-87500668	ATATGGGCAGAGCTTCCGTA	CAGTACAAACGCCCAGACCT
Cmtm6	chr9:114640156-114640556	CCGAGAGTTTTAGCTGGGTGA	AGCTGCAAGCCTTTGAGGAT
Diap1	chr18:38039780-38040180	ACAGGCAGCCTTGCTTAAAA	CAAGGCCGGAATAAAACAGA
Eif1a	chr18:46757183-46757583	TACTCCCCGGTGGTAGAGAG	CAGAGGGCTTTAGCATCCAG
Foxk1	chr5:142843084-142843484	ACAACGTCCTCAAGGCTCAT	GGAAGGGGCACTAGTCAGGA
Nfkbiz	chr16:55822180-55822580	GCTGCTGCAAGAACAGGTC	GAAATTGAGTCCAGGCCAGA
Pih1d1	chr7:52409473-52409873	GCGAGAGGTATGGGGATTTA	CGTGATTTCCCTACAGTGC
Setmar	chr6:108014985-108015385	GCAGCATCTGAGGAGGAATC	CAGCCCTTTCAGCCACTTAG
Skap2	chr6:51962503-51962903	GAGCGAATTGGAGCTGTGTC	AACCTTGGTGGAAAAGACCA
Smardc2	chr11:106134199-106134599	ACCAGCACCTCCCATAACTG	TTGAAGACGCAGAATTGACG
Control	chr19:34317846-34317997	CTTCTGCATCCTGTCAGCAA	CTTTTCCAGGGATGGAGTCA
Fas (control)	chr19:34328661+34328879	TGAAAGGAGCGTTGTCAGT	ATTTTTGGCACCAGATGAGC

Supplementary Table 5. Summary of the genes regulated by STAT3 in all four cell types.

Gene Symbol	Annotation	Notes	Function
1810013L24Rik	NM_001081400	Unknown	Unknown
Aars	NM_146217	alanyl-tRNA synthetase is important for protein translation (1)	Protein translation
Amn1	NM_001113424	In yeast, Failure of Amn1 function results in defects of both the spindle assembly and nuclear orientation checkpoints and delays turning off Cdc14 in G1. Thus, Amn1 is part of a daughter-specific switch that helps cells exit from mitotic exit and reset the cell cycle. Co activator of ste12 (control stat1-like transcription)	Cell cycle control
Azin1	ENSMUSG00000037458	Ornithine decarboxylase (ODC) catalyzes the conversion of ornithine to putrescine in the first and apparently rate-limiting step in polyamine biosynthesis. Ornithine decarboxylase antizymes play a role in the regulation of polyamine synthesis by binding to and inhibiting ornithine decarboxylase. The protein encoded by this gene is highly similar to ODC. It binds to ODC antizyme and stabilizes ODC, thus inhibiting antizyme-mediated ODC degradation (2).	Metabolism and cell growth
Bcl3	NM_033601	B cell leukemia/lymphoma 3. This protein is an atypical member of the Inhibitor of Kappa-B (IkappaB) family of proteins. It is believed to repress the activation of the NFkappa-B signaling cascade by direct binding to the dimeric transcription factors NFKB1, NFKB2, RELA, RELB or c-Rel (3).	Transcription factor (proto-oncogene)
Bcl6	NM_009744	B cell leukemia/lymphoma 6. Bcl6 prevents premature activation and differentiation of germinal center B cells and provides an environment tolerant of the DNA breaks associated with immunoglobulin gene remodeling mechanisms involved in the production of high-affinity antibodies of different isotypes. Acts as an oncogene when overexpressed (4).	Transcription factor (oncogene)
Cic	NM_027882	Also known as capicua, Transcriptional repressor, generally a negative repressor of receptor kinase. Inactivated by tor kinase downstream of PI3K (5)	Transcription factor
Cmtm6	NM_026036	Also known in mouse as CKLF-like MARVEL transmembrane domain containing 6 chemokine-like factor superfamily.	Cytokine regulator
Diap1	ENSMUSG00000024456	Also known as p140mDia, p140mDia, is a downstream effector of Rho. It is a mammalian homolog of Drosophila diaphanous, a protein required for cytokinesis, and belongs to a family of formin-related proteins containing repetitive polyproline stretches. p140mDia binds selectively to the GTP-bound form of Rho and also binds to profilin. p140mDia, profilin and RhoA are co-localized in the spreading lamellae of cultured fibroblasts. They are also co-localized in membrane ruffles of phorbol ester-stimulated sMDCK2 cells, which extend these structures in a Rho-dependent manner. The three proteins are recruited around phagocytic cups induced by fibronectin-coated beads. It suggest that Rho regulates actin polymerization by targeting profilin via p140mDia beneath the specific plasma membranes. (6)	Cytoskeleton and trafficking
Eif1a	NM_010120	Eukaryotic initiation factor 1 assists in targeting the ribosome to the AUG start codon (7).	Protein translation
Fos	NM_010234	Transcription factor, member of AP-1 transcriptional complex. Wide roles in biology.	Transcription factor
Foxk1	ENSMUSG00000075577	Transcriptional co-repressor.	Transcription factor (repressor)
Irf2	NM_008391	Transcriptional co-repressor.	Transcription factor (repressor)

Junb	NM_008416	Transcription factor, member of the AP-1 transcriptional complex.	Transcription factor
Mnt	NM_010813	<i>Mus musculus</i> max binding protein (Mnt) repress Myc activity by binding to Max (8).	Transcription factor (repressor)
Mrpl52	NM_026851	Mitochondrial ribosomal protein L52 (Mrpl52), potentially important in ribosomal synthesis.	Metabolism and cell growth
Neat1	NR_003513 ENSMUSG000 00092274	Architectural long noncoding RNA NEAT1 (Mene/β) present in paraspeckles, subnuclear bodies that alter gene expression via the nuclear retention of RNA (9).	Transcription factor
Nfkbiz	NM_001159395	Also known as I-kappa-B-zeta. It is an important regulator of NFKB in immune cells by binding to it as a co-transcription factor (10).	Transcription factor
Pih1d1	NM_029406	Regulator of the anti-apoptotic protein PIH1D1 (chaperone like protein), a subunit of R2TP complex, it is an anti apoptotic protein and also contributes to the assembly of the RNA pol II complex. Involved in cell growth (11).	Metabolism and cell growth
Ptpn1	NM_011201	A protein tyrosine phosphatase, PTP1B (encoded by Ptpn1) is involved in modulating signaling from many tyrosine kinases and in particular JAK-STAT pathways through the tyrosine dephosphorylation of JAK2 and STAT3. It is a modulator of cell metabolism through its action on tyrosine phosphorylated proteins. (12)	Metabolism and cell growth
Sbno1	NM_001081203	Mouse ortholog of the strawberry notch homolog 1 in <i>Drosophila</i> (Sbno1). It was detected as a Notch pathway modulator in fly and a target of myc-jmjC transcription complex. It is a positive modulator of cell growth (13).	Transcription factor (repressor)
Setmar	NM_178391	SET domain and mariner transposase fusion gene (Setmar). Also known as Metnase, acts as an antiapoptosis protein by promoting non-homologous end joining (NHEJ) repair.	DNA repair and chromatin remodeling
Skap2	NM_018773	Partner of PTP-PEST and involved in recognizing actin fibers. It is an integrin regulated gene involve in cell migration and cell adhesion. (14)	Cytoskeleton and trafficking
Smarcd2	NM_031878	Also known as BAF60B. It is a member of the SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily d, member 2 (Smarcd2). Chromatin remodeling. (15)	DNA repair and chromatin remodeling
Socs3	NM_007707	Negative regulator of JAK-STAT. (16)	Cytokine regulator
Stat1	NM_009283	Member of the STAT family of transcription factors.	Transcription factor
Stat3	NM_213659	STAT3 binds to its own promoter to regulate its own transcription (17).	Transcription factor
Tcf4	NM_013685	Beta-catenin binding transcription factor (18).	Transcription factor
Tiparp	NM_178892	TCDD-inducible poly(ADP-ribose) polymerase (Tiparp) (dioxin like inducible). Involved in the response to dioxin and potentially contributes to the immunomodulation of AHR (Aryl hydrocarbon receptor) as one of its target genes (19).	Metabolism and cell growth
Tut1	NM_197993	Transcription <i>Mus musculus</i> terminal uridylyl transferase 1, U6 snRNA-specific (Tut1), involved in miRNA processing (20).	RNA modulator
Vps28	NM_025842	Acting on protein trafficking and recycling through the ESRT-1 complex.	Cytoskeleton and trafficking
Zfp36	NM_011756	Multiple names, primarily known as tristetraproline. A major negative regulator of IL-10 mRNA in activated macrophages, suppresses the anti-inflammatory response (21).	RNA modulator
Fam86	NM_027446	AdoMet_MTases; S-adenosylmethionine-dependent methyltransferases (SAM or AdoMet-MTase), class I; AdoMet-MTases are enzymes that use S-adenosyl-L-methionine (SAM or AdoMet) as a	Metabolism and cell growth

		substrate for methyltransfer, creating the product S-adenosyl-L-homocysteine (AdoHcy). They are used to methylate a large number of biomolecules (protein to tRNA to nucleotides etc.).	
Xrcc6bp1	ENSMUSG00000025436	Mitochondrial inner membrane protease ATP23 homolog. Associated with DNA repair gene KU70 also known as KUB3. Acts as an oncogene when overexpressed.	DNA repair and chromatin Remodeling (oncogene)
Zfp217	ENSMUSG00000052056	Involved with Oct4 in embryonic stem cell maintenance (22).	Transcription factor

Total genes	35
Transcription factors	15
DNA repair and chromatin remodeling	3
Metabolism and cell growth	6
RNA modulator	2
Cytoskeleton and trafficking	3
Cytokine regulator	2
Protein translation	2
Cell cycle control	1
Unknown	1

REFERENCES

1. Yadavalli, S.S. and Ibba, M. (2012) Quality control in aminoacyl-tRNA synthesis its role in translational fidelity. *Advances in protein chemistry and structural biology*, **86**, 1-43.
2. Perez-Leal, O. and Merali, S. (2012) Regulation of polyamine metabolism by translational control. *Amino acids*, **42**, 611-617.
3. Maldonado, V. and Melendez-Zajgla, J. (2011) Role of Bcl-3 in solid tumors. *Molecular cancer*, **10**, 152.
4. Basso, K. and Dalla-Favera, R. (2012) Roles of BCL6 in normal and transformed germinal center B cells. *Immunological reviews*, **247**, 172-183.
5. Jimenez, G., Shvartsman, S.Y. and Paroush, Z. (2012) The Capicua repressor - a general sensor of RTK signaling in development and disease. *Journal of cell science*, **125**, 1383-1391.
6. Watanabe, N., Madaule, P., Reid, T., Ishizaki, T., Watanabe, G., Kakizuka, A., Saito, Y., Nakao, K., Jockusch, B.M. and Narumiya, S. (1997) p140^{Diaph}, a mammalian homolog of *Drosophila* diaphanous, is a target protein for Rho small GTPase and is a ligand for profilin. *The EMBO journal*, **16**, 3044-3056.
7. Hinnebusch, A.G. (2011) Molecular mechanism of scanning and start codon selection in eukaryotes. *Microbiology and molecular biology reviews : MMBR*, **75**, 434-467, first page of table of contents.

8. Walker, W., Zhou, Z.Q., Ota, S., Wynshaw-Boris, A. and Hurlin, P.J. (2005) Mnt-Max to Myc-Max complex switching regulates cell cycle entry. *The Journal of cell biology*, **169**, 405-413.
9. Passon, D.M., Lee, M., Rackham, O., Stanley, W.A., Sadowska, A., Filipovska, A., Fox, A.H. and Bond, C.S. (2012) Structure of the heterodimer of human NONO and paraspeckle protein component 1 and analysis of its role in subnuclear body formation. *Proceedings of the National Academy of Sciences of the United States of America*, **109**, 4846-4850.
10. Kannan, Y., Yu, J., Raices, R.M., Seshadri, S., Wei, M., Caligiuri, M.A. and Wewers, M.D. (2011) IkappaBzeta augments IL-12- and IL-18-mediated IFN-gamma production in human NK cells. *Blood*, **117**, 2855-2863.
11. Boulon, S., Bertrand, E. and Pradet-Balade, B. (2012) HSP90 and the R2TP co-chaperone complex: building multi-protein machineries essential for cell growth and gene expression. *RNA biology*, **9**, 148-154.
12. Lessard, L., Stuble, M. and Tremblay, M.L. (2010) The two faces of PTP1B in cancer. *Biochimica et biophysica acta*, **1804**, 613-619.
13. Takano, A., Zochi, R., Hibi, M., Terashima, T. and Katsuyama, Y. (2010) Expression of strawberry notch family genes during zebrafish embryogenesis. *Developmental dynamics : an official publication of the American Association of Anatomists*, **239**, 1789-1796.
14. Zhou, L., Zhang, Z., Zheng, Y., Zhu, Y., Wei, Z., Xu, H., Tang, Q., Kong, X. and Hu, L. (2011) SKAP2, a novel target of HSF4b, associates with NCK2/F-actin at membrane ruffles and regulates actin reorganization in lens cell. *Journal of cellular and molecular medicine*, **15**, 783-795.
15. Lores, P., Visvikis, O., Luna, R., Lemichez, E. and Gacon, G. (2010) The SWI/SNF protein BAF60b is ubiquitinated through a signalling process involving Rac GTPase and the RING finger protein Unkempt. *The FEBS journal*, **277**, 1453-1464.
16. Shuai, K. and Liu, B. (2003) Regulation of JAK-STAT signalling in the immune system. *Nature reviews. Immunology*, **3**, 900-911.
17. Hutchins, A.P., Poulain, S. and Miranda-Saavedra, D. (2012) Genome-wide analysis of STAT3 binding in vivo predicts effectors of the anti-inflammatory response in macrophages. *Blood*, **119**, e110-119.
18. Shitashige, M., Hirohashi, S. and Yamada, T. (2008) Wnt signaling inside the nucleus. *Cancer science*, **99**, 631-637.
19. Diani-Moore, S., Ram, P., Li, X., Mondal, P., Youn, D.Y., Sauve, A.A. and Rifkind, A.B. (2010) Identification of the aryl hydrocarbon receptor target gene TiPARP as a mediator of suppression of hepatic gluconeogenesis by 2,3,7,8-tetrachlorodibenzo-p-dioxin and of nicotinamide as a corrective agent for this effect. *The Journal of biological chemistry*, **285**, 38801-38810.
20. Wyman, S.K., Knouf, E.C., Parkin, R.K., Fritz, B.R., Lin, D.W., Dennis, L.M., Krouse, M.A., Webster, P.J. and Tewari, M. (2011) Post-transcriptional generation of miRNA variants by multiple nucleotidyl transferases contributes to miRNA transcriptome complexity. *Genome research*, **21**, 1450-1461.
21. Gaba, A., Grivennikov, S.I., Do, M.V., Stumpo, D.J., Blackshear, P.J. and Karin, M. (2012) Cutting Edge: IL-10-Mediated Tristetraprolin Induction Is Part of a Feedback Loop That Controls Macrophage STAT3 Activation and Cytokine Production. *J Immunol*.
22. Pardo, M., Lang, B., Yu, L., Prosser, H., Bradley, A., Babu, M.M. and Choudhary, J. (2010) An expanded Oct4 interaction network: implications for stem cell biology, development, and disease. *Cell stem cell*, **6**, 382-395.