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Supplemental Information

CDK8 Kinase Phosphorylates Transcription Factor STAT1 to Selectively Regulate the Interferon Response

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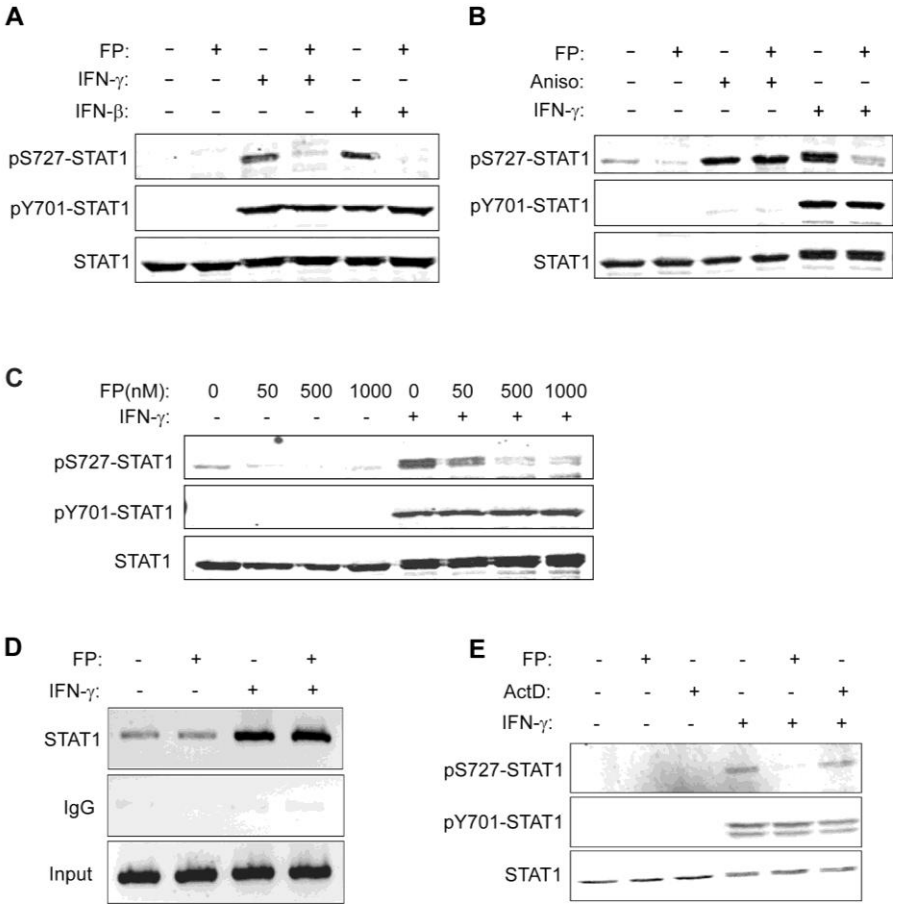

Figure S1. Analysis of Flavopiridol Effects on IFN- and Stress-Induced S727 Phosphorylation of STAT1 in Fibroblasts (A, B and C), of Flavopiridol Effects on STAT1 Promoter Recruitment (D), and of the Effects of Transcription Inhibition on S727 Phosphorylation of STAT1 (E)

(A) Flavopiridol inhibits IFN-γ- and IFN-β-induced S727 phosphorylation of STAT1 in fibroblasts. Mouse fibroblasts were stimulated for 40 min with IFN-γ or IFN-β after pretreatment or control treatment for 15 min with flavopiridol (FP) (500 nM). Cell extracts were analyzed by Western blotting using antibodies to phosphorylated S727 of STAT1 (pS727-STAT1), phosphorylated

Y701 of STAT1 (pY701-STAT1) and STAT1 C-terminal antibody (not recognizing the STAT1β isoform).

(B) Flavopiridol inhibits IFN-γ- but not stress-induced S727 phosphorylation of STAT1 in fibroblasts. Mouse fibroblasts were stimulated for 40 min with the stress inducer anisomycin (Aniso) or IFN-γ after pretreatment or control treatment for 15 min with flavopiridol (FP). Cell extracts were analyzed as in (A).

(C) Mouse fibroblasts were stimulated for 40 min with IFN-γ or left untreated followed 15 min-pretreatment with flavopiridol (FP) at indicated concentrations. Cell extracts were analyzed as in (A).

(D) STAT1 promoter recruitment is not impaired by flavopiridol. MEFs were stimulated for 30 min with IFN-γ after pretreatment or control treatment for 30 min with flavopiridol (FP). Chromatin recruitment of STAT1 was analyzed by ChIP using STAT1 antibody or unspecific IgG. A representative gel with PCR-amplified *Irf1* promoter using immunoprecipitated DNA as template is shown. Total chromatin DNA was amplified for input control.

(E) Ongoing transcription is not required for IFN-γ-induced S727 phosphorylation of STAT1. MEFs were stimulated for 40 min with IFN-γ after pretreatment or control treatment for 15 min with actinomycin D (ActD). Cell extracts were analyzed by Western blotting using antibodies to phosphorylated S727 of STAT1 (pS727-STAT1), phosphorylated Y701 of STAT1 (pY701-STAT1) and total STAT1.

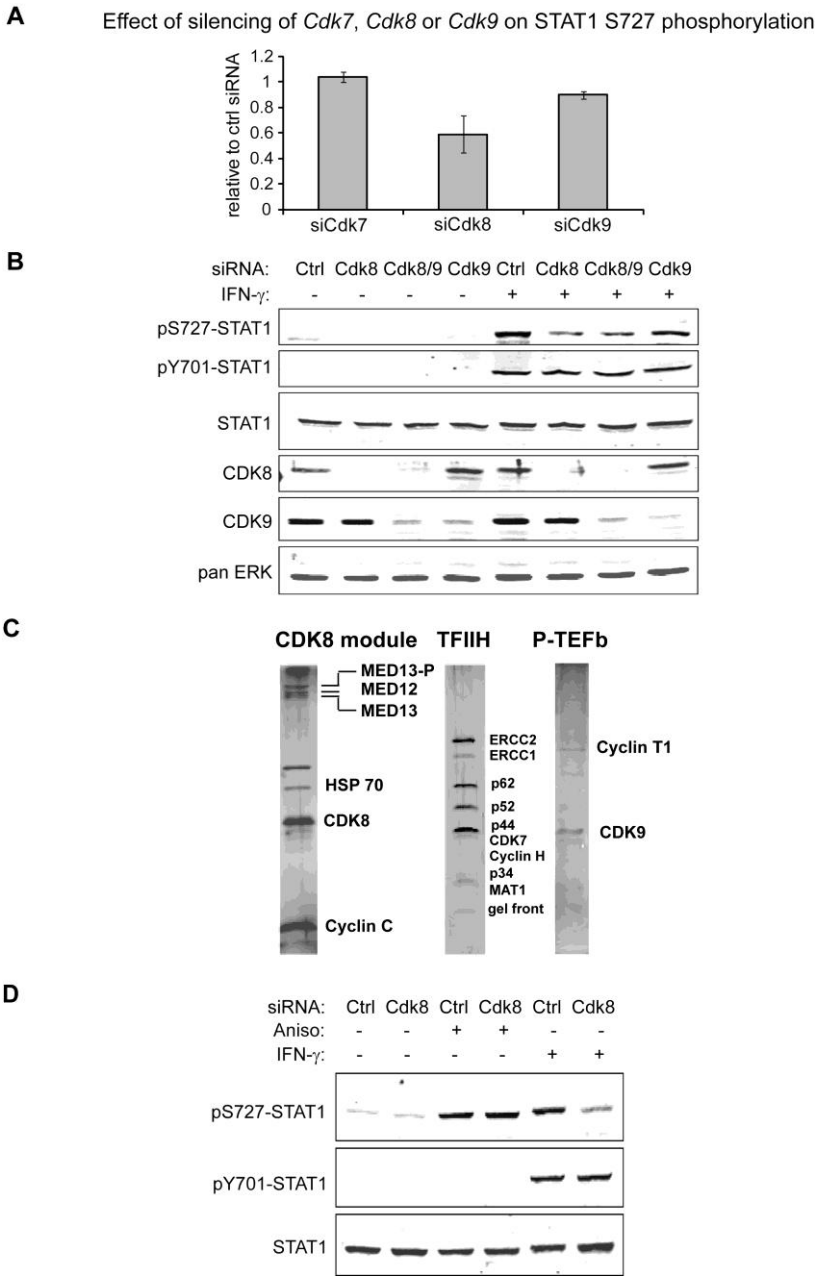

Figure S2. Effects of *Cdk7*, *Cdk8* and *Cdk9* Silencing and of Combined *Cdk8* and *Cdk9* Silencing on STAT1 S727 Phosphorylation (A, B, D and E), and Silver-Stained Gels of Purified Kinase Complexes Used for In Vitro Kinase Assays (C)

(A) Quantitative analysis of effects of *Cdk7*, *Cdk8* and *Cdk9* silencing on IFN-γ-induced STAT1 S727 phosphorylation. MEFs were treated for 48 h with siRNA to *Cdk7*, *Cdk8*, *Cdk9* or control siRNA (Ctrl) and subsequently stimulated for 40 min with IFN-γ. Cell extracts of three experiments were analyzed by Western blotting using antibodies to phosphorylated S727 of STAT1 (pS727-STAT1), phosphorylated Y701 of STAT1 (pY701-STAT1) and total STAT1. The Western blot signal was quantified using the Odyssey Imager (LI-COR Biosciences), and the pS727 signals were normalized to total STAT1 signals. Values of the normalized pS727 signals

for the individual Cdk siRNA relative to control siRNA (Ctrl) are depicted. Error bars represent standard deviations (SDs) (n = 3).

(B) Combined silencing of *Cdk8* and *Cdk9* does not result in more efficient inhibition of IFN-γ-induced STAT1 S727 phosphorylation than silencing of *Cdk8* alone. MEFs were treated for 48 h with siRNA to *Cdk8*, *Cdk9*, both *Cdk8* + *Cdk9* (Cdk8/9), or control siRNA (Ctrl) and subsequently stimulated for 40 min with IFN-γ or left unstimulated. Cell extracts were analyzed by Western blotting using antibodies to phosphorylated S727 of STAT1 (pS727-STAT1), phosphorylated Y701 of STAT1 (pY701-STAT1) and total STAT1. Silencing was confirmed by Western blotting of the same extracts using antibodies to CDK8 and CDK9. Equal loading was controlled by antibodies to ERK1/ERK2 (pan ERK).

(C) Silver stained gels of purified CDK8 module, TFIIH, and P-TEFb used for kinase assays.

(D) Stress-induced STAT1 S727 phosphorylation is not impaired in fibroblasts silenced for *Cdk8*. Fibroblasts silenced for the expression of *Cdk8* or control-silenced cells were treated for 30 min with anisomycin (Aniso) or IFN-γ or left untreated. Cell extracts were analyzed using antibodies to phosphorylated S727 of STAT1 (pS727-STAT1), phosphorylated Y701 of STAT1 (pY701-STAT1) and total STAT1. Note that anisomycin does not cause Y701 phosphorylation.

Figure S3

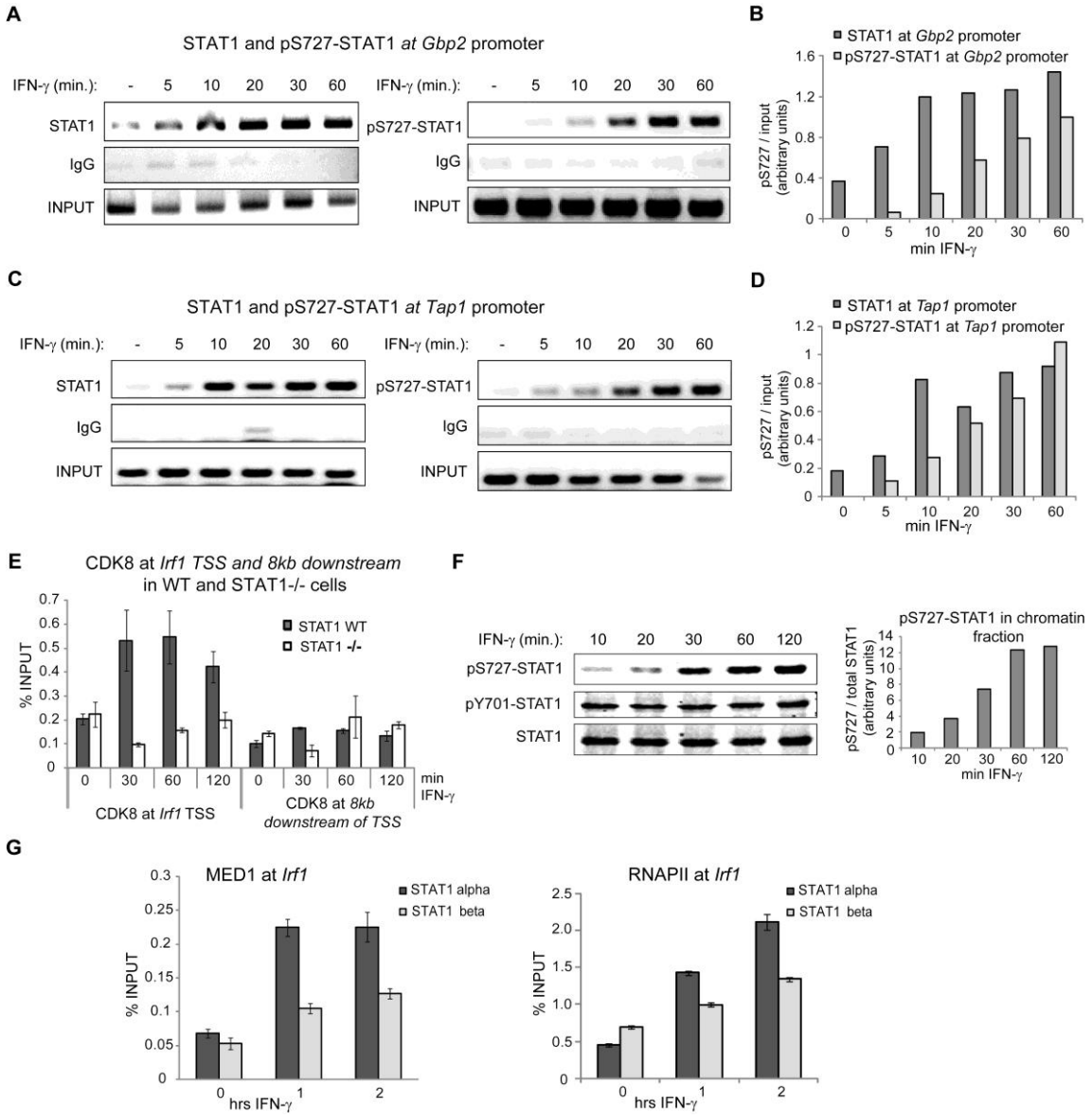

Figure S3. Recruitment of S727-Phosphorylated STAT1 to *Gbp2* (A, B) and *Tap1* (C, D) Promoters and to Chromatin (F), STAT1-Dependent Recruitment of CDK8 to TSS and Gene Body of *Irf1* (E) and Effect of Missing TAD on Recruitment of MED1 and RNAPII (G)

(A–D) Recruitment of STAT1 precedes accumulation of S727-phosphorylated STAT1 at the *Ggp2* and *Tap1* promoters. Mouse fibroblasts were treated for indicated times with IFN-γ or left untreated. Association of STAT1 and S727-phosphorylated STAT1 with the *Gbp2* (A) and *Tap1* (C) promoters was examined by ChIP using respective antibodies or unspecific IgG. A representative gel with PCR-amplified *Gbp2* or *Tap1* promoters using immunoprecipitated DNA as template is shown. Total chromatin DNA was amplified for input control. Quantitative analysis (using ImageJ) of data shown in (A) and (C) is depicted in (B) and (D), respectively: the pS727 signal was normalized to input DNA after subtracting the signals of IgG.

(E) IFN-γ induces STAT1-dependent CDK8 recruitment to the *Irf1* transcription start site (TSS) but not to the gene body. WT and STAT1$^{-/-}$ MEFs (right panel) were treated for indicated times

with IFN-γ, and CDK8 recruitment to the TSS or the gene body of the *Irf1* gene was determined by ChIP. CDK8 increased after IFN-γ treatment at the start site but not at the gene body in WT cells. No increase of CDK8 was observed in STAT1-/- cells throughout the gene. CDK8 recruitment was determined by ChIP using CDK8 antibodies or unspecific IgG. Immunoprecipitated DNA was analyzed by qPCR for the *Irf1* TSS and gene body (8 kb downstream of TSS), carried out in triplicates. Signals were normalized to input DNA. Error bars represent standard deviations (SDs) (n = 3).

(F) Accumulation of S727-phosphorylated STAT1 on chromatin reaches a plateau at approximately 60 min of IFN-γ treatment. MEFs were treated for indicated times with IFN-γ and processed as for ChIP analysis. The chromatin fractions were analyzed by Western blotting using antibodies to phosphorylated S727 of STAT1 (pS727-STAT1), phosphorylated Y701 of STAT1 (pY701-STAT1) and total STAT1 (left panel), and quantitated using Image Studio (Odyssey system from LI-COR) by normalizing the pS727-STAT1 signal to the STAT1 signal (right panel).

(G) MED1 and RNAPII are less efficiently recruited by STAT1beta than by STAT1alpha. MEFs derived from mice expressing solely STAT1alpha or STAT1beta were treated for indicated times with IFN-γ. Association of MED1 (left panel) and RNAPII (right panel) with the *Irf1* TSS was examined by ChIP. Error bars represent SDs (n = 3).

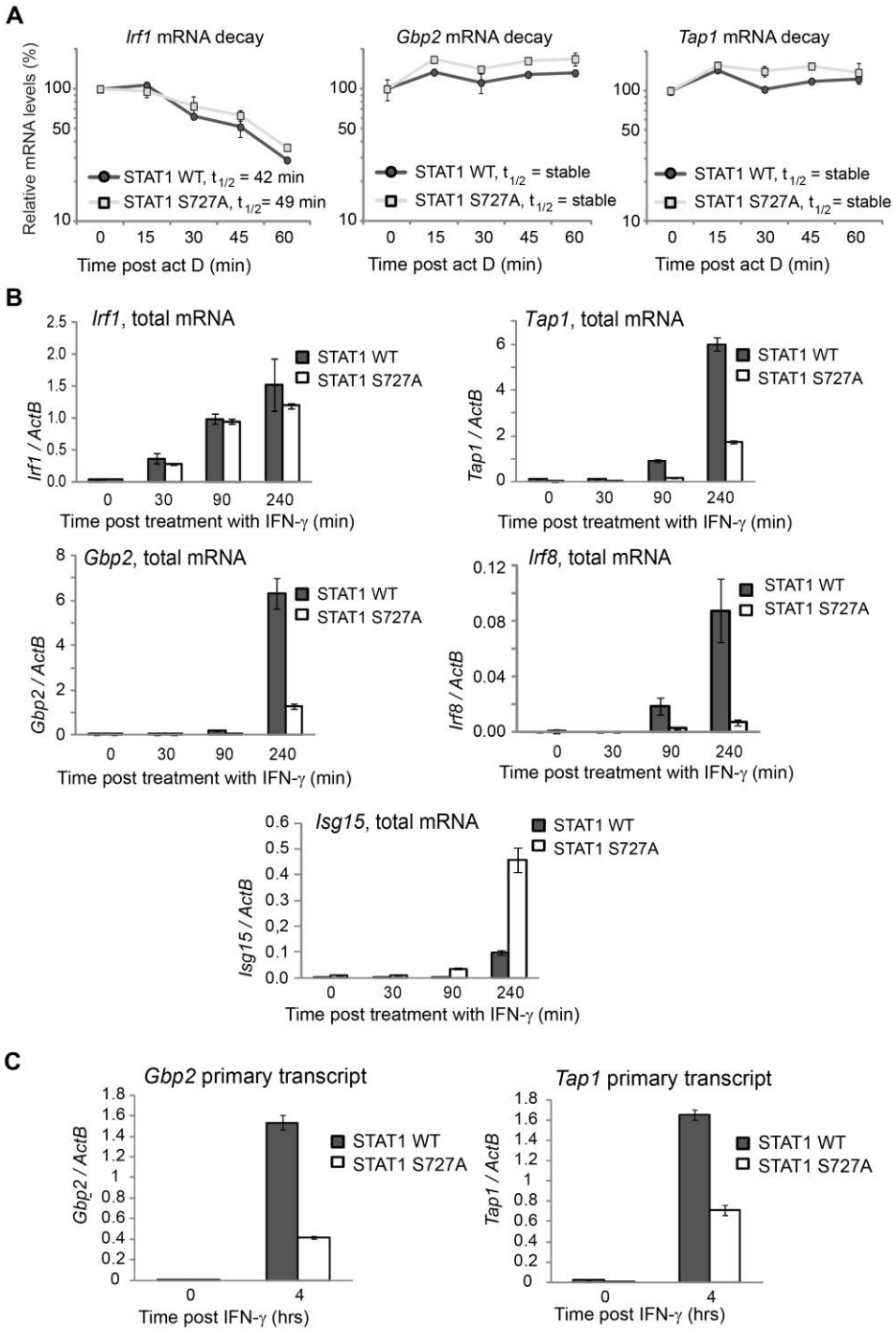

Figure S4. Measurement of mRNA Stability (A), Total RNA Fractions from Analysis of Newly Transcribed mRNA (B) and Amounts of Primary Transcripts (C)

(A) *Irf1*, *Gbp2* and *Tap1* mRNA stability in STAT1 WT and S727A cells. STAT1 WT and S727A MEFs were treated with IFN-γ for 4 h and actinomycin D (act D) was added for the indicated times. RNA was isolated, and the amounts of *Irf1*, *Gbp2* and *Tap1* mRNA were determined by qRT-PCR. Relative values to *Hprt* are shown. Error bars represent standard deviations (SDs) (n = 3).

(B) 4sU was added to the cell culture medium simultaneously with IFN-γ, or 60 min and 210 min after IFN-γ stimulation, or without IFN-γ treatment. The labeling was performed in WT and S727A MEFs for 30 min followed by RNA isolation and separation to collect the 4sU-labeled RNA fractions and total RNA fractions. Total RNA representing accumulated RNA at 0, 30 min, 90 min and 240 min of IFN-γ treatment is shown for *Irf1*, *Tap1*, *Gbp2*, *Irf8* and *Isg15*. mRNA was quantitated by qRT-PCR. *ActB* was used for normalization. Error bars represent SDs (n = 3).

(C) S727A mutation affects levels of primary transcripts. STAT1 WT and S727A MEFs were treated with IFN-γ for 4 h or left untreated. RNA was isolated, and the amounts of primary transcripts of *Tap1* and *Gbp2* genes were determined by qRT-PCR for intronic amplicons. Relative values to *ActB* are shown. Error bars represent standard deviations (SDs) (n = 3).

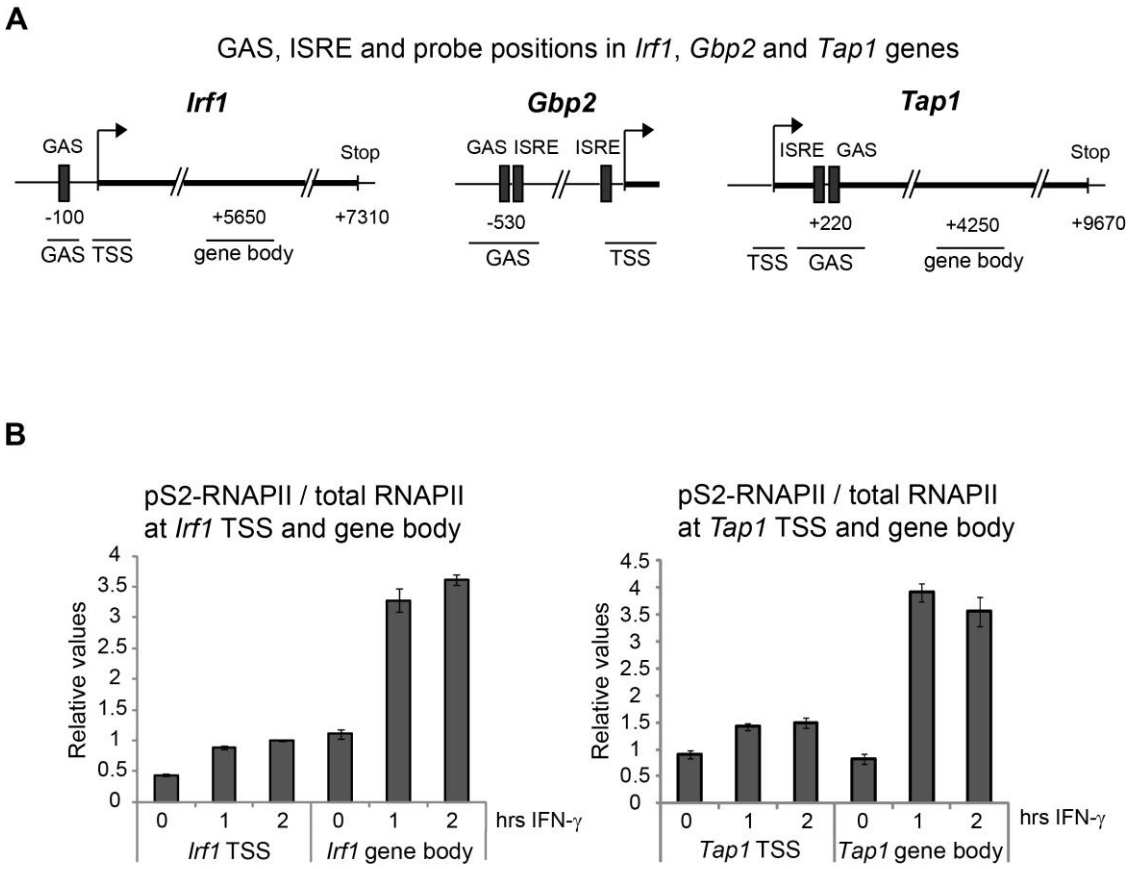

Figure S5. Schematic Representation of the *Irf1*, *Gbp2* and *Tap1* Gene Loci (A) and Positions of ChIP Amplicons and Relative Abundance of S2-Phosphorylated RNAPII at the TSS and the Gene Body of *Irf1* and *Tap1* (C)

(A) Positions of the regulatory GAS and ISRE elements are marked. Note that GAS and ISRE in the Tap1 gene are downstream of the transcription start site. "Stop" marks the end of *Irf1* (GenBank NM_001159393.1) and *Tap1* (GenBank NM_013683.2) transcripts. Amplicons for ChIP analyses are depicted as TSS (transcription start site), GAS (GAS elements) and gene body with the approximate position relative to TSS.

(B) Ratios of S2-phosphorylated RNAPII to total RNAPII at TSS and the gene body of the *Irf1* and *Tap1* genes. WT MEFs treated for indicated times with IFN-γ were examined by ChIP using antibodies to RNAPII and pS2-RNAPII. Immunoprecipitated DNA was analyzed by qPCR for the both TSS and the gene body of *Irf1* and *Tap1*, normalized to input DNA, and the ratios S2-phosphorylated RNAPII to total RNAPII were calculated. Error bars represent SDs (n = 3).

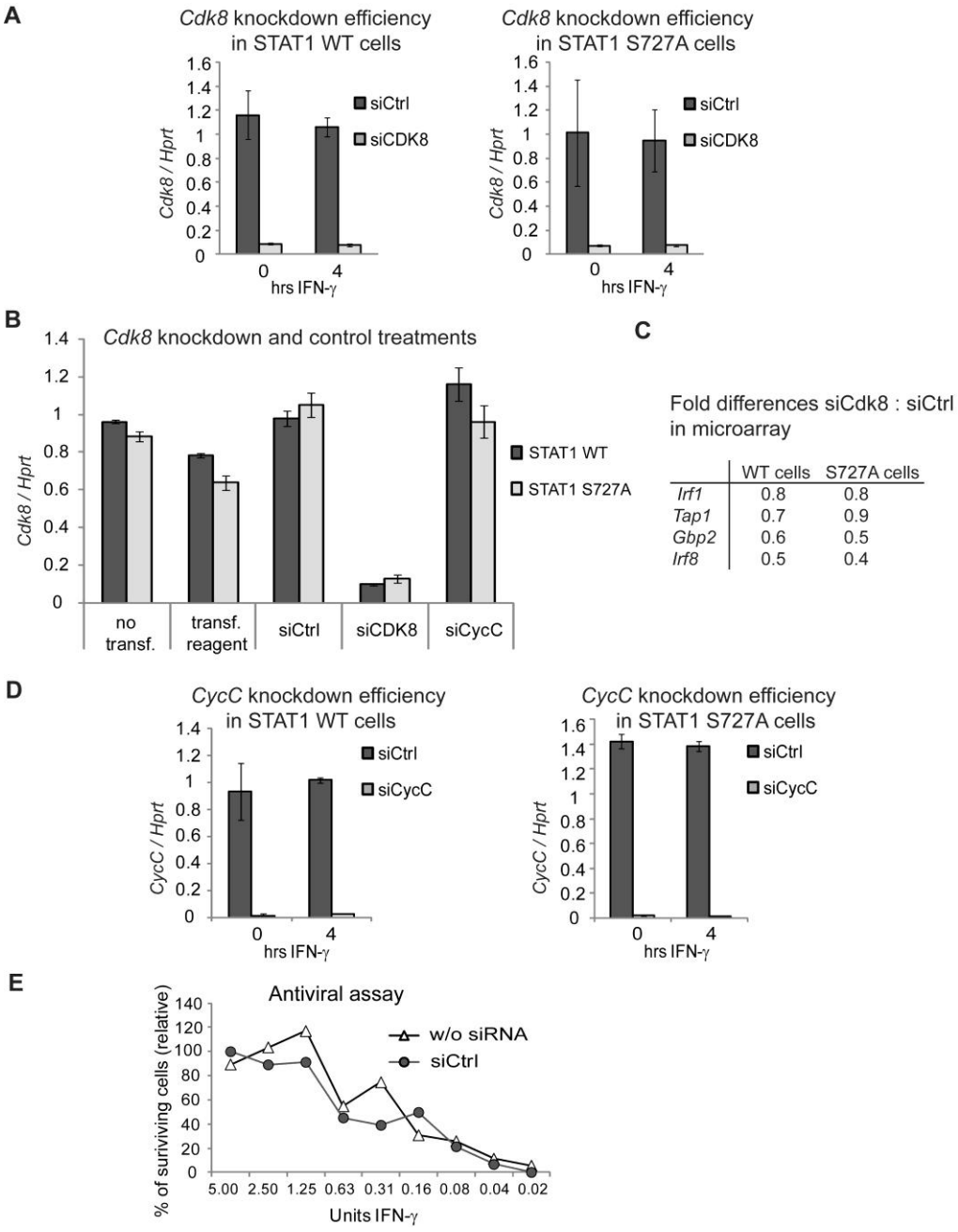

Figure S6. Control Experiments Showing Silencing Efficiency for *Cdk8* and *CycC* (A and D), Fold Differences in Microarray (C) and no Effects of the Transfection Procedure (B and E)

(A) Silencing efficiency of *Cdk8* by siRNA in microarray experiments. Efficiency of silencing of *Cdk8* in STAT1 WT (left panel) or STAT1 S727A (right panel) cells stimulated with IFN-γ or left unstimulated was assessed with measurements of *Cdk8* mRNA levels using qRT-PCR. Relative values to *Hprt* are shown. Error bars represent standard deviations (SDs) of biological triplicates (n = 3).

(B) siRNA transfection procedure has no effect on *Cdk8* expression. STAT1 WT and STAT1 S727A cells were left untreated (no transf.), treated with transfection reagent alone (transf. reagent), control siRNA (siCtrl), siRNA for *Cdk8* (siCdk8), or siRNA for *CycC* (siCycC). *Cdk8* mRNA levels were determined by qRT-PCR. Relative values to *Hprt* are shown. Error bars represent standard deviations (SDs) (n = 3).

(C) Differences in expression of *Irf1*, *Tap1*, *Gbp2* and *Irf8* observed in the microarray experiment shown in Figure 7A and 7B. Differences in IFN-γ-induced expression levels of the indicated genes between siCdk8- and siCtrl-treated WT and S727A cells are depicted. The values are antilog numbers extracted from Table S2.

(D) Silencing efficiency of *CycC* by siRNA in experiments showing similar effect of CycC and CDK8 on expression of IFN-γ-induced genes. Efficiency of silencing of *CycC* in STAT1 WT (left panel) or STAT1 S727A (right panel) cells stimulated with IFN-γ or left unstimulated was controlled by measurements of *CycC* mRNA levels using qRT-PCR. Relative values to *Hprt* are shown. Error bars represent standard deviations (SDs) (n = 3).

(E) The procedure of siRNA transfection does not alter sensitivity of cells to VSV infection. STAT1 WT cells were treated with control siRNA (siCtrl) or were left untreated. After 24 h of incubation with IFN-γ at indicated concentrations cells were infected with VSV (MOI = 0.1), and the cell survival was monitored as in (Figure 7F).

Table S1. IFN-γ-Induced Genes Significantly ($p < 0.05$) Downregulated at Least 2-fold by the STAT1 S727A Mutation

Genbank AC	Gene symbol	WT-g/WT-0	SA-g/WT-g
NM_001034859	*Gm4841*	9.8	-3.0
NM_001033767	*Gm4951*	8.7	-1.1
NM_010260	*Gbp2*	8.1	-1.8
NM_018734	*Gbp3*	7.0	-1.3
NM_194336	*Mpa2l*	6.8	-2.7
NM_001101475	*F830016B08Rik*	6.5	-2.0
NM_145545	*Gbp6*	6.3	-1.0
NM_001039647	*Gbp11*	6.3	-2.9
NM_001168294	*Serpina3f*	6.2	-1.1
NM_010724	*Psmb8*	6.1	-1.6
NM_013585	*Psmb9*	5.7	-2.1
NM_001135115	*Gm12250*	5.2	-1.1
NM_030738	*Vmn1r65*	5.2	-1.6
NM_001037713	*Xaf1*	4.9	-1.1
NM_194336	*Mpa2l*	4.8	-2.3
NM_013683	*Tap1*	4.8	-2.2
NM_001256005	*Gbp4*	4.6	-3.2
NM_008320	*Irf8*	4.6	-2.1
NM_009277	*Trim21*	4.2	-1.4
NM_009896	*Socs1*	3.6	-1.0
NM_001045540	*Gm12185*	3.5	-1.2
NM_011530	*Tap2*	3.2	-2.2
NM_177820	*Apol10b*	2.9	-1.9
NM_020557	*Cmpk2*	2.9	-2.1
NM_021443	*Ccl8*	2.5	-2.0
NM_181545	*Slfn8*	2.5	-1.8
NM_020557	*Cmpk2*	2.5	-1.8
NM_023835	*Trim12a*	2.5	-1.5
NM_001199940	*Serpina3i*	2.3	-1.2
NM_001081083	*Armc3*	2.2	-1.6
NM_023835	*Trim12a*	2.1	-1.4
ENSMUST00000114230	*Psmb9*	1.9	-1.0
NM_199146	*Trim30d*	1.9	-2.4
NM_001037713	*Xaf1*	1.9	-1.3
XM_136331	*Gm4955*	1.9	-1.3
NM_001146007	*9230105E10Rik*	1.7	-1.6
NM_181542	*Slfn10-ps*	1.7	-1.3
NM_001146007	*9230105E10Rik*	1.7	-1.3
NM_001013828	*Iigp1b*	1.6	-1.0
XM_136331	*Gm4955*	1.6	-1.4

NM_011333	*Ccl2*	1.6	-1.6
NM_029419	*Apol7a*	1.6	-1.8
NM_013819	*H2-M3*	1.6	-1.5
NM_001146007	*9230105E10Rik*	1.5	-1.3
NM_183087	*Fam189a1*	1.5	-3.3
NM_001039646	*Gbp10*	1.4	-1.3
NM_178745	*Tmem229b*	1.4	-1.6
NM_007987	*Fas*	1.4	-1.7
NM_025829	*Eif4e3*	1.4	-2.3
NM_013654	*Ccl7*	1.4	-2.3
NM_001190466	*Dact1*	1.3	-3.6
NM_053109	*Clec2d*	1.3	-1.1
NR_033577	*Gm8221*	1.3	-1.3
NM_010171	*F3*	1.3	-2.1
NM_175291	*Dock10*	1.3	-2.1
NM_001190466	*Dact1*	1.3	-3.2
NM_010555	*Il1r2*	1.1	-1.3
NM_033541	*Oas1c*	1.1	-1.9
NM_001083925	*Oas1b*	1.1	-1.1
NM_008362	*Il1r1*	1.0	-1.4
NM_029419	*Apol7a*	1.0	-1.0

Genes are ordered according to their induction (log 2-transformed) by IFN-γ in WT cells (column: WT-g/WT-0). Fold difference (log 2) between S727A (SA) and WT cells is shown in the column "SA-g/WT-g". Genes that appear more than once have different probe set IDs for each listing. Data are extracted from the Table S4.

Table S2. IFN-γ-Induced Genes Significantly ($p < 0.05$) Upregulated at Least 2-fold by the STAT1 S727A Mutation

Genbank AC	Gene symbol	WT-g/WT-0	SA-g/WT-g
NM_021274	*Cxcl10*	6.2	2.6
NM_029000	*Gvin1*	6.0	4.3
NM_009251	*Serpina3g*	5.3	1.2
NM_197986	*Tmem140*	4.4	1.1
NM_001045481	*Ifi203*	4.2	2.6
NM_028967	*Batf2*	4.1	1.7
NM_008329	*Ifi204*	4.0	2.8
NM_015783	*Isg15*	4.0	1.3
NM_015783	*Isg15*	3.9	1.5
NM_001033450	*Mnda*	3.7	2.3
NM_001004174	*AA467197*	3.6	4.0
BC010546	*Ifi204*	3.5	2.6
AK019325	*Gm9706*	3.4	1.3
NM_029000	*Gvin1*	3.3	3.9
NM_007609	*Casp4*	3.1	3.5
XM_001000891	*Gm1966*	3.0	4.2
NM_007609	*Casp4*	2.9	3.5
NM_001045481	*Ifi203*	2.9	2.5
NM_001204910	*AI607873*	2.8	2.8
NM_001139519	*Zbp1*	2.7	1.6
XM_003084464	*Gm16340*	2.5	2.8
NM_178005	*Lrrtm2*	2.3	1.0
NM_033601	*Bcl3*	2.1	2.3
NM_178446	*Rbm47*	2.1	1.9
NM_172393	*Aim1*	2.0	3.6
NM_199015	*D14Ertd668e*	1.9	5.1
NM_023137	*Ubd*	1.9	1.3
ENSMUST00000104958	*Psme2*	1.8	2.3
AK087205	*9530082P21Rik*	1.7	1.1
NM_175475	*Cyp26b1*	1.7	1.9
AK156907	*Cxcl10*	1.5	2.1
NM_011019	*Osmr*	1.4	1.1
NM_013498	*Crem*	1.4	2.2
NM_008381	*Inhbb*	1.4	1.9
NM_009344	*Phlda1*	1.3	1.9
NM_013498	*Crem*	1.3	2.0
NM_178446	*Rbm47*	1.2	1.8
NM_010392	*H2-Q2*	1.2	1.0
NM_010942	*Nsg1*	1.2	2.1
NM_178005	*Lrrtm2*	1.2	1.0
NM_172875	*Adc*	1.2	1.5
NM_026637	*Ggct*	1.1	1.5

NM_009256	*Serpinb9*	1.1	2.1
NM_011580	*Thbs1*	1.1	1.5
NM_009780	*C4b*	1.0	1.9
NM_001033207	*Nlrc5*	1.0	1.2
NM_008599	*Cxcl9*	1.0	2.2
NM_207648	*H2-Q6*	1.0	1.1

Genes are ordered according to their induction (log 2-transformed) by IFN-γ in WT cells (column: WT-g/WT-0). Fold difference (log 2) between S727A (SA) and WT cells is shown in the column "SA-g/WT-g". Genes that appear more than once have different probe set IDs for each listing. Data are extracted from the Table S4

Table S3. IFN-γ-Induced Genes Not Significantly Affected by the STAT1 S727A Mutation

Genbank AC	Gene symbol	WT-g/WT-0
NM_001145164	*Tgtp2*	9.5
NM_018738	*Igtp*	8.6
NM_001146275	*Iigp1*	7.7
NM_019440	*Irgm2*	7.5
NM_001033207	*Nlrc5*	6.8
NM_011854	*Oasl2*	6.7
NM_008330	*Ifi47*	6.1
NM_008326	*Irgm1*	5.8
NM_011579	*Tgtp1*	5.7
NM_021893	*Cd274*	5.7
NM_001145164	*Tgtp2*	5.5
NM_001039530	*Parp14*	5.4
NM_008326	*Irgm1*	5.2
ENSMUST00000073997	*BC023105*	5.2
NM_001168294	*Serpina3f*	5.0
NM_023386	*Rtp4*	5.0
NM_008331	*Ifit1*	4.7
NM_001146275	*Iigp1*	4.5
NM_008390	*Irf1*	4.3
NM_030253	*Parp9*	4.2
NM_010501	*Ifit3*	4.1
NM_001013371	*Dtx3l*	4.1
NM_001163576	*Parp10*	3.8
AK034303	*9330175E14Rik*	3.8
NM_001005858	*I830012O16Rik*	3.7
NM_001168660	*Apol9b*	3.5
NM_001199940	*Serpina3i*	3.5
NM_009283	*Stat1*	3.3
NM_011909	*Usp18*	3.3
NM_019963	*Stat2*	3.3
NM_001163621	*Apol6*	3.2
NM_029219	*Rnf19b*	3.1
NM_173786	*Apol9a*	3.1
NM_173786	*Apol9a*	3.1
NM_013606	*Mx2*	3.0
NM_001114679	*9930111J21Rik1*	3.0
NM_001159417	*Irf9*	3.0
NM_016850	*Irf7*	2.9
NM_030684	*Trim34a*	2.9
NR_033332	*Gm12216*	2.8
AK135804	*Gm10839*	2.7
NM_023279	*Tubb3*	2.7
NM_027835	*Ifih1*	2.7

NM_021394	*Zbp1*	2.7
NM_172729	*Nod1*	2.6
NM_008358	*Il15ra*	2.6
NM_010156	*Samd9l*	2.6
NM_023738	*Uba7*	2.6
NM_013640	*Psmb10*	2.5
NM_001005858	*I830012O16Rik*	2.5
NM_145391	*Tapbpl*	2.5
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NM_198095	*Bst2*	2.2
NM_172893	*Parp12*	2.1
NM_001013371	*Dtx3l*	2.1
NM_010681	*Lama4*	2.1
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NM_153564	*Gbp5*	2.0
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NM_145227	*Oas2*	2.0
NM_172689	*Ddx58*	2.0
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NM_009396	*Tnfaip2*	2.0
NM_175449	*Fam26f*	1.9
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NM_008223	*Serpind1*	1.9
NM_199252	*Unc93a*	1.8
AK017289	*5430410E06Rik*	1.8
NM_001141949	*Nmi*	1.8
NM_027320	*Ifi35*	1.8
NM_001025313	*Tapbp*	1.8
NM_009808	*Casp12*	1.7
NM_011486	*Stat3*	1.7
NM_001159393	*Irf1*	1.7
NM_011832	*Insrr*	1.6
NM_146125	*Itpka*	1.6
NM_008357	*Il15*	1.6
NR_045032	*Gdap10*	1.6
NM_019949	*Ube2l6*	1.6
NM_001005748	*Phactr1*	1.6
NM_001005748	*Phactr1*	1.6
NM_198004	*5133401N09Rik*	1.6
NM_001177351	*AW112010*	1.5

NM_213659	*Stat3*	1.5
NM_126166	*Tlr3*	1.5
NM_145211	*Oas1a*	1.5
NM_009546	*Trim25*	1.5
NM_027835	*Ifih1*	1.5
ENSMUST00000170226	*Plec*	1.5
NM_183162	*BC006779*	1.5
ENSMUST00000112869	*Prune2*	1.5
NM_001005748	*Phactr1*	1.4
NM_011163	*Eif2ak2*	1.4
NM_010531	*Il18bp*	1.4
NM_018851	*Samhd1*	1.4
NM_194346	*Rnf31*	1.4
NM_194346	*Rnf31*	1.3
NM_026913	*Mitd1*	1.3
NM_183426	*Sbno2*	1.3
NM_001033196	*Znfx1*	1.3
NM_011190	*Psme2*	1.3
NM_001139520	*Samhd1*	1.3
NM_009895	*Cish*	1.3
NM_028261	*Tmem173*	1.3
NM_001025208	*LOC547349*	1.3
NM_010398	*H2-T23*	1.3
NM_008230	*Hdc*	1.3
NM_011710	*Wars*	1.3
NM_011190	*Psme2*	1.3
NM_007707	*Socs3*	1.3
NM_001014996	*Cenpj*	1.3
NM_009834	*Ccrn4l*	1.3
NM_008744	*Ntn1*	1.3
ENSMUST00000100186	*LOC100503847*	1.2
NM_001199967	*Gm11127*	1.2
NM_001243760	*Ciita*	1.2
NM_001038587	*Adar*	1.2
NM_028035	*Snx10*	1.2
ENSMUST00000054384	*Trim56*	1.2
NM_001141981	*Rbm43*	1.2
NM_001164314	*Wars*	1.2
NM_028807	*1200009I06Rik*	1.2
NM_028035	*Snx10*	1.2
NM_030743	*Rnf114*	1.1
NM_201373	*Trim56*	1.1
NM_030711	*Erap1*	1.1
NM_001243916	*Trim34b*	1.1
NM_172767	*Vwa5a*	1.1
NM_172767	*Vwa5a*	1.1

NM_001001892	*H2-K1*	1.1
NM_145153	*Oas1f*	1.1
NM_011189	*Psme1*	1.1
NM_011390	*Slc12a7*	1.1
NM_010392	*H2-Q2*	1.1
NM_144830	*Tmem106a*	1.1
NM_011150	*Lgals3bp*	1.1
NM_001033136	*Fam82a2*	1.0
NM_181402	*Parp11*	1.0
NM_001081032	*Gm8909*	1.0
NM_010393	*H2-Q5*	1.0
NR_038025	*4933412E12Rik*	1.0

Genes are ordered according to their induction (log 2-transformed) by IFN-γ in WT cells (column: WT-g/WT-0). Genes that appear more than once have different probe set IDs for each listing. Data are extracted from the Table S4.

Table S4. Microarray Evaluation Showing the Effect of S727A Mutation and Cdk8 Silencing on Expression of IFN-γ-Induced Genes

Probe set ID	Genbank AC	Gene symbol	Gene name	WT-siCtrl-g/WT-siCtrl-0	SA-siCtrl-g/SA-siCtrl-0	SA-siCtrl-g/WT-siCtrl-g	WT-siCdk8-g/WT-siCtrl-g	SA-siCdk8-g/SA-siCtrl-g	WT-siCdk8-0/WT-siCtrl-0	SA-siCdk8-0/SA-siCtrl-0	p-value: WT-siCtrl-g/WT-siCtrl-0	p-value: SA-siCtrl-g/WT-siCtrl-g
A_55_P1981461	AK017289	*5430410E06Rik*	RIKEN cDNA 5430410E06 gene	1.8	1.7	0.8	0.0	-0.1	0.0	0.3	0.00	0.00
A_66_P101942	AK019325	*Gm9706*	predicted gene 9706	3.4	3.9	1.3	-0.2	-0.1	-0.1	-0.4	0.00	0.01
A_55_P2276224	AK034303	*9330175E14Rik*	RIKEN cDNA 9330175E14 gene	3.8	2.7	-0.3	0.0	-0.2	-0.1	-0.4	0.00	0.45
A_55_P2470474	AK087205	*9530082P21Rik*	RIKEN cDNA 9530082P21 gene	1.7	2.0	1.1	-0.2	0.0	-0.3	-0.3	0.00	0.00
A_66_P106060	AK090152	*Dtx3l*	deltex 3-like (Drosophila)	2.3	1.8	0.4	-0.2	-0.1	0.0	-0.6	0.00	0.52
A_55_P2079535	AK135804	*Gm10839*	predicted gene 10839	2.7	3.0	0.3	0.3	-0.1	0.1	0.2	0.00	0.48
A_55_P2016459	AK156907	*Cxcl10*	chemokine (C-X-C motif) ligand 10	1.5	3.2	2.1	-0.2	-0.8	0.0	0.1	0.00	0.00
A_55_P2066578	BC010546	*Ifi204*	interferon activated gene 204	3.5	2.7	2.6	0.1	0.0	0.9	0.0	0.00	0.00
A_66_P124724	ENSMUST00000030584	*Rnf19b*	ring finger protein 19B	2.4	1.9	0.2	0.0	-0.4	0.1	0.1	0.00	0.48
A_55_P2358679	ENSMUST00000054384	*Trim56*	tripartite motif-containing 56	1.2	1.1	-0.2	-0.2	-0.2	0.0	-0.2	0.00	0.28
A_52_P480044	ENSMUST00000073997	*BC023105*	cDNA sequence BC023105	5.2	4.7	-0.6	-1.1	-0.9	-0.1	0.2	0.00	0.08
A_51_P159503	ENSMUST00000093902	*Rnf213*	ring finger protein 213	1.9	1.8	0.1	-0.4	-0.1	0.1	0.1	0.00	0.88
A_55_P2035003	ENSMUST00000100186	*LOC100503847*	hypothetical LOC100503847	1.2	1.3	-0.3	0.0	0.4	-0.1	0.0	0.02	0.61
A_55_P2141943	ENSMUST00000102642	*Ube2l6*	ubiquitin-conjugating enzyme E2L 6	2.1	2.4	-0.8	-0.3	-0.1	-0.5	-0.1	0.00	0.08
A_55_P2025612	ENSMUST00000104958	*Psme2*	proteasome (prosome, macropain) 28 subunit, beta	1.8	0.6	2.3	-0.1	0.1	0.0	-0.1	0.00	0.00
A_55_P2042096	ENSMUST00000112869	*Prune2*	prune homolog 2	1.5	2.2	0.8	-0.7	-0.5	-0.1	0.2	0.01	0.06

			(Drosophila)									
A_55_P2038983	ENSMUST00000114230	*Psmb9*	proteasome (prosome, macropain) subunit, beta type 9 (large multifunctional peptidase 2)	1.9	0.8	-1.0	-0.4	-0.1	0.1	-0.2	0.00	0.00
A_55_P2006983	ENSMUST00000170226	*Plec*	plectin	1.5	1.4	0.0	0.0	0.1	0.2	0.2	0.00	0.98
A_55_P2049647	NM_001001892	*H2-K1*	histocompatibility 2, K1, K region	1.1	0.6	0.9	-0.2	-0.2	0.1	0.0	0.00	0.00
A_55_P2137049	NM_001004174	*AA467197*	expressed sequence AA467197	3.6	3.8	4.0	-1.1	-0.5	0.3	0.5	0.00	0.00
A_52_P605517	NM_001005748	*Phactr1*	phosphatase and actin regulator 1	1.6	0.3	-0.4	-0.1	-0.3	-0.1	-0.9	0.00	0.29
A_51_P182572	NM_001005748	*Phactr1*	phosphatase and actin regulator 1	1.6	0.3	-0.5	-0.3	-0.3	-0.2	-0.9	0.00	0.17
A_55_P2068233	NM_001005748	*Phactr1*	phosphatase and actin regulator 1	1.4	0.4	-0.4	-0.1	-0.3	-0.2	-0.8	0.00	0.36
A_66_P117933	NM_001005858	*I830012O16Rik*	RIKEN cDNA I830012O16 gene	3.7	3.5	0.6	-0.8	-0.5	-0.6	-0.7	0.00	0.36
A_55_P1972872	NM_001005858	*I830012O16Rik*	RIKEN cDNA I830012O16 gene	2.5	2.8	0.4	-1.0	-0.3	-0.5	-0.2	0.01	0.72
A_55_P2174541	NM_001013371	*Dtx3l*	deltex 3-like (Drosophila)	4.1	3.6	0.6	-0.2	-0.3	0.4	0.1	0.00	0.05
A_55_P2059154	NM_001013371	*Dtx3l*	deltex 3-like (Drosophila)	2.1	2.4	0.5	-0.2	-0.2	0.0	0.2	0.00	0.06
A_55_P2112787	NM_001013828	*Iigp1b*	interferon inducible GTPase 1B	1.6	0.8	-1.0	-0.7	-0.5	-0.1	0.1	0.00	0.01
A_51_P174434	NM_001014996	*Cenpj*	centromere protein J	1.3	1.2	-0.3	-0.2	0.0	0.1	0.4	0.00	0.37
A_55_P1966660	NM_001025208	*LOC547349*	similar to MHC class I antigen precursor	1.3	0.9	0.8	-0.3	-0.4	-0.4	-0.3	0.00	0.00
A_55_P2149763	NM_001025313	*Tapbp*	TAP binding protein	1.8	1.0	0.9	0.0	0.0	0.2	0.0	0.00	0.00
A_51_P233027	NM_001033136	*Fam82a2*	family with sequence similarity 82, member A2	1.0	0.7	-0.2	0.0	0.0	0.3	0.1	0.01	0.72
A_55_P2076757	NM_001033196	*Znfx1*	zinc finger, NFX1-type containing 1	1.3	1.4	-0.4	-0.1	-0.1	0.0	-0.1	0.00	0.11
A_66_P113043	NM_001033207	*Nlrc5*	NLR family, CARD domain containing 5	6.8	5.3	0.1	-0.3	-0.4	0.2	0.0	0.00	0.88

A_55_P2016034	NM_001033207	*Nlrc5*	NLR family, CARD domain containing 5	1.0	1.9	1.2	0.0	0.0	0.2	-0.3	0.00	0.00
A_55_P1962918	NM_001033450	*Mnda*	myeloid cell nuclear differentiation antigen	3.7	2.7	2.3	0.0	-0.1	0.3	0.2	0.00	0.00
A_55_P2133195	NM_001033767	*Gm4951*	predicted gene 4951	8.7	7.3	-1.1	-1.1	-1.3	-0.2	-0.3	0.00	0.00
A_55_P2073024	NM_001034859	*Gm4841*	predicted gene 4841	9.8	6.8	-3.0	-1.2	-2.0	-0.1	0.0	0.00	0.00
A_55_P1966838	NM_001037713	*Xaf1*	XIAP associated factor 1	4.9	5.1	-1.1	-0.3	-0.2	0.0	-0.2	0.00	0.01
A_55_P1966833	NM_001037713	*Xaf1*	XIAP associated factor 1	1.9	0.9	-1.3	-0.3	0.1	0.2	0.2	0.00	0.00
A_55_P1969078	NM_001038587	*Adar*	adenosine deaminase, RNA-specific	1.2	1.4	-0.1	-0.2	-0.3	-0.1	0.0	0.01	0.91
A_51_P514712	NM_001039530	*Parp14*	poly (ADP-ribose) polymerase family, member 14	5.4	4.7	0.2	-0.5	-0.5	0.0	0.0	0.00	0.68
A_55_P1978521	NM_001039646	*Gbp10*	guanylate-binding protein 10	1.4	0.5	-1.3	-0.6	-0.1	0.0	0.1	0.00	0.00
A_55_P2042813	NM_001039647	*Gbp11*	guanylate binding protein 11	6.3	2.7	-2.9	-0.3	-0.2	0.0	-0.6	0.00	0.00
A_55_P1966731	NM_001045481	*Ifi203*	interferon activated gene 203	4.2	6.0	2.6	0.4	-0.3	0.1	0.1	0.00	0.00
A_55_P1988202	NM_001045481	*Ifi203*	interferon activated gene 203	2.9	4.9	2.5	0.4	0.0	0.0	0.2	0.00	0.00
A_52_P494730	NM_001045540	*Gm12185*	predicted gene 12185	3.5	1.4	-1.2	-1.0	-0.2	0.1	0.0	0.00	0.00
A_55_P1956160	NM_001081032	*Gm8909*	predicted gene 8909	1.0	0.8	0.6	-0.2	-0.3	-0.3	-0.3	0.03	0.08
A_55_P2008016	NM_001081083	*Armc3*	armadillo repeat containing 3	2.2	0.7	-1.6	0.1	0.0	0.1	-0.1	0.00	0.00
A_55_P1959064	NM_001083925	*Oas1b*	2'-5' oligoadenylate synthetase 1B	1.1	0.1	-1.1	-0.1	0.0	0.0	-0.1	0.00	0.00
A_66_P125389	NM_001101475	*F830016B08Rik*	RIKEN cDNA F830016B08 gene	6.5	4.5	-2.0	-1.2	-1.5	-0.2	-0.2	0.00	0.00
A_55_P2015405	NM_001114679	*9930111J21Rik1*	RIKEN cDNA 9930111J21 gene 1	3.0	1.2	-0.3	-0.6	-0.2	0.1	0.0	0.00	0.37
A_55_P2057936	NM_001135115	*Gm12250*	predicted gene 12250	5.2	4.1	-1.1	-0.5	-0.6	-0.1	-0.1	0.00	0.01
A_55_P1994042	NM_001139519	*Zbp1*	Z-DNA binding protein 1	2.7	4.2	1.6	0.1	-0.4	0.0	0.1	0.00	0.00

A_55_P2019699	NM_001139520	*Samhd1*	SAM domain and HD domain, 1	1.3	1.5	0.5	-0.4	-0.3	-0.1	-0.1	0.00	0.16
A_55_P2034705	NM_001141949	*Nmi*	N-myc (and STAT) interactor	1.8	1.5	0.3	-0.1	-0.1	0.2	0.0	0.00	0.23
A_55_P2017491	NM_001141981	*Rbm43*	RNA binding motif protein 43	1.2	0.7	-0.1	0.1	0.2	0.2	0.0	0.00	0.79
A_55_P2062246	NM_001145164	*Tgtp2*	T-cell specific GTPase 2	9.5	9.2	-0.6	-0.8	-0.8	1.1	0.0	0.00	0.07
A_55_P1989225	NM_001145164	*Tgtp2*	T-cell specific GTPase 2	5.5	4.9	-0.6	-1.3	-0.5	-0.1	0.0	0.00	0.06
A_55_P2039061	NM_001146007	*9230105E10Rik*	RIKEN cDNA 9230105E10 gene	1.7	0.8	-1.6	0.1	0.2	0.1	-0.1	0.00	0.00
A_55_P2163857	NM_001146007	*9230105E10Rik*	RIKEN cDNA 9230105E10 gene	1.7	0.8	-1.3	-0.2	0.1	0.1	0.1	0.00	0.00
A_55_P2064652	NM_001146007	*9230105E10Rik*	RIKEN cDNA 9230105E10 gene	1.5	0.5	-1.3	0.5	0.1	0.0	-0.2	0.01	0.00
A_55_P1990633	NM_001146275	*Iigp1*	interferon inducible GTPase 1	7.7	7.3	-0.7	-1.3	-1.1	0.8	0.2	0.00	0.57
A_55_P2410304	NM_001146275	*Iigp1*	interferon inducible GTPase 1	4.5	4.0	-0.7	-1.2	-1.2	-0.2	-0.4	0.00	0.06
A_55_P2000067	NM_001159393	*Irf1*	interferon regulatory factor 1	1.7	1.7	-0.1	-0.3	-0.3	-0.1	0.1	0.00	0.87
A_55_P2114938	NM_001159417	*Irf9*	interferon regulatory factor 9	3.0	2.1	-0.1	-0.3	-0.4	-0.2	-0.5	0.00	0.81
A_55_P2130970	NM_001163576	*Parp10*	poly (ADP-ribose) polymerase family, member 10	3.8	2.9	0.0	-0.2	-0.2	0.7	0.1	0.00	0.99
A_66_P104314	NM_001163621	*Apol6*	apolipoprotein L 6	3.2	3.3	0.6	0.0	0.2	0.4	0.2	0.00	0.19
A_55_P1972275	NM_001164314	*Wars*	tryptophanyl-tRNA synthetase	1.2	1.1	-0.6	-0.1	0.0	0.2	0.2	0.01	0.09
A_55_P2104975	NM_001168294	*Serpina3f*	serine (or cysteine) peptidase inhibitor, clade A, member 3F	6.2	4.7	-1.1	-1.1	-1.5	-0.1	-0.3	0.00	0.01
A_55_P2142226	NM_001168294	*Serpina3f*	serine (or cysteine) peptidase inhibitor, clade A, member 3F	5.0	3.1	-0.5	-1.2	-1.3	-0.2	-0.7	0.00	0.16
A_66_P110633	NM_001168660	*Apol9b*	apolipoprotein L 9b	3.5	4.1	0.6	0.0	0.0	0.0	0.0	0.00	0.05
A_52_P1020860	NM_001177351	*AW112010*	expressed sequence AW112010	1.5	1.2	-0.3	0.1	0.0	0.4	0.2	0.04	0.66
A_51_P175567	NM_001190466	*Dact1*	dapper homolog 1,	1.3	1.6	-3.6	-0.5	0.0	0.2	0.3	0.00	0.00

			antagonist of beta-catenin (xenopus)									
A_55_P2177899	NM_001190466	*Dact1*	dapper homolog 1, antagonist of beta-catenin (xenopus)	1.3	1.3	-3.2	-0.4	-0.1	0.3	0.3	0.00	0.00
A_55_P1966774	NM_001199940	*Serpina3i*	serine (or cysteine) peptidase inhibitor, clade A, member 3l	3.5	1.4	-1.0	-0.9	-1.0	-0.8	-1.4	0.01	0.37
A_55_P2142232	NM_001199940	*Serpina3i*	serine (or cysteine) peptidase inhibitor, clade A, member 3l	2.3	1.5	-1.2	-0.8	-0.7	-0.4	0.0	0.00	0.00
A_55_P2125049	NM_001199967	*Gm11127*	predicted gene 11127	1.2	0.7	0.9	-0.3	-0.3	-0.2	-0.1	0.00	0.00
A_55_P2081105	NM_001204910	*AI607873*	expressed sequence AI607873	2.8	3.7	2.8	0.8	0.2	0.5	0.6	0.00	0.00
A_55_P2179074	NM_001243760	*Ciita*	class II transactivator	1.2	1.3	0.1	-0.2	-0.3	-0.2	0.0	0.02	0.90
A_55_P1973229	NM_001243916	*Trim34b*	tripartite motif-containing 34B	1.1	0.7	-0.3	-0.2	0.1	0.2	-0.2	0.00	0.31
A_55_P2103837	NM_001256005	*Gbp4*	guanylate binding protein 4	4.6	1.4	-3.2	-0.6	-0.6	0.0	-0.1	0.00	0.00
A_55_P2091461	NM_007609	*Casp4*	caspase 4, apoptosis-related cysteine peptidase	3.1	2.0	3.5	0.3	-0.1	0.4	0.2	0.00	0.00
A_55_P1984168	NM_007609	*Casp4*	caspase 4, apoptosis-related cysteine peptidase	2.9	2.0	3.5	0.3	0.0	0.3	0.3	0.00	0.00
A_51_P474459	NM_007707	*Socs3*	suppressor of cytokine signaling 3	1.3	1.4	0.6	-0.2	-0.4	0.0	-0.2	0.00	0.01
A_55_P2091676	NM_007987	*Fas*	Fas (TNF receptor superfamily member 6)	1.4	1.8	-1.7	0.3	-0.8	0.3	-0.6	0.01	0.00
A_51_P468140	NM_008223	*Serpind1*	serine (or cysteine) peptidase inhibitor, clade D, member 1	1.9	1.8	0.0	-0.5	-0.1	0.0	0.0	0.00	0.95
A_51_P254656	NM_008230	*Hdc*	histidine decarboxylase	1.3	0.8	-0.5	-0.3	0.2	0.0	0.2	0.00	0.03
A_52_P354823	NM_008320	*Irf8*	interferon regulatory factor 8	4.6	2.7	-2.1	-0.9	-1.3	-0.1	0.0	0.00	0.00
A_55_P1981479	NM_008326	*Irgm1*	immunity-related GTPase family M member 1	5.8	4.5	-0.4	-0.4	-0.2	0.3	-0.1	0.00	0.13
A_51_P262171	NM_008326	*Irgm1*	immunity-related	5.2	4.3	-0.1	-0.3	-0.3	0.2	-0.2	0.00	0.70

			GTPase family M member 1									
A_55_P1975560	NM_008329	*Ifi204*	interferon activated gene 204	4.0	3.1	2.8	0.4	0.1	1.0	0.2	0.00	0.00
A_55_P1998416	NM_008330	*Ifi47*	interferon gamma inducible protein 47	6.1	5.9	-0.3	0.0	0.0	0.6	0.2	0.00	0.68
A_51_P327751	NM_008331	*Ifit1*	interferon-induced protein with tetratricopeptide repeats 1	4.7	4.4	0.5	-0.5	-0.6	-0.3	-0.5	0.00	0.47
A_52_P15461	NM_008357	*Il15*	interleukin 15	1.6	1.1	-0.4	0.0	0.4	-0.1	0.2	0.00	0.10
A_55_P2041738	NM_008358	*Il15ra*	interleukin 15 receptor, alpha chain	2.6	2.4	-0.2	-0.7	-0.7	-0.2	-0.3	0.00	0.59
A_51_P271503	NM_008362	*Il1r1*	interleukin 1 receptor, type I	1.0	0.7	-1.4	0.2	-0.7	0.3	-0.2	0.01	0.00
A_55_P2096422	NM_008381	*Inhbb*	inhibin beta-B	1.4	-0.2	1.9	0.0	0.3	0.2	0.3	0.00	0.00
A_55_P2000062	NM_008390	*Irf1*	interferon regulatory factor 1	4.3	3.8	0.0	-0.1	-0.1	0.1	0.1	0.00	0.95
A_51_P461665	NM_008599	*Cxcl9*	chemokine (C-X-C motif) ligand 9	1.0	3.1	2.2	0.3	-0.7	-0.1	0.1	0.00	0.00
A_55_P2162935	NM_008744	*Ntn1*	netrin 1	1.3	0.6	0.0	-0.1	-0.2	0.0	0.2	0.00	0.96
A_51_P326191	NM_009251	*Serpina3g*	serine (or cysteine) peptidase inhibitor, clade A, member 3G	5.3	4.0	1.2	-0.9	-1.1	-0.5	-1.1	0.00	0.00
A_55_P2134246	NM_009256	*Serpinb9*	serine (or cysteine) peptidase inhibitor, clade B, member 9	1.1	0.6	2.1	-0.2	-0.2	-0.2	-0.2	0.01	0.00
A_55_P1962344	NM_009277	*Trim21*	tripartite motif-containing 21	4.2	3.8	-1.4	-0.3	-0.2	0.3	0.1	0.00	0.00
A_55_P1955906	NM_009283	*Stat1*	signal transducer and activator of transcription 1	3.3	2.9	-0.4	-0.5	-0.4	0.0	0.2	0.00	0.33
A_51_P195958	NM_009344	*Phlda1*	pleckstrin homology-like domain, family A, member 1	1.3	0.1	1.9	-0.4	-0.1	-0.1	0.1	0.01	0.00
A_55_P2098697	NM_009396	*Tnfaip2*	tumor necrosis factor, alpha-induced protein 2	2.0	0.7	-0.6	0.1	-0.2	0.3	0.2	0.00	0.02
A_51_P364485	NM_009396	*Tnfaip2*	tumor necrosis factor, alpha-	2.0	0.7	-0.6	0.1	-0.2	0.3	0.2	0.00	0.02

			induced protein 2									
A_55_P2098071	NM_009546	*Trim25*	tripartite motif-containing 25	1.5	1.4	-0.7	-0.2	-0.3	-0.2	-0.4	0.00	0.01
A_55_P2078633	NM_009780	*C4b*	complement component 4B (Childo blood group)	1.0	0.9	1.9	0.0	0.0	0.4	-0.2	0.04	0.00
A_55_P1983853	NM_009808	*Casp12*	caspase 12	1.7	1.2	0.6	0.0	-0.1	0.2	-0.3	0.00	0.00
A_55_P1968723	NM_009834	*Ccrn4l*	CCR4 carbon catabolite repression 4-like (S. cerevisiae)	1.3	1.2	0.8	0.1	0.0	0.1	0.4	0.00	0.01
A_51_P470715	NM_009895	*Cish*	cytokine inducible SH2-containing protein	1.3	1.4	0.5	-0.1	-0.2	0.0	-0.2	0.00	0.01
A_51_P279606	NM_009896	*Socs1*	suppressor of cytokine signaling 1	3.6	2.8	-1.0	-0.2	-0.2	-0.1	-0.2	0.00	0.00
A_66_P121787	NM_010156	*Samd9l*	sterile alpha motif domain containing 9-like	2.6	2.7	0.1	0.0	-0.1	0.2	0.0	0.00	0.85
A_55_P2151601	NM_010156	*Samd9l*	sterile alpha motif domain containing 9-like	2.4	2.6	0.2	0.1	0.0	0.1	0.0	0.00	0.56
A_65_P08971	NM_010171	*F3*	coagulation factor III	1.3	1.0	-2.1	-0.2	-0.1	0.2	0.0	0.01	0.00
A_51_P203955	NM_010260	*Gbp2*	guanylate binding protein 2	8.1	8.0	-1.8	-0.8	-1.1	-0.2	-0.2	0.00	0.00
A_51_P425048	NM_010392	*H2-Q2*	histocompatibility 2, Q region locus 2	1.2	0.6	1.0	-0.3	-0.1	-0.1	-0.1	0.00	0.00
A_51_P219789	NM_010392	*H2-Q2*	histocompatibility 2, Q region locus 2	1.1	0.6	0.9	-0.2	0.0	0.0	0.0	0.00	0.00
A_51_P400752	NM_010393	*H2-Q5*	histocompatibility 2, Q region locus 5	1.0	0.6	0.8	-0.3	-0.1	0.0	0.0	0.00	0.00
A_51_P237754	NM_010398	*H2-T23*	histocompatibility 2, T region locus 23	1.3	0.7	0.8	-0.3	-0.3	-0.2	-0.1	0.00	0.00
A_51_P359570	NM_010501	*Ifit3*	interferon-induced protein with tetratricopeptide repeats 3	4.1	2.8	0.9	-0.6	-0.5	-0.2	-0.3	0.00	0.07
A_52_P577384	NM_010531	*Il18bp*	interleukin 18 binding protein	1.4	0.9	0.2	0.1	0.1	0.1	0.1	0.00	0.41
A_51_P470079	NM_010555	*Il1r2*	interleukin 1 receptor, type II	1.1	0.1	-1.3	0.8	0.1	0.4	-0.1	0.00	0.00

A_51_P212420	NM_010681	*Lama4*	laminin, alpha 4	2.1	1.2	0.4	0.6	-0.2	1.3	-0.2	0.00	0.43
A_51_P345367	NM_010724	*Psmb8*	proteasome (prosome, macropain) subunit, beta type 8 (large multifunctional peptidase 7)	6.1	5.2	-1.6	-0.2	-0.3	0.5	0.1	0.00	0.00
A_51_P390538	NM_010821	*Mpeg1*	macrophage expressed gene 1	2.4	2.7	0.3	-0.4	-0.1	0.0	0.2	0.00	0.59
A_52_P467726	NM_010942	*Nsg1*	neuron specific gene family member 1	1.2	0.8	2.1	0.0	0.1	0.3	0.1	0.00	0.00
A_51_P319460	NM_011019	*Osmr*	oncostatin M receptor	1.4	1.1	1.1	0.1	-0.4	0.1	-0.5	0.00	0.00
A_51_P359636	NM_011150	*Lgals3bp*	lectin, galactoside-binding, soluble, 3 binding protein	1.1	1.1	-0.1	0.5	0.4	0.6	0.4	0.02	0.81
A_52_P559919	NM_011163	*Eif2ak2*	eukaryotic translation initiation factor 2-alpha kinase 2	1.4	1.4	0.3	-0.3	0.0	-0.2	-0.4	0.00	0.31
A_51_P101196	NM_011189	*Psme1*	proteasome (prosome, macropain) 28 subunit, alpha	1.1	1.0	-0.1	-0.1	-0.2	0.0	0.0	0.00	0.72
A_55_P1996862	NM_011190	*Psme2*	proteasome (prosome, macropain) 28 subunit, beta	1.3	1.0	0.2	-0.1	0.0	0.2	0.1	0.00	0.58
A_55_P2025611	NM_011190	*Psme2*	proteasome (prosome, macropain) 28 subunit, beta	1.3	0.9	0.0	-0.1	0.0	0.1	0.0	0.00	0.98
A_51_P286737	NM_011333	*Ccl2*	chemokine (C-C motif) ligand 2	1.6	2.7	-1.6	0.4	-0.3	0.9	0.6	0.00	0.00
A_51_P421734	NM_011390	*Slc12a7*	solute carrier family 12, member 7	1.1	0.3	0.6	0.2	0.2	0.5	0.3	0.00	0.00
A_55_P1991219	NM_011486	*Stat3*	signal transducer and activator of transcription 3	1.7	0.7	-0.2	-0.3	0.1	0.1	0.0	0.00	0.67
A_55_P2017645	NM_011530	*Tap2*	transporter 2, ATP-binding cassette, sub-family B (MDR/TAP)	3.2	3.3	-2.2	-0.4	-0.2	0.2	-0.2	0.00	0.00

A_51_P478722	NM_011579	*Tgtp1*	T-cell specific GTPase 1	5.7	5.3	-0.4	-1.0	-0.6	0.1	0.2	0.00	0.40
A_55_P2017636	NM_011580	*Thbs1*	thrombospondin 1	1.1	0.0	1.5	0.5	-0.7	0.8	-0.7	0.01	0.00
A_55_P2082902	NM_011710	*Wars*	tryptophanyl-tRNA synthetase	1.3	1.0	-0.4	-0.3	0.1	0.2	0.2	0.00	0.23
A_55_P1983708	NM_011832	*Insrr*	insulin receptor-related receptor	1.6	0.8	-0.6	-0.1	0.0	-0.1	-0.1	0.00	0.02
A_51_P387123	NM_011854	*Oasl2*	2'-5' oligoadenylate synthetase-like 2	6.7	6.3	-0.1	-0.4	-0.2	-0.2	-0.2	0.00	0.93
A_55_P2114953	NM_011909	*Usp18*	ubiquitin specific peptidase 18	3.3	3.8	0.8	-0.6	-0.3	-0.3	-0.1	0.00	0.19
A_51_P423976	NM_013498	*Crem*	cAMP responsive element modulator	1.4	1.7	2.2	-0.4	-0.2	-0.2	0.1	0.00	0.00
A_52_P460957	NM_013498	*Crem*	cAMP responsive element modulator	1.3	1.6	2.0	-0.3	-0.1	-0.3	0.0	0.00	0.00
A_51_P369803	NM_013585	*Psmb9*	proteasome (prosome, macropain) subunit, beta type 9 (large multifunctional peptidase 2)	5.7	5.1	-2.1	-0.3	-0.1	0.1	0.1	0.00	0.00
A_51_P514085	NM_013606	*Mx2*	myxovirus (influenza virus) resistance 2	3.0	3.6	0.6	0.0	0.0	0.1	0.0	0.00	0.27
A_52_P570266	NM_013640	*Psmb10*	proteasome (prosome, macropain) subunit, beta type 10	2.5	2.2	0.4	-0.2	-0.2	0.0	-0.2	0.00	0.12
A_51_P436652	NM_013654	*Ccl7*	chemokine (C-C motif) ligand 7	1.4	3.2	-2.3	0.8	-0.2	1.3	0.6	0.00	0.00
A_51_P100327	NM_013683	*Tap1*	transporter 1, ATP-binding cassette, sub-family B (MDR/TAP)	4.8	4.3	-2.2	-0.5	-0.1	0.7	0.2	0.00	0.00
A_51_P469968	NM_013819	*H2-M3*	histocompatibility 2, M region locus 3	1.6	1.6	-1.5	0.2	0.4	0.4	0.5	0.00	0.00
A_66_P128537	NM_015783	*Isg15*	ISG15 ubiquitin-like modifier	4.0	4.4	1.3	-0.2	0.0	-0.2	-0.5	0.00	0.01
A_55_P2103698	NM_015783	*Isg15*	ISG15 ubiquitin-like modifier	3.9	4.7	1.5	-0.1	-0.1	-0.2	-0.1	0.00	0.00
A_51_P421876	NM_016850	*Irf7*	interferon regulatory factor 7	2.9	3.4	-0.2	-0.7	-0.1	-0.2	-0.1	0.00	0.72
A_55_P2472435	NM_018734	*Gbp3*	guanylate binding protein 3	7.0	6.7	-1.3	-0.6	-0.6	-0.1	-0.2	0.00	0.00

A_51_P112355	NM_018738	*Igtp*	interferon gamma induced GTPase	8.6	8.8	-0.5	-0.4	-0.5	0.6	0.2	0.00	0.13
A_52_P466090	NM_018851	*Samhd1*	SAM domain and HD domain, 1	1.4	1.5	0.7	-0.3	-0.2	0.1	0.0	0.00	0.01
A_55_P2137611	NM_019440	*Irgm2*	immunity-related GTPase family M member 2	7.5	7.2	-0.8	-0.6	-0.5	0.2	-0.1	0.00	0.03
A_55_P2031125	NM_019949	*Ube2l6*	ubiquitin-conjugating enzyme E2L 6	1.6	1.4	-0.9	-0.2	-0.2	-0.3	-0.4	0.00	0.00
A_55_P2059606	NM_019963	*Stat2*	signal transducer and activator of transcription 2	3.3	2.5	-0.5	-0.3	-0.2	-0.1	-0.2	0.00	0.08
A_55_P2158404	NM_020557	*Cmpk2*	cytidine monophosphate (UMP-CMP) kinase 2, mitochondrial	2.9	0.8	-2.1	-0.2	0.0	0.0	-0.5	0.00	0.00
A_52_P186937	NM_020557	*Cmpk2*	cytidine monophosphate (UMP-CMP) kinase 2, mitochondrial	2.5	0.7	-1.8	-0.1	0.1	-0.1	-0.5	0.00	0.00
A_55_P2016462	NM_021274	*Cxcl10*	chemokine (C-X-C motif) ligand 10	6.2	5.6	2.6	-0.6	-0.8	-0.5	-0.2	0.00	0.00
A_66_P139683	NM_021394	*Zbp1*	Z-DNA binding protein 1	2.7	3.5	0.8	-0.5	-0.4	0.0	0.2	0.00	0.13
A_51_P464703	NM_021443	*Ccl8*	chemokine (C-C motif) ligand 8	2.5	2.0	-2.0	0.0	-0.2	0.1	-0.1	0.00	0.00
A_51_P248666	NM_021893	*Cd274*	CD274 antigen	5.7	4.4	-0.9	-0.8	-0.8	-0.2	0.1	0.00	0.04
A_52_P338066	NM_023137	*Ubd*	ubiquitin D	1.9	3.2	1.3	0.3	0.2	-0.1	0.3	0.00	0.00
A_55_P2041828	NM_023279	*Tubb3*	tubulin, beta 3	2.7	1.3	-0.6	-0.4	0.4	0.0	0.5	0.00	0.05
A_51_P304170	NM_023386	*Rtp4*	receptor transporter protein 4	5.0	5.1	-0.1	-0.2	-0.1	0.0	-0.2	0.00	0.96
A_55_P2026233	NM_023738	*Uba7*	ubiquitin-like modifier activating enzyme 7	2.6	1.3	0.0	-0.3	0.0	0.2	-0.4	0.00	0.98
A_52_P267391	NM_023835	*Trim12a*	tripartite motif-containing 12A	2.5	2.5	-1.5	0.0	0.1	-0.1	0.1	0.00	0.00
A_55_P2064659	NM_023835	*Trim12a*	tripartite motif-containing 12A	2.1	1.5	-1.4	-0.1	0.2	0.2	0.0	0.00	0.00
A_51_P187842	NM_025829	*Eif4e3*	eukaryotic translation initiation factor 4E member 3	1.4	0.6	-2.3	0.1	0.4	0.0	0.0	0.00	0.00
A_52_P679860	NM_025992	*Herc6*	hect domain and	2.2	2.1	0.4	-0.2	0.1	0.0	0.7	0.00	0.19

			RLD 6									
A_52_P64514	NM_025992	*Herc6*	hect domain and RLD 6	2.2	2.0	0.6	-0.5	0.1	0.1	0.3	0.00	0.20
A_52_P641758	NM_026637	*Ggct*	gamma-glutamyl cyclotransferase	1.1	1.0	1.5	0.2	-0.6	0.5	-0.4	0.02	0.00
A_66_P122110	NM_026913	*Mitd1*	MIT, microtubule interacting and transport, domain containing 1	1.3	1.1	-0.6	-0.3	0.0	-0.2	-0.2	0.00	0.00
A_51_P414889	NM_027320	*Ifi35*	interferon-induced protein 35	1.8	1.7	-0.1	-0.3	0.0	0.1	-0.2	0.00	0.86
A_55_P1978987	NM_027835	*Ifih1*	interferon induced with helicase C domain 1	2.7	1.4	0.7	-0.2	0.1	0.4	0.6	0.00	0.06
A_55_P2005783	NM_027835	*Ifih1*	interferon induced with helicase C domain 1	1.5	1.1	0.5	-0.4	0.4	0.2	0.5	0.00	0.02
A_51_P120093	NM_028035	*Snx10*	sorting nexin 10	1.2	1.0	0.5	-0.2	-0.1	-0.2	0.0	0.00	0.00
A_66_P110343	NM_028035	*Snx10*	sorting nexin 10	1.2	0.9	0.6	-0.1	-0.2	-0.1	-0.1	0.00	0.00
A_51_P240801	NM_028261	*Tmem173*	transmembrane protein 173	1.3	1.2	0.3	-0.1	-0.2	-0.1	-0.3	0.00	0.38
A_55_P2022604	NM_028807	*1200009I06Rik*	RIKEN cDNA 1200009I06 gene	1.2	0.4	-0.8	0.2	-0.4	0.1	-0.2	0.00	0.00
A_51_P165182	NM_028967	*Batf2*	basic leucine zipper transcription factor, ATF-like 2	4.1	5.5	1.7	-0.6	-1.2	-0.1	-0.2	0.00	0.00
A_55_P1996973	NM_029000	*Gvin1*	GTPase, very large interferon inducible 1	6.0	2.5	4.3	-0.2	-0.2	0.5	-0.2	0.00	0.00
A_52_P535484	NM_029000	*Gvin1*	GTPase, very large interferon inducible 1	3.3	2.6	3.9	-0.2	-0.3	0.1	-0.1	0.00	0.00
A_51_P444290	NM_029084	*Slamf8*	SLAM family member 8	2.4	1.9	-0.3	0.2	0.2	-0.1	0.0	0.00	0.52
A_55_P2068607	NM_029219	*Rnf19b*	ring finger protein 19B	3.1	2.1	0.5	-0.1	-0.2	0.2	-0.1	0.00	0.05
A_55_P1964262	NM_029419	*Apol7a*	apolipoprotein L 7a	1.6	1.6	-1.8	-0.1	0.1	0.2	0.4	0.00	0.00
A_51_P497724	NM_029419	*Apol7a*	apolipoprotein L 7a	1.0	0.3	-1.0	0.0	0.3	0.3	0.3	0.02	0.00
A_55_P2142863	NM_030253	*Parp9*	poly (ADP-ribose) polymerase family, member 9	4.2	3.3	0.6	-0.3	-0.1	0.5	0.0	0.00	0.01
A_66_P105689	NM_030684	*Trim34a*	tripartite motif-	2.9	2.8	-0.6	0.0	-0.2	0.4	-0.1	0.00	0.06

			containing 34A									
A_65_P04284	NM_030711	*Erap1*	endoplasmic reticulum aminopeptidase 1	1.1	1.0	-0.7	0.2	0.4	0.5	0.5	0.00	0.00
A_55_P2166049	NM_030738	*Vmn1r65*	vomeronasal 1 receptor 65	5.2	3.1	-1.6	-0.9	-1.6	-0.2	-0.6	0.00	0.00
A_55_P1958255	NM_030743	*Rnf114*	ring finger protein 114	1.1	1.0	-0.1	-0.1	0.2	0.1	0.1	0.00	0.78
A_55_P1998957	NM_033541	*Oas1c*	2'-5' oligoadenylate synthetase 1C	1.1	1.0	-1.9	0.2	0.5	0.3	0.2	0.00	0.00
A_55_P2066116	NM_033601	*Bcl3*	B-cell leukemia/lymphoma 3	2.1	1.5	2.3	-0.4	-0.2	-0.7	-0.2	0.00	0.00
A_55_P2115442	NM_053109	*Clec2d*	C-type lectin domain family 2, member d	1.3	2.2	-1.1	0.1	-0.3	-0.1	-0.4	0.03	0.01
A_52_P85174	NM_126166	*Tlr3*	toll-like receptor 3	1.5	1.4	0.1	-0.3	0.1	0.3	0.1	0.00	0.95
A_55_P2037121	NM_144830	*Tmem106a*	transmembrane protein 106A	1.1	0.9	0.0	-0.3	0.2	0.2	0.2	0.00	1.00
A_51_P154842	NM_145153	*Oas1f*	2'-5' oligoadenylate synthetase 1F	1.1	1.2	-0.2	0.0	0.1	0.3	0.1	0.04	0.71
A_55_P1998943	NM_145211	*Oas1a*	2'-5' oligoadenylate synthetase 1A	1.5	1.7	0.4	0.2	0.1	-0.1	-0.1	0.03	0.55
A_55_P2019719	NM_145227	*Oas2*	2'-5' oligoadenylate synthetase 2	2.0	1.8	-0.3	-0.1	0.3	-0.1	-0.1	0.01	0.79
A_51_P505795	NM_145391	*Tapbpl*	TAP binding protein-like	2.5	1.9	-0.3	-0.2	-0.1	0.1	-0.1	0.00	0.28
A_51_P463846	NM_145545	*Gbp6*	guanylate binding protein 6	6.3	6.3	-1.0	-0.8	-0.5	0.0	-0.1	0.00	0.03
A_51_P273609	NM_146125	*Itpka*	inositol 1,4,5-trisphosphate 3-kinase A	1.6	1.5	0.3	-0.4	-0.1	0.0	0.1	0.00	0.39
A_52_P327664	NM_153564	*Gbp5*	guanylate binding protein 5	2.0	1.5	-0.3	0.0	-0.3	-0.1	-0.5	0.00	0.50
A_55_P2116059	NM_172393	*Aim1*	absent in melanoma 1	2.0	0.2	3.6	-0.4	0.0	-0.4	0.0	0.00	0.00
A_52_P385536	NM_172689	*Ddx58*	DEAD (Asp-Glu-Ala-Asp) box polypeptide 58	2.0	2.4	0.4	-0.5	-0.3	-0.4	-0.6	0.00	0.22
A_55_P1965000	NM_172689	*Ddx58*	DEAD (Asp-Glu-Ala-Asp) box polypeptide 58	2.0	2.5	0.1	-0.5	-0.2	-0.5	-0.3	0.00	0.92
A_51_P234113	NM_172729	*Nod1*	nucleotide-binding	2.6	2.7	0.7	-0.3	-0.8	-0.2	-0.3	0.00	0.10

			oligomerization domain containing 1									
A_55_P2131088	NM_172767	*Vwa5a*	von Willebrand factor A domain containing 5A	1.1	1.1	-0.3	-0.5	-0.3	-0.4	-0.4	0.04	0.62
A_66_P131754	NM_172767	*Vwa5a*	von Willebrand factor A domain containing 5A	1.1	1.2	0.1	-0.4	-0.2	-0.3	-0.2	0.04	0.95
A_66_P140742	NM_172875	*Adc*	arginine decarboxylase	1.2	0.5	1.5	0.0	0.0	0.2	-0.2	0.01	0.00
A_51_P214747	NM_172893	*Parp12*	poly (ADP-ribose) polymerase family, member 12	2.1	2.1	-0.1	-0.6	-0.2	-0.2	0.1	0.00	0.94
A_55_P2107775	NM_173786	*Apol9a*	apolipoprotein L 9a	3.1	3.8	0.5	-0.1	0.0	0.1	0.3	0.00	0.15
A_55_P2043367	NM_173786	*Apol9a*	apolipoprotein L 9a	3.1	3.7	0.6	0.0	0.0	0.0	0.0	0.00	0.02
A_52_P650028	NM_175291	*Dock10*	dedicator of cytokinesis 10	1.3	0.0	-2.1	0.5	0.0	0.8	0.2	0.01	0.00
A_51_P100852	NM_175449	*Fam26f*	family with sequence similarity 26, member F	1.9	2.1	0.3	-0.2	0.0	0.0	-0.2	0.00	0.58
A_51_P501844	NM_175475	*Cyp26b1*	cytochrome P450, family 26, subfamily b, polypeptide 1	1.7	0.4	1.9	0.4	-0.5	0.6	-0.5	0.00	0.00
A_55_P2006494	NM_177820	*Apol10b*	apolipoprotein L 10b	2.9	2.1	-1.9	0.3	0.0	0.4	0.0	0.00	0.00
A_55_P2084418	NM_178005	*Lrrtm2*	leucine rich repeat transmembrane neuronal 2	2.3	1.7	1.0	-0.4	-1.1	-0.4	-0.8	0.00	0.00
A_55_P2084413	NM_178005	*Lrrtm2*	leucine rich repeat transmembrane neuronal 2	1.2	1.6	1.0	-0.5	-0.9	0.0	-0.2	0.00	0.00
A_55_P1959303	NM_178446	*Rbm47*	RNA binding motif protein 47	2.1	0.5	1.9	-0.1	-0.1	-0.1	0.2	0.00	0.00
A_55_P1959305	NM_178446	*Rbm47*	RNA binding motif protein 47	1.2	0.5	1.8	0.2	0.0	0.2	0.4	0.04	0.00
A_52_P220783	NM_178745	*Tmem229b*	transmembrane protein 229B	1.4	0.8	-1.6	-0.1	-0.1	0.1	-0.1	0.00	0.00
A_55_P2113256	NM_181402	*Parp11*	poly (ADP-ribose) polymerase family, member 11	1.0	0.6	0.0	-0.1	0.0	0.3	0.0	0.01	0.99
A_55_P2135200	NM_181542	*Slfn10-ps*	schlafen 10, pseudogene	1.7	0.6	-1.3	-0.2	0.2	-0.1	-0.3	0.03	0.01

A_55_P2117656	NM_181545	*Slfn8*	schlafen 8	2.5	0.8	-1.8	-0.2	0.1	0.1	0.6	0.00	0.00
A_55_P2026572	NM_183087	*Fam189a1*	family with sequence similarity 189, member A1	1.5	0.8	-3.3	0.7	0.5	0.9	0.4	0.00	0.00
A_55_P1959953	NM_183162	*BC006779*	cDNA sequence BC006779	1.5	1.6	0.2	-0.1	0.0	0.1	0.1	0.00	0.64
A_52_P616392	NM_183426	*Sbno2*	strawberry notch homolog 2 (Drosophila)	1.3	0.9	0.2	0.0	-0.2	0.2	-0.3	0.00	0.68
A_55_P2052385	NM_194336	*Mpa2l*	macrophage activation 2 like	6.8	4.3	-2.7	-0.6	-0.2	0.1	-0.1	0.00	0.00
A_55_P2052380	NM_194336	*Mpa2l*	macrophage activation 2 like	4.8	2.3	-2.3	-0.9	-0.6	-0.4	-0.4	0.00	0.00
A_55_P2165074	NM_194346	*Rnf31*	ring finger protein 31	1.4	1.1	0.0	0.1	0.0	0.2	0.0	0.00	0.95
A_51_P191469	NM_194346	*Rnf31*	ring finger protein 31	1.3	1.1	0.0	0.1	0.0	0.1	0.0	0.00	1.00
A_52_P463977	NM_197986	*Tmem140*	transmembrane protein 140	4.4	3.6	1.1	-0.4	-0.4	0.2	-0.1	0.00	0.01
A_52_P335609	NM_198004	*5133401N09Rik*	RIKEN cDNA 5133401N09 gene	1.6	1.5	-0.9	-0.3	-0.4	-0.1	-0.2	0.00	0.00
A_51_P169693	NM_198095	*Bst2*	bone marrow stromal cell antigen 2	2.2	1.6	0.5	0.1	0.2	0.6	0.2	0.00	0.03
A_55_P2015687	NM_199015	*D14Ertd668e*	DNA segment, Chr 14, ERATO Doi 668, expressed	1.9	3.7	5.1	0.1	0.2	0.0	0.6	0.00	0.00
A_52_P199633	NM_199146	*Trim30d*	tripartite motif-containing 30D	1.9	0.2	-2.4	-0.1	0.2	0.1	-0.2	0.00	0.00
A_52_P326664	NM_199252	*Unc93a*	unc-93 homolog A (C. elegans)	1.8	1.8	-0.2	-0.6	-0.2	0.2	0.1	0.01	0.83
A_55_P2139763	NM_201373	*Trim56*	tripartite motif-containing 56	1.1	1.0	-0.4	-0.2	-0.3	-0.1	-0.3	0.00	0.17
A_55_P1978506	NM_207648	*H2-Q6*	histocompatibility 2, Q region locus 6	1.0	0.5	1.1	-0.2	-0.1	-0.1	0.0	0.00	0.00
A_51_P201480	NM_213659	*Stat3*	signal transducer and activator of transcription 3	1.5	0.8	-0.1	-0.1	-0.3	0.0	-0.2	0.00	0.93
A_55_P2100620	NR_033332	*Gm12216*	predicted gene 12216	2.8	2.1	-0.4	0.1	-0.2	0.0	-0.2	0.00	0.24
A_52_P69558	NR_033577	*Gm8221*	apolipoprotein L, 3-like	1.3	0.6	-1.3	-0.2	0.3	0.2	0.0	0.00	0.00
A_55_P2213828	NR_038025	*4933412E12Rik*	RIKEN cDNA 4933412E12 gene	1.0	1.2	0.1	-0.1	-0.2	-0.1	-0.2	0.00	0.87

A_55_P2243431	NR_045032	*Gdap10*	ganglioside-induced differentiation-associated-protein 10	1.6	1.4	-0.9	-0.3	-0.2	0.0	0.1	0.00	0.00
A_52_P431615	XM_001000891	*Gm1966*	predicted gene 1966	3.0	2.8	4.2	-0.2	-0.1	0.4	0.1	0.00	0.00
A_55_P2173210	XM_003084464	*Gm16340*	predicted gene 16340	2.5	3.3	2.8	0.4	0.0	0.4	0.2	0.00	0.00
A_55_P1972582	XM_136331	*Gm4955*	predicted gene 4955	1.9	0.6	-1.3	-0.6	-0.3	0.0	0.1	0.00	0.00
A_55_P2004007	XM_136331	*Gm4955*	predicted gene 4955	1.6	0.2	-1.4	-0.7	0.0	-0.2	-0.1	0.00	0.00

Genes significantly (p-value < 0.05) induced at least 2-fold by IFN-γ are shown (in alphabetical order). Fold differences (log 2-transformed) and p-values derived from three biological replicates for each condition are depicted. Key: WT = WT MEFs; SA = S727A MEFs; siCtrl = sample treated with control siRNA; siCdk8 = sample treated with Cdk8 siRNA; g = sample stimulated for 4 h with IFN-γ; 0 = sample not stimulated with IFN-γ

Table S5. **Overlap of Genes Similarly Affected by S727A Mutation and *Cdk8* Silencing**

Genbank AC	Gene symbol	Type of change
NM_001146007	*9230105E10Rik*	down
NM_029419	*Apol7a*	down
NM_020557	*Cmpk2*	down
NM_020557	*Cmpk2*	down
NM_001190466	*Dact1*	down
NM_001190466	*Dact1*	down
NM_010171	*F3*	down
NM_001101475	*F830016B08Rik*	down
NM_001039646	*Gbp10*	down
NM_001039647	*Gbp11*	down
NM_010260	*Gbp2*	down
NM_018734	*Gbp3*	down
NM_001256005	*Gbp4*	down
NM_145545	*Gbp6*	down
NM_001045540	*Gm12185*	down
NM_001135115	*Gm12250*	down
NM_001034859	*Gm4841*	down
NM_001033767	*Gm4951*	down
XM_136331	*Gm4955*	down
XM_136331	*Gm4955*	down
NR_033577	*Gm8221*	down
NM_001013828	*Iigp1b*	down
NM_008320	*Irf8*	down
NM_194336	*Mpa2l*	down
NM_194336	*Mpa2l*	down
NM_001083925	*Oas1b*	down
NM_010724	*Psmb8*	down
ENSMUST00000114230	*Psmb9*	down
NM_013585	*Psmb9*	down
NM_001168294	*Serpina3f*	down
NM_001199940	*Serpina3i*	down
NM_181542	*Slfn10-ps*	down
NM_181545	*Slfn8*	down
NM_009896	*Socs1*	down
NM_013683	*Tap1*	down
NM_011530	*Tap2*	down
NM_178745	*Tmem229b*	down
NM_023835	*Trim12a*	down
NM_009277	*Trim21*	down
NM_199146	*Trim30d*	down
NM_030738	*Vmn1r65*	down

NM_001037713	*Xaf1*	down
NM_001037713	*Xaf1*	down
NM_001204910	*AI607873*	up
NM_007609	*Casp4*	up
NM_007609	*Casp4*	up
NM_008599	*Cxcl9*	up
NM_175475	*Cyp26b1*	up
NM_199015	*D14Ertd668e*	up
NM_026637	*Ggct*	up
XM_003084464	*Gm16340*	up
NM_001045481	*Ifi203*	up
NM_001045481	*Ifi203*	up
NM_008329	*Ifi204*	up
BC010546	*Ifi204*	up
NM_011019	*Osmr*	up
NM_178446	*Rbm47*	up
NM_011580	*Thbs1*	up
NM_023137	*Ubd*	up
NM_001139519	*Zbp1*	up

IFN-γ-induced genes (in alphabetical order) either down-regulated by both, the S727A mutation and *Cdk8* silencing, or up-regulated under the same conditions. Genes that appear more than once have different probe set IDs for each listing. Data are extracted from the Table S4.

Supplemental Experimental Procedures

RNAi-Mediated Silencing

Approx. 2x 10^5 (or 5x 10^5) MEFs were seeded in 3,5 cm (or 6 cm) format in DMEM supplemented with 10% FCS without antibiotics. Next day the medium was replaced with 2.5 ml (or 5 ml) fresh medium and cells were transfected with 50 pmol (or 100 pmol) ON-TARGET plus™ SMART pool siRNA (Dharmacon) using Lipofectamine™ RNAiMAX Reagent in Opti-MEM I (both Invitrogen). After 48 hours cells were used for whole cell extract preparation or RNA isolation.

Immunoblotting

Procedures for whole cell extracts, immunoprecipitation and immunoblotting were as described (Sadzak et al., 2008). Primary antibodies used to detect proteins are described in antibody list (below).

Chromatin Immunoprecipitation

Chromatin Immunoprecipitation assay (ChIP) was performed as in (Hauser et al., 2002) with the following modifications. To pull down the antibodies Protein G Dynabeads (Invitrogen) were used. The amount of immunoprecipitated DNA was quantified in qPCR using Kapa Sybr Fast qPCR Universal Mix (Peqlab) and primers described in the primer list (below). All qPCRs were run on Mastercycler ep realplex^2 (Eppendorf). Values of immunoprecipitated DNA were shown as % input. Antibodies used in ChIP assay are specified in the antibody list (below).

Purification of Recombinant Proteins

Plasmids encoding STAT1 GST fusion proteins (GST-STAT1-WT aa711-750 and the corresponding S727A mutant) were described (Kovarik et al., 1999). STAT3 and STAT5a GST fusion proteins (GST-STAT3-WT aa715-770 and the corresponding S727A mutant, GST-STAT5a-WT aa704-793 and the corresponding S725A and S779A single mutants and S725A/S779A double mutant) were obtained by cloning the TADs into pGEX-4T1 (Promega). Standard techniques for expression and purification of GST fusion proteins were used. The four protein CDK8 module was expressed and purified according to (Knuesel et al., 2009b). The TFIIH complex was purified from HeLa cells as described in (Knuesel et al., 2009a). P-TEFb was isolated following recombinant expression in insect cells. Sf9 cells were co-infected with high-titer virus at a multiplicity of infection ratio of 1:2 (CDK9:Cyc T1) for 48 h at 27^{o}C. P-TEFb was purified from Sf9 cell pellets as described (Tahirov et al.).

Kinase Assays

Reactions were performed with 1 µl CDK8 module, 1 µl TFIIH, and 0.75 µl P-TEFb with 500 ng GST-RNAPII CTD and 750 ng of GST-STAT-TAD (STAT1, STAT3, STAT5a and the corresponding mutants) or GST only in kinase buffer (25 mM Tris pH 8.0, 100 mM KCl, 100 µM ATP, 10 mM $MgCl_2$, and 2 mM DTT) with 2.5 µCi [γ-32P]ATP at 30^{o}C for 60 min. SDS-PAGE was used to separate proteins and the gels were subsequently silver stained, dried at 55^{o}C for 60 min, exposed on a phosphor-imager screen for 18 h, and imaged using a Typhoon 9400 scanner. Quantitation of auto-rad bands was performed using ImageJ.

Microarray Analysis

STAT1 WT and STAT1 S727A MEFs were treated with siRNA as described above and stimulated with IFN-γ for 4 h or left untreated. Total RNA was isolated from cells using TRIzol reagent (Invitrogen) following the manufactures protocol and used for expression analysis using Agilent Whole Mouse Genome Microarrays, 8x60K. Standard protocols for labeling and hybridization were followed. In brief, fluorescent cRNA was generated using Low Input Quick

Amp Labeling Kit (Agilent). The amplified cyanine 3-labeled cRNA samples were then purified using SV Total RNA Isolation System (Promega) and hybridized to microarray slides. Microarray slides were washed and scanned with an Agilent Scanner.
Information from probe features was extracted from microarray scan images using the Agilent Feature Extraction software v10.7.3. Further analyses were performed using R and Bioconductor (Gentleman et al., 2004). Arrays were assessed for quality, weighted and quantile normalized. Subsequently the data were log transformed and filtered for low expression. Residual variances were adjusted using an empirical bayes method (Smyth, 2004) to obtain approximately t-distributed differences in gene expression values. P-values were adjusted for multiple testing using the false discovery rate (Reiner et al., 2003). Microarray data have been deposited in Gene Expression Omnibus under the accession number GSE40728 (GEO, http://www.ncbi.nlm.nih.gov/geo/info/linking.html).

Quantitation of Gene Expression by Quantitative RT-PCR (qRT-PCR)

To measure mRNA expression total RNA was reverse transcribed using oligo (dT)18 primer and Mu-MLV reverse transcriptase (Fermentas). cDNA was amplified with GoTaq qPCR Master Mix (Promega) and primers described in the primer list (below). qRT-PCR was performed using Mastercycler ep realplex2 (Eppendorf). To measure the abundance of primary transcript RNA was digested with DNase I (Roche), purified with RNeasy MiniElute Cleanup Kit (Qiagen) and reverse transcribed using random primers (nonamers) and Superscript III Reverse Transcriptase (Invitrogen).

Metabolic labeling of RNA

Metabolic labeling, biotinylation and purification of nascent RNA were performed as described (Dolken et al., 2008). Briefly, 4-thiouridine (4sU) (100 µM) was added to the cell culture medium 30 min prior to IFN-γ stimulation, simultaneously with IFN-γ, or 60 min and 210 min after IFN-γ stimulation. Labeling was stopped after 30 minutes and total cellular RNA was isolated from cells using TRIzol reagent (Invitrogen) following manufacturer's protocol. RNA was treated with recombinant RNase-free DNase I (Roche) 0.2 U/µl for 30 minutes at 37°C in order to remove genomic DNA contamination.
Biotinylation was carried out in biotinylation buffer (10 mM Tris, 1 mM EDTA) and 0.2 mg/mL Biotin-HPDP at a final RNA concentration of 100 ng/µL for 2 h at 25°C with shaking. Unbound biotin was removed with chloroform/isoamylalcohol. RNA was precipitated at 16000g at 4°C with equal volume of isopropanol and 1:10 volume of 5M sodium chloride. Biotinylated RNA was captured using µMACS streptavidin beads and columns (Miltenyi). Nascent RNA was eluted from streptavidin beads by applying twice 100 µl of 100 mM dithiothreitol (DTT) to the column. RNA was recovered from eluates using the RNeasy MinElute Spin columns (Qiagen). RNA was reverse transcribed using SuperScript III (Invitrogen) and oligo-dT(18) primers following manufacturer´s instructions. For reverse transcription reaction 100 ng of nascent RNA or 1 µg of Total RNA was used. *ActB* was used for normalization. qRT-PCR was performed on Realplex system (Eppendorf) using GoTaq MasterMix (Promega).

mRNA Stability

Approx. 1x 10^6 MEFs were seeded in 6 cm format were stimulated with IFN-γ for 4 h and actinomycin D (Sigma) was added (5 µg/ml). After 0, 15 30, 45 and 60 min of act D treatment RNA was isolated and processed for qRT-PCR analysis.

Antiviral Assay with Vesicular Stomatitis Virus

MEFs were seeded on 3.5 cm dishes at 30% confluence and 24 h later they were treated with Cyclin C siRNA, control siRNA or left untreated. siRNA transfection was performed using Lipofectamine RNAiMAX (Invitrogen) according the manufacturer protocol and 50 pmol siRNA

per dish. After 48 hours of siRNA transfection cells were seeded on 96 well plates in normal medium and 5 x 10^3 cells per well. Four hours after seeding the medium was replaced with new medium that was supplemented with fresh siRNA and IFN-γ in two-fold serial dilutions starting at 10 units. The medium was again replaced 24 h later with medium without siRNA and without IFN-γ. VSV was then added at the multiplicity of infection (MOI) of 0.1 and the cells were incubated for additional 39 h. The plates were then washed 2x with PBS (Dulbecco´s PBS, PAA) and surviving cells were stained for 1 h at room temperature in the dark with Crystal violet (40 ml 1% crystal violet and 80 ml methanol, 300 ml dH_2O). Cells were then washed twice with PBS, air dried and subsequently incubated with 100 µl solubilization buffer (50/50 mixture of 0.1 M NaH2PO4, pH = 4.5 and 50% ethanol) per well. Crystal violet intensity, that was proportional to number of surviving cells, was determined at 595 nm using a microplate reader (BIO-RAD iMark).

List of Antibodies Used for Western Blotting

pS727 STAT1 (Kovarik et al., 1998), dilution 1:1000
pY701 STAT1 (Cell Signalling, Cat. Nr. 9171), dilution 1:1000
C-terminus STAT1 (Kovarik et al., 1998), dilution 1:1000
N-terminus STAT1 (BD Biosciences, Cat. Nr. 610115), dilution 1:1000
pS727 STAT3 (Cell Signaling Cat. Nr. 9134), dilution 1:500
pY705 STAT3, (Cell Signaling, Cat. Nr. 9131), dilution 1:1000
STAT3 (Cell Signaling, Cat. Nr. 9139), dilution 1:1000
pS722 STAT4 (Santa Cruz, Cat. Nr. sc-28296), dilution 1:500
pY694 STAT4 (Cell Signaling, Cat. Nr. 5267), dilution 1:1000
STAT4 (Cell Signaling, Cat. Nr. 2653), dilution 1:1000
pS725/730 STAT5a/b (Abcam, Cat. Nr. ab36153), dilution 1:1000
pY694/699 STAT5a/b (Upstate-Millipore, Cat. Nr. 05-886), dilution 1:1000
STAT5a/b (Santa Cruz, Cat. Nr. sc-835), dilution 1:1000
CDK7 (Santa Cruz, Cat. Nr. sc-529), dilution 1:1000
CDK8 (Santa Cruz, Cat. Nr. sc-1521), dilution 1:500
CDK8 (Santa Cruz, Cat. Nr. sc-5612), dilution 1:300
CDK9 (Santa Cruz, Cat. Nr. sc-484), dilution 1:1000
pan ERK (BD Biosciences, Cat. Nr. 610123), dilution 1:2000

List of Antibodies Used for Chromatin Immunoprecipitation (ChIP)

pS727 STAT1 (Kovarik et al., 1998), 5 µl serum/ChIP
C-terminus STAT1 (Kovarik et al., 1998), 5 µl serum/ChIP
RNAPII (Santa Cruz, Cat. Nr. sc-899), 4 µg/ChIP
pS2 RNAPII (Bethyl, Cat. Nr. A300-654A), 0,7 µg/ChIP
CDK8 (Santa Cruz, Cat. Nr. sc-1521), 5 µg/ChIP
MED1 (also called TRAP220) (Santa Cruz, Cat Nr. Sc-5334X), 5 µg/ChIP
Control rabbit IgG (Santa Cruz, Cat. Nr. sc-2027), 4 µg/ChIP
Control goat IgG (Santa Cruz, Cat. Nr. sc-2028), 5 µg/ChIP
Pre-immune serum (Kovarik et al., 1998), 1-2 µl serum/ChIP

List of Primers Used for ChIP

Irf1 (GAS): Fwd- GGAGCACAGCTGCCTTGTACTT, Rev- CCCACTCGGCCTCATCATT
Irf1 (TSS): Fwd- TCCCGCTAAGTGTTTAGATTTC, Rev- TTCGGTTCGGCTTAGACTG
Irf1 (gene body): Fwd- TGCCTAGTTGCTTGTCTCTG , Rev- CTCCTGTGTGTCGCTGTC
Tap1 (TSS): Fwd- GGTCCTGCCCTCAATCTG, Rev- GCCTGTCGTGTTCTTCTCC
Tap1 (GAS): Fwd- AGGCGTGTCTAGTGATTCG, Rev- CGTGAGCTGTCCAGAGTC
Tap1 (gene body): Fwd- TAGTGTTAAGAATCAGCCTTC, Rev- ATCCTGGAATCTCGGTTAC

Gbp2 (GAS): Fwd- AGTGGTGCTAAAATTGTTGTGG, Rev- AGAAAGGAAGGAGAAAGATGGG
Gbp2 (TSS): Fwd- TCTACCTGAGAAGTCCTGAG, Rev- TTGCCAGAGAACTTGTGAG
All primers are written in 5´- 3´, and were designed using Beacon Designer software except for *Irf1* (GAS) which is from (Liu et al., 2004). Position in the gene locus is depicted in Figure S4.

List of Primers Used for Quantitation of Gene Expression (qRT-PCR)

Irf1: Fwd- CCGAAGACCTTATGAAGCTCTTTG, Rev: GCAAGTATCCCTTGCCATCG
Tap1: Fwd- CTGGCAACCAGCTACGGGT, Rev- TGAGAAAGAGGATGTGGTGGG
Gbp2: Fwd- TGCTAAACTTCGGGAACAGG, Rev- GAGCTTGGCAGAGAGGTTTG
Irf8 (Ouyang et al., 2011): Fwd- GAGCGAAGTTCCTGAGATGG, Rev- TGGGCTCCTCTTGGTCATAC
Isg15 (Wood et al., 2012): Fwd- ATGGCCTGGGACCTAAAG, Rev- TTAGGCACACTGGTCCCC
Hprt: Fwd- GGATTTGAATCACGTTTGTGTCAT, Rev- ACACCTGCTAATTTTACTGGCAA
ActB: Fwd- CAACGAGCGGTTCCGATG, Rev- GCCACAGGATTCCATACCCA
Gbp2 (Primary Transcript): Fwd- ACAGCATCATTATTACATCAGG, Rev- ATACCGAGCCAGATAGGG
Tap1 (Primary Transcript): See *Tap1* (gene body) used for ChIP

List of QuantiTect Primer Assays (Qiagen) for qRT-PCR

Cdk8: Mm_Cdk8_1_SG, Cat. Nr. QT00158697
CycC: Mm_Ccnc_1_SG, Cat. Nr. QT00161420

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