Supplementary information

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Figure S1. Composition of the murine genome by promoter, exon, intron, and intergenic sequences. The percentage of DNA sequences that belong to promoter, exon, intron, or intergenic region is calculated from murine genome, and shown in a pie chart.

Figure S2. STAT4 binds to multiple sites in the extended *Ifng* locus. The locations of conserved non-coding sequences (CNS) are as designated by Wilson et al (Wilson et al., 2009).

Figure S3. Confirmation of STAT4 and STAT6 binding by chromatin precipitation and quantitative PCR. (A, B) Specific STAT binding to selected regions that shown in Figure 3 was verified by quantitative PCR. The sequences of PCR primers used are listed in Table S3. The amount of precipitated DNA was calculated as % input. Blue bars represent wild type cells, and red bars represent STAT-deficient cells. **A**: STAT4 IP, **B**: STAT6 IP.

Figure S4. Overview of data presented in this report, highlighting representative genes that belong to each cluster. In this report, integration of 3 biological readouts; (1) STAT binding, (2) patterns of epigenetic modifications and (3) gene expression change, was resulted in the identification of gene clusters. These represent various actions of STAT, both activating and repressing gene transcription.

Figure S5. STAT-bound and negatively regulated genes. (A, B) Pie charts showing the number of genes that exhibited STAT binding but whose expression were inhibited by the respected STAT. The genes were further divided based on the their relative expression ratio in Th1 and Th2 cells (> 2 fold difference) and whether or not they were bound by both STATs. **(A)** STAT4-bound and negatively regulated genes. **(B)** STAT6-bound and negatively regulated genes.

Table S1. Summary of unique tag counts and total peak counts identified by ChIP-seq. A total of 16 samples were analyzed for ChIP-seq, and for each sample, the total unique tag counts (original tag counts) and the total peak counts (computed peak counts) are shown. For STAT peaks, CisGenome (Ji et al., 2008) was used to compute the peaks. For histone marks, an islands calling program (SICER) (Zang et al., 2009) was used to compute the peaks.

Table S2. List of STAT4 and STAT6 bound genes. STAT4 bound genes are listed under the tab denoted as *"S4WTTh1NRS.genes"*, and STAT6 bound genes are listed under *"S6WTTh2NRS.genes"*.

Table S3. Primer sequences used for ChIP-qPCR in Figure S3.

Table S4. STAT-bound genes and their gene expression and epigenetic changes. All STAT-bound genes are listed under the epigenetic cluster identified in Figure 4. The tabs representing each cluster are: *K4 High.Stat4.g, K27 Low.Stat4.g, K27 High.Stat4.g, K36 High.Stat4.g, K36 Low.Stat4.g, Indeterminate.Stat4.g* for STAT4-bound genes; *K36 High.Stat6.g, K36 Low.Stat6.g, K27 High.Stat6.g, K27 Low.Stat6.g, Indeterminate.Stat6.g* for STAT6-bound genes. For each gene, 3 sets of numbers (WT, KO, WT/KO ratio) are listed for gene expression as well as for 3 epigenetic marks (K4, K27, K36).

Table S5. Global STAT-dependent gene expression changes in Th1 and Th2 cells. Microarray gene expression analysis from WT-Th1, STAT4KO-Th1, WT-Th2 and STAT6KO-Th2 are listed for 22433 genes depicted by Affymetrix Mouse Genome 430 2.0 Array.