

**Supplemental Figure 1.** IFN $\gamma$  and TNF drive loss of MART-1 and gain of NGFR expression in baseline differentiated cell lines and baseline differentiation status of cell lines is not governed by their mutation status. A) Flow cytometry plots of baseline differentiated cell lines (left) and baseline undifferentiated cell lines (right) upon IFN $\gamma$  or TNF exposure. B) Mutation status of the eight cell lines for select relevant genes.

**Supplemental Figure 2.** A) PCA of gene expression on all genes. B) Signature score of each sample based on genes in “GO\_Interferon-gamma mediated signaling pathway” shows all samples upregulated IFN $\gamma$ -related response genes. C) TNF samples (left) for IFN $\gamma$  signature genes. D) IFN $\gamma$  samples (right) for TNF signature genes.

**Supplemental Figure 3.** A) K-means clustering of the induced ATAC-seq peaks, with their positions relative to the transcriptional start sites. B) Top enriched motifs in the hyperaccessible ATAC peaks of TNF- and IFN $\gamma$ -exposed cell lines.

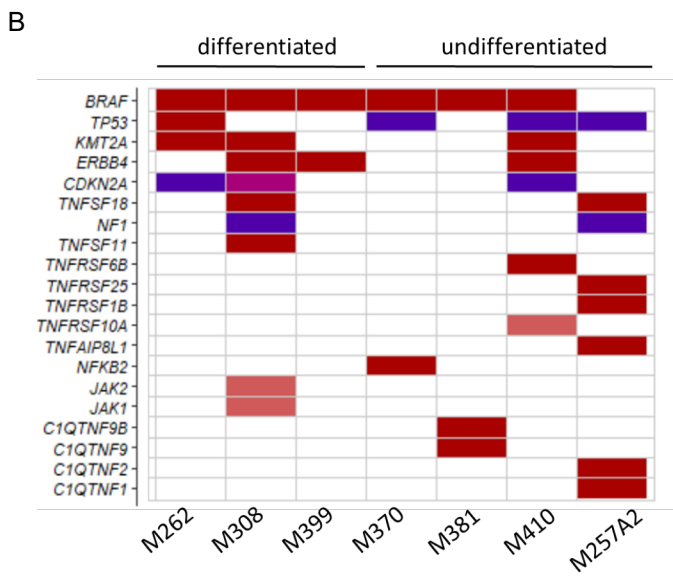
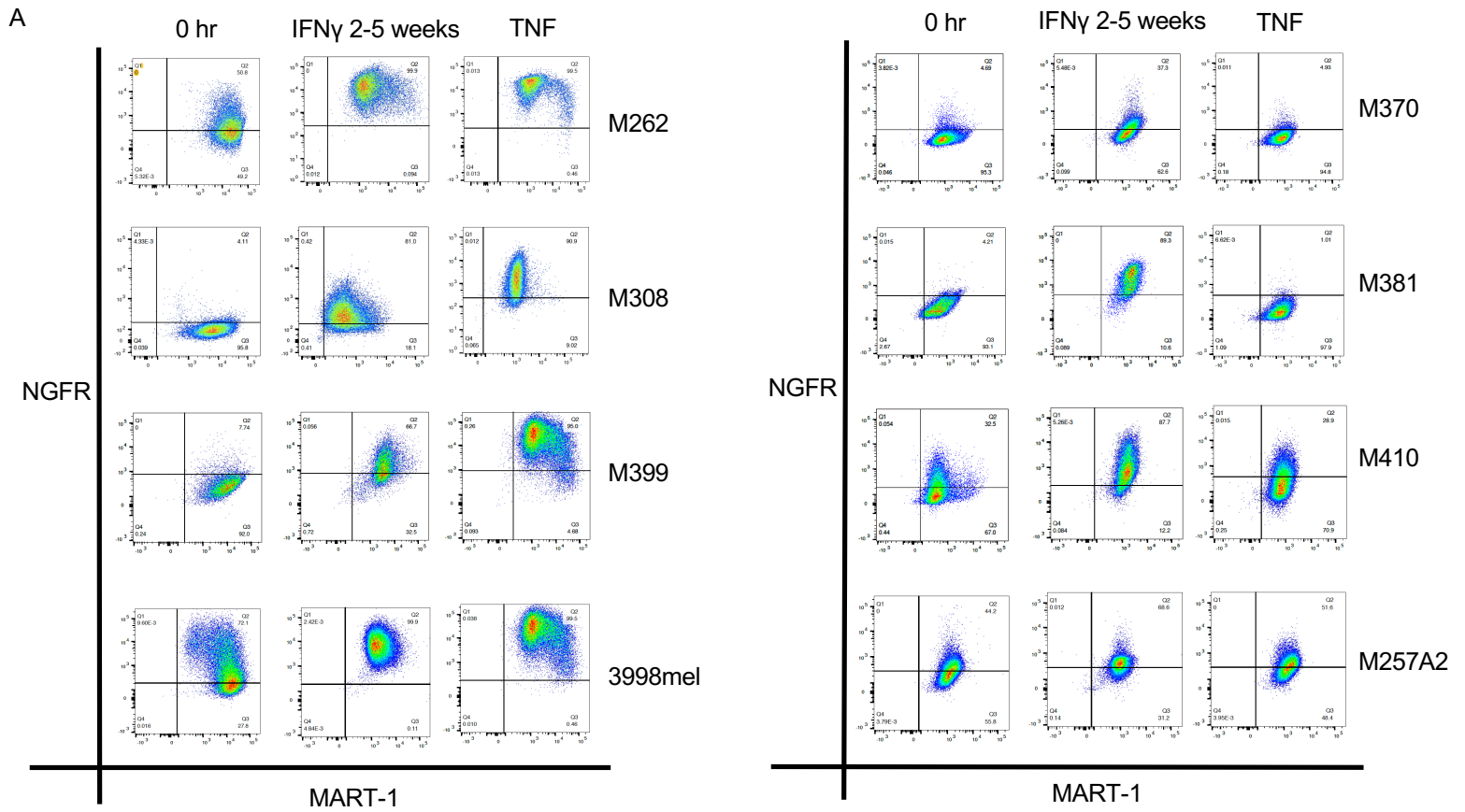
**Supplemental Figure 4.** A-B) VIPER analysis plots showing inferred TF activity for differentiated versus undifferentiated lines for (A) TNF or (B) IFN $\gamma$ . C-D) TNF and IFN $\gamma$  comparisons of each baseline differentiation status.

## **Supplemental Tables**

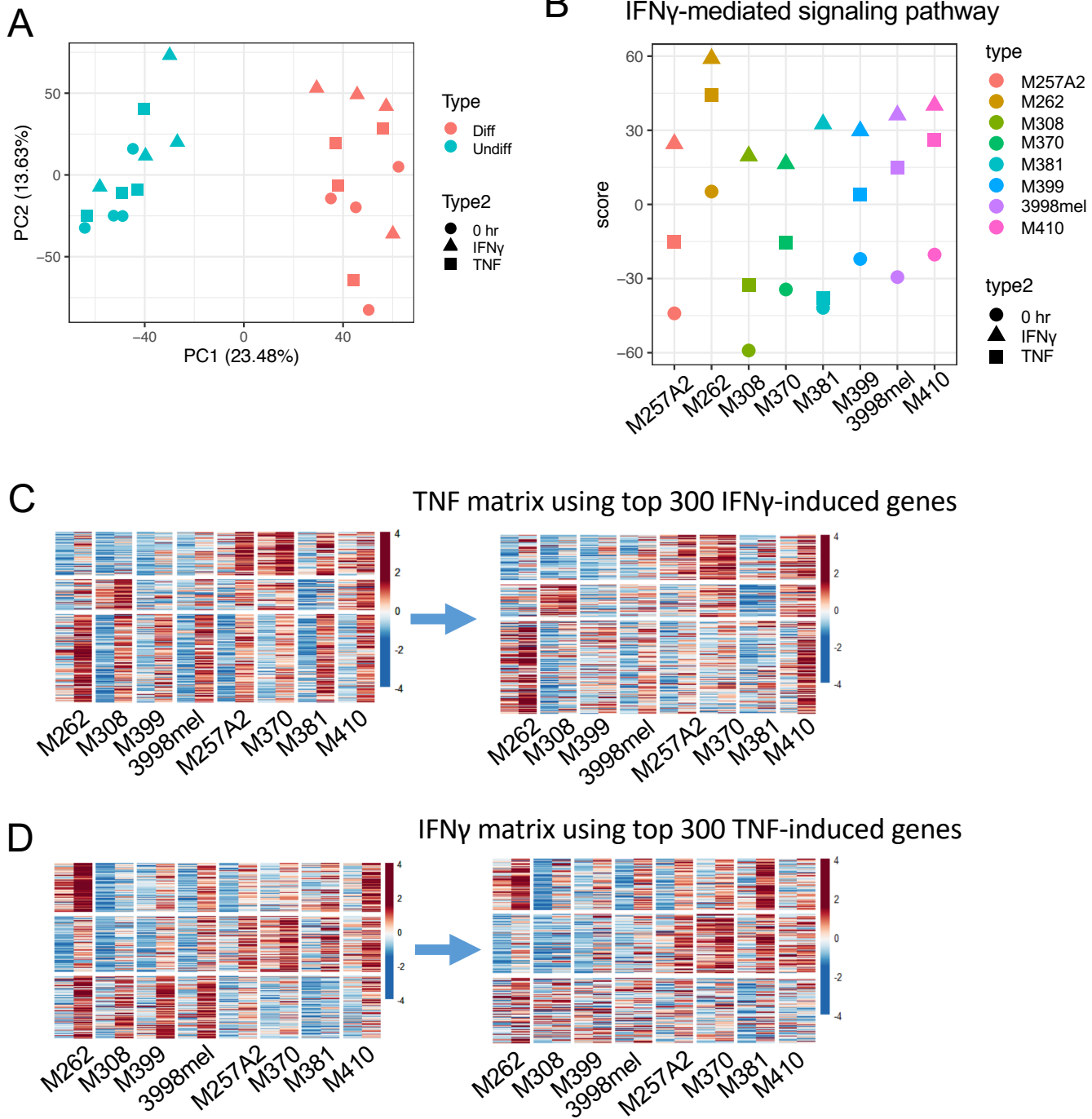
**Supplemental Table 1.** Gene expression loadings.

**Supplemental Table 2.** Gene set enrichment analysis results.

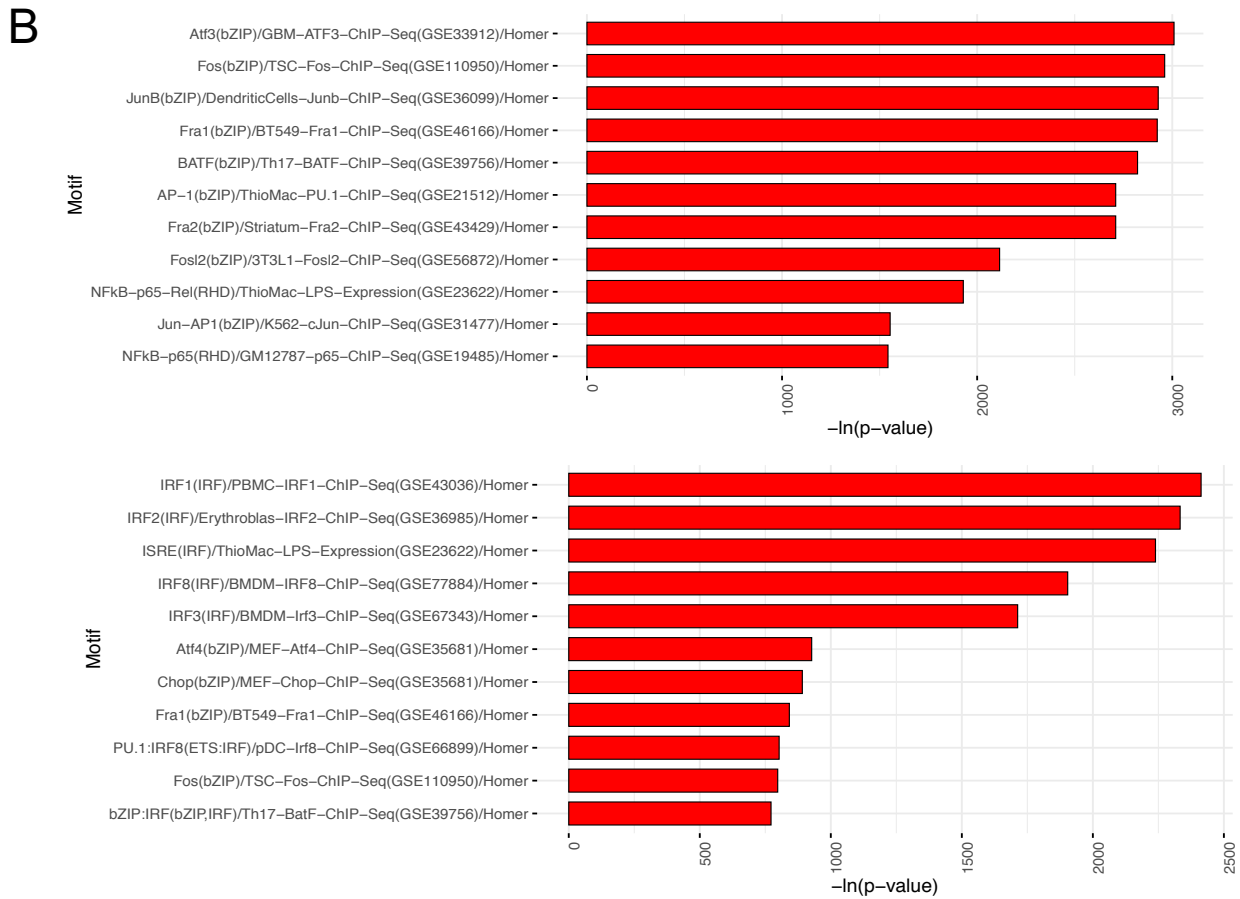
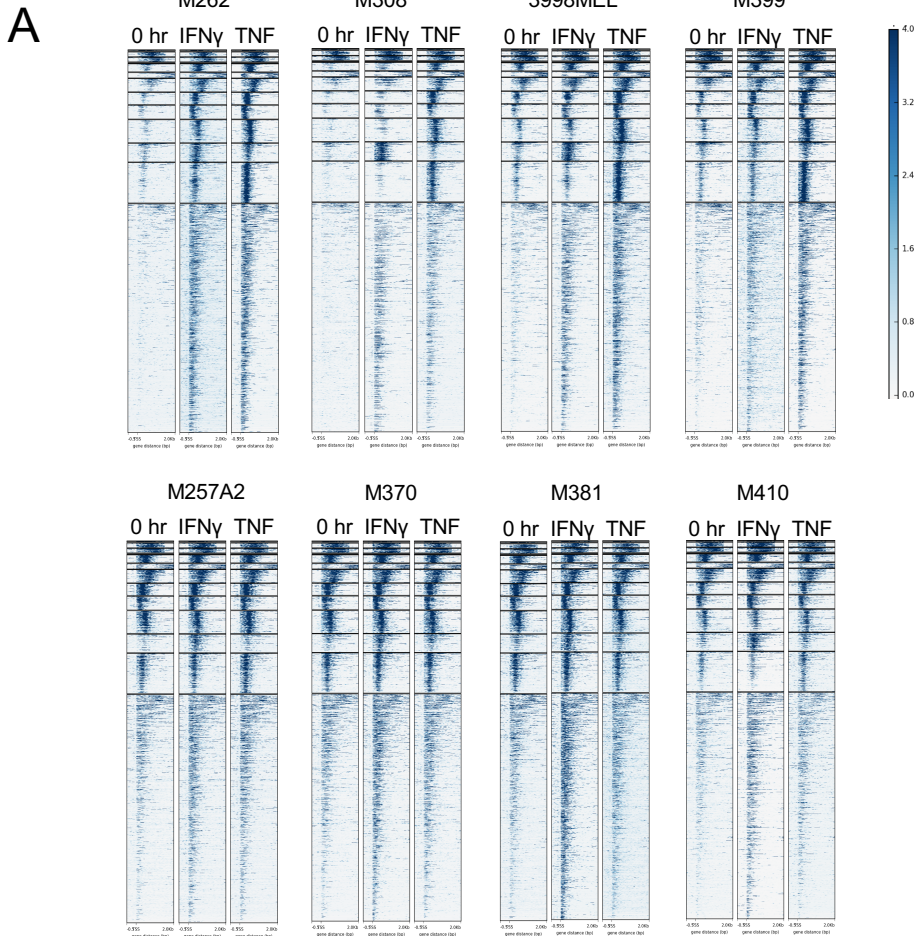
Supp. Fig 1



Supp. Fig 2

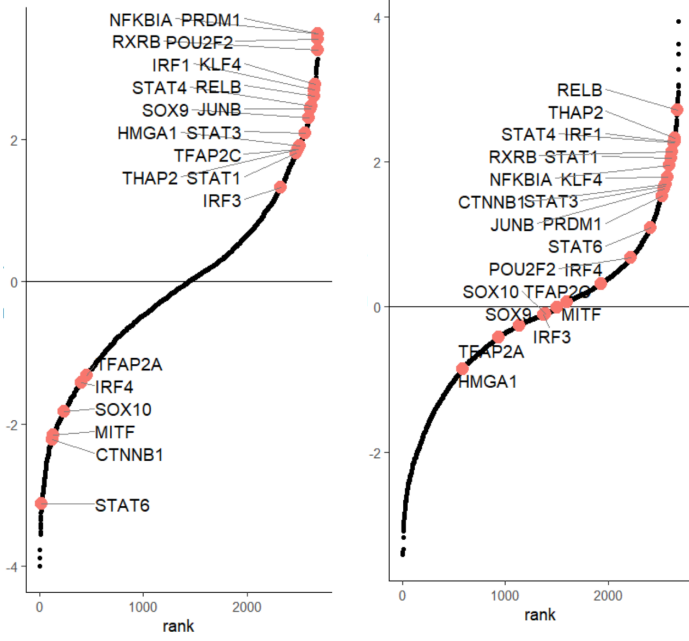


# Supp. Fig 3

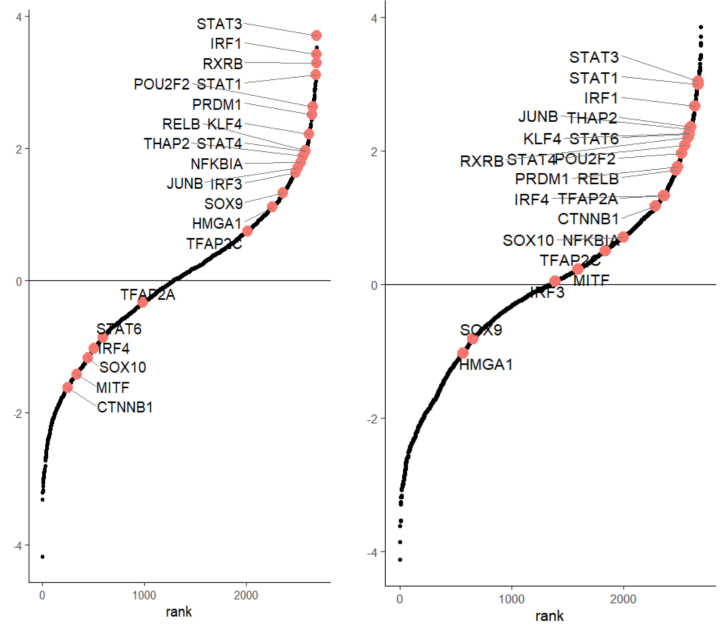


Supp. Fig 4

A

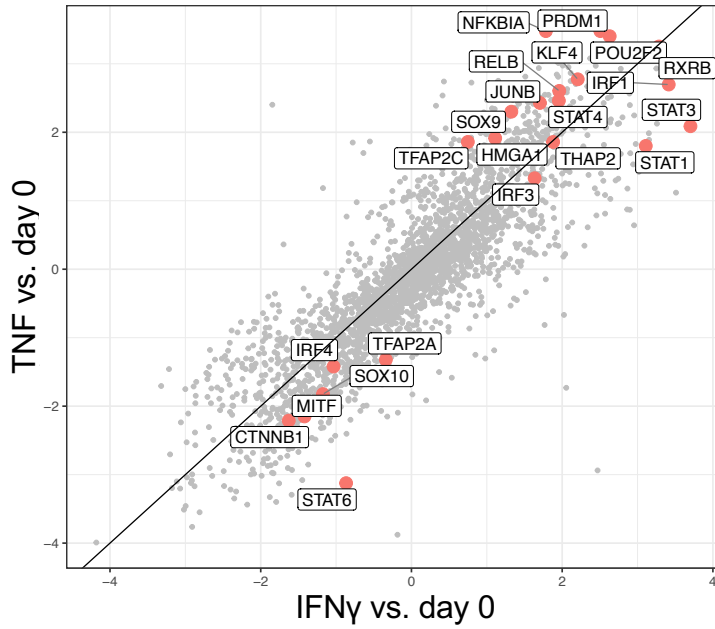


B



C

Baseline Differentiated



D

Baseline Undifferentiated

