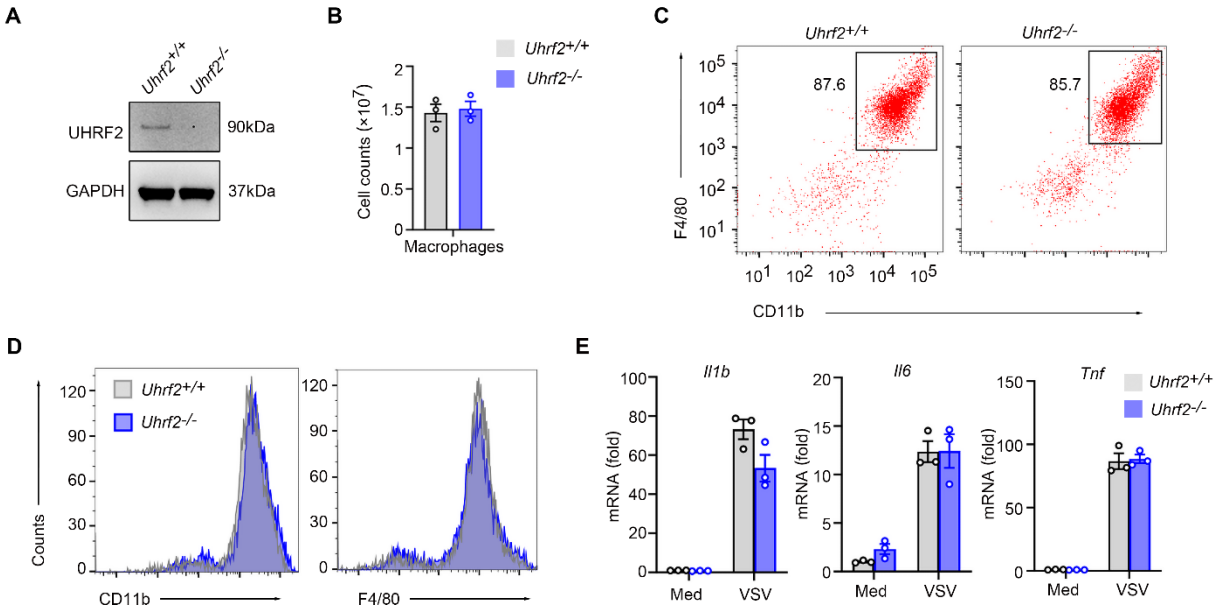


## Supplementary Materials for

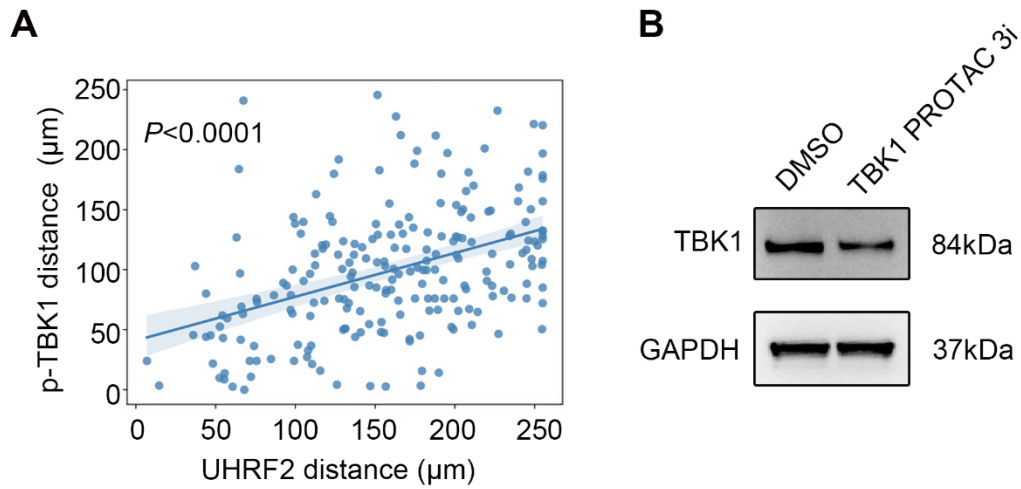
# **E3 ligase UHRF2 hijacks nuclear TBK1 to epigenetically repress type I interferons expression**

Wenwen Huang *et al.*

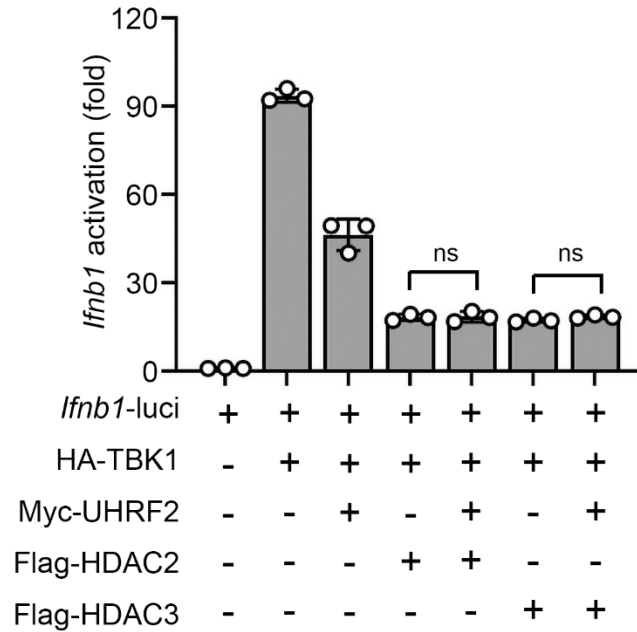
Corresponding author email: [qianzhang@immunol.org](mailto:qianzhang@immunol.org); [caoxt@immunol.org](mailto:caoxt@immunol.org)



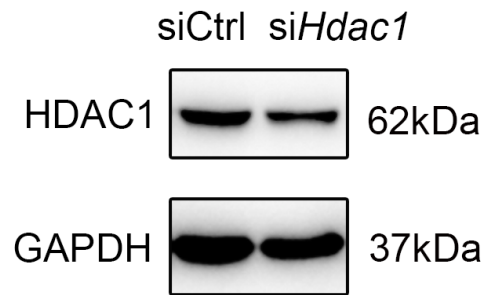
**Fig. S1. *Uhrf2* knockout mice have no abnormal differentiation of macrophages.** (A) Immunoblot analysis of UHRF2 expression in mouse peritoneal macrophages from *Uhrf2* knockout (*Uhrf2*<sup>-/-</sup>) and control littermate (*Uhrf2*<sup>+/+</sup>) mice. (B) Cell counts of peritoneal macrophages in *Uhrf2*<sup>+/+</sup> and *Uhrf2*<sup>-/-</sup> mice. (C, D) FACS analysis of CD11b, F4/80 expression in *Uhrf2*<sup>+/+</sup> and *Uhrf2*<sup>-/-</sup> peritoneal macrophages. (E) RT-qPCR analysis of mRNA levels of indicated genes in *Uhrf2*<sup>+/+</sup> or *Uhrf2*<sup>-/-</sup> macrophages infected with VSV for 12 h. Data were presented as mean+s.d (B, E) or images (A, C, D) from one representative of three independent experiments with biological replicates.



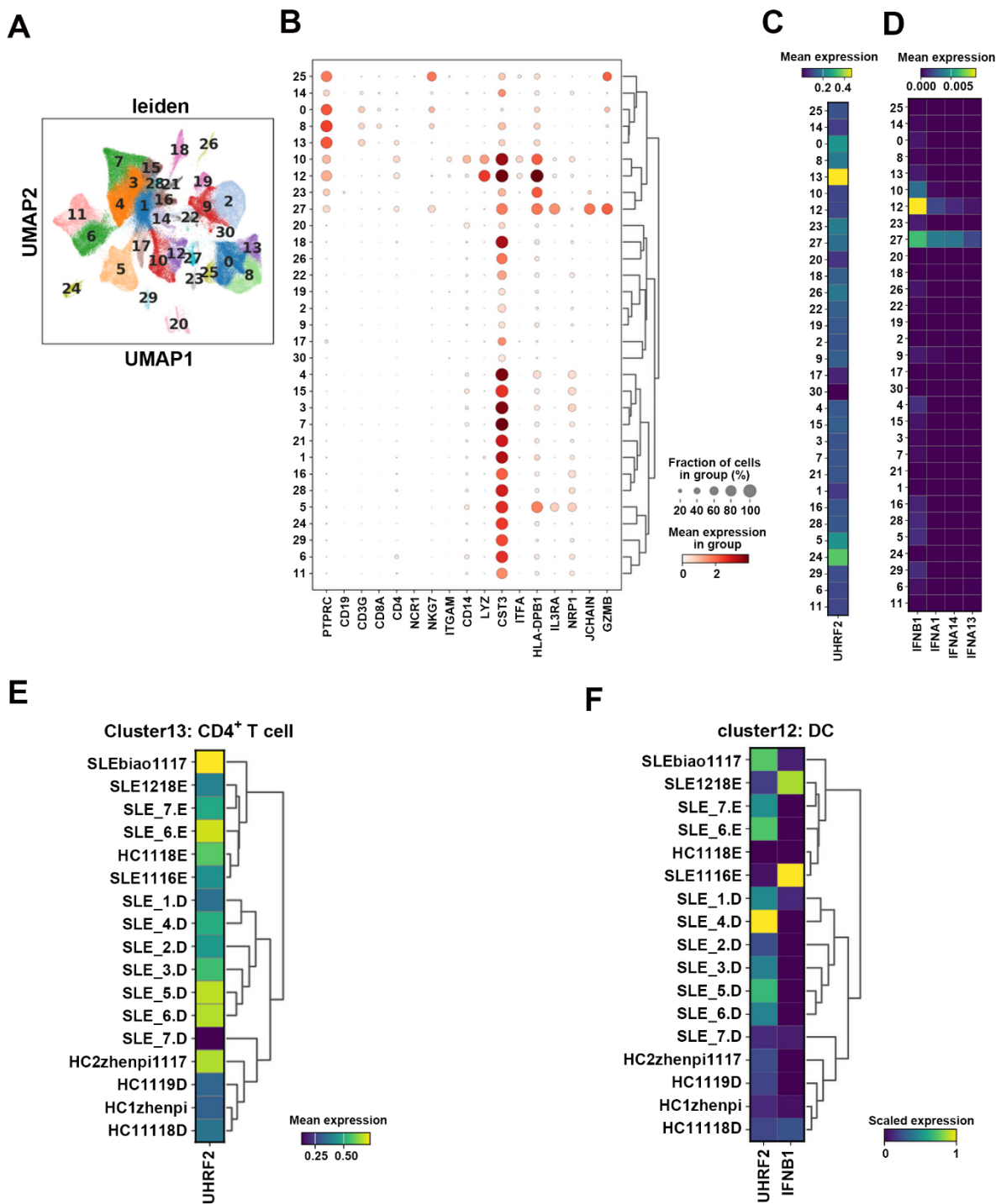
**Fig. S2. Inducing degradation of TBK1 protein in macrophages.** (A) Pearson correlation analysis of co-localization of UHRF2 and p-TBK1 (n=217). Statistical significance was determined using a two-tailed Pearson correlation test (Pearson  $r=0.4241$ ,  $P<0.0001$ ). (B) Immunoblot assays of total TBK1 protein in lysates of mouse macrophages pretreated with DMSO or TBK1 degrader (TBK1 PROTAC 3i) for 6 h and infected with VSV for 12 h. Data were presented as images (B) from one representative of three independent experiments with biological replicates.



**Fig. S3. HDAC2/3 independently inhibit TBK1-activated *Ifnb1* promoter activity.** Luciferase activity of the *Ifnb1* promoter reporter in HEK293T cells transiently transfected with indicated plasmids and assessed by dual-luciferase assay. Data were presented as mean+s.d from one representative of three independent experiments with biological replicates.



**Fig. S4. Silencing *Hdac1* expression in macrophages.** Immunoblot assays of HDAC1 in lysates of mouse macrophages transfected with control or *Hdac1*-specific siRNAs for 36 h and infected with VSV for 12 h. Data were presented as images from one representative of three independent experiments with biological replicates.



**Fig. S5. Expression variations of UHRF2 in SLE samples.** (A) UMAP of cell subsets in skin biopsies from SLE patients (SLE) and healthy donors (HC) in a published scRNA-seq dataset (GSE179633). (B) Dotplot showing mRNA levels of indicated genes in each of the cell clusters.

**(C-F)** Matrixplots showing mRNA levels of indicated genes in all clusters (**C, D**) or the indicated clusters in all the skin samples of the two groups (**E, F**).