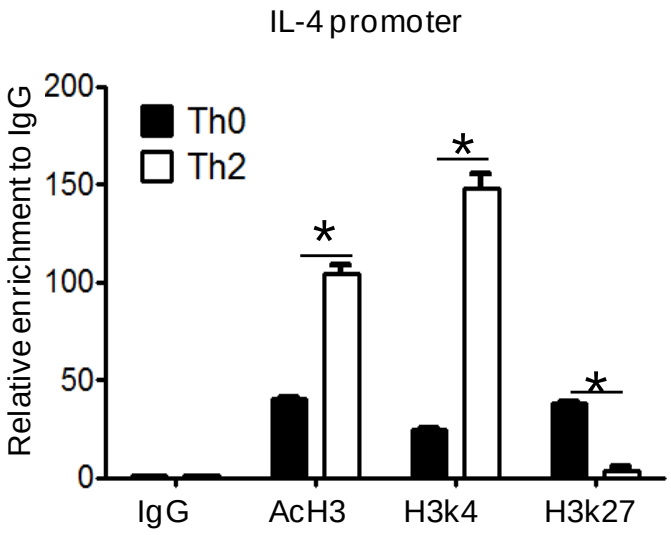
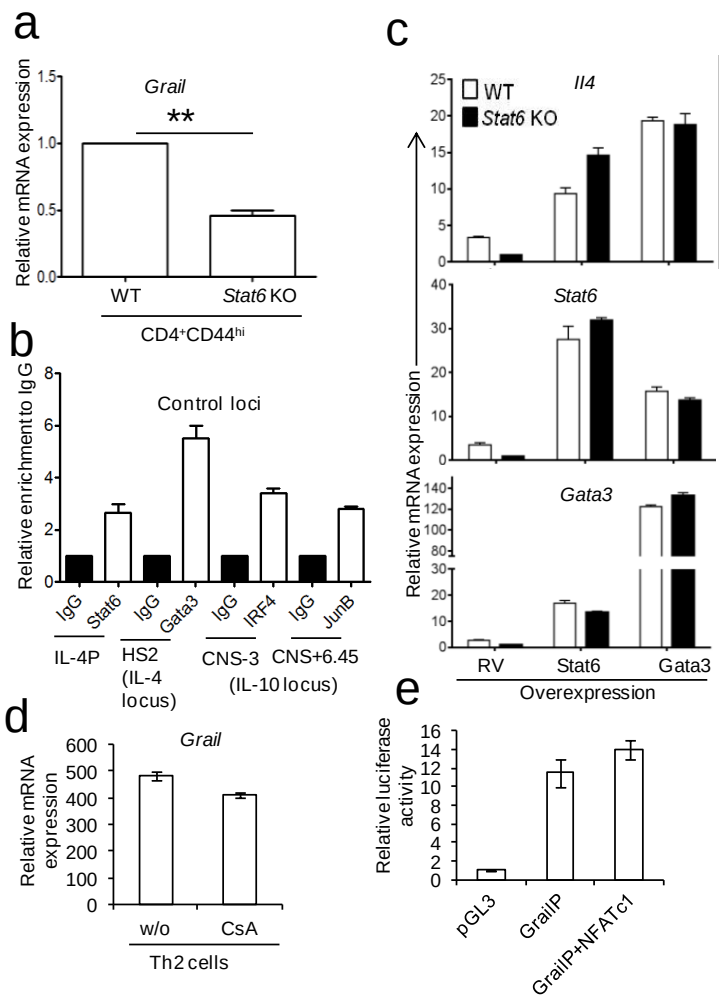


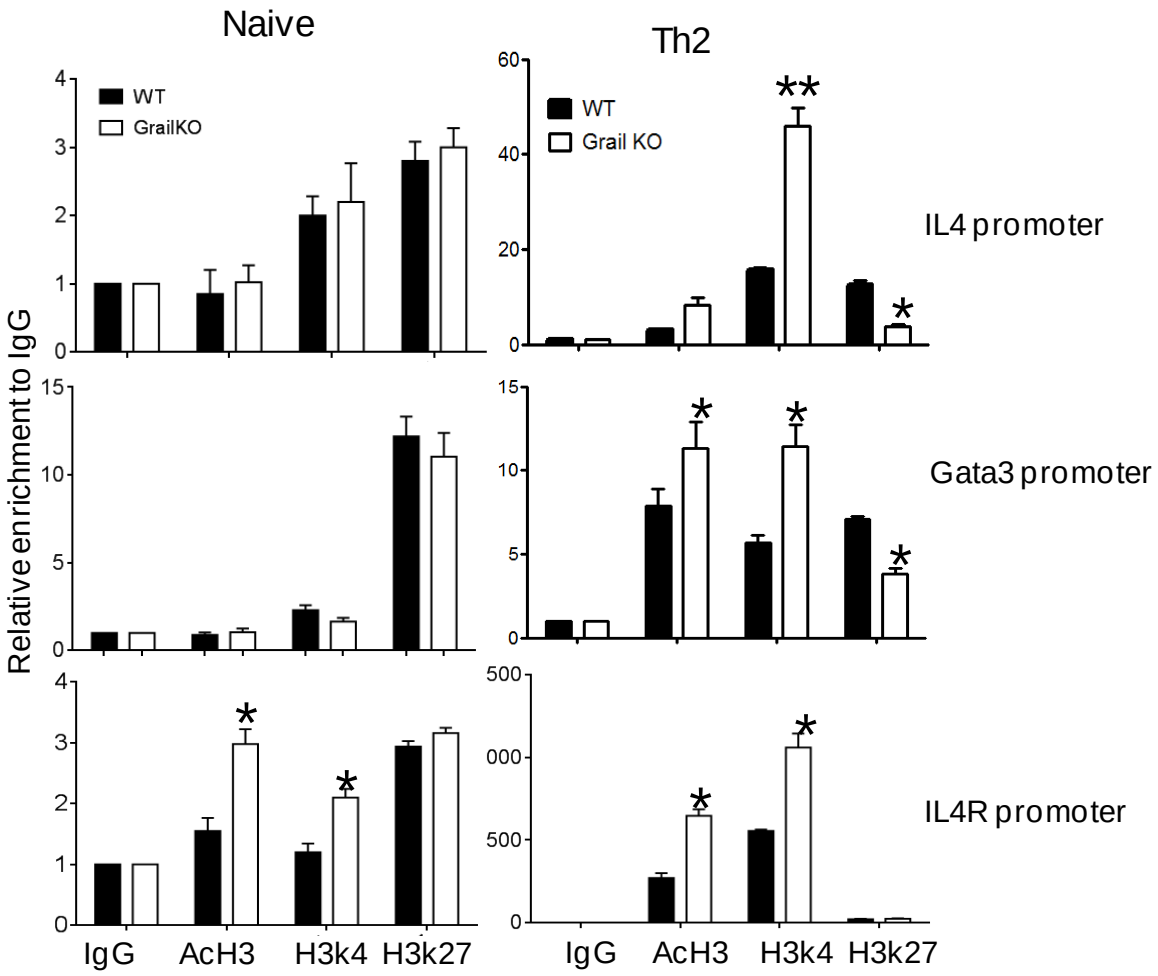

**SupplementaryFigure 1. Chromatin immunoprecipitation analysis at Th2 control gene loci.**

Naïve $CD4^{+}CD25^{-}CD62L^{hi}CD44^{lo}$ T cells from C57BL/6 mice were cultured for 4 days under Th0 and Th2 polarizing cell conditions. On day 4, cells were restimulated with anti-CD3 for 4hrs and chromatin immunoprecipitation (ChIP) analysis was performed. Enrichment of histone H3 acetylation (AcH3), Anti-trimethyl histone H3 lysine 4 (H3k4) and Anti-trimethyl histone H3 lysine 27 (H3K27) at IL-4 promoter locus was analyzed. The data from each replicate were normalized to the input control and the graphs represent fold enrichment of the indicated proteins to control antibody (rabbit IgG) at the designated locus. The results shown are mean ± SEM. P values: *<0.05. Student's t-test was performed to detect between-group differences. The data are representative of at least three independent experiments with consistent results.



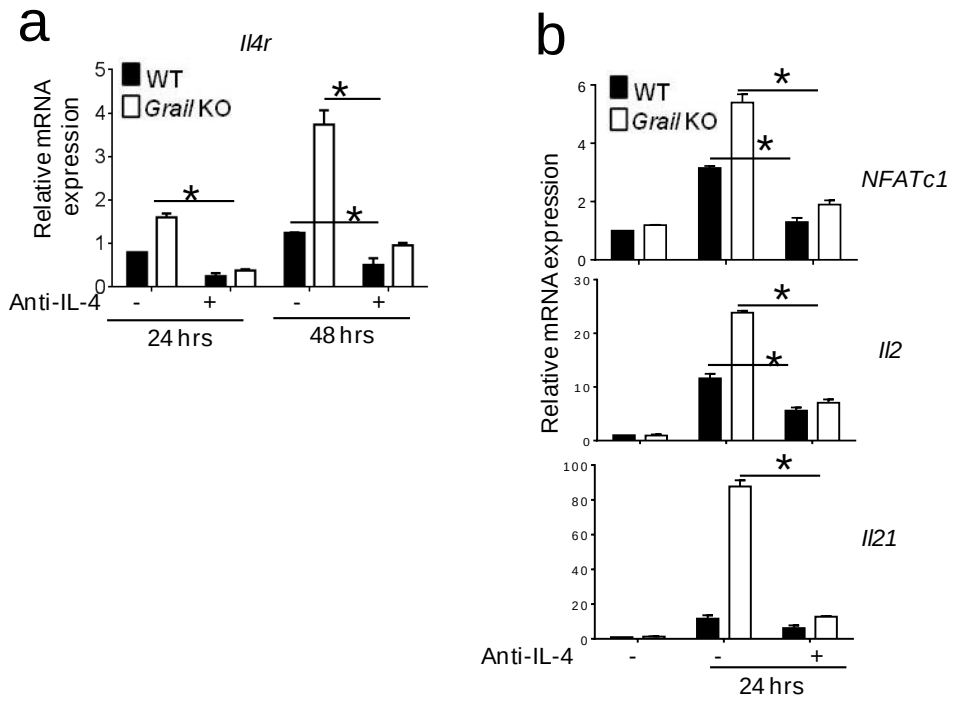

**Supplementary Figure 2. Role of Th2 related transcription factors in *Grail* expression.**

(**a**) FACS sorted $CD4^{+}CD44^{hi}$ effector memory T cells from WT and *Stat6* KO mice were analyzed for *Grail* mRNA expression by qRT-PCR. (**b**) Naïve T cells from C57BL/6 mice were cultured for 4 days under Th0 and Th2 polarizing cell conditions and ChIP analysis was performed as indicated. The data from each replicate were normalized to the input control and the graphs represent fold enrichment of the indicated proteins to control antibody (rabbit IgG) at the designated locus. **(c)** mRNA expression levels of *Il4*, *Stat6* and *Gata3* in naïve $CD4^{+}$ T lymphocytes from WT and *Stat6* KO mice infected with bicistronic retroviruses expressing the indicated factors. **(d)** *Grail* expression was analyzed in Th2 cells cultured in the presence or absence of cyclosporine A (CsA). **(e)** Luciferase assay in EL-4 cells transfected with Grail promoter (Grail-P) containing luciferase vector along with NFATc1 expression plasmid. Luciferase activity is expressed relative to the expression of cotransfected renilla luciferase plasmid as a control for transfection efficiency. Relative luciferase units are expressed as a fold difference to the control (vector only, pGL3) value. The results shown are mean ± SEM. P values: **<0.01. Student's t-test was performed to detect between-group differences. The data are representative of mean of at least three independent experiments with consistent results.



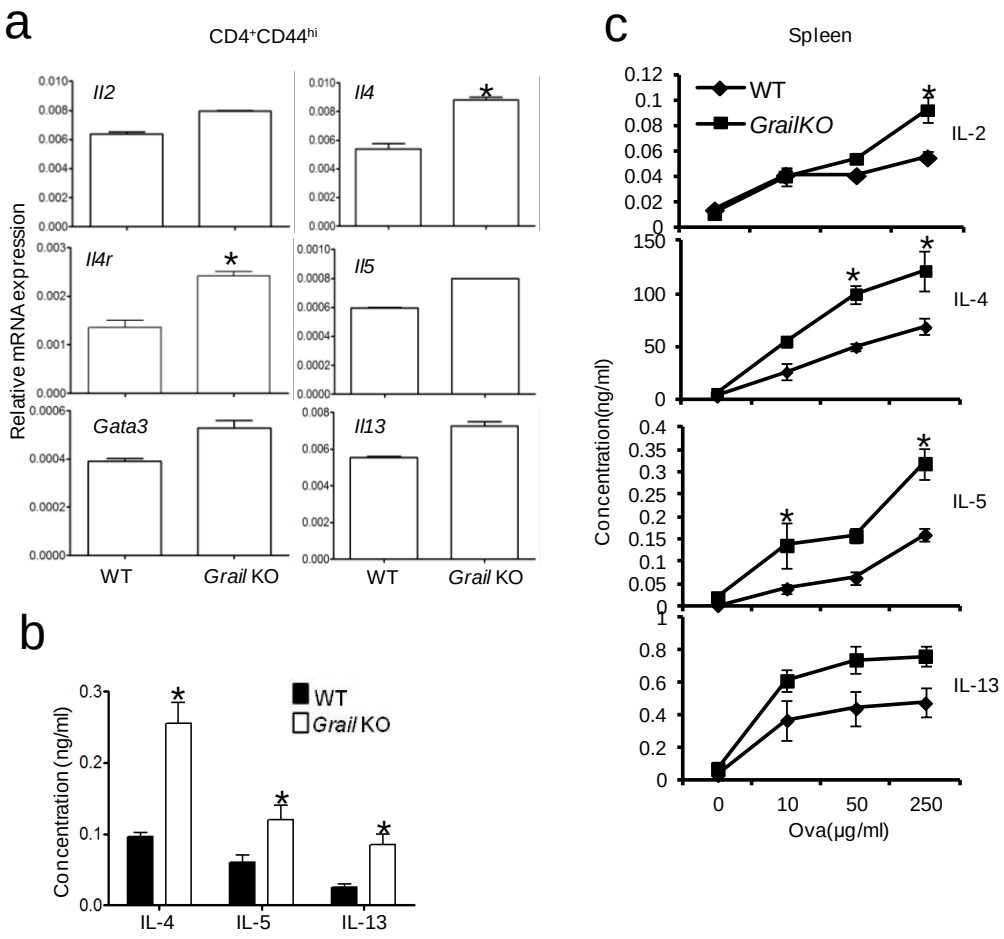

**Supplementary Figure 3. Chromatin configuration of signature Th2 genes in WT and *Grail* KO naïve and Th2 cells.**

Naïve $CD4^{+}CD25^{-}CD62L^{hi}CD44^{lo}$ T cells from WT and *Grail* KO mice were isolated and cultured for 4 days under Th2 polarizing cell conditions. ChIP analysis of histone H3 acetylation (AcH3), Anti-trimethyl histone H3 lysine 4 (H3k4) and Anti-trimethyl histone H3 lysine 27 (H3K27) methylation was performed at IL-4, Gata3 and IL-4 receptor (IL4R) promoter loci in both naïve (left panel) and differentiated Th2 cells (right panel). The data from each replicate were normalized to the input control and the graphs represent fold enrichment of the indicated proteins to control antibody (rabbit IgG) at the designated locus. The results shown are mean ± SEM. P values: *<0.05, **<0.01. Student's t-test was performed to detect between-group differences.. The data are representative of mean of at least three independent experiments with consistent results.



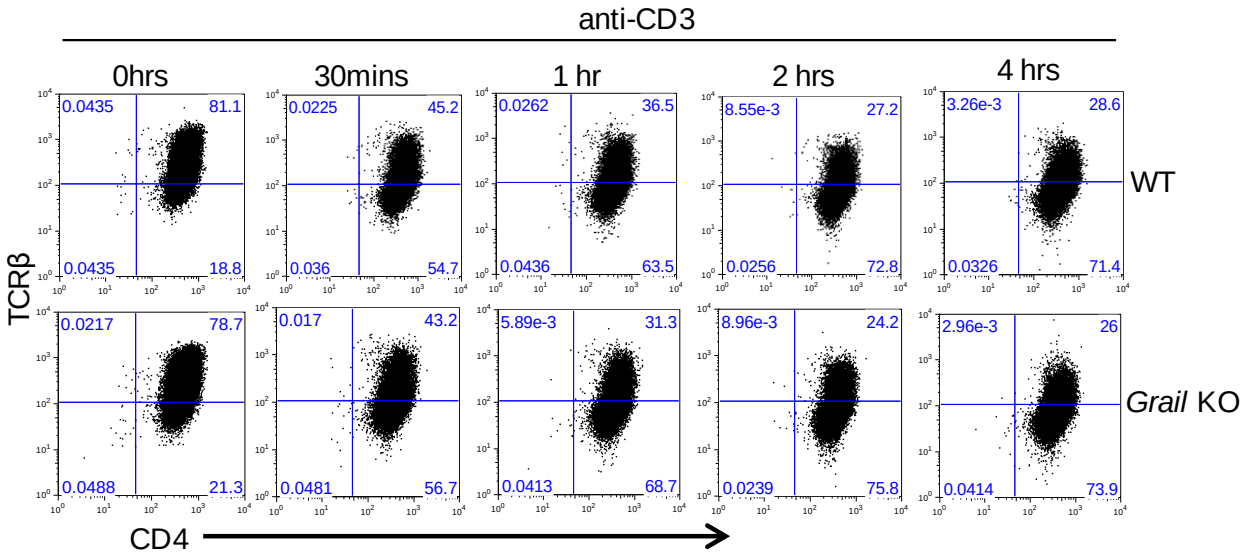

**Supplementary Fig. 4. IL-4 requirement for Th2 programming in Grail deficient cells.**

(**a-b**) Naïve $CD4^+$ T cells from WT and *Grail* KO mice were activated with anti-CD3 and anti-CD28 in the presence or absence of anti-IL-4 antibody for 24 and 48 hrs and mRNA expression of the indicated genes was analyzed by qRT-PCR. The data shown were normalized by the expression of a reference gene *Actb*. The results shown are mean ± SEM. P values: *<0.05. Student's t-test was performed to detect between-group differences. The data are representative of at least three independent experiments with consistent results.



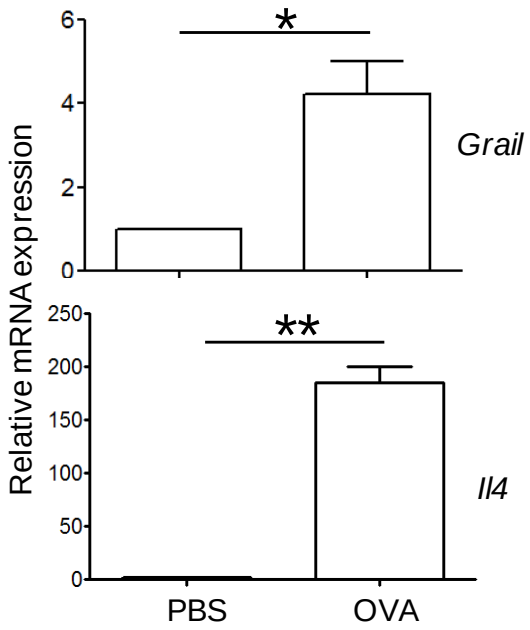

**Supplementary Figure 5. Elevated Th2 cytokine expression in *Grail* KO T cells *in vivo*.**

(**a-b**) FACS sorted $CD4^{+}CD44^{hi}$ effector memory T cells from WT and *Grail* KO mice were restimulated with anti-CD3 and analyzed for the expression of the indicated genes by qRT-PCR (**a**) and ELISA (**b**). **(c)** Groups of male WT and *Grail* KO mice (6-8 weeks old, n=5 per group) were intraperitoneally sensitized with Ova in alum at 2 weeks interval, followed by intranasal challenge with Ova. Splenocytes from asthmatic mice were restimulated with different concentrations of Ova for 72 hrs and IL-2, IL-4, IL-5 and IL-13 levels were measured by ELISA. The results shown are mean ± SEM. P values: *<0.05. Student's t-test was performed to detect between-group differences. The data are representative of at least three independent experiments with consistent results**.**



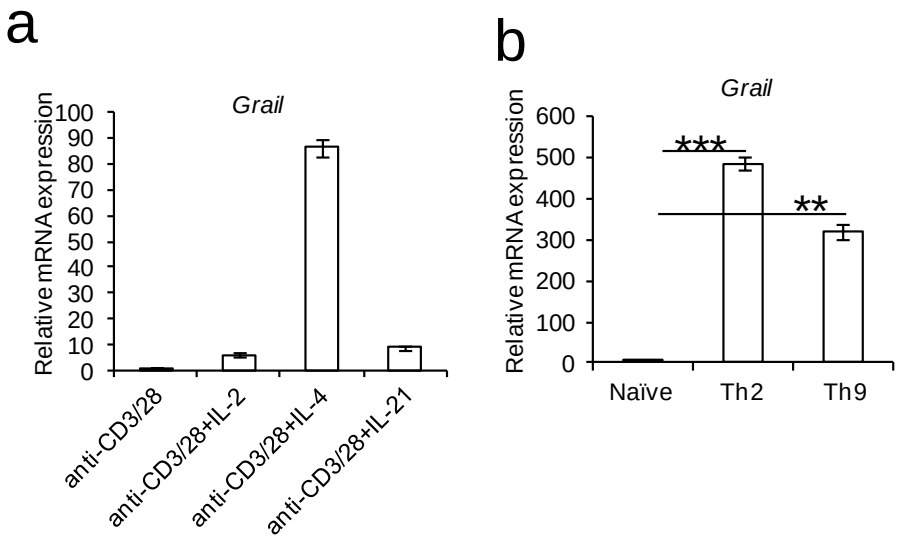

**Supplementary Figure 6. Regulation of cell-surface TCR expression by Grail in Th2 cells.**

Naïve $CD4^{+}CD25^{-}CD62L^{hi}CD44^{lo}$ T cells from C57BL/6 mice were cultured for 4 days under Th2 polarizing cell conditions. The cells were then restimulated for indicated time points with anti-CD3, and the expression of TCRβ was determined by flow cytometry. Numbers in dot plot quadrants represent the percentages. The results shown are representative of at least three independent experiments.



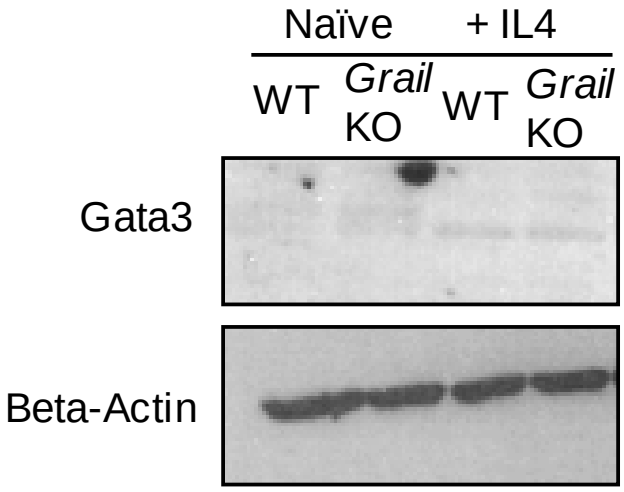

**Supplementary Figure 7. *Grail* expression in lungs of asthmatic mice.**

Groups of WT and *Grail* KO mice (6-8 weeks old, n=5 per group) were subjected to asthma. The mice were intraperitoneally sensitized with Ova in alum at 2 weeks interval, followed by intranasal challenge with Ova. Total lungs were harvested and *Grail* and *Il4* mRNA levels were analyzed by qRT-PCR analysis. The results shown are mean ± SEM. P values: *<0.05, **<0.01. Student's t-test was performed to detect between-group differences. The data are representative of at least three independent experiments with consistent results.



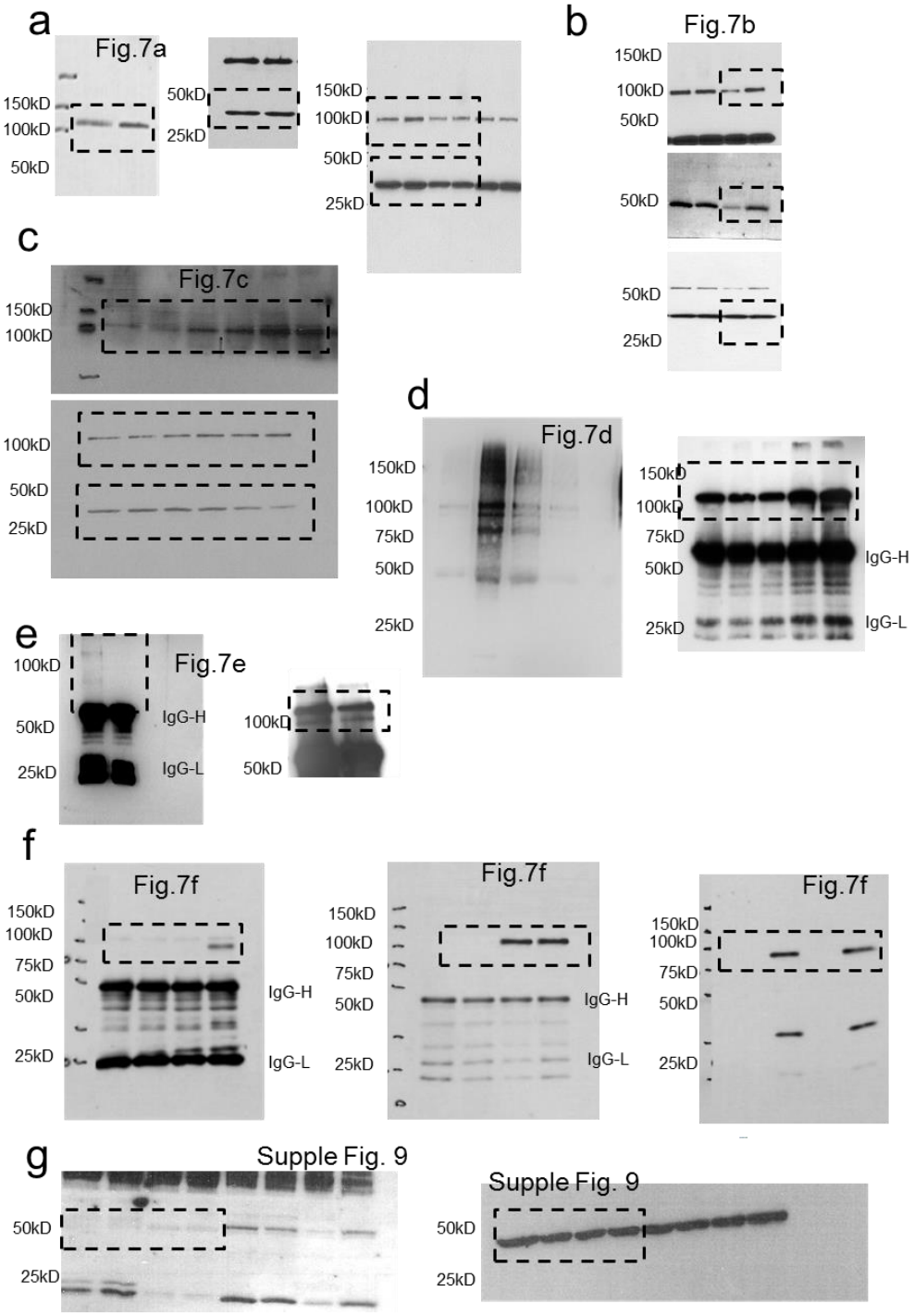

**Supplementary Figure 8. *Grail* expression in Th2 and Th9 cells.**

**(a)** Naïve $CD4^+$ T cells from C57BL/6 mice were activated with anti-CD3 and anti-CD28 alone or in the presence of indicated cytokines for 72 hrs and analyzed for *Grail* mRNA expression. **(b)** Naïve $CD4^+$ T cells from WT and *Grail* KO mice were activated with anti-CD3 and anti-CD28 under Th2 and Th9 (anti-IFN-γ - Bioexcel,10μg/ml, IL-4 - Peprotech, 10ng/ml, TGF-β-Peprotech,2ng/ml, hIL-2- Peprotech,50U/ml) polarizing conditions. Grail expression was analyzed by qRT-PCR. The data shown was normalized by the expression of a reference gene *Actb*. The results shown are mean ± SEM. P values: **<0.01, ***<0.001. Student's t-test was performed to detect between-group differences. The data are representative of at least three independent experiments with consistent results.




**Supplementary Figure 9. Gata3 expression in WT and Grail deficient T cells.**

Gata3 protein expression was detected in naïve $CD4^+$ T cells or in cells activated with anti-CD3/anti-CD28 in the presence of IL-4 for 24 hours from WT and *Grail* KO mice by western blot analysis. Actin levels were analyzed as control. The data is representative of at least three independent experiments with consistent results.




**Supplementary Figure 10. Uncropped gel images.**

IgG-H and IgG-L represent the heavy and light chains of IgG respectively. The blots are representative of at least three independent experiments with consistent results.