**Extended Data Figure 1. Wtap depletion in T cells induces inflammation of the gut. a**, **b** Deletion efficiency of floxed Wtap alleles in thymocytes and splenic T cells showing an immunoblot (**a**) with Wtap specific antibodies using Gapdh as a loading control or flow cytometry (**b**) with Wtap-specific antibodies on thymocytes, CD4 and CD8 SP thymocytes, thymic Treg cells as well as splenic CD4+ and peripheral CD4+Foxp3+ Treg cells. **c**, qPCR analysis of the indicated cytokine gene expression within mRNA prepared from colon tissue. Results are to *Ywhaz* expression and presented relative to wild-type. Data were derived from three independent experiments. **d**, **e**, IFN and IL-17a production in CD4+ T cells from the lamina propria of the colon. Percentages of IFN+IL-17a+ cells are shown in **e**. Data are representative of three independent experiments. **f-i**, Stainings to detect CD4+CD25+Foxp3+ Treg cells in spleen (**f**), colon (**i**) and splenocytes (**g**, **h**) from *Foxp3*-Cre and *Wtap*fl/fl; *Foxp3*-Cre mice. Numbers adjacent to outlined areas indicate the percentage of cells in each gate. Data are representative of three independent experiments. **j**, Flow cytometry to detect RORγt and Helios for CD4+YFP+Foxp3+ or YFP–Foxp3+ T cells in mLNs from female *Wtap*fl/fl; *Foxp3*-Crehet mice. Data are representative of two independent experiments. **k**, IFN and IL-17a production in CD4+Foxp3+ T cells in lamina propria of the colon. Percentages of IFN+ or IL17a+ cells are shown in the right panel. Data are representative of three to four biological replicates.

**Extended Data Figure 2. Analyzing Wtap effects on thymic Treg cells and intracellular TCR expression.** **a**, Staining to detect CD4+CD25+Foxp3+ Treg cells in thymus from *Wtap*fl/fl and *Wtap*fl/fl; *Cd4*-Cre mice. Numbers adjacent to outlined areas indicate the percentage of cells in each gate. Data are representative of three independent experiments. **b**, Intracellular staining of TCRβ on gated CD4 SP CD24- or CD8 SP CD24- thymocytes. Data are representative of two independent experiments. **c**, **d**, Flow cytometry analysis (**c**) and cellularity (**d**) of thymocytes from bone marrow chimeras, assessed for expression of CD4 and CD8 (right) after gating on CD45.1 or CD45.2 (left). Numbers adjacent to outlined areas indicate percentage of cells in each gate. Data are representative of three biological replicates.

**Extended Data Figure 3. Virma expression is essential for m6A modification.** **a, b,** Percentage of the different congenic marked hematopoetic CD45+ cells (**a**) and flow cytometry analysis of splenocytes (**b**) from bone marrow chimeras harboring WT (CD45.1+) and *Wtap*fl/fl; *Cd4*-Cre (CD45.2+) hematopoetic cells, assessed for expression of CD4 and CD8 after identifying CD45.1 or CD45.2 congenic cells. Numbers adjacent to outlined areas indicate the percentages of cells in each gate. Data are representative of three biological replicates. **c**, Surface staining of CD44 and CD62L on CD4+ and CD8+ T cells after gating on CD45.1 or CD45.2 congenic splenocytes of the bone marrow chimeras. Numbers adjacent to outlined areas indicate percentage of cells in each gate. Data are representative of three biological replicates. **d**, Immunoblot analysis of Virma protein in extracts from MEF cells showing Gapdh as a loading control. Data are representative of two independent experiments. **e**,m6A abundance as determined by LC/MS/MS analysis in the oligo-dT-purified mRNAs of Virma-depleted and Cre expressing or wildtype MEF cells. Data were derived from three biological replicates. **f**, Stainings to identify CD4+CD25+Foxp3+ Treg cells among thymocytes of *Virma*fl/fl or *Virma*fl/fl; *Cd4*-Cre mice. Numbers adjacent to outlined areas indicate the percentages of cells in each gate. Data are representative of three independent experiments.

**Extended Data Figure 4. The m6A methyltransferase complex controls T cell survival. a**, Flow cytometry of CD4+ and CD8+ T cells from *Cd4-*CreERt2 and *Wtap*fl/fl; *Cd4*-CreERt2 mice stained with anti-WTAP antibody seven days after the last gavage. Data are representative of three independent experiments. **b**, **c**, Flow cytometry of cells from lymphoid organs of tamoxifen-gavaged Rag1−/− (**b**) or CD45.1 (**c**) mice 9 days after transfer of naive CD4+ T cells from *Cd4-*CreERt2 or *Wtap*fl/fl; *Cd4*-CreERt2 mice, assessed for expression of Wtap after gating on CD4 and TCR in **b** or CD45.1 and CD45.2 in **c**. Data were derived from two to three independent experiments. **d**,Histogram of Ki67 expression in CD4+ T cells from *Cd4-*CreERt2 and *Wtap*fl/fl; *Cd4*-CreERt2 mice that received tamoxifen gavage and anti-CD3 antibody injection. Data are representative of three independent experiments. **e**, Cellularity of pLNs from *Cd4*-CreERt2 and *Wtap*fl/fl; *Cd4*-CreERt2 mice that received tamoxifen gavage and anti-CD3 antibody injection. Data were derived from three independent experiments.

**Extended Data Figure 5. Analyzing TCR induced apoptosis and activation markers after Virma or Mettl3 deletion in CD4+ T cells.** **a**, Flow cytometry of CD4+ T cells from *Cd4-*CreERt2 and *Virma*fl/fl; *Cd4-*CreERt2 mice, stained with anti-VIRMA antibody three days after the last gavage. Data are representative of three independent experiments. **b**, Flow cytometry of CD4+ T cells from *Cd4-*CreERt2 and *Virma*fl/fl; *Cd4-*CreERt2 mice, stained with AnnexinV and LIVE/DEAD Fixable dye on day 4. Percentage of AnnexinV+ population is shown in the right. Data are representative of three independent experiments. **c**, Percentage of AnnexinV+ naive CD4+ T cells during the naive T cell culture without IL-7 at the indicated days. Data presented were derived from two independent experiments. **d**, Surface staining of activation marker CD5 and CD25 in CD4+ T cells. Data are representative of four biological replicate. **e**, Surface staining of activation marker CD69 in CD4+ T cells from *Cd4-*CreERt2 and *Wtap*fl/fl; *Cd4-*CreERt2 mice that received tamoxifen gavage. Data are representative of three independent experiments.

**Extended Data Figure 6. Wtap depletion induces apoptosis *in vitro*.** **a,** Experimental scheme of *in vitro* deletion of Wtap induced by 4'-hydroxy-tamoxifen in iKO CD4+ T cells. **b**, Flow cytometry of CD4+ T cells prepared from *in vitro* 4’OH-tamoxifen induced Wtap deletion, stained with anti-WTAP antibody on day 4. **c**, Flow cytometry of iKO and control CD4+ T cells, stained with AnnexinV and LIVE/DEAD Fixable dye on day 4. Percentage of AnnexinV+ cell populations is shown in the right panel. Data are representative of two independent experiments. **d**, Measurement of m6A abundance on mRNAs in CD4+ T cells prepared from *in vitro* 4’OH-tamoxifen induced Wtap deletion. Data are representative of three biological replicates.

**Extended Data Figure 7. Strategy and validation of the CLIP analyses. a**, Reproducibility of enriched peaks in m6A- or Ythdf2-iCLIP. Data were prepared from three biological replicate for m6A-CLIP and two replicate for Ythdf2-CLIP. **b,** Flow chart of the CLIP analysis. **c,** Venn diagram showing the overlap of m6A target mRNAs from Yao et al.[23](#_ENREF_23) and this study. **d,** Integrative Genomics Viewer (IGV) tracks of *Tnf* displaying m6A-CLIP and Ythdf2-CLIP reads distribution. The read coverage is shown for merged replicates. Predicted DRACH sites in the peak region overlaps of the two CLIP experiments are marked with red arrowheads.

**Extended Data Figure 8. Regulation of m6A modified mRNAs by Wtap deletion.** **a,** qPCR analysis of iKO and control CD4+ T cells. Results are presented relative to *Ywhaz* expression. Data were derived from two independent experiments. **b**, mRNA decay curves of *Tnfrsf1b* mRNA in iKO and control CD4+ T cells using Actinomycin D to terminate transcription of newly synthesized mRNAs. Data presented were derived from two independent experiments.