**SUPPLEMENTARY INFORMATION**

**Supplementary Figure 1. TOLLIP expression in murine colon.** Flow cytometry gating representation for assessing TOLLIP protein synthesis in epithelial cells, neutrophils, and macrophages in colons from *Camp+/+* and *Camp-/-* mice.

**Supplementary Figure 2.** (**A**) Full image for the western blot for **Fig 1B**. (**B**) TOLLIP protein synthesis in bone marrow-derived macrophages isolated from *Camp+/+* and *Camp-/-* mice determined by western blotting. Blots were normalized to GAPDH with ratios at the bottom. (**C-D**) Flowcytometry analysis of (**C**) (CD45+CD11b+LyG+TOLLIP+) neutrophils and (**D**) resident (CD45+CD11+CX3CR1+TOLLIP+) macrophages expressing TOLLIP protein in the colonic mucosa of *Camp+/+* and *Camp-/-* mice after oral gavage with PBS or *C. rodentium* at 7 days post-infection (~5x108 CFU in 200 mL of PBS). Box and whisker plots represent the means ± SEM (bars) (n = 4-7 mice/group). (**E**) TOLLIP mRNA expression in colonic epithelial cells from *Camp+/+* and *Camp-/-* mice determined by qPCR. Data are shown relative to GAPDH as means ± SEM (n= 4-7 mice/group). (**F**) TOLLIP mRNA quantification in HT29 cells treated with LL-37 (2 μM; for up to 8 h) determined by qPCR and represented relative to GAPDH expression. *P* < 0.05 (two-way ANOVA or one-way ANOVA post hoc Bonferroni correction for multiple group comparison) was considered significant unless noted differently for specific figure.

**Supplementary Figure 3. Cathelicidins induce TOLLIP expression in human colonic epithelial HT29 cells and murine fibroblasts. Assessment in HT29 cells of knockdown expression in LL-37 and TOLLIP, cytokine quantification in Sham and ShTOLLIP transfected cells post LL-37, and overexpression of miR-31-5p.** (**A-B**) TOLLIP synthesis in (**A**) HT29 cells treated with LL-37 at variable concentrations and (**B**) murine L929 fibroblasts treated with LL-37 at 2 μM for variable times determined by western blotting. LPS (1 μg/mL) was used as positive control for TOLLIP expression. In (**A**), a bar graph depicting quantification of TOLLIP protein next to the blot. Silencing efficiency in HT29 cells sham transfected or knock down in (**C**) LL-37 or (**D**) TOLLIP determined by western blotting. (**E**) Quantification of CXCL1, IL10, IL8, and IL-1Ra in HT29 cell supernatants and lysates (for IL-Ra) at variable times post LL-37 treatment measured by ELISAs. Data are represented as absolute values (pg/mL). (**F**) A bar graph showing increased miR-31-5p expression in HT29 cells determined by qPCR. U6 snRNA was used as normalization control. *P* < 0.05 (one-way ANOVA post hoc Bonferroni correction for multiple group comparison) was considered significant.

**Supplementary Figure 4. Shotgun proteomic in murine colons.** Experimental workflow for proteomic analysis in colons from *C. rodentium* infected *Camp+/+* and *Camp-/-* mice (7 days post-infection) and the Metascape analysis of different pathways and STRING analysis of Ago2 protein-protein interaction with Ybx3, Zc3hav1, Pabpn1, and Tdrd1.

**Supplementary Figure 5. Colonic epithelial cell apoptosis in *Camp+/+* and *Camp-/-* mice infected by *C. rodentium*.** Apoptotic cells in colons of *Camp+/+* and *Camp-/-* mice orally challenged with PBS or *C. rodentium* (~1x108 CFU in 200 μL of PBS). Cells were identified at 7 days post infection by (**A**) TUNEL assay and (**B**) counted and illustrated using ImageJ 1.53c software (National Institute of Health, USA). Data are represented as number of apoptotic cells per 100 crypts. Data are means ± SEM (n= at least 3 mice/group). *P* < 0.05 (Kruskal-Wallis test for mean comparison) was considered significant. ns= not significant.