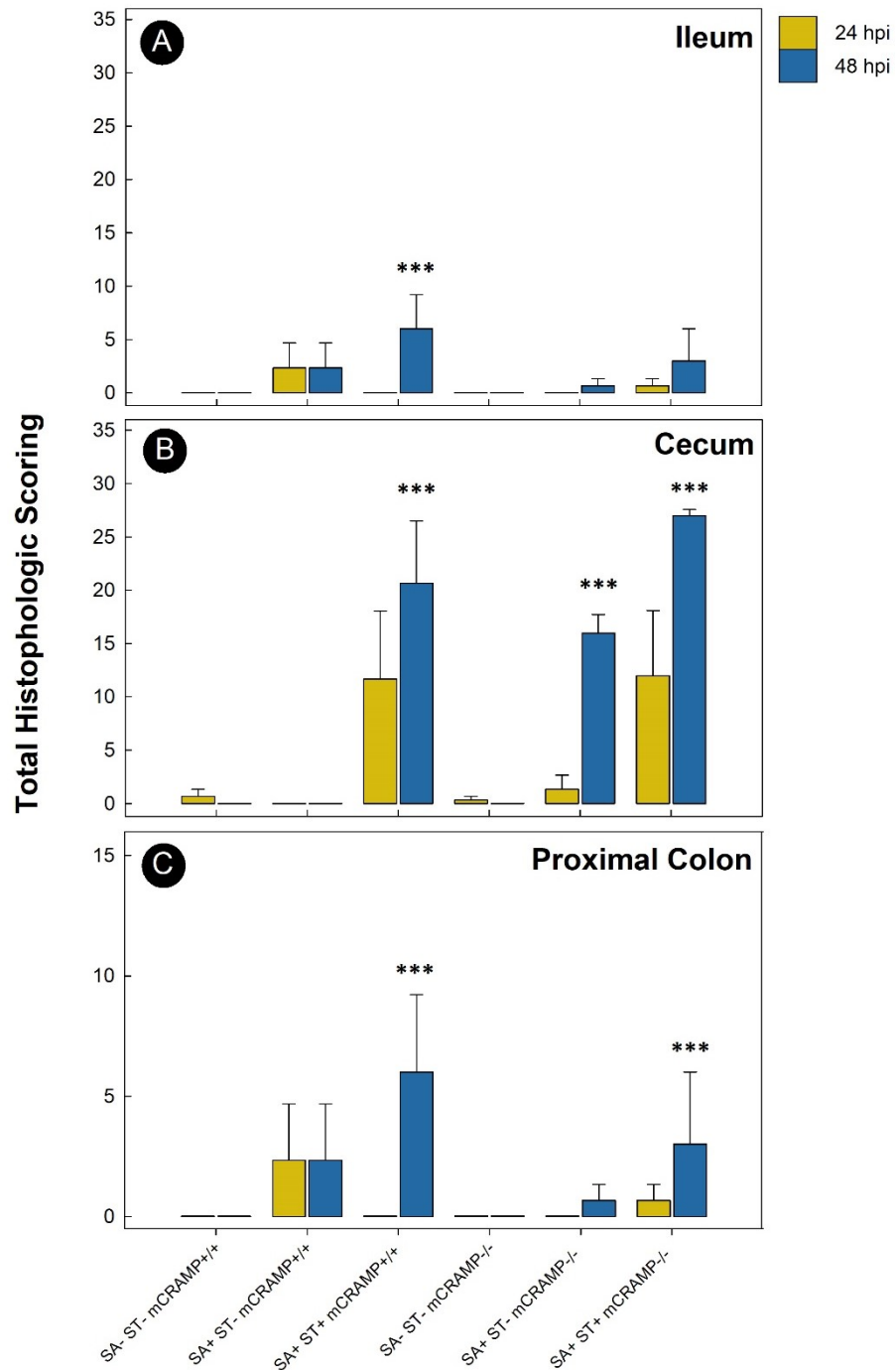
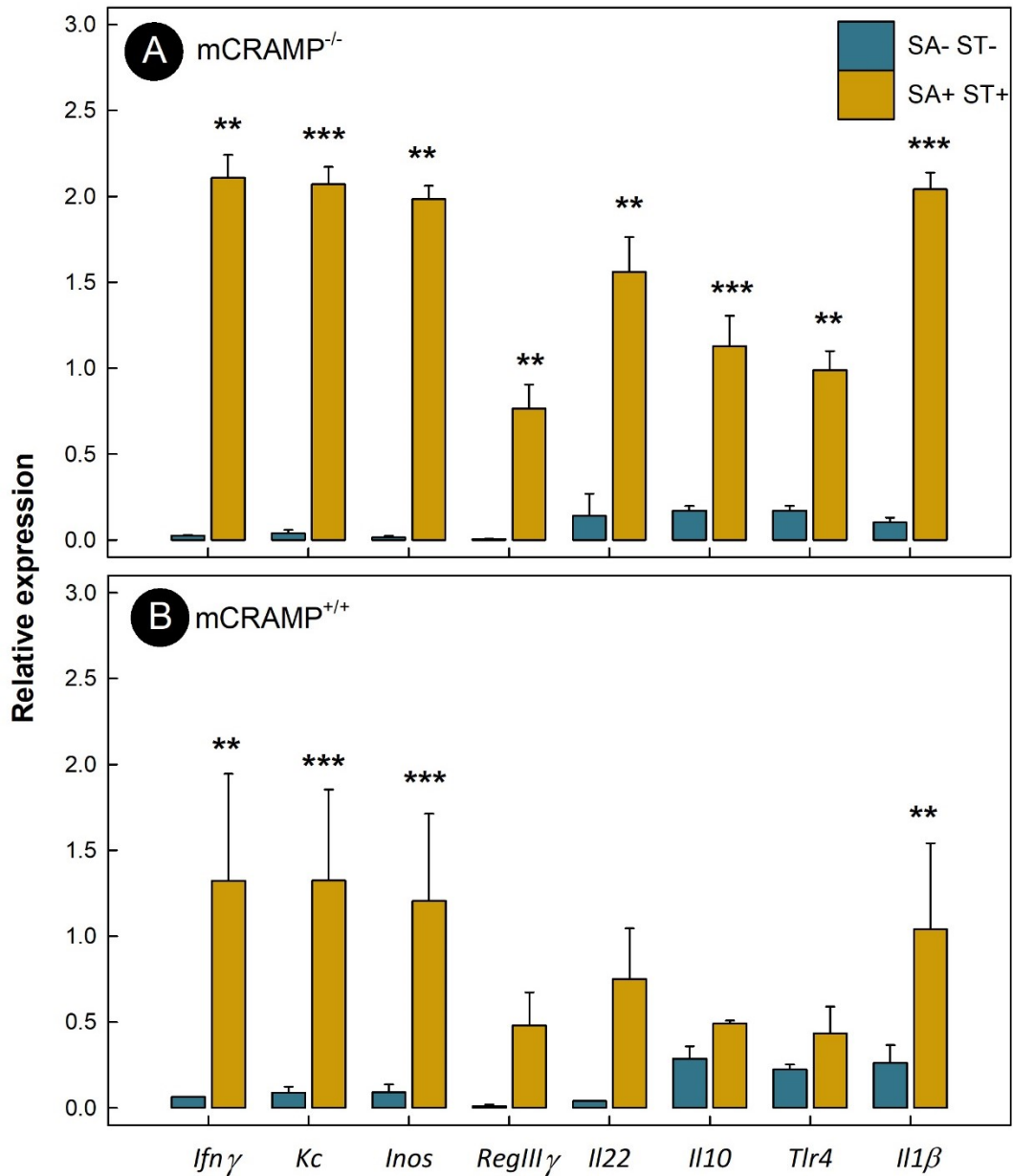


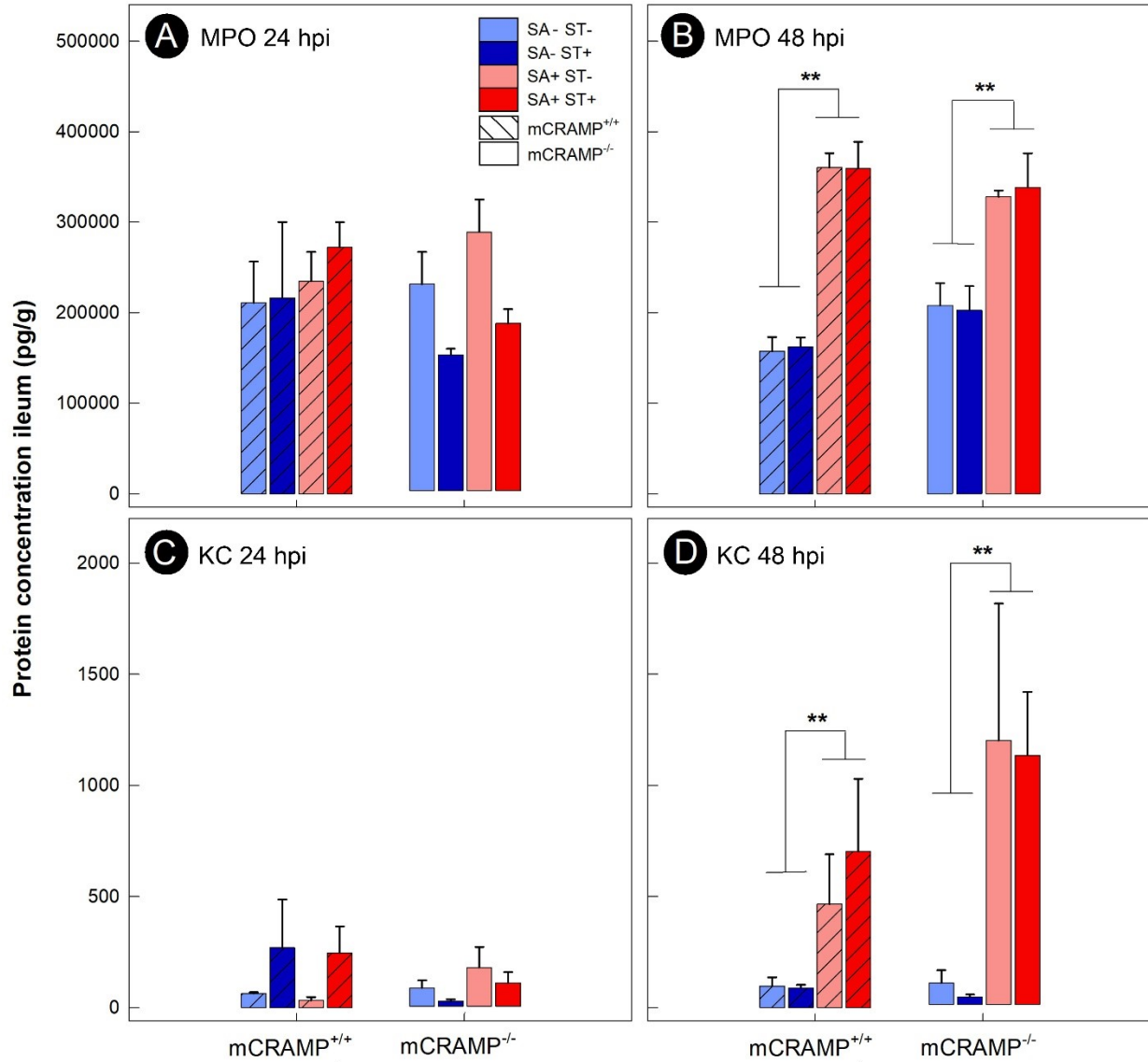
## Supplemental material



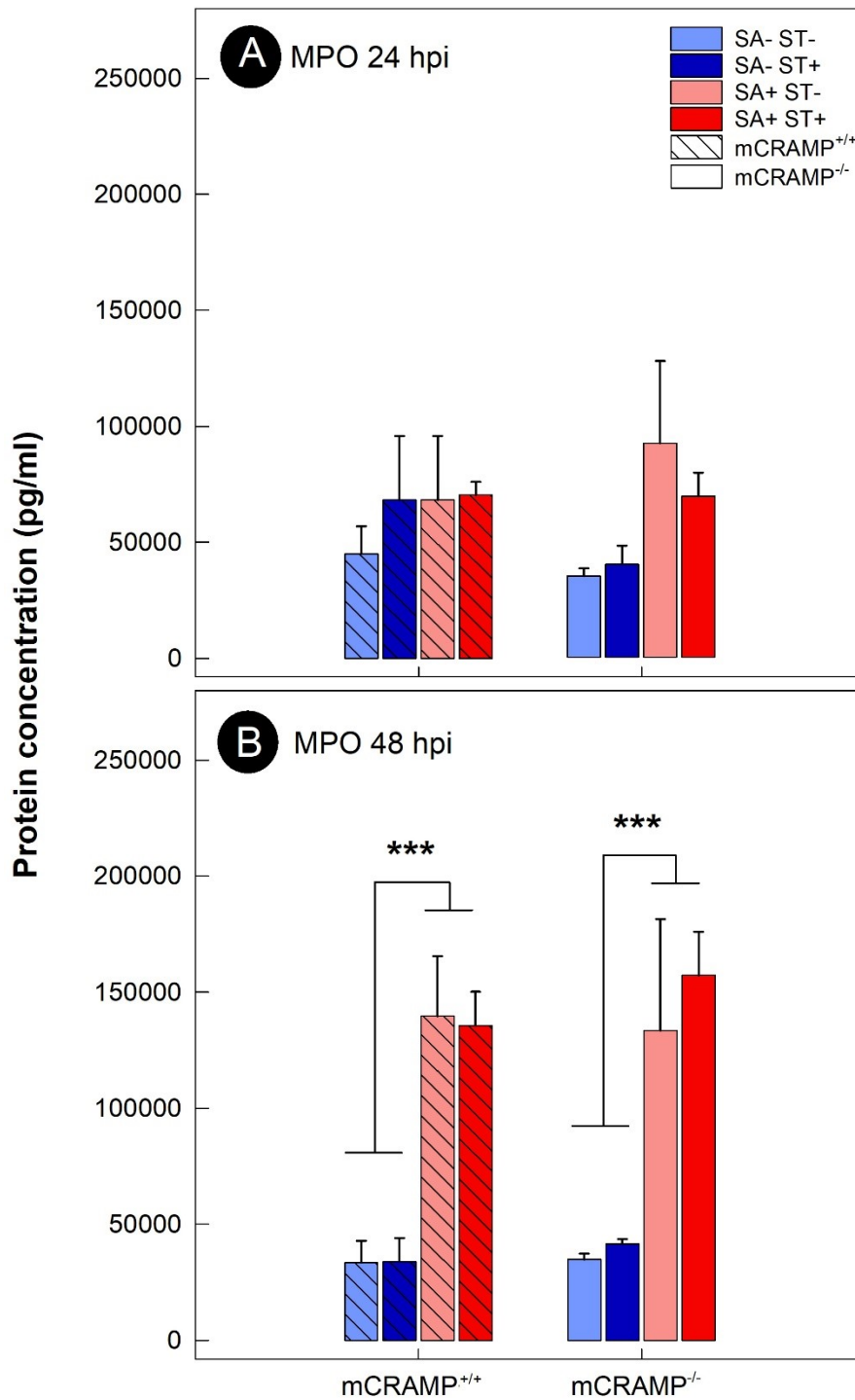
**Fig S1** Total histopathologic scores in mCRAMP<sup>-/-</sup> and mCRAMP<sup>+/+</sup> mice that were inoculated with *Salmonella enterica* Typhimurium (SA+) or medium alone (SA-), and pre-treated with streptomycin (ST+) or water alone (ST-) at 24 vs 48 hours post-inoculation. (A) Ileum; (B) Cecum; (C) Proximal Colon. Vertical lines associated with markers are standard errors of the mean. Histogram bars with asterisks indicate that treatments differ (\*\*\*) P < 0.001).



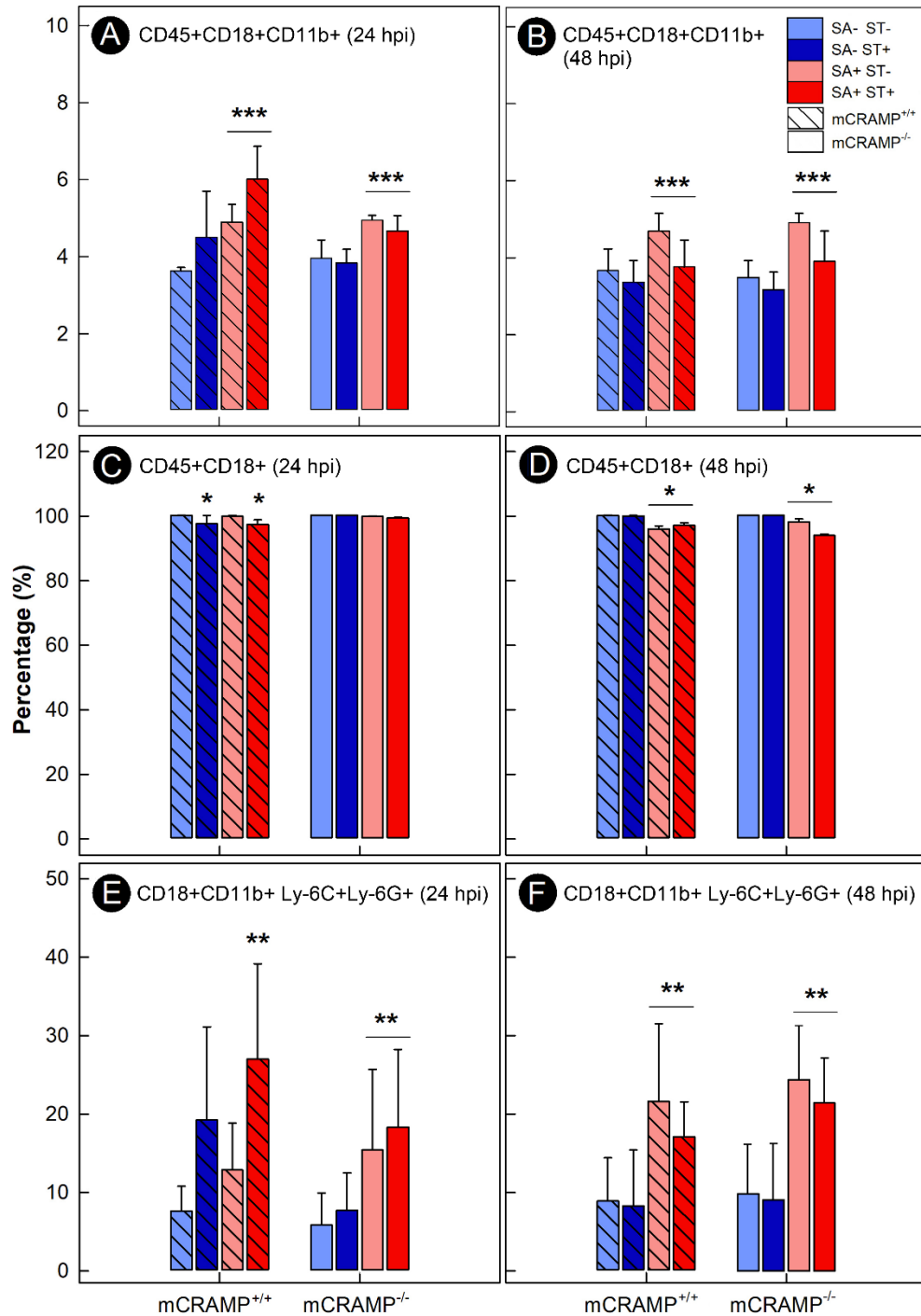
**Fig S2** Relative gene expression in cecum of mCRAMP<sup>+/+</sup> and mCRAMP<sup>-/-</sup> mice that were inoculated with *Salmonella enterica* Typhimurium (SA+) or medium alone (SA-) and pretreated with streptomycin (ST+) or water alone (ST-) at 48 hours post-inoculation. (A) mCRAMP<sup>-/-</sup> (B) mCRAMP<sup>+/+</sup>. Vertical lines associated with markers are standard errors of the mean. Histogram bars with asterisks indicate that treatments differ (\*P<0.050, \*\*P<0.010).



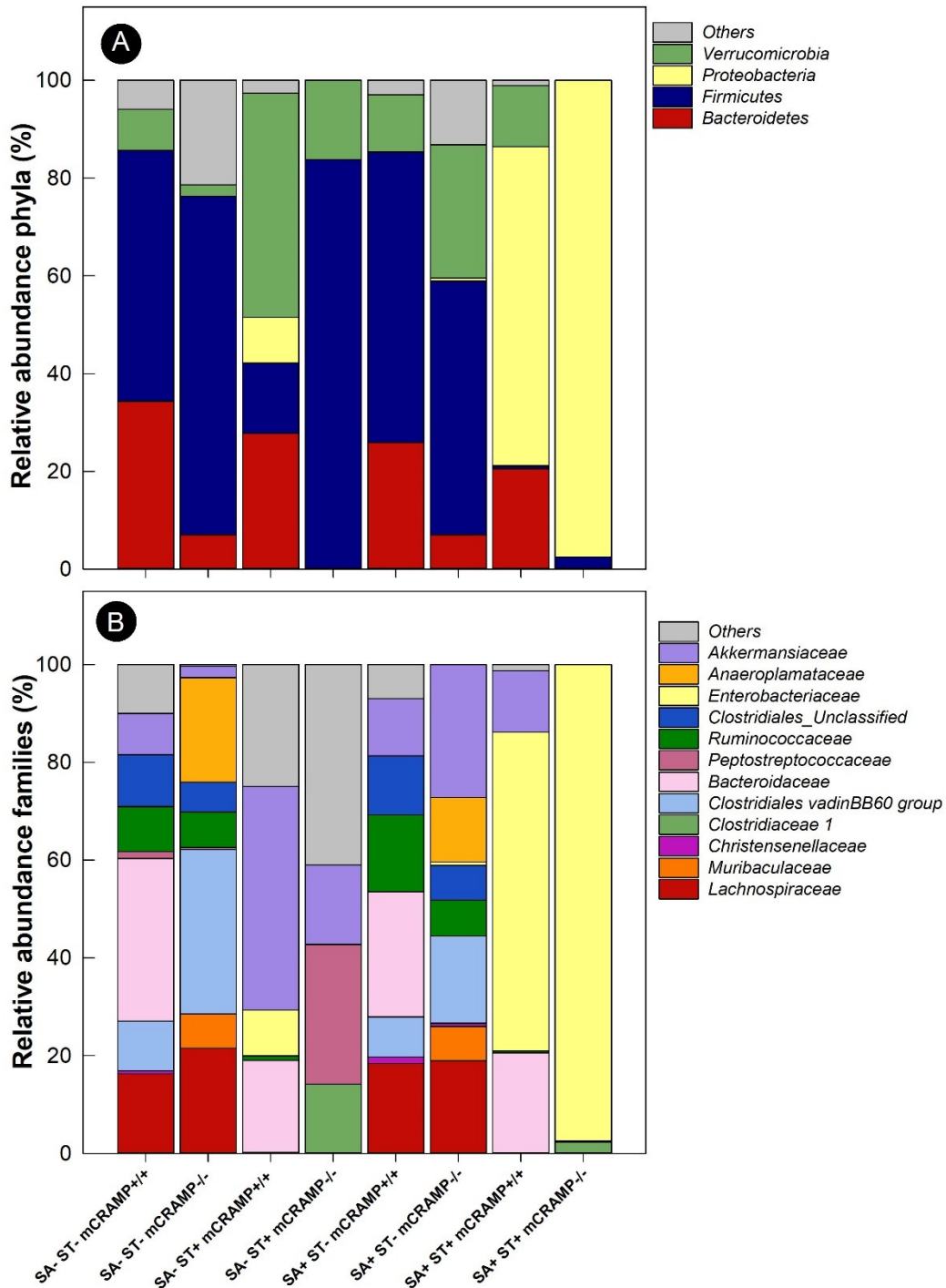
**Fig S3** Protein concentrations of MPO and KC in the ileum of mCRAMP<sup>+/+</sup> and mCRAMP<sup>-/-</sup> mice that were orally inoculated with *Salmonella enterica* Typhimurium (SA+) or medium alone (SA-), and pretreated with streptomycin (ST+) or water alone (ST-). (A) MPO at 24 hours post-inoculation (hpi); (B) MPO at 48 hpi; (C) KC at 24 hpi; (D) KC at 48 hpi. Vertical lines associated with markers are standard errors of the mean. Histogram bars with asterisks indicate that treatments differ (\*P<0.050, \*\*P<0.010, \*\*\*P<0.001).



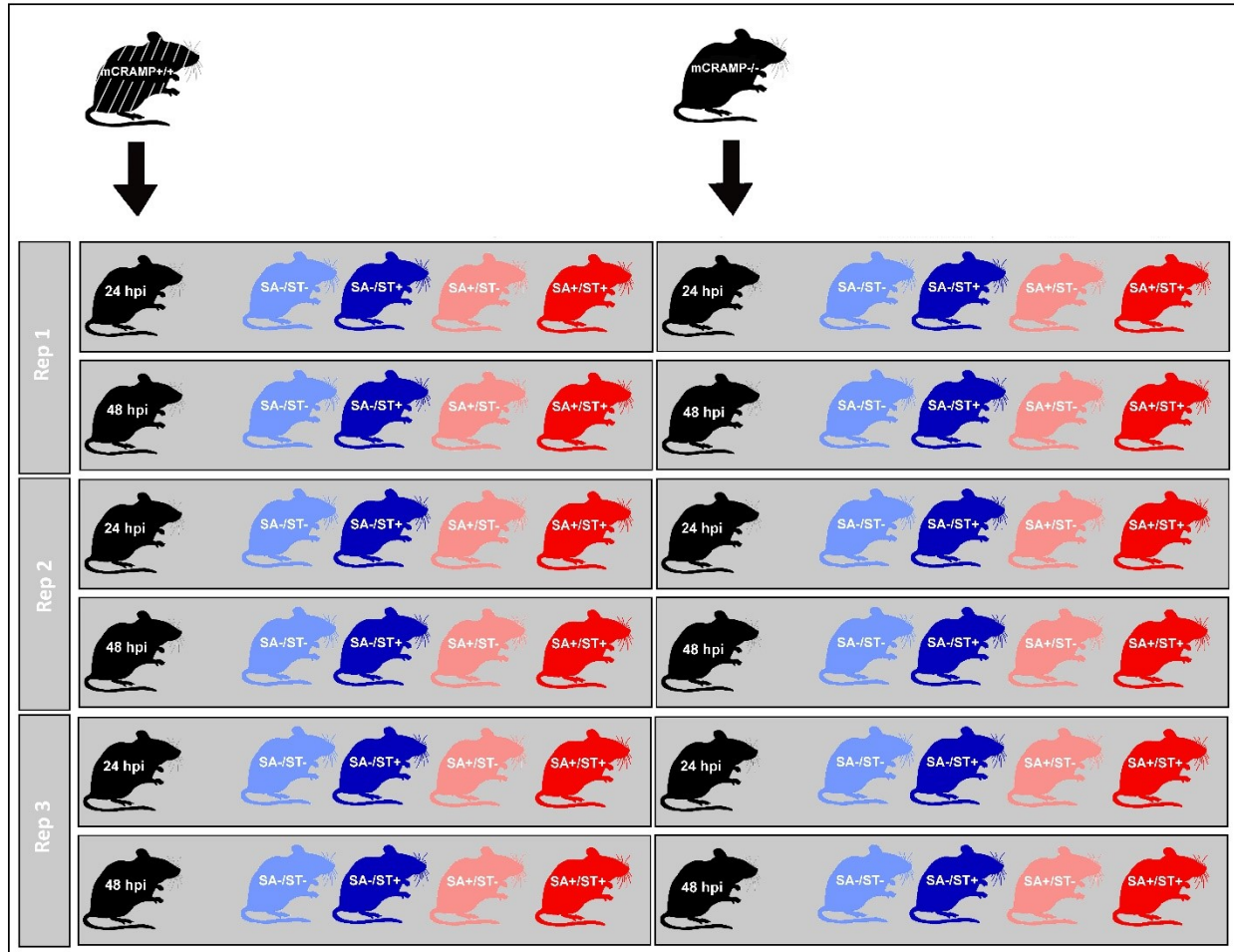
**Fig S4** Protein concentrations of MPO in the serum of mCRAMP<sup>+/+</sup> and mCRAMP<sup>-/-</sup> mice that were orally inoculated with *Salmonella enterica* Typhimurium (SA+) or medium alone (SA-), and pretreated with streptomycin (ST+) or water alone (ST-). (A) MPO at 24 hours post-inoculation (hpi); (B) MPO at 48 hpi. Vertical lines associated with markers are standard errors of the mean. Histogram bars with asterisks indicate that treatments differ (\*P<0.050, \*\*P<0.010, \*\*\*P<0.001).



**FIG S5** Percentage of splenic immune cell populations in mCRAMP<sup>-/-</sup> and mCRAMP<sup>+/+</sup> mice, that were orally inoculated with *Salmonella enterica* Typhimurium (SA+) or medium alone (SA-), and pretreated with streptomycin (ST+) or water alone (ST-). (A) CD45<sup>+</sup>CD18<sup>+</sup>CD11b<sup>+</sup> leukocytes at 24 hours post-inoculation (hpi); (B) CD45<sup>+</sup>CD18<sup>+</sup>CD11b<sup>+</sup> leukocytes at 48 hpi; (C) CD45<sup>+</sup>CD18<sup>+</sup> leukocytes at 24 hpi; (D) CD45<sup>+</sup>CD18<sup>+</sup> leukocytes at 48 hpi; (E) CD18<sup>+</sup>CD11b<sup>+</sup> Ly-6C<sup>+</sup>Ly-6G<sup>+</sup> neutrophils at 24 hpi; (F) CD18<sup>+</sup>CD11b<sup>+</sup> Ly-6C<sup>+</sup>Ly-6G<sup>+</sup> neutrophils at 48 hpi. Vertical lines associated with markers are standard errors of the mean. Histogram bars with asterisks indicate that treatments differ (\*P<0.050, \*\*P<0.010, \*\*\*P<0.001).



**FIG S6** Relative abundance (%) of bacterial phyla and families in cecum digesta of mCRAMP<sup>+/+</sup> and mCRAMP<sup>-/-</sup> mice that were orally inoculated with *Salmonella enterica* Typhimurium (SA+) or medium alone (SA-), and pretreated with streptomycin (ST+) or water (ST-) alone at 48 hours post-inoculation. (A) Phyla; (B) Families.



**FIG S7** Schematic representation of the experimental design. The experiment was arranged as a two ( $\pm$  mCRAMP) by two ( $\pm$  *Salmonella*) by two ( $\pm$  streptomycin) by two (sample time) factorial experiment. The experiment was run on three separate occasions, and comprised 48 mice in total. The figure represents only one replicate.

**Table S1** Splenic immune cell populations at 48 hours post-inoculation.

Cell phenotype	mCRAMP <sup>+/+</sup>								mCRAMP <sup>-/-</sup>							
	ST- SA-		ST+ SA-		ST- SA+		ST+ SA+		ST- SA-		ST+ SA-		ST- SA+		ST+ SA+	
	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
CD3 <sup>+</sup> T cells (% of live lymphocytes)	1.21	0.2	1.45	0.39	1.59	0.28	1.55	0.36	0.94	0.3	0.76	0.06	1.16	0.14	0.97	0.09
CD4 <sup>+</sup> T helper cells (% of CD3 <sup>+</sup> cells)	38.0	6.15	44.3	1.05	43.7	5.08	52.0	8.47	42.36	5.24	49.33	9.70	45.96	7.87	53.13	5.34
CD8 <sup>+</sup> cytotoxic T cells (% of CD3 <sup>+</sup> cells)	3.4	1.20	2.42	0.55	4.10	1.44	4.20	0.92	4.88	2.57	4.04	1.60	5.06	1.91	5.43	1.76
CD3 <sup>+</sup> CD4 <sup>+</sup> TCR <sup>+</sup> γδ T cells (% of CD4 <sup>+</sup> cells)	90.9	0.68	87.9	1.96	94.0	2.70	94.6	0.77	89.26	2.23	89.90	1.70	91.56	3.73	93.93	0.56
IL-23R <sup>+</sup> γδ T cells (% of CD4 <sup>+</sup> TCR <sup>+</sup> cells)	43.5	12.7	32.0	15.1	34.3	16.7	24.2	10.1	34.6	13.1	34.9	7.3	29.73	10.8	17.3	8.27
CD3 <sup>+</sup> CD161 <sup>+</sup> NK cells (% of live CD3 <sup>+</sup> cells)	4.00	0.30	3.06	0.18	3.16	0.34	2.46	0.14	3.72	0.18	3.56	0.11	3.48	0.49	3.03	0.34
CD3 <sup>+</sup> CD11b <sup>+</sup> CD11c <sup>-</sup> monocytes (% of live CD3 <sup>+</sup> CD161 <sup>-</sup> cells)	0.10	0.07	0.86	0.64	0.21	0.11	0.35	0.30	0.11	0.08	0.07	0.05	0.94	0.89	0.66	0.56
CD3 <sup>+</sup> CD11b <sup>+</sup> CD11c <sup>+</sup> mDC (% of live CD3 <sup>+</sup> CD161 <sup>-</sup> cells)	0.17	0.12	0.20	0.09	0.13	0.08	0.10	0.07	0.14	0.11	0.16	0.13	0.10	0.05	0.10	0.06
CD3 <sup>+</sup> CD11b <sup>+</sup> CD11c <sup>+</sup> pDC (% of live CD3 <sup>+</sup> CD161 <sup>-</sup> cells)	0.20	0.03	0.19	0.01	0.26	0.04	0.29	0.11	6.10	5.95	0.15	0.04	0.27	0.13	0.22	0.03
CD68 <sup>+</sup> macrophages (% of CD11b <sup>+</sup> CD11c <sup>+</sup> cells)	0.16	0.12	0.10	0.07	0.13	0.08	0.20	0.09	0.14	0.10	0.16	0.13	0.09	0.05	0.10	0.06

pDC, plasmacytoid dendritic cells; mDC, myeloid dendritic cells.



**Table S2** P values for Alpha and Beta Diversity measurements.

Treatments		Alpha Diversity			Beta Diversity
		Pielou's evenness	Faith's index	ASVs counts	UniFrac weighted
24 hpi	SA- ST-	0.563	0.248	0.248	0.201
	SA- ST+	0.512	0.055	0.126	0.511
	SA+ ST-	0.512	0.017	0.049	0.003
	SA+ ST+	0.049	0.126	0.275	0.306
48 hpi	SA- ST-	0.512	0.126	0.126	0.100
	SA- ST+	0.827	0.055	0.268	0.222
	SA+ ST-	0.563	0.017	0.563	0.003
	SA+ ST+	0.512	0.827	0.512	0.587

**Table S3** Histopathologic scoring system

Score	Inflammatory cell infiltrate		Epithelial changes			Mucosal architecture	
	Severity	Extent	Hyperplasia	Goblet cell loss	Epithelial injury	Irregular crypt*	Crypt loss
0	normal	normal	normal	normal	none	–	normal
1	Minimal: <10%	Mucosal	Minimal: <25%	Minimal <20%	rare (i.e. < 10 surface epithelial cells shedding)	–	decrease of <10%
2	Mild: 10-25%; scattered neutrophils	Mucosal and submucosal	Mild: 25-35%	Mild 21-35%	mild (i.e. focal epithelial erosions; 11-50 surface epithelial cells shedding)	–	decrease of ≥10%
3	Moderate: 26-50%	Mucosal, submucosal and transmural	Moderate: 36-50%; mitoses in middle/upper third of crypt epithelium, distant from crypt base	Moderate 36-50%	moderate (i.e. multi focal surface epithelium erosion; < 50 of surface epithelial cells shedding)	–	
4	Marked: >51%; dense infiltrate	–	Marked: >51%; mitoses in upper third of crypt epithelium, distant from crypt base	Marked >50%	severe (i.e. multi focal to coalescing surface epithelium erosions; >50 of surface epithelial cells shedding).	Yes	
5	–	–				Yes	

\*Non-parallel crypts, variable crypt diameters, bifurcation and branched crypts