Supplemental 1: qPCR analysis of pro-inflammatory genes in acute DSS colitis. (A)

MESO scale analysis of proinflammatory cytokines in the distal colon of WT and MPO KO mice on day 7, 2 days after DSS was removed. (B) qPCR analysis of proinflammatory cytokines in the distal colon of WT and MPO KO mice following acute DSS colitis. (C) MESO scale analysis of proinflammatory cytokines in the distal colon of WT and MPO KO mice at Day 21, 16 days after DSS was removed. n = 3-4 mice per group panel A and C. n = 8-10 mice per group b. Data is expressed as mean ± SD and the p-value determined by T-test (B, C) or 1-Way ANOVA (A). *p < 0.05, ** p < 0.01, *** p < 0.001.
Supplemental 2: qPCR analysis of pro-inflammatory genes in chronic DSS colitis. (A)
Fecal blood scores from WT and MPO KO mice during each round of DSS colitis. (B and C)
qPCR analysis of proinflammatory cytokines in the distal colon of WT and MPO KO mice
following the second and third round of DSS colitis. n= 6-14 mice per group panel A, n = 4-5
mice per group panel B, and n = 11 mice per group panel C. Data is expressed as mean ±
SD and the p-value determined by T-test (B, C) or 2-Way ANOVA (A) were appropriate. *p <
0.05, ** p < 0.01.
Supplemental 3: Analysis of PMN infiltrate in acute and chronic DSS colitis. Flow cytometry analysis of tissue PMN in water control (A) and after the 1\textsuperscript{st}, 2\textsuperscript{nd}, and 3\textsuperscript{rd} round of DSS colitis (B) in WT and MPO KO mice. \( n = 5\text{-}10 \) mice per group. (C) Analysis of granulomas, normalized to colon length, in MPO KO and WT mice treated with 1 (acute) or 3 (chronic) rounds of DSS. \( n = 10\text{-}24 \) mice. Data is expressed as mean ± SD and the \( p \)-value determined by T-test (B) or 1-Way ANOVA (A, C). * \( p < 0.05 \).
A

- **MPO KO Acute**
- **WT Acute**
- **MPO KO Chronic**
- **WT Chronic**

B

- **PMN # (Whole Colon)**
  - WT H2O
  - MPO H2O

C

- **PMN # (Whole Colon)**
  - WT Rd 1
  - WT Rd 2
  - WT Rd 3
  - MPO Rd 1
  - MPO Rd 2
  - MPO Rd 3

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**A**

- *ns*
- **ns**

**B**

- *ns*

**C**

- *ns*
Supplemental 4: qPCR analysis of pro-inflammatory genes in IPA treated mice. qPCR analysis of proinflammatory cytokines in the distal colon of WT and MPO KO mice treated with 0.1 mg/mL IPA in drinking water following chronic DSS colitis. n = 3-12 mice per group. Data is expressed as mean ± SD and the p-value determined by 1-Way ANOVA. *p < 0.05, ** p < 0.01, *** p < 0.001, **** p < 0.0001.
**Supplemental 5: Analysis of 3-Cl-Tyr in Occludin.** (A and B) EC-HPLC tracings of 1µM and 100nM standards of Tyr (~3min retention time) and 3-Cl-Tyr (~5min retention time). (C) Analysis of 3-Cl-Tyr in ZO-1 from T84 IEC exposed to PMN or activated MPO, n = 3 biological replicates. (D) Analysis of 3-Cl-Tyr in occludin, claudin-1, and JAM1 from water treated WT and MPO KO mice. Data is expressed as mean ± SD and the p-value determined by 1-Way ANOVA.
Supplemental 6: TJ rations of ZO-1 and occludin in T84 IEC. (A) Model of occludin peptide disrupting the TJ. (B) Analysis of ZO-1 TJ ratio in T84 IEC treated with 200 µg/ml scrambled, non-chlorinated, or chlorinated occludin peptide for 6hr. (C) Analysis of occludin TJ ratio in T84 IEC treated with 200 µg/ml scrambled, non-chlorinated, or chlorinated occludin peptide for 6hr. Arrows marks regions of decreased expression, non-linear staining, diffuse staining, or formation of puncta. Data includes individual measurements across 3 biological replicates. >30 total TJ measured across biological replicates, a total of 3 biological replicates (cells cultured at different time points) used. Data is expressed as mean ± SD and the p-value determined by 1-Way ANOVA. *** p < 0.001 and **** p < 0.0001.
Scrambled Peptide - Chlorinated Peptide

A

H-CLHYC-OH

Enterocyte

Occludin

H-CLHYC-OH

Enterocyte

TJ Length Ratio

ns

Control Peptide - Peptide - Chlorinated Peptide

B

ZO-1 TJ Ratio

Scrambled Peptide - Peptide - Chlorinated Peptide

C

Occludin TJ Ratio

Scrambled Peptide - Peptide - Chlorinated Peptide
Supplemental 7: Occludin and ZO-1 staining in MPO treated IEC. (A) T84 IEC grown on 0.4 µm transwell inserts were grown to confluency and then treated with control, pH 5.0, 1 µg/ml MPO, 200 µM H$_2$O$_2$, or a combination of pH 5.0/MPO/H$_2$O$_2$ for 6hr. Following treatment the inserts were fixed in 1:1 methanol/acetic acid and stained for occludin. (B) Caco-2 IEC grown on 0.4 µm transwell inserts were grown to confluency and then treated with control, pH 5.0, 1 µg/ml MPO, 200 µM H$_2$O$_2$, or a combination of pH 5.0/MPO/H$_2$O$_2$ for 6hr. Following treatment the inserts were fixed in 1:1 methanol/acetic acid and stained for ZO-1. Arrows marks regions of mislocalization or decreased expression.