

**Figure S1.** Targeting of the mouse histamine N-methyltransferase (*Hnmt*) locus. **(A)** Schematic of the targeted mouse *Hnmt* genomic locus with coding exons in blue, untranslated regions in light blue, and loxP sites denoted by black arrowheads. **(B)** Location and exact sequences of gRNA target regions within intron 2 and intron 3; dotted red line denotes DSB, PAM is highlighted and sequences corresponding to gRNA protospacer are underlined. **(C)** Sanger sequencing chromatograms of targeted regions after PCR cloning from G1 offspring gDNA, highlighted regions mark LoxP sequences. **(D)** Sanger sequencing of PCR amplicons spanning the 401 bp deletion region following Cre/LoxP recombination from a sample of *CMV<sup>Cre(+)</sup>;Hnmt<sup>fl/fl</sup>* animal. Dotted line denotes deletion breakpoint. Shaded region is the single LoxP site remaining after recombination. **(E)** Deletion of the *Hnmt* floxed region driven by *Sox10<sup>CreERT2</sup>* in intestinal tissue. Genomic DNA (gDNA) was extracted from Ileum rod samples from *Sox10<sup>CreERT2</sup>;Hnmt* mice. Note a lower molecular weight band is present in samples positive for *Sox10<sup>CreERT2</sup>*. Abbreviations: DSB - double strand DNA break, gRNA - guide RNA, PAM - protospacer adjacent motif.

**Figure S2.** Effects of enteric glial histamine N-methyltransferase (*Hnmt*) relative expression in mouse colon. **(A and B)** Representative qPCR gels utilizing *Hnmt* exon 1 primers from colon samples in WT and *CMV<sup>Cre</sup>;Hnmt* mice in males **(A)** and females **(B)**. **(C and D)** Representative qPCR gels utilizing *Hnmt* exon 3 primers from colon samples in WT and *CMV<sup>Cre</sup>;Hnmt* mice in males **(C)** and females **(D)**. **(E and F)** Representative qPCR gels utilizing *Hnmt* exon 2-4 primers from colon samples in WT and *CMV<sup>Cre</sup>;Hnmt* mice in males **(E)** and females **(F)**. **(G)** Quantification of qPCR data of relative expression

of *Hnmt* exon 2-4 normalized to *Rps6* in WT, *CMV<sup>Cre(-)</sup>;Hnmt<sup>f/Δ</sup>*, and *CMV<sup>Cre(+)</sup>;Hnmt<sup>f/f</sup>* mice. (**H** and **I**) Quantification of qPCR data of relative expression of *Hnmt* exon 3 and exon 2-4 to *Hnmt* exon 1 in WT, *CMV<sup>Cre(-)</sup>;Hnmt<sup>f/Δ</sup>*, and *CMV<sup>Cre(+)</sup>;Hnmt<sup>f/f</sup>* mice (**H** and **I**, respectively). n = 5-9 animals per group, \*\*P < 0.01, \*\*\*P < 0.001, One-way ANOVA.

**Figure S3.** Effects of glial histamine N-methyltransferase (*Hnmt*) ablation on Diamine oxidase (*Dao*) and N-acetyltransferase 2 (*Nat2*) relative expression in mouse ileum of *Sox10<sup>CreERT2</sup>;Hnmt* and WT littermates. (**A** and **B**) Quantification of qPCR data of relative expression of *Dao* and *Nat2* normalized to *Rps6* (**A** and **B**, respectively) in males and females from WT littermates and *Sox10<sup>CreERT2</sup>;Hnmt*. n = 6 animals per group, 2-way ANOVA.

Figure S1.

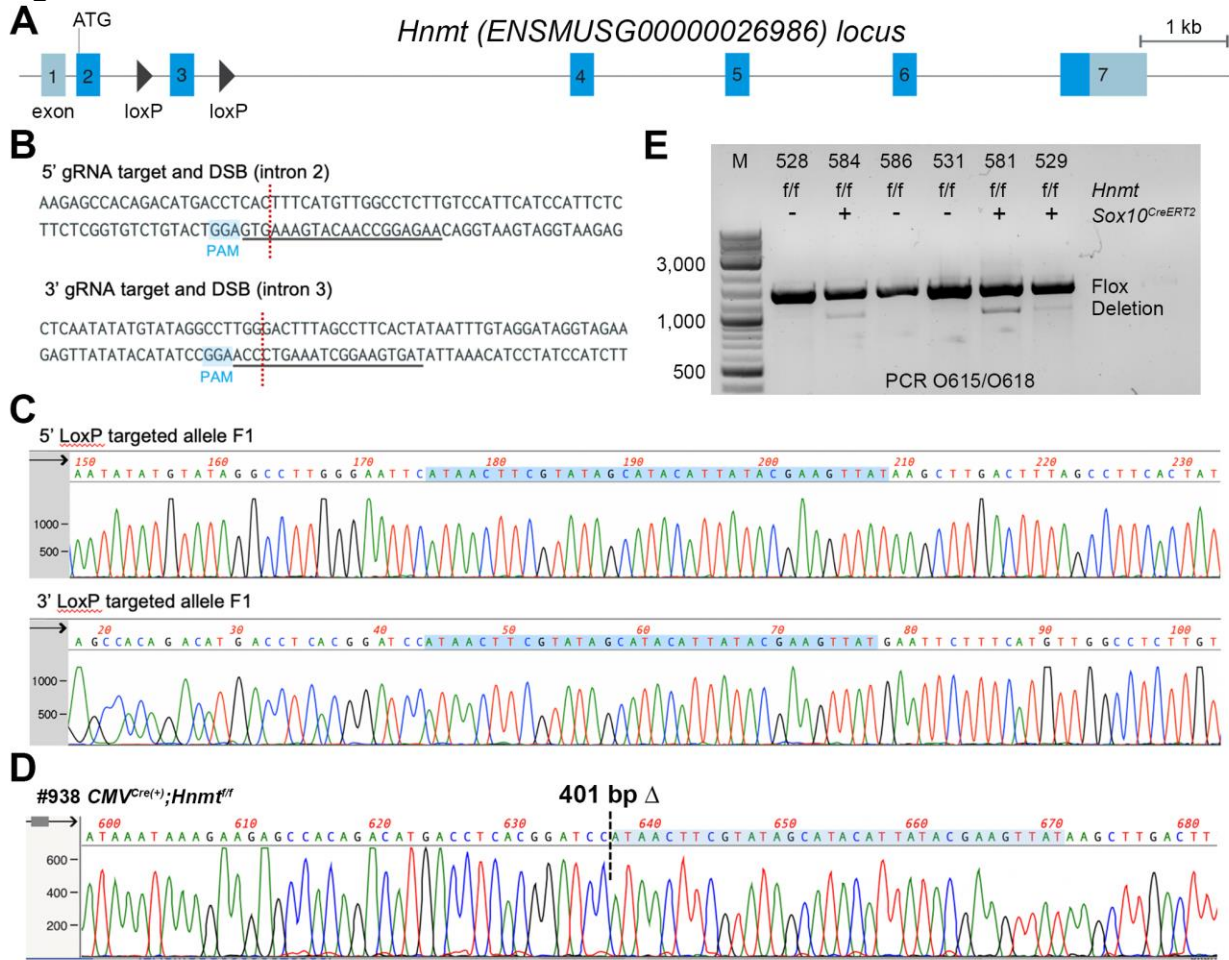
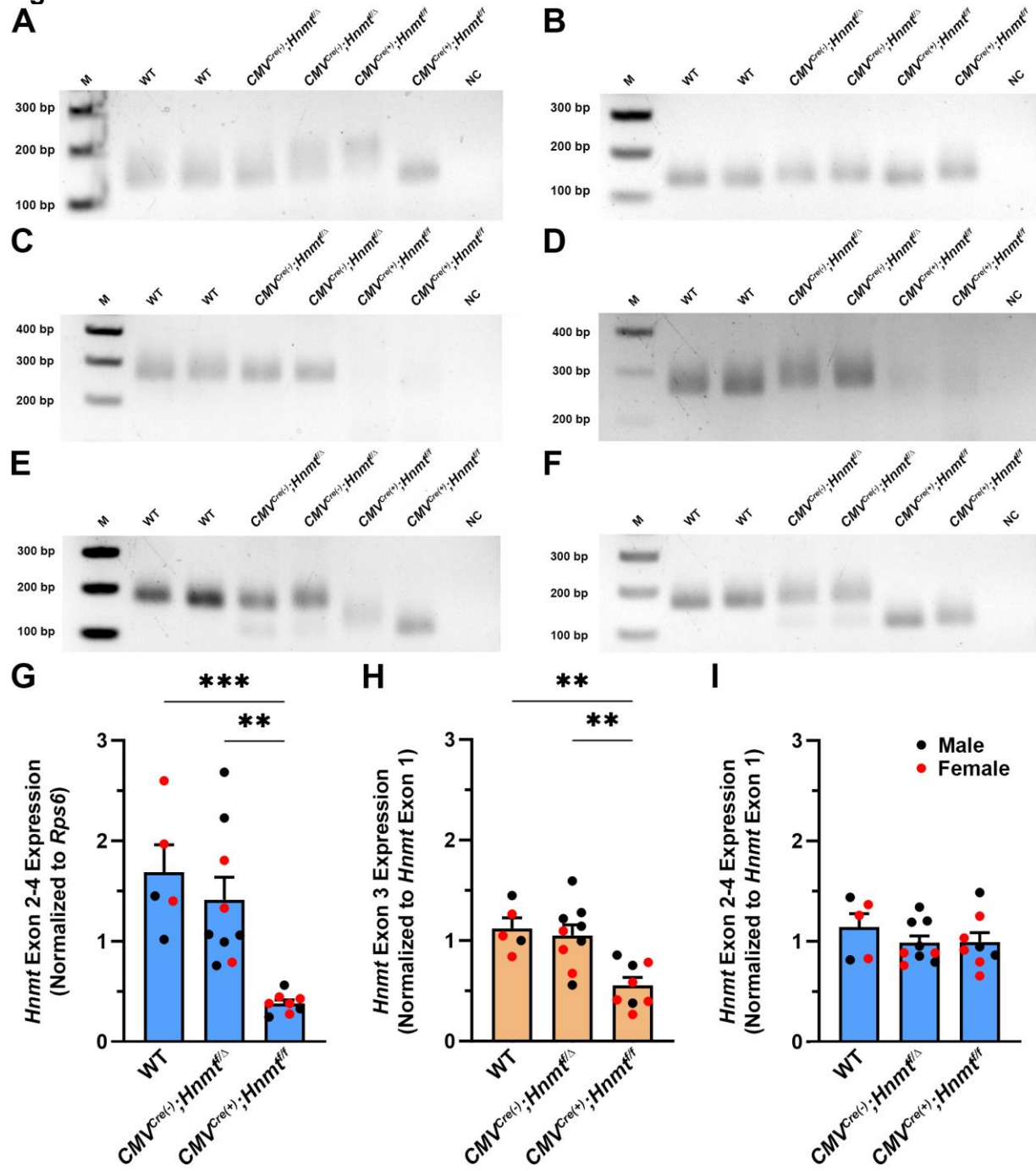


Figure S2.



**Figure S3.**

