

**Figure S1.** Mutation spectrum in the lower bowel of *H. hepaticus*-infected RagIl10gpt mice and uninfected controls at 21 WPI, (A) Male and (B) Female. Smaller numbers represent percentages of each mutation type in the total mutations of the respective groups, where numbers in red and blue stand for percentages of total transversions and total transitions in the corresponding groups, respectively. *H. hepaticus* infection elevated prevalence of the overall transversion mutations in the cecum and colon of the infected males but not of the females compared with their controls.

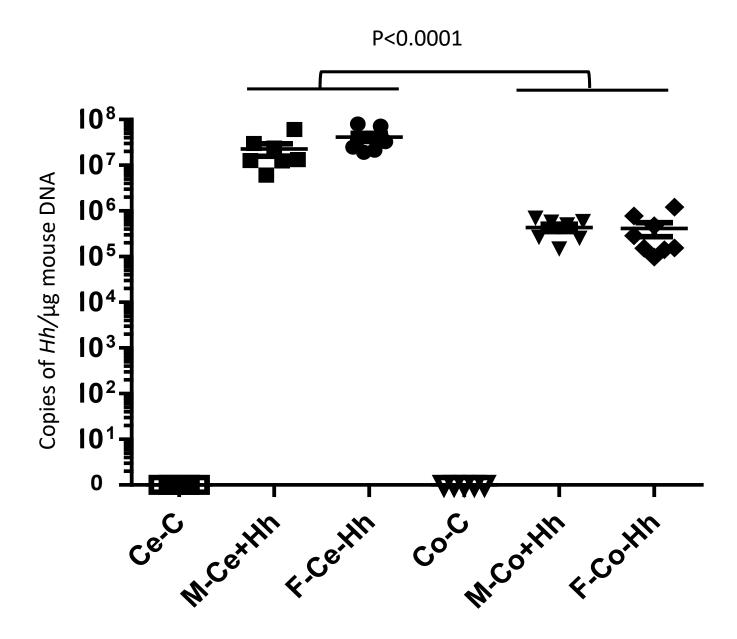


Figure S2. Mucosa-associated *H. hepaticus* levels in the lower bowel of the infected RagII10gpt mice at 21 WPI. There were significant differences in *H. hepaticus* colonization levels between the cecum and colon of the infected mice. *H. hepaticus* colonization levels in the cecum and colon were comparable between the infected males and the infected females. The numbers on the y axis represent the copies of the *H. hepaticus* genome expressed per μg murine DNA in the samples.

## RagIl10gpt mice Males Females CDT+Hh infection pks+ E. coli Inflammation Atm ↓ DSBs DNA damage Mutation Frequency

**Promotion of intestinal carcinogenesis** 

**Figure S3.** A working model outlining proposed pathways in the *H. hepaticus*-induced male-biased promotion of mutation frequencies in the lower bowel of RagIl10gpt mice. Up and down arrows in black denote elevated or reduced cellular events in the lower bowel of the infected RagIl10gpt mice compared to the sham controls, respectively. These responses are stronger (represented by bigger up arrows) in the males versus females.