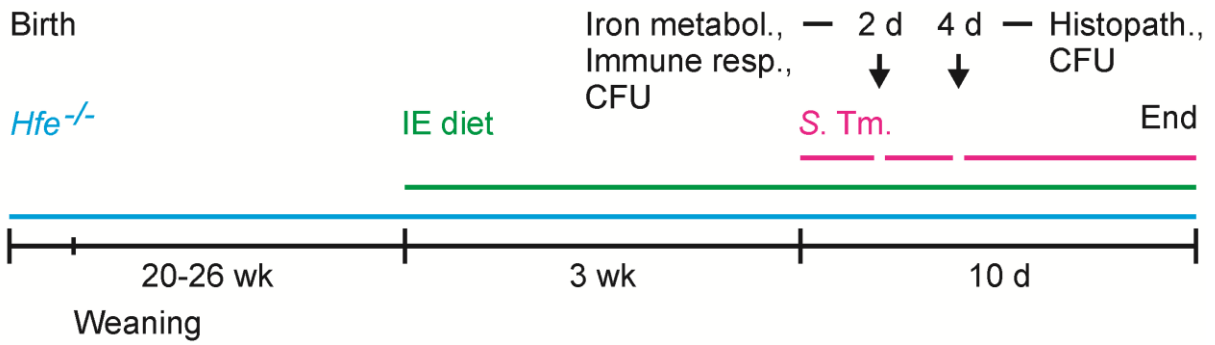


1 **Supplementary figure 1.**

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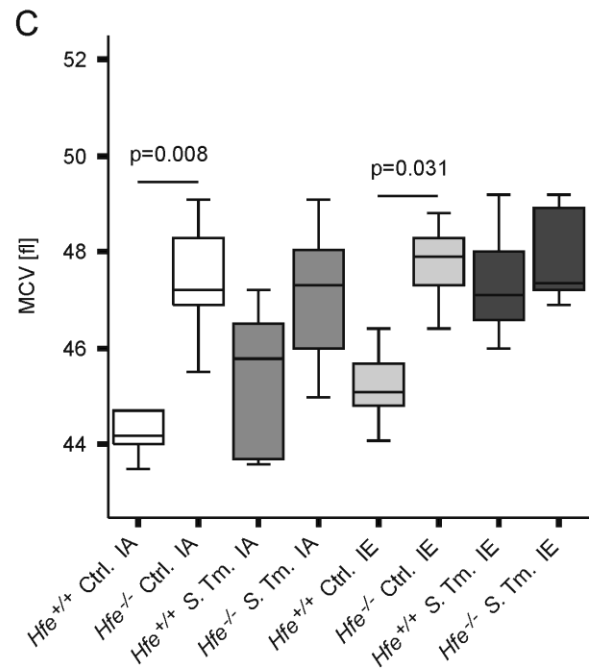
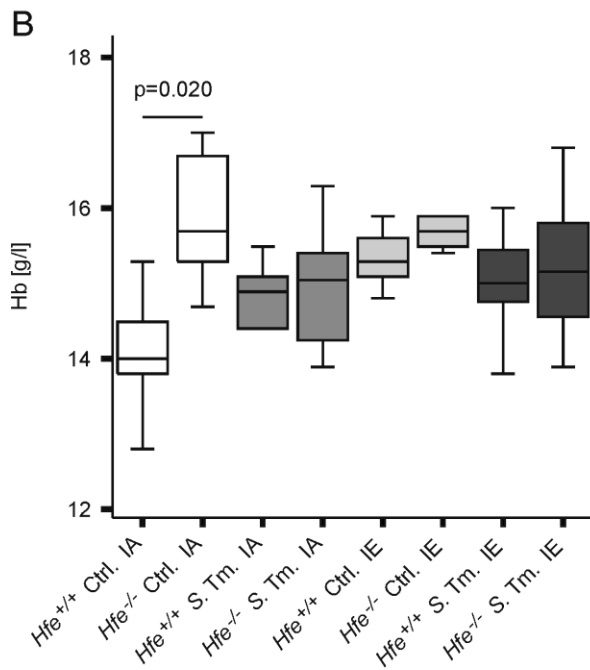
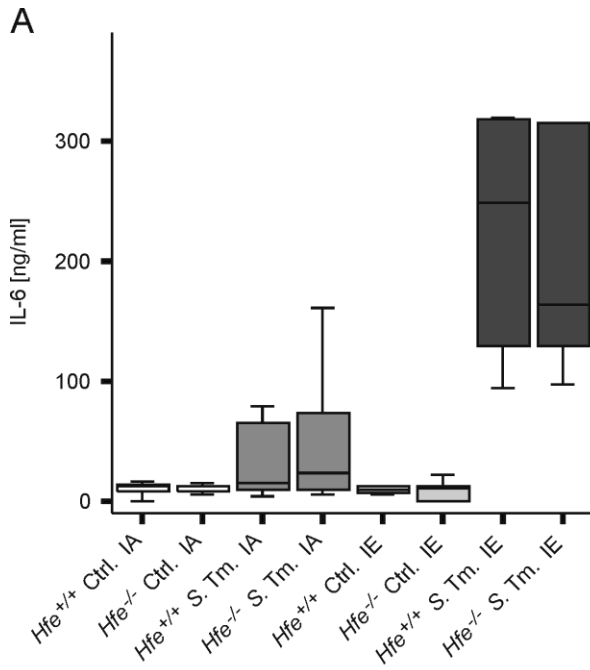
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1 **Supplementary figure 2.**

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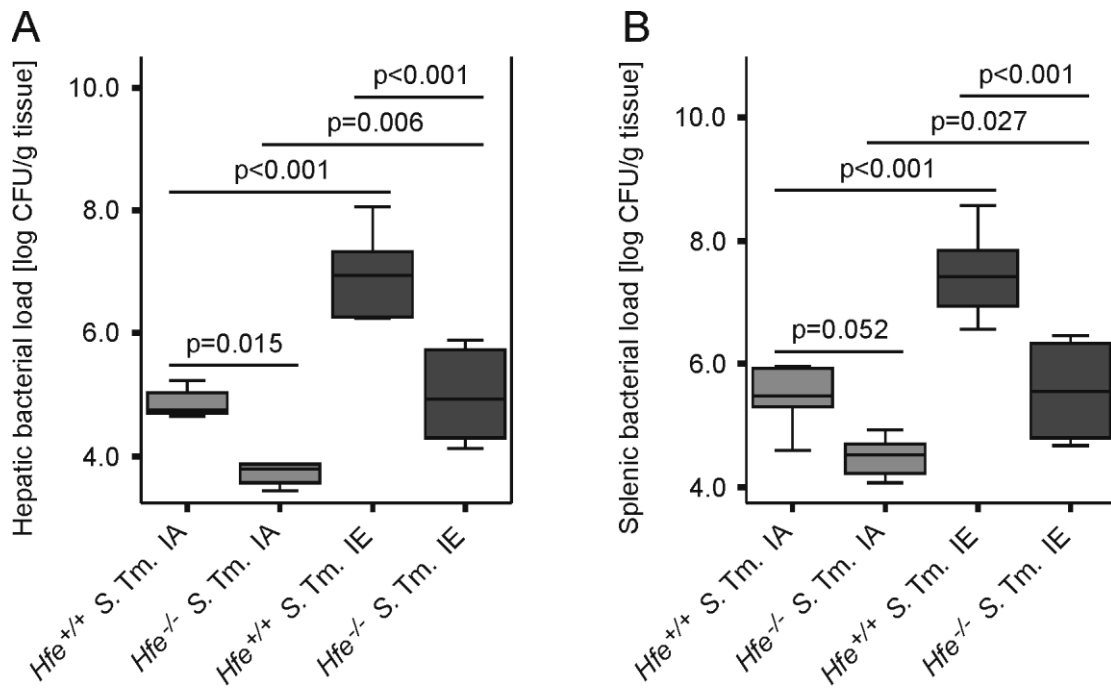
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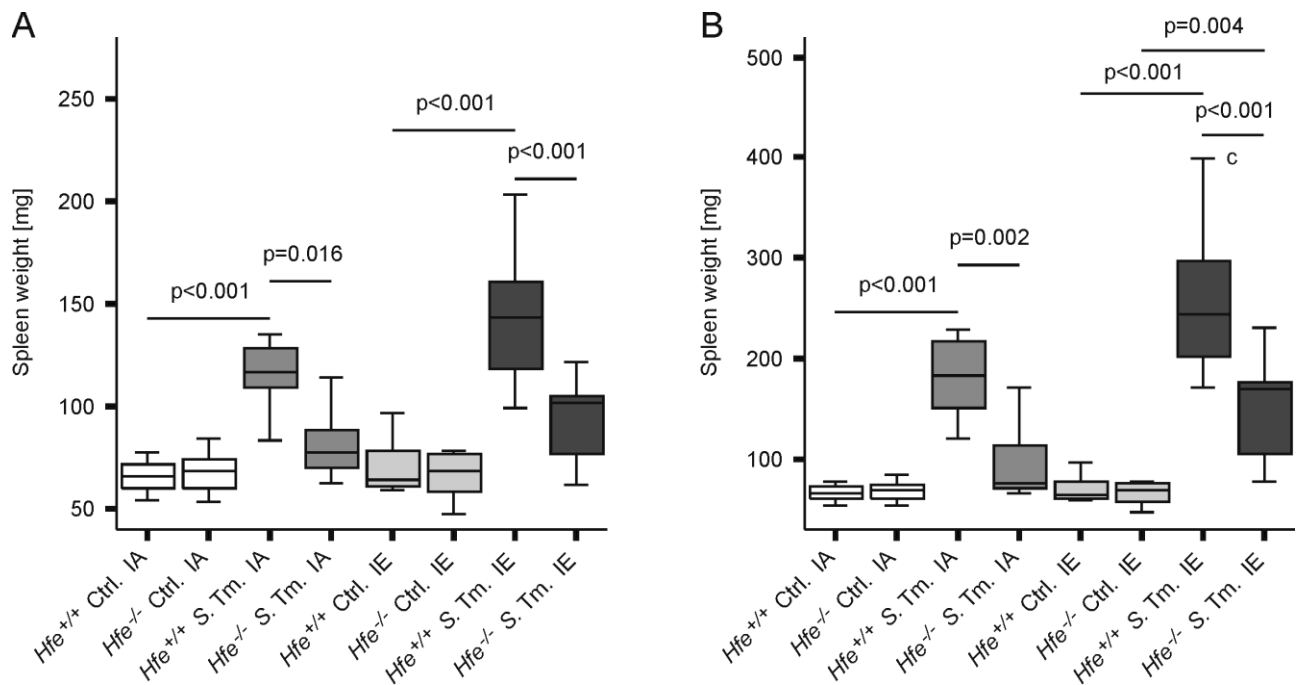
1 **Supplementary figure 3.**

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5 **Supplementary figure 4.**

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1 **Supplementary figure 1.**

2 **Experimental design.**

3 Male *Hfe*^{-/-} and congenic C57BL/6 WT animals (*Hfe*^{+/+}) were weaned at 4 wk of age
4 and then kept on a standard iron-adequate (IA) rodent diet before enrollment in the study at
5 20-26 wk of age. Subsequently, mice were either maintained on the IA diet or switched to an
6 iron-enriched diet (IE) for 3 wk prior to and during the actual infection. Mice were then
7 infected i.p. with 500 CFU of *S. Typhimurium* (*S. Tm.*) or injected with phosphate-buffered
8 saline (PBS) as diluent. Mice were monitored for up to 10 d. On d 2 (48 h) and d 4 (96 h)
9 after the inoculation, randomly selected mice were sacrificed to enumerate colony-forming
10 units (CFU) of bacteria (d 2 and d 4) and study iron metabolism and the immune response (d
11 2) as well as histopathologic findings (d 4). The expression of bacterial iron metabolic genes
12 was also evaluated on d 2 post-infection. Note that the x-axis representing the timeline has an
13 arbitrary rather than linear scale.

14

15 **Supplementary figure 2.**

16 **Serum IL-6, hemoglobin and mean corpuscular volume**

17 *Hfe*^{-/-} and congenic C57BL/6 WT animals (*Hfe*^{+/+}) were fed either a standard iron-
18 adequate diet (IA) or an iron-enriched diet (IE) and infected i.p. with 500 CFU of *S.*
19 *Typhimurium* (*S. Tm.*). Mock-infected controls (Ctrl.) received diluent. Serum IL-6 levels
20 (A), hemoglobin (Hb) concentration (B), and mean corpuscular volume (MCV), an
21 erythrocyte index (C), were measured at baseline (PBS) and 48 h after infection. Data are
22 presented and compared exactly as in figure 1. Intriguingly, hemoglobin (Hb) levels were
23 unaffected by iron and infection, although under steady-state conditions, *Hfe*^{-/-} mice tended to
24 have higher Hb levels as compared to congenic WT mice (Suppl. fig. 2B). Similarly,
25 erythrocytes of *Hfe*^{-/-} mice had higher mean corpuscular volumes (MCV) as compared to WT
26 mice (Suppl. fig. 2C).

27

28 **Supplementary figure 3.**

29 **Bacterial load in livers and spleens on d 4 of infection**

30 Bacterial loads of at least 6 animals per group were determined in livers (A) and
31 spleens (B) of randomly selected animals on d 4 post-infection. CFU data were log-
32 transformed and compared by means of ANOVA with Tukey's post hoc test. All statistically
33 significant differences are indicated as lines as in figure 3.

34

1 **Supplementary figure 4.**

2 **Spleen weight on d 2 and d 4 of infection as a measure of disease severity**

3 *Hfe*^{-/-} and congenic C57BL/6 WT animals (*Hfe*^{+/+}) were fed either a standard iron-
4 adequate diet (IA) or an iron-enriched diet (IE) and infected i.p. with 500 CFU of *S.*
5 Typhimurium (*S. Tm.*). Mock-infected controls (Ctrl.) received diluent. Spleen weights of at
6 least 6 mice per group were determined on d 2 (A) and d 4 (B) post-infection. Data are
7 presented and compared as in figure 1.