

**Supplementary figure S1. Change of gut microbiota membership.** (A) The number of observed amplicon sequence variants (ASVs). (B) Faith's phylogenetic diversity. Boxes and whiskers were denoted as per Figure 5 and outliers are shown as individual data points. Data at different time points within the same treatment group were compared using the Wilcoxon matched-pairs signed-ranks test (two-tailed) and that of either the same treatment or sex groups at the same time point were compared using the Mann-Whitney test (two-tailed). \*  $p < 0.05$  and \*\*  $p < 0.01$ .  $n=4-6/\text{group}$ .

**Supplementary figure S2. Triplot of redundancy analysis (RDA) of the microbiota composition in male (A) and female (B) mice.** 7,8-DHF and time were entered as environmental variables. Samples are indicated by open triangles and circles. Amplicon sequence variants (ASVs) with at least 50% of the variability in their abundance explained by RDA1 and RDA2 are indicated by blue arrows.

**Supplementary figure S3. Cumulative distribution curves of eigenvector centrality in each network.** Kolmogorov-Smirnov tests were performed to test the differences.

**Supplementary Table S1. Topological parameters of each network.**

**Supplementary Table S2. Neighbors of 7,8-DHF-responding ASVs in female mice in different networks**

**Supplementary Table S3. Neighbors of 7,8-DHF-responding ASVs in male mice in different networks**