Myricetin alleviates high-fat diet-induced atherosclerosis in ApoE$^{-/-}$ mice by regulating bile acid metabolism involved in gut microbiota remodeling

Yilong Liu[a], Ruoqi Wang[a], Jinren Zhou[b], Qiang Lyu[c], Xiaoyong Zhao[a], Xiaochun Yang[d,e], Kunsong Chen[a], Zhiwei Gao[b*], and Xian Li[a,e*]

[a] Zhejiang Key Laboratory of Horticultural Crop Quality Improvement, Zhejiang University, Hangzhou 310058, China

[b] Department of Vascular Surgery, the Second Affiliated Hospital of Zhejiang University School of Medicine, Hangzhou 310009, China

[c] School of Pharmacy, Zhejiang Chinese Medical University, 548, Binwen Road, Hangzhou 310053, China

[d] Center for Drug Safety Evaluation and Research, College of Pharmaceutical Sciences, Zhejiang University, Hangzhou, China

[e] Shandong (Linyi) Institute of Modern Agriculture, Zhejiang University, Linyi 276000, China

[*]Correspondence should be addressed to Xian Li; xianli@zju.edu.cn and Zhiwei Gao; 2317157@zju.edu.cn

Supporting Information

Table S1. The sequences of the primers for RT-qPCR analysis of gene expression in liver.

Gene name	5'-Forward Primer-3'	5'-Reverse Primer-3'
CYP7A1	AGCAACTAAACAACCTGCCAGTA	GTCCGGATATTCAAGGATGCA
CYP27A1	GCCTTGGAAGCCATCACCTA	AGATCTGATGAAGGCGGCAG
CYP7B1	CCCTGCGTGACGAAATTGAC	AGAATAGTGCTTTCCAGGCAGA
CYP8B1	TTGCAAATGCTGCCTCAACC	AGTGGGAAATTAACAGTCGCA

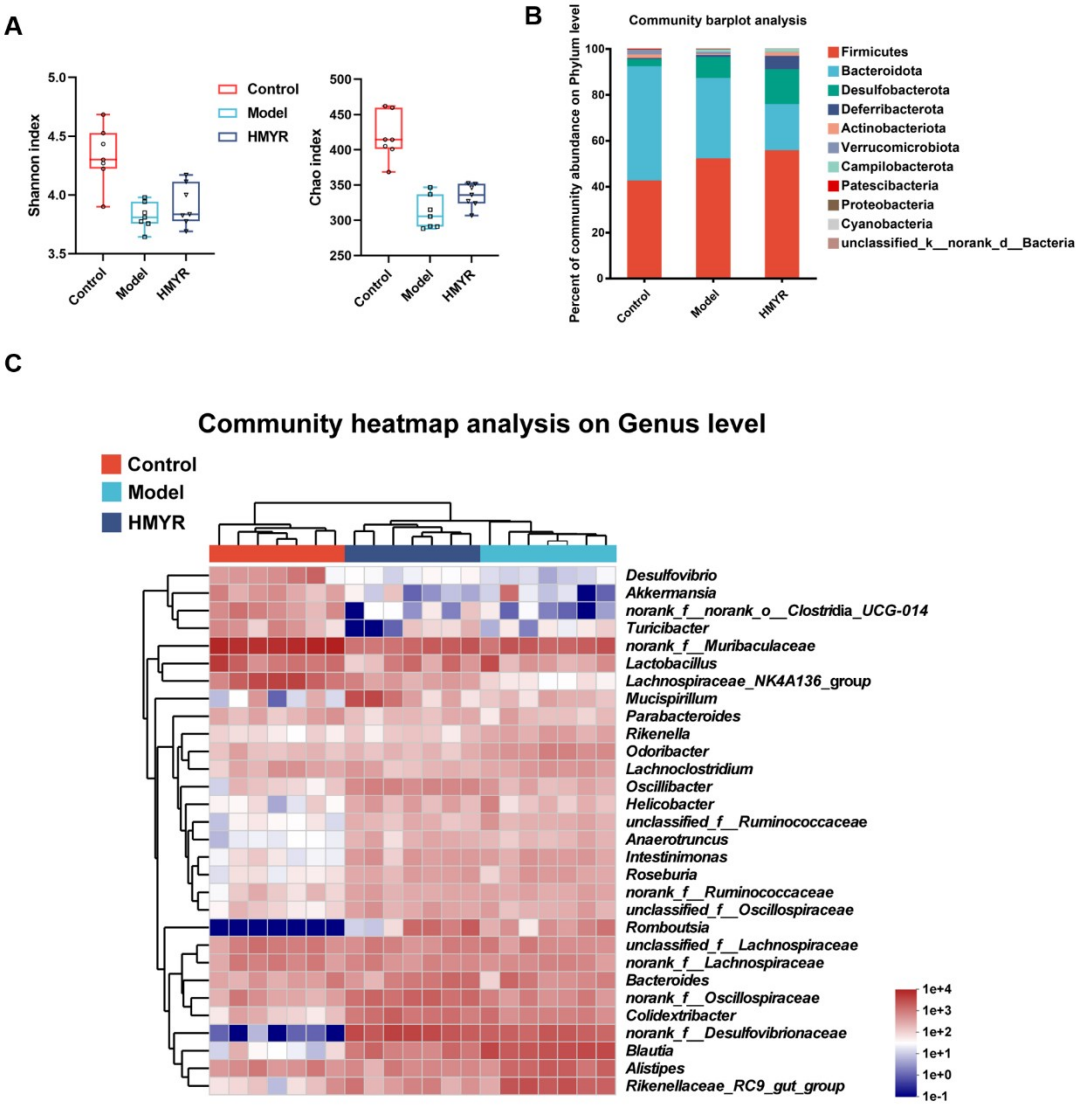

Fig. S1. Effects of MYR on the composition of gut microbiota in ApoE$^{-/-}$ mice. (A) α-diversity of the gut microbiota measured by Shannon, Chao index. (B) Relative abundance of dominant bacteria at the phylum level. (C) Heatmap of gut microbiota (top 30 genus) at the genus level. Data are expressed as the mean ± SEM.

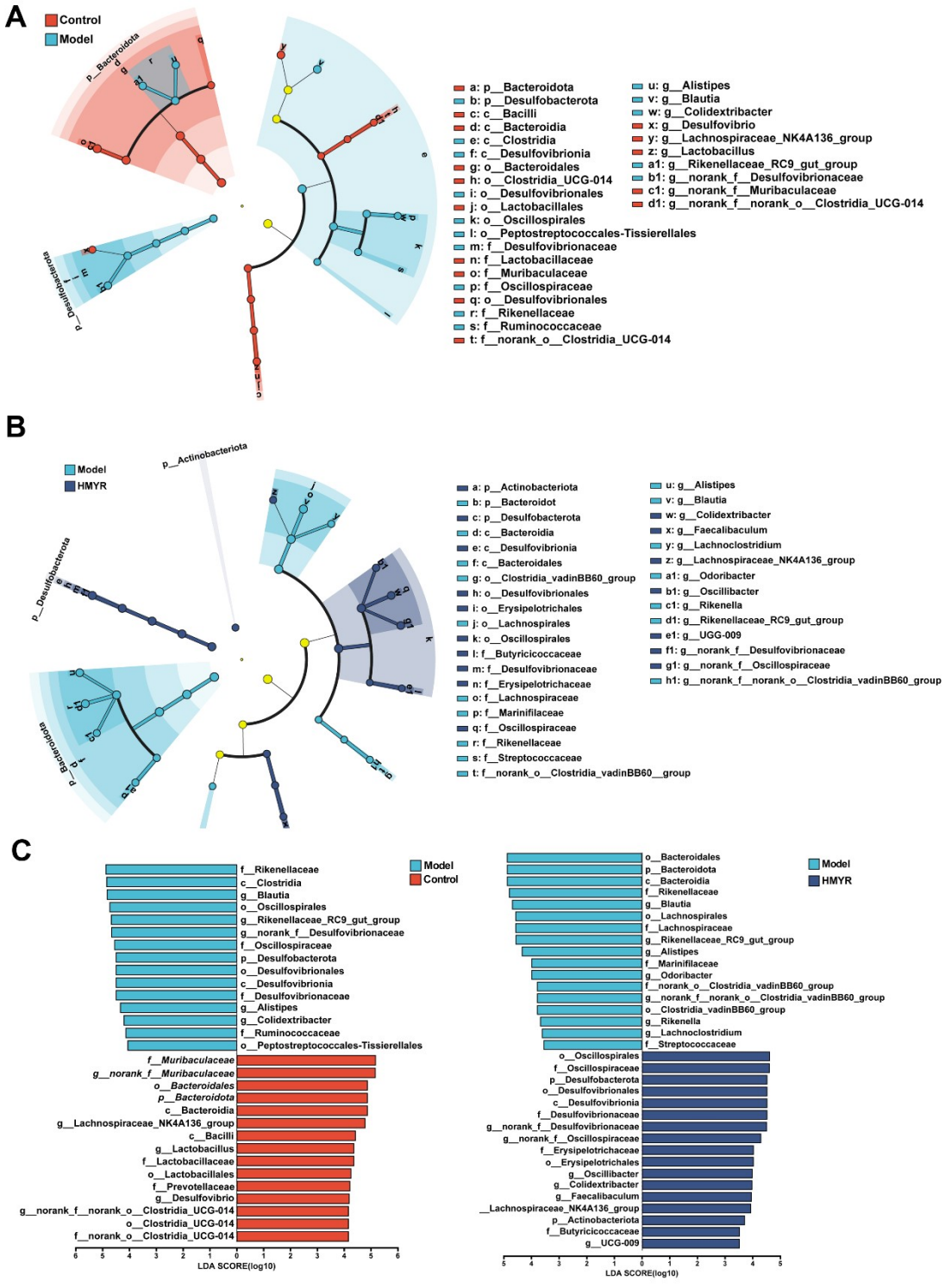

Fig. S2. Identification of the most characteristic gut microbiota in MYR-treated ApoE$^{-/-}$ mice analyzed by LEfSe at different taxonomy levels. (A) Evolutionary branch diagram of gut microbiota between control and model. (B) Evolutionary branch

diagram of gut microbiota between HMYR and model. (C) LDA value distribution histogram of comparison of gut microbiota of model respectively compared with control and HMYR. Taxa meeting LDA score threshold > 3.5 being listed. p, phylum; c, class; o, order; f, family; and g, genus.

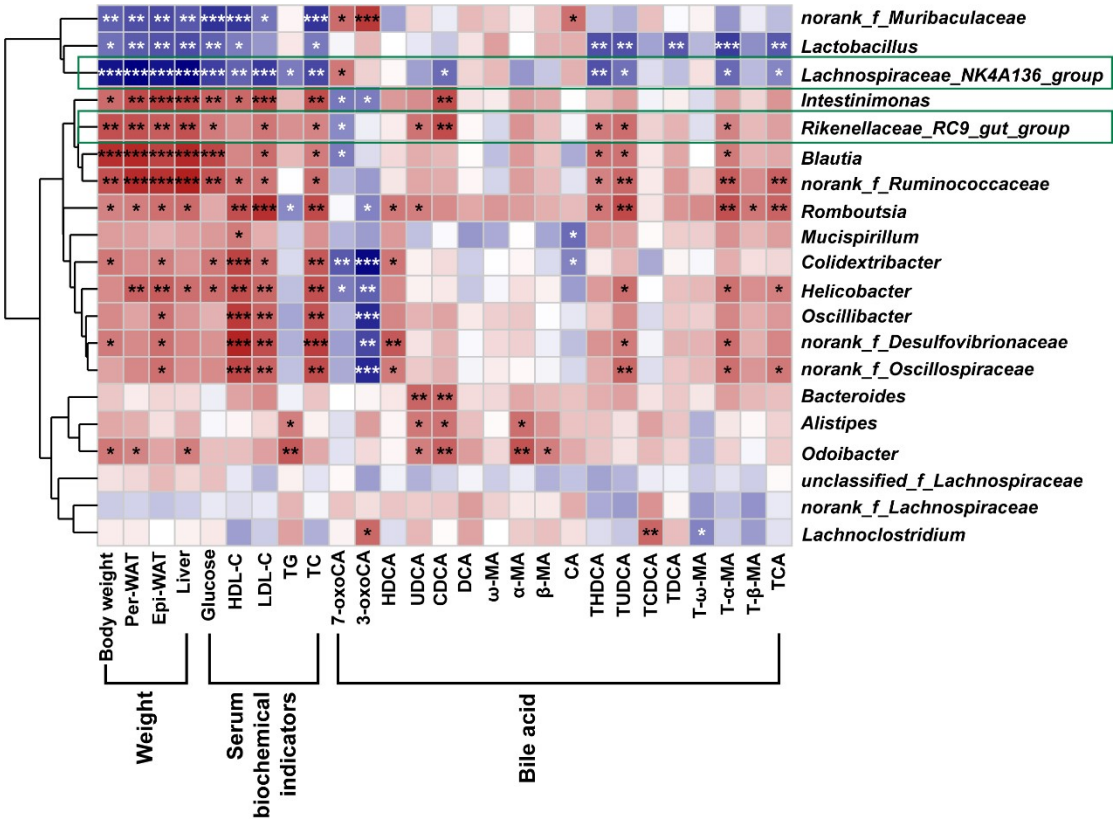

Fig. S3. Correlations between the relative abundance of gut microbiota (top 30 genera) and hepatic bile acids in MYR-treated ApoE$^{-/-}$ mice.