Hydroxyurea ameliorates atherosclerosis in ApoE$^{-/-}$ mice by potentially modulating Niemann-Pick C1-like 1 protein through the gut microbiota

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Supplementary information

Figure legends

Supplementary Figure 1: Body weight and food intake of mice during the experiment. **(A)** Weight change of mice of each group. **(B)** Changes in the food intake of mice in each group (n = 7).

Supplementary Figure 2： Plasma IL-6 and TNF-α levels after two months of drug administration. (n = 7, IL-6: interleukin-6; TNF-α: tumor necrosis factor-α).

Supplementary Figure 3： Plasma ALT, AST and creatinine levels after two months of drug administration. (n = 7, *: compared to the model group, *P < 0.05, ALT: alanine transaminase, AST: aspartate aminotransferase).

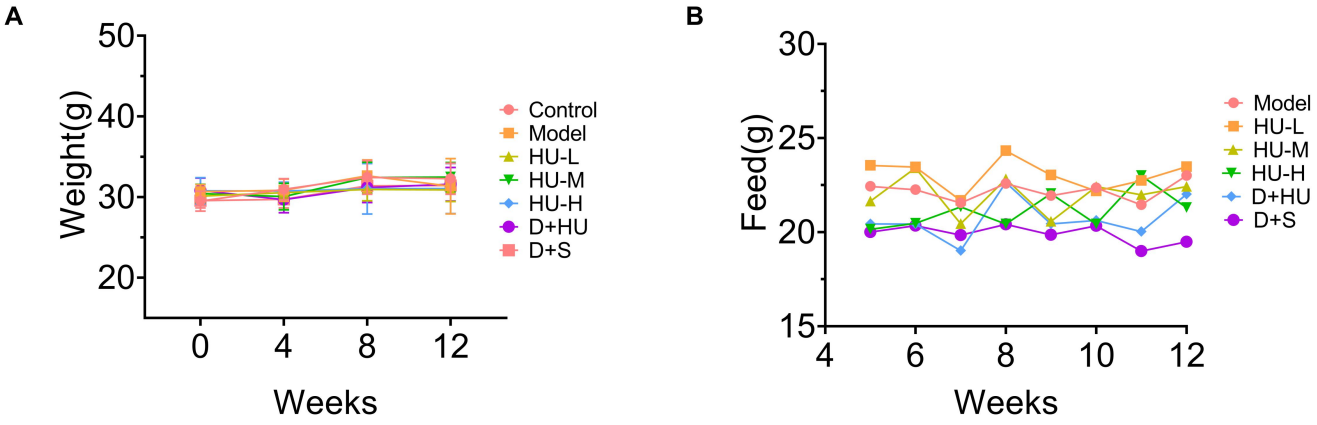
Supplementary Figure 4： OPLS-DA model showing the group separation between the model group and the medication group. **(A)** OPLS-DA model of model group vs HU-L group. **(B)** OPLS-DA model of model group vs HU-M group. **(C)** OPLS-DA model of model group vs HU-H group. **(D)** OPLS-DA model of model group vs D+HU group (n = 5, OPLS-DA: orthogonal partial least squares-discriminant analysis).

Supplementary Figure 5: LDLR and Srebp2 levels in mouse livers. **(A)** Hepatic LDLR levels among each group (n = 7, *: compared to the model group, $^{*}P < 0.05$, ns: not significant). **(B)** Hepatic LDLR levels among each group (n = 7, *: compared to the model group, $^{*}P < 0.05$, LDLR: low density lipoprotein receptor, SREBP2: Sterol-regulatory element binding proteins 2).

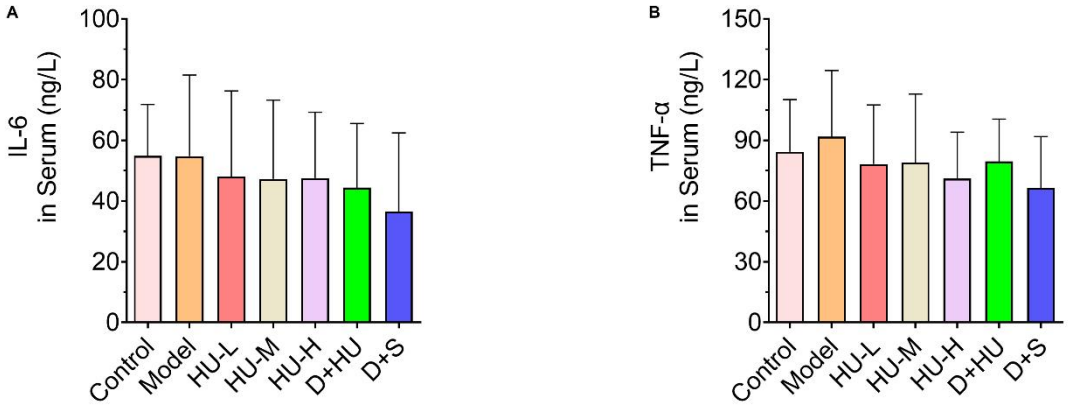
Table legend

Supplementary Table 1: Differential bacteria associated with lipid metabolism and atherosclerotic diseases

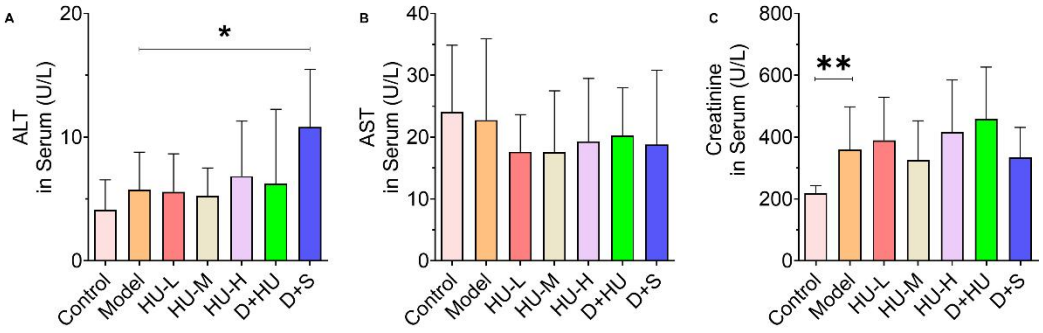
Supplementary Figure 1



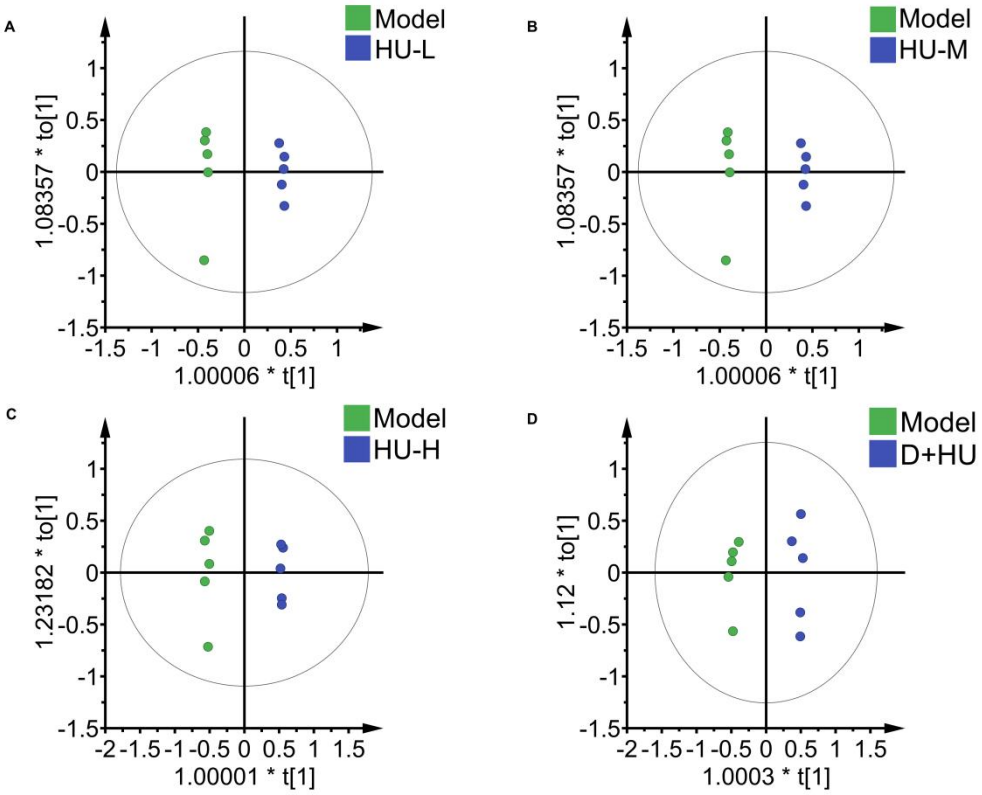
Supplementary Figure 2



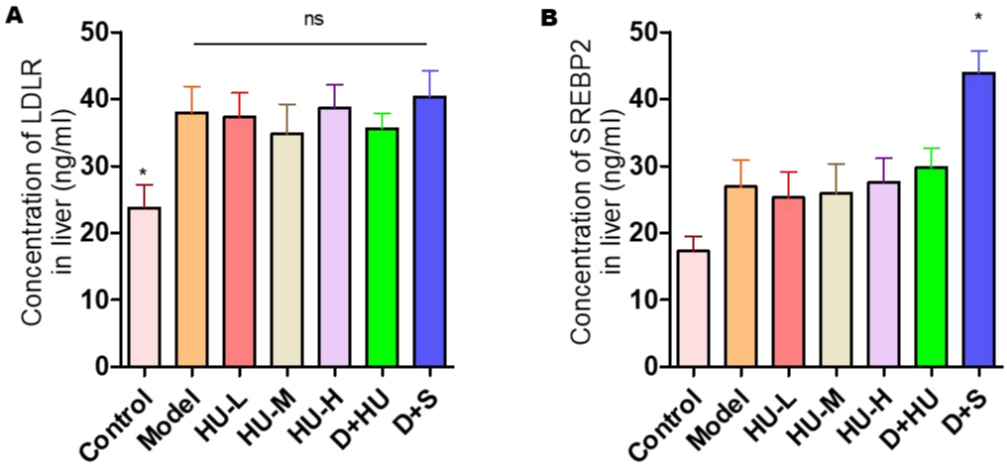
Supplementary Figure 3



Supplementary Figure 4



Supplementary Figure 5



Supplementary Table 1 Differential bacteria associated with lipid metabolism and atherosclerotic diseases

Organism	Qualititative outcome	Diseases/Traits	Method	First author	Year of publication	Type	Host
Lactobacillus	Elevated	Coronary artery disease	16S rRNA sequencing	Liu Z[1]	2019	Faeces	Human
	Elevated	Coronary artery disease	16S rRNA sequencing	Zhu Q[2]	2018	Faeces	Human
Prevotella	Elevated	Coronary artery disease	16S rDNA pyrosequencing	Toya T[3]	2020	Faeces	Human
Lachnospiraceae	Reduced	Coronary artery disease	16S rRNA sequencing	Zhu Q[2]	2018	Faeces	Human
	Reduced	Coronary artery disease	16S rRNA sequencing	Liu H[4]	2019	Faeces	Human
Bacteroides	Reduced	Atherosclerosis	16S rRNA sequencing	Jie Z[5]	2017	Faeces	Human
	Elevated	Coronary artery disease	16S rRNA sequencing	Liu Z[1]	2019	Faeces	Human
	Reduced	Coronary artery disease	16S rRNA sequencing	Liu Z[1]	2019	Faeces	Human
	Reduced	Coronary artery disease	TRFLP	Emoto T[6]	2017	Faeces	Human
	Reduced	Hyperlipidemia	16S rRNA sequencing	Gargari G[7]	2018	Faeces	Human
Blautia	Reduced	Coronary artery disease	16S rRNA sequencing	Zheng Y-Y[8]	2020	Faeces	Human
Akkermansia	Elevated	Coronary artery disease	16S rRNA sequencing	Zheng Y-Y[8]	2020	Faeces	Human
	Elevated	Ischemic stroke	16S rRNA sequencing	Tan C[9]	2020	Faeces	Human
	Reduced	Hyperlipidemia	16S rRNA sequencing	Gargari G[7]	2018	Faeces	Human
Roseburia	Reduced	Coronary artery disease	16S rRNA sequencing	Zhu Q[2]	2018	Faeces	Human
	Reduced	Atherosclerosis	Shotgun sequencing	Karlsson F[10]	2012	Faeces	Human
	Reduced	Hyperlipidemia	16S rRNA sequencing	Gargari G[7]	2018	Faeces	Human
Odoribacter	Elevated	Coronary artery disease	16S rRNA sequencing	Zheng Y-Y[8]	2020	Faeces	Human
Desulfovibrio	Elevated	Coronary artery disease	16S rRNA sequencing	Zheng Y-Y[8]	2020	Faeces	Human
Parabacteroides	Elevated	Coronary artery disease	16S rRNA sequencing	Liu Z[1]	2019	Faeces	Human
	Elevated	Coronary artery disease	MiSeq sequencing	Kehrmann J[11]	2019	Faeces	Human

	Reduced	Coronary artery disease	16S rRNA sequencing	Zhang Y[12]	2019	Faeces	Human
Lactococcus	Elevated	Coronary artery disease	16S rRNA sequencing	Zhu Q[2]	2018	Faeces	Human
Ruminococcus	Elevated	Coronary artery disease	16S rDNA pyrosequencing	Toya T[3]	2020	Faeces	Human
	Elevated	Atherosclerosis	16S rRNA sequencing	Jie Z[5]	2017	Faeces	Human
Streptococcus	Reduced	Coronary artery disease	16S rRNA sequencing	Liu Z[1]	2019	Faeces	Human
	Elevated	Coronary artery disease	16S rRNA sequencing	Liu H[4]	2020	Faeces	Human
	Elevated	Atherosclerosis	16S rRNA sequencing	Jie Z[5]	2017	Faeces	Human
Enterococcus	Elevated	Coronary artery disease	16S rRNA sequencing	Zhu Q[2]	2018	Faeces	Human
	Elevated	Coronary artery disease	16S rRNA sequencing	Liu Z[1]	2019	Faeces	Human

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