SUPPLEMENTARY INFORMATION

Histamine deficiency exacerbates myocardial injury in acute myocardial infarction through impaired macrophage infiltration and increased cardiomyocyte apoptosis

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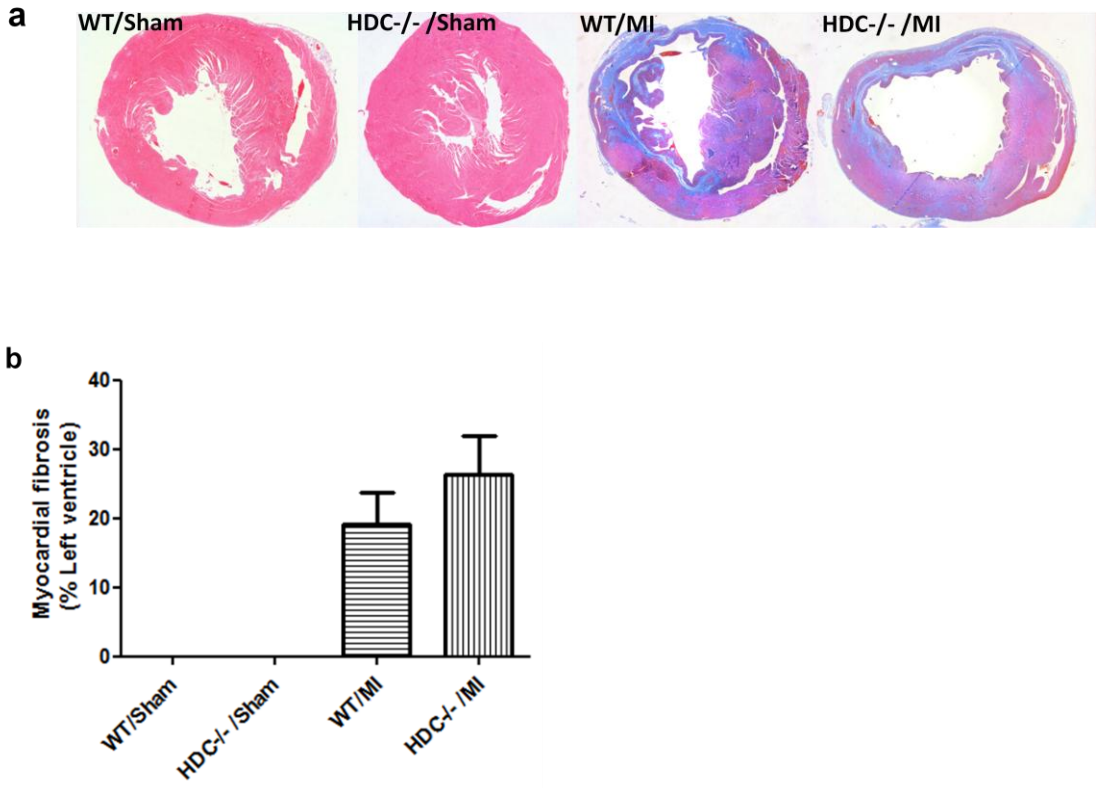
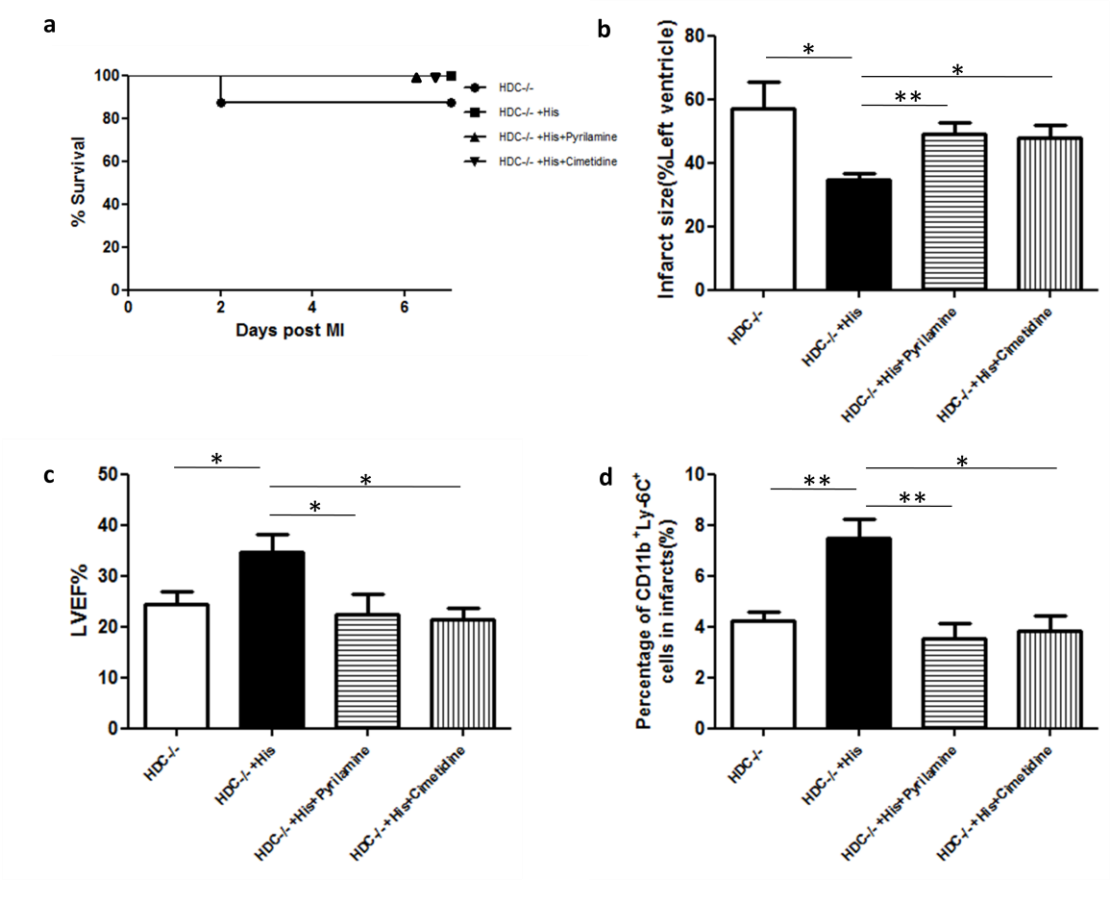
Supplementary Figures S1-3



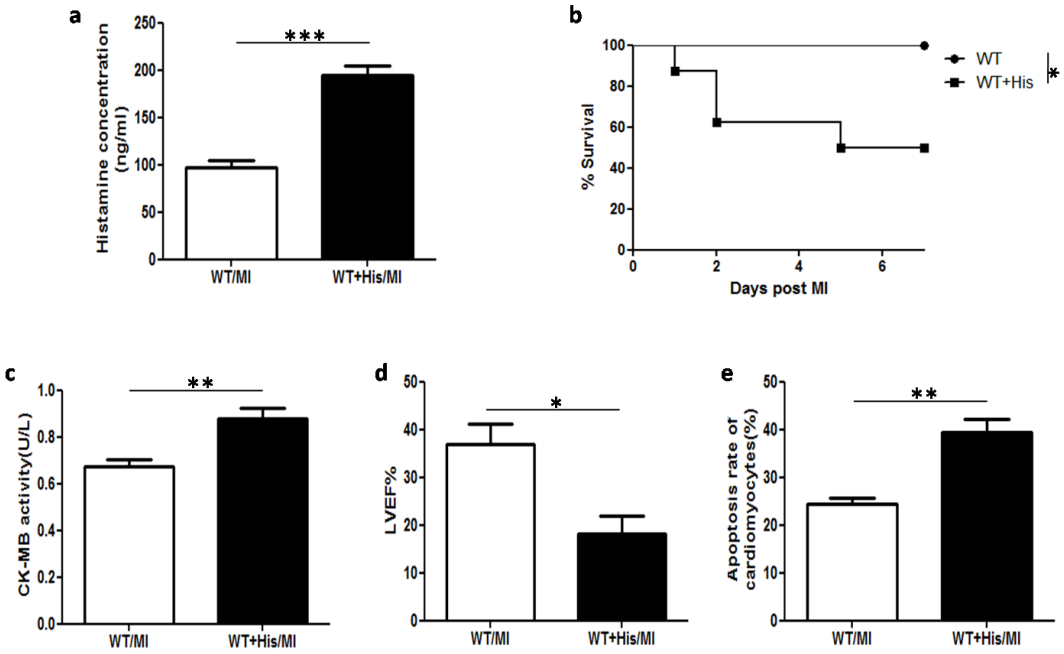
Supplementary Figure S1: The effect of histamine deficiency on myocardial fibrosis following AMI

a, Representative images of Masson staining. **b**, The extent of fibrosis slightly increased in the infarcted heart of $HDC^{-/-}$ mice 7 days after MI, though it did not reach a significant level (p=0.37, n=4).



Supplementary Figure S2: The effects of histamine receptors antagonists on HDC$^{-/-}$ mice plus exogenous histamine

a, Histamine receptors antagonists did not compromise the survival of HDC$^{-/-}$ mice plus exogenous histamine. **b**, The infarct size was increased by the administering of pyrilamine and cimetidine (**p<0.01 vs HDC$^{-/-}$ +His, *p<0.05 vs HDC$^{-/-}$ +His; n=4). **c**, LVEF% (7d post MI) was decreased by the administering of pyrilamine and cimetidine (*p<0.05 vs HDC$^{-/-}$ +His; n=6-8). **d**, The administering of pyrilamine and cimetidine both suppressed the infiltration of macrophages in the infarcts 1d post MI (**p<0.01 vs HDC$^{-/-}$ +His, *p<0.05 vs HDC$^{-/-}$ +His; n=4).



Supplementary Figure S3: Excessive exogenous histamine could be detrimental to the mice subjected to MI

a, Exogenous histamine administration (4mg/kg, intraperitoneal injection) increased the levels of histamine in WT mice significantly (***p<0.001 vs WT; n=5). **b**, Exogenous histamine compromised the survival of WT mice after AMI (*p<0.05 vs WT; n=8). **c**, The level of CK-MB activity was increased by the administering of exogenous histamine (**p<0.01 vs WT; n=5 and 7). **d**, LVEF% (7d post MI) was decreased by the administering of exogenous histamine (*p<0.05 vs WT; n=4 and 6). **e**, The administering of exogenous histamine increased the apoptosis of cardiomyocytes (**p<0.01 vs WT; n=4).