Supplementary Figure Captions

Fig. S1. Overall condition of experimental mice and single cell sequencing of heart tissue. (A) Status diagram of mice. (B) Body weight of mice (n=6). (C) Heart to body weigh ratio (n=6). (D) The gross image of mice heart (n=6). UMAP plots illustrate the distribution of 15 distinct immune cell clusters in the hearts of (E) control mice and at (F) 3 days and (G) 7 days after CLP surgery (n = 3). (H) Quantification of cell numbers within each cluster shown in E-G. (I) Quantitative analysis of cardiac M2-polarized macrophages across all groups, assessed by (J) flow cytometry (n=3). For (B-C), the data are normalized to the respective controls. The data are presented as means ± SD. One-way ANOVA followed by Dunnett's post hoc test was used to determine statistical significance ($P < 0.05$). ***P < 0.001, **P < 0.01, *P < 0.05. Abbreviations: CLP-3d, cecal ligation and puncture three days later; CLP-7d, cecal ligation and puncture seven days later; SS, steady state. Source data are available online for this figure.

Fig. S2. Molecular docking and experimental validation of FX effects on BET family proteins. High affinity docking models and schematic interactions of FX with (A) BRD3 and (B) BRD4. The protein levels of (C) BRD3 and (D) BRD4 in hearts of LPS-treated mice with or without FX administration. The protein levels of (E) BRD2, (F) BRD3 and (G) BRD4 in LPS-induced M1-polarized macrophages treated with FX. For (C–G), the data are normalized to respective controls and presented as means ± SD (n = 3). One-way ANOVA followed by Dunnett's post hoc test was used to determine statistical significance ($P < 0.05$). ****P < 0.0001, ***P < 0.001, **P < 0.01, *P < 0.05. Abbreviations: BRD3, bromodomain containing 3; BRD4, bromodomain containing 4. Other abbreviations are the same as in Figs. 1, 3, 6 & 7. Source data are available online for this figure.

Fig. S3 Validation of BRD2 overexpression and knockdown efficiency in macrophages. (A) The transfection efficiency of plasmid in macrophages. (B) The protein level of BRD2 following siRNA transfection at different concentrations (3, 4, and 5 μL) in LPS-treated macrophages. The data are presented as means ± SD. One-way ANOVA followed by Dunnett's post hoc test was used to determine statistical significance ($P < 0.05$). ****P < 0.0001. The abbreviations are the same as in Figs. 1, 5 & 7. Source data are available online for this figure.