PNAS

Supporting Information for
Targeting STING oligomerization with small-molecule inhibitors

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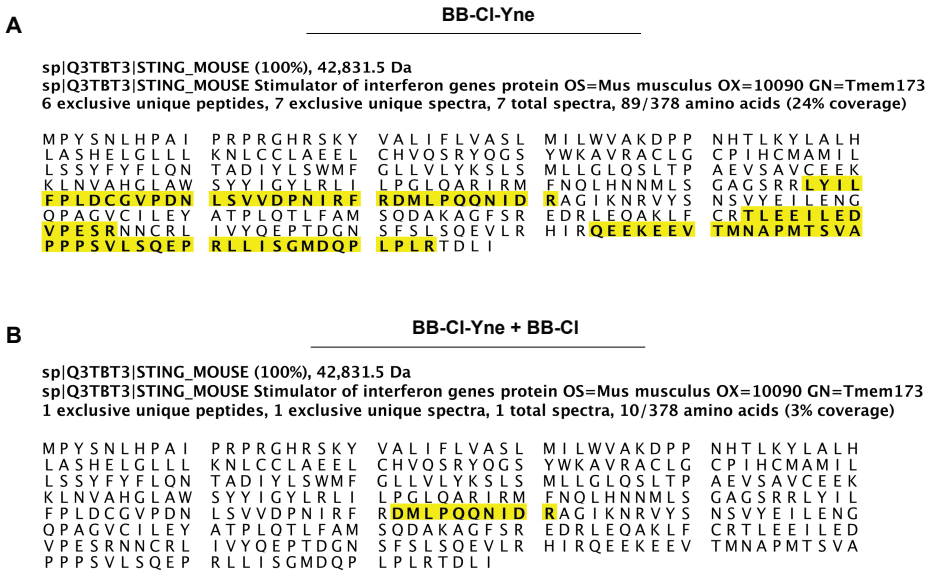
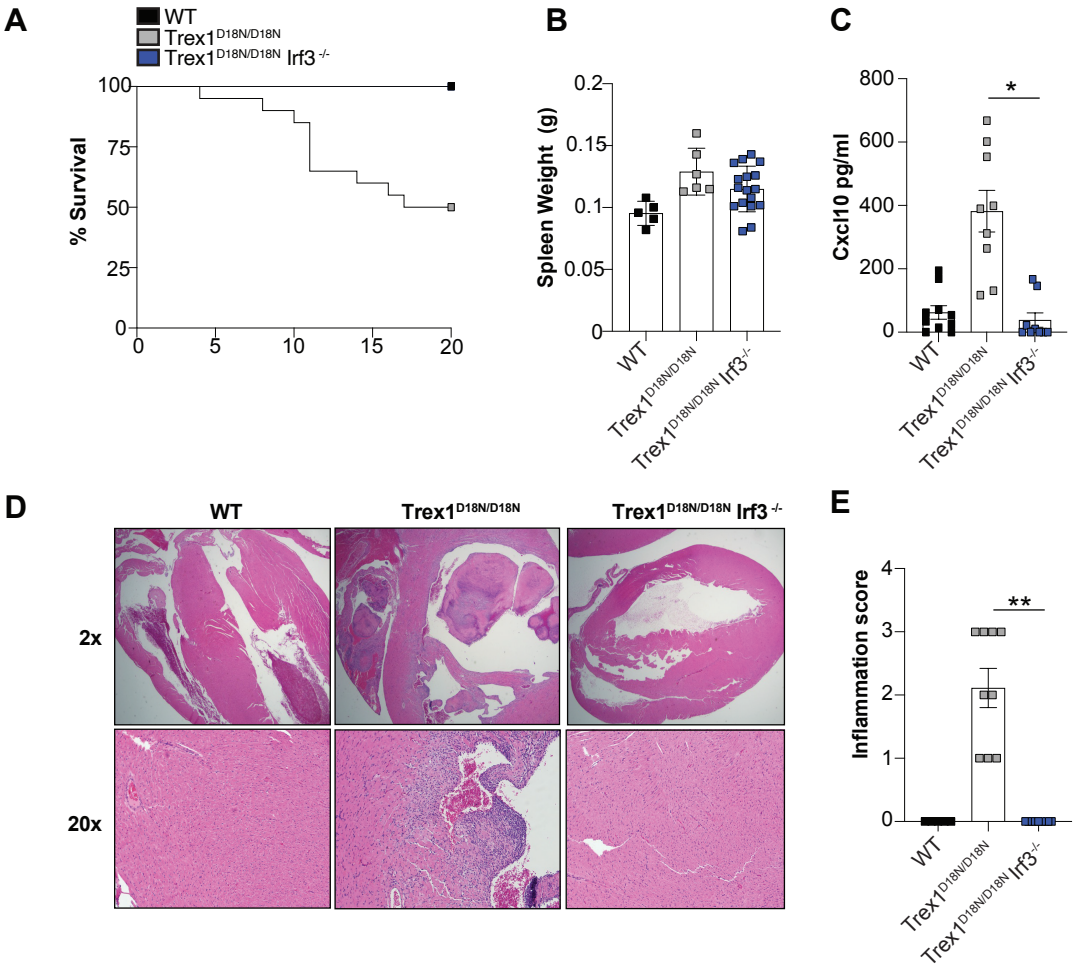
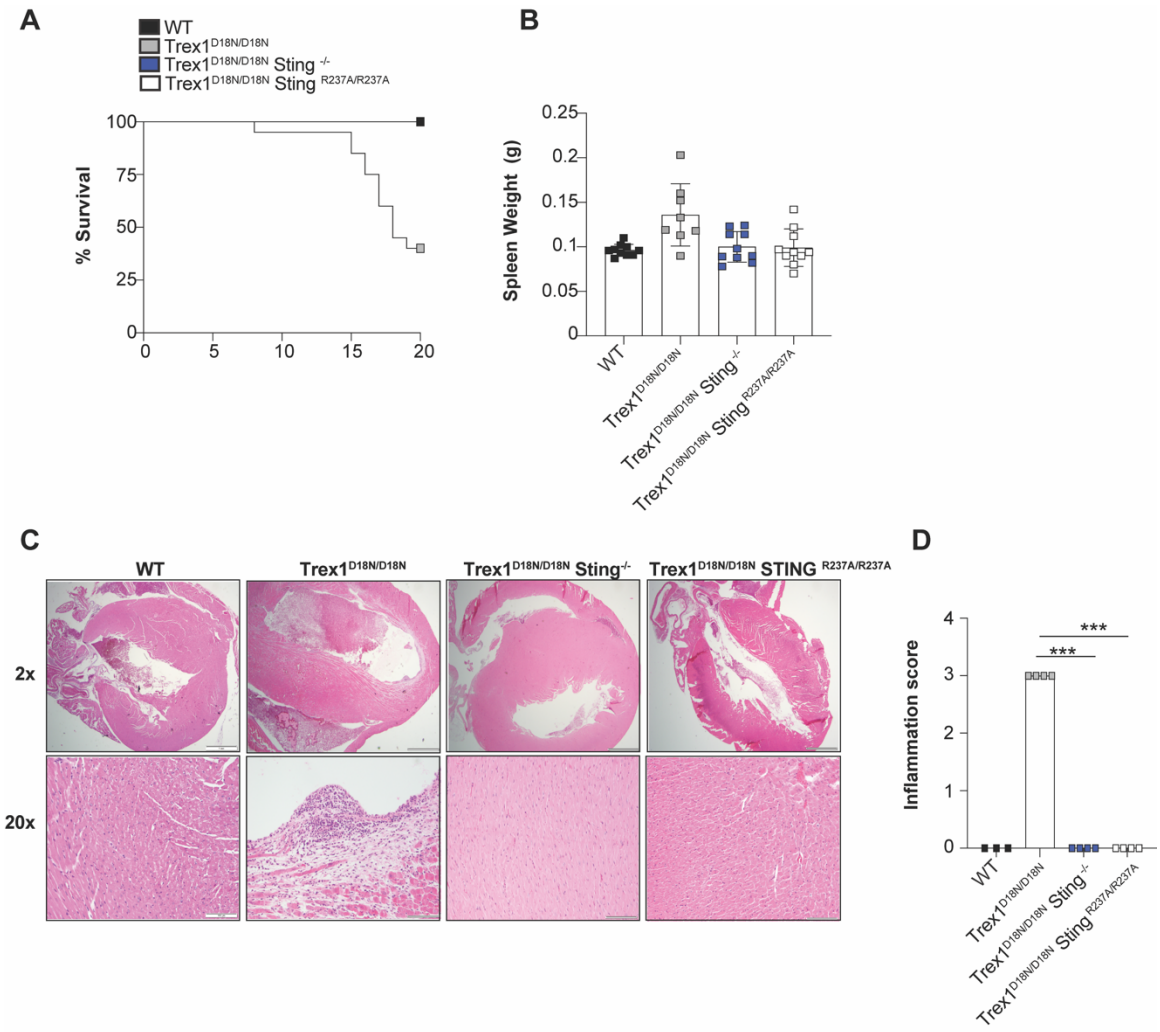


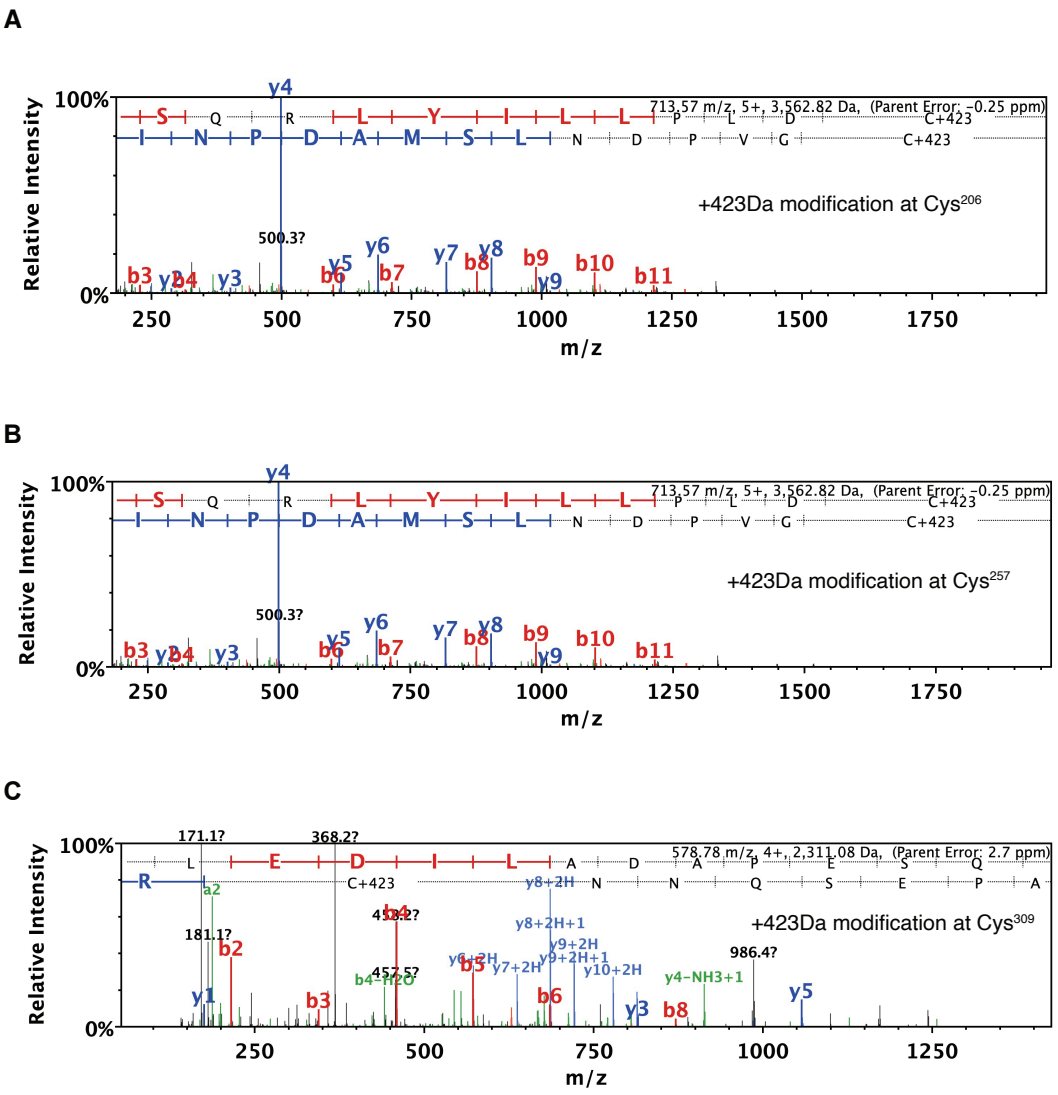
Supplementary Figure 1. BB-Cl-amidine binds to STING. (**A–B**) Sequence coverage of STING from analysis of peptides identified in streptavidin bead pull-downs from clicked lysates of BMDMs treated with BB-Cl-Yne (A) or BMDMs co-treated with BB-Cl-amidine and BB-Cl-Yne (B) (related to Figure 4). Representative of 3 independent replicates.



Supplementary Figure 2. IRF3 deficiency protects against experimental AGS in Trex1D18N/D18N mice. (**A**) Survival analysis of WT (n=20), Trex1$^{D18N/D18N}$ (n=20), *Trex1*$^{D18N/D18N}$/*Irf3*$^{-/-}$ mice (n=20). (**B**) Spleen weights of WT (n=5), *Trex1*$^{D18N/D18N}$ (n=6), *Trex1*$^{D18N/D18N}$/*Irf3*$^{-/-}$ mice (n=17) (**C**) ELISA analysis of serum Cxcl10 in WT (n=10), *Trex1*$^{D18N/D18N}$ (n=9), *Trex1*$^{D18N/D18N}$/*Irf3*$^{-/-}$ mice (n=9). (**D–E**) Representative H&E staining of tissue sections from hearts (D) and pathology evaluation of heart sections (E) from WT (n=5) and *Trex1*$^{D18N/D18N}$ *(n=9)* and Trex$^{D18N/D18N}$/*Irf3*$^{-/-}$ mice (n=9). *, *P*<0.05, **, *P*<0.01 by two-way ANOVA. Error bars show means ± SEM.



Supplementary Figure 3. STING deficiency and cGAMP binding blockade protect against experimental AGS in Trex1$^{D18N/D18N}$ mice. (**A**) Survival analysis of WT (n=10), Trex$^{D18N/D18N}$ (n=20) and Trex1$^{D18N/D18N}$/STING$^{-/-}$ (n=10) and Trex1$^{D18N/D18N}$/STING$^{R237A/R237A}$ (n=10) mice. (**B**) Spleen weights of WT (n=10), Trex1$^{D18N/D18N}$ (n=8), Trex1$^{D18N/D18N}$/STING$^{-/-}$ (n=10) and Trex1$^{D18N/D18N}$/STING$^{R237A/R237A}$ (n=10) mice. (**C–D**) Representative H&E staining (C) and pathology scoring of tissue sections from hearts (D) of WT (n=3), Trex1$^{D18N/D18N}$ (n=4) and Trex1$^{D18N/D18N}$/STING$^{-/-}$ (*n=4*) and Trex1$^{D18N/D18N}$/STING $^{R237A/R237A}$ (n=4) mice., ***, *P*<0.001. two-way ANOVA. Error bars show means ± SEM.



Supplementary Figure 4. BB-Cl-amidine modifies Cys^{206}, Cys^{257} and Cys^{309} in STING. (**A–C**) Representative mass spectrometry spectra of STING modified by BB-Cl-amidine AT Cys^{206} (A), Cys^{257} (B) and Cys^{309} (C) identified in tryptic digests from recombinant STING (10 μg) incubated with BB-Cl-amidine (10 μM) for 1 h at 37 °C.