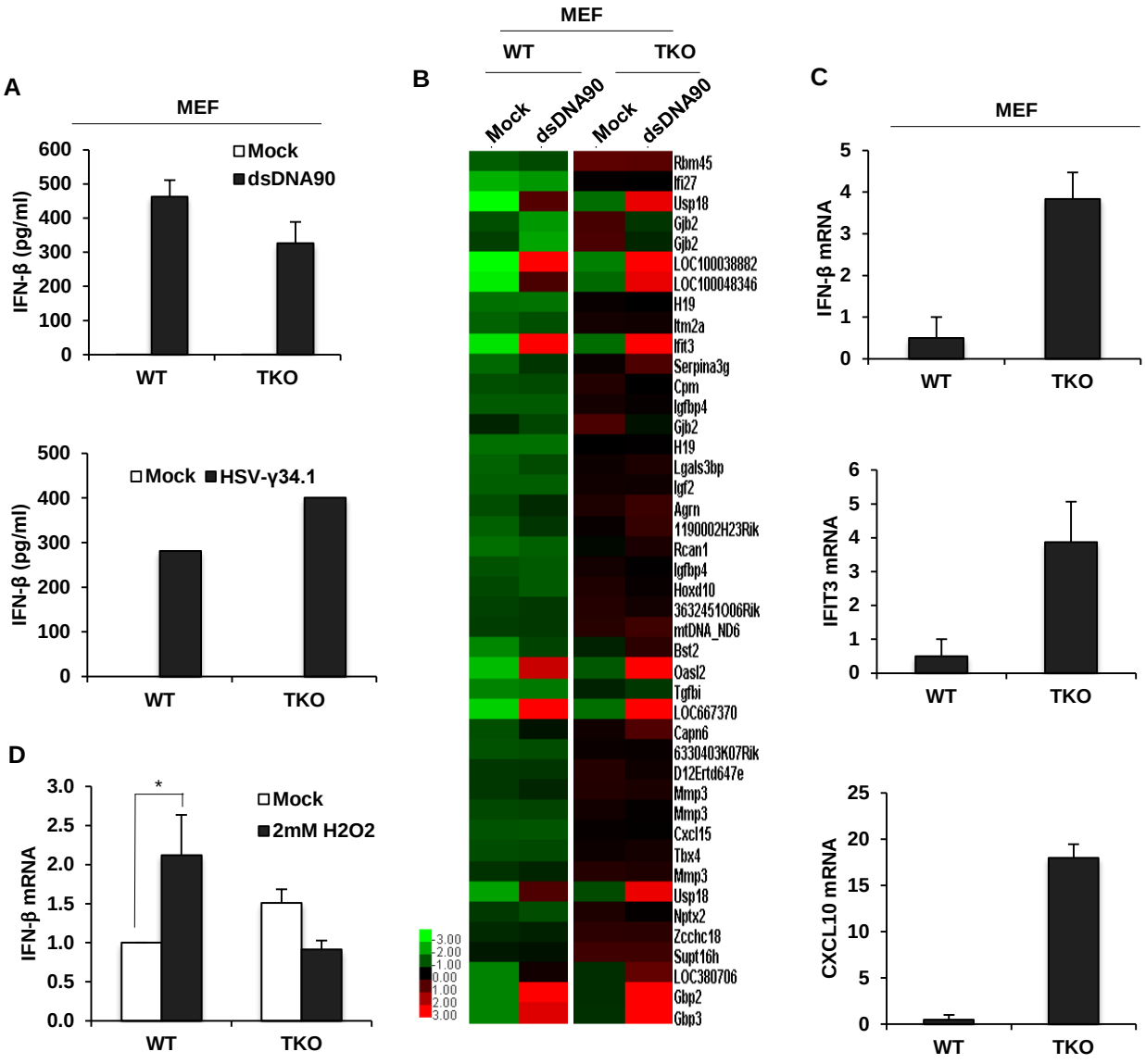
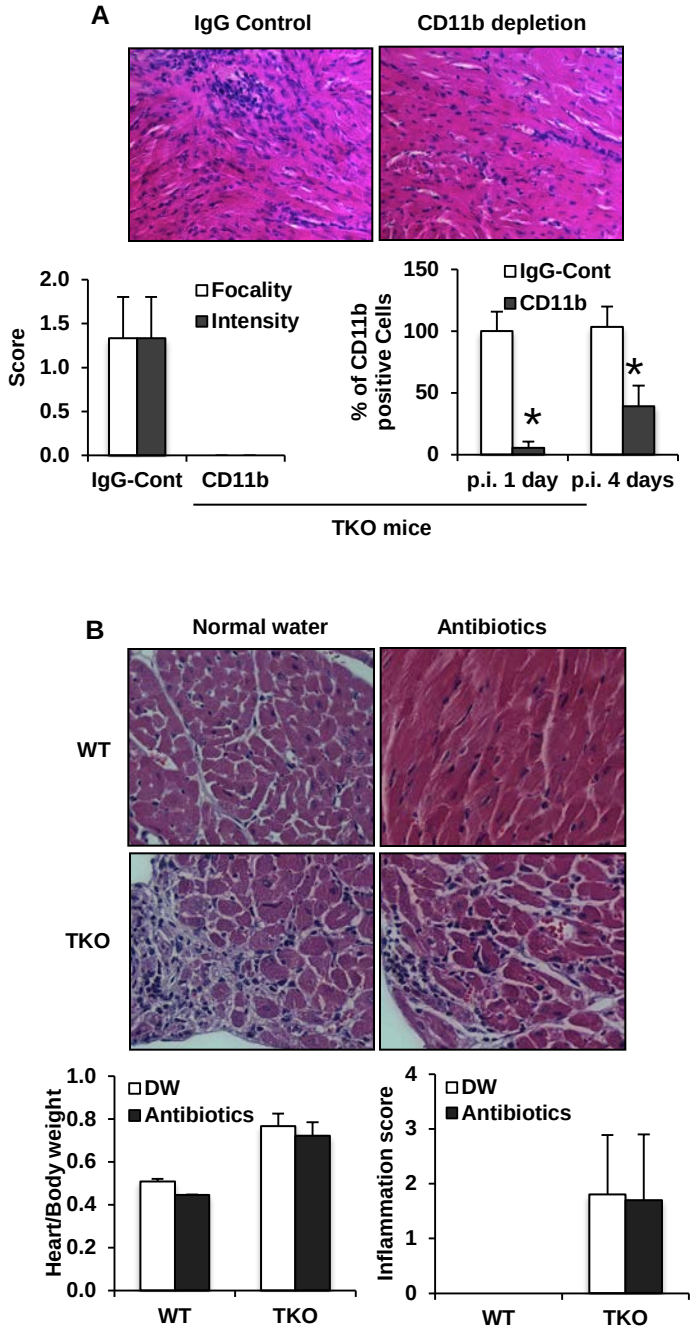
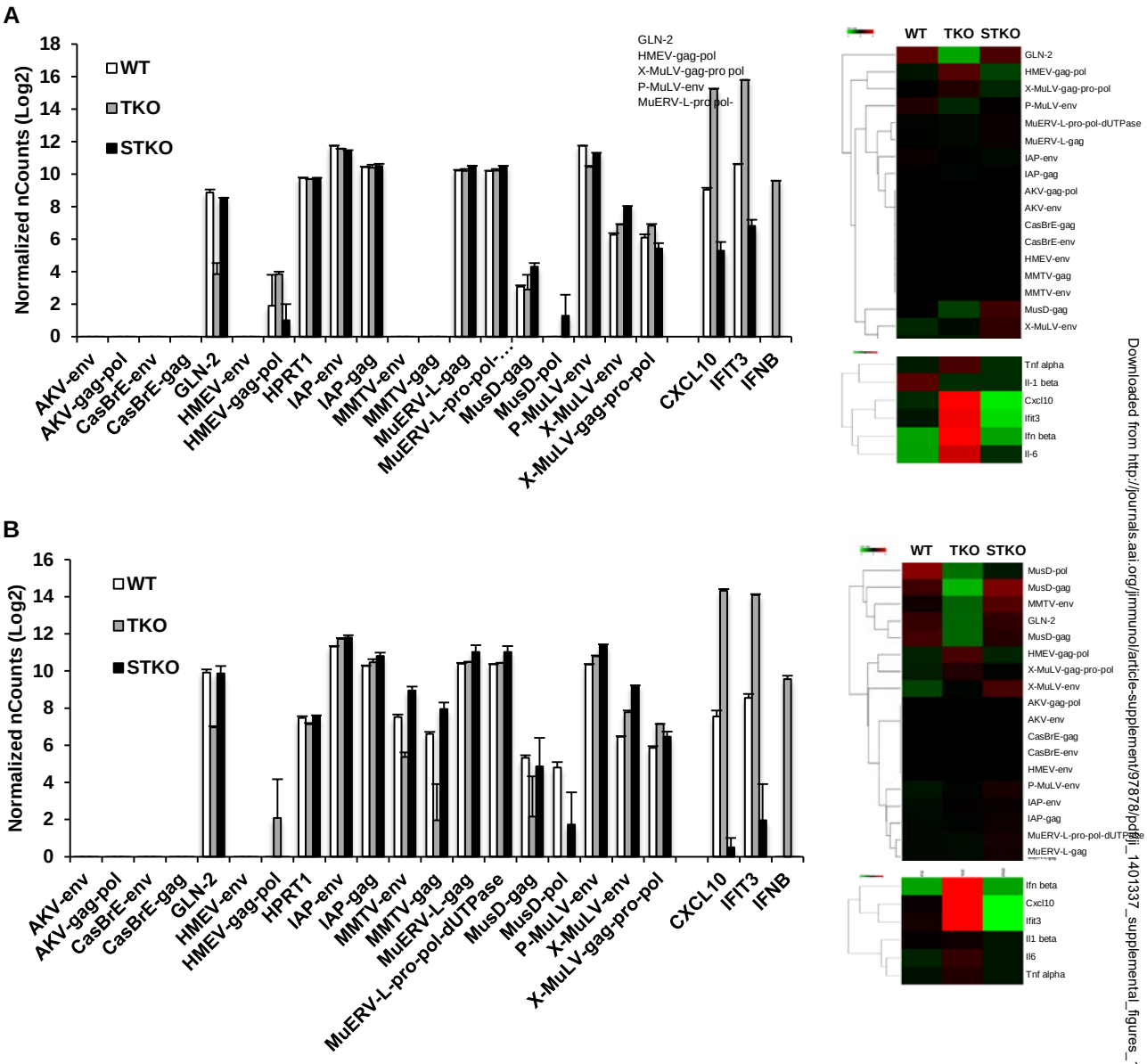





**Supplemental Fig. 1. TREX1 do not generate higher levels of cytokines by STING agonists. (A)** ELISA of IFN-β *and* **(B)** Gene array analysis in WT and TKO mouse embryonic fibroblasts (MEFs) treated with or without dsDNA90 (4ug/ml) or HSV-γ34.5 (MOI=1). Total RNA was purified and transcripts analyzed by Illumina Sentrix Chip Array (Mouse WG6 version2). **(C)** qPCR analysis of IFN-β, IFIT3, and CXCL10 in WT and TKO. (**D**) IFN-β mRNA levels in WT and TKO bone marrow derived macrophages (BMDM) added with necrotic thymocytes treated with $H_2O_2$ (2mM) for 1h. Error Bars indicated s.d. * ; p<0.05 Student's t-test.



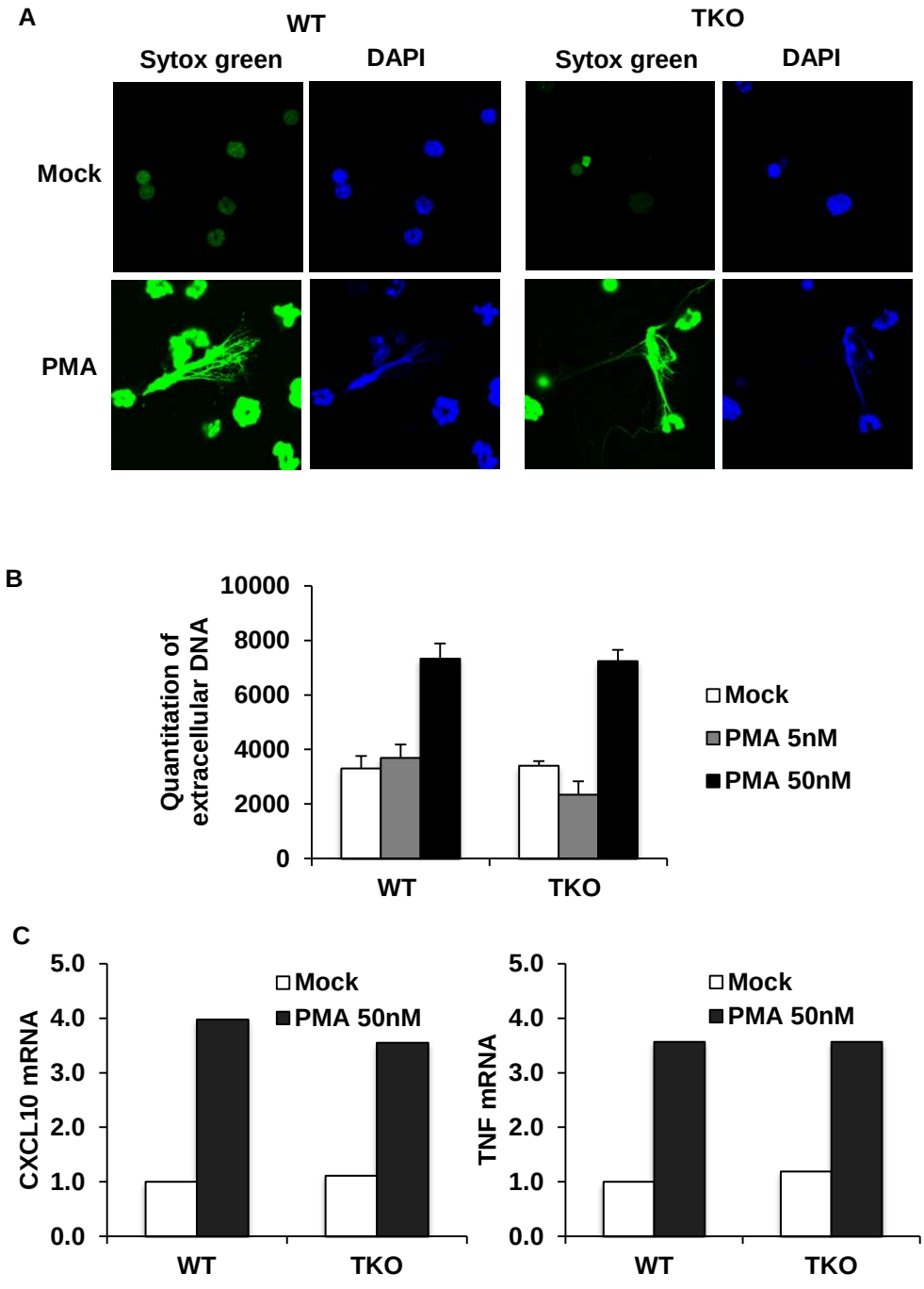

**Supplemental Fig. 2. (A) Depletion of CD11b$^+$ cells decreased heart inflammation by Trex1 deficiency.** CD11b (eBioscience 16-0112) or IgG2b Isotype control (eBioscience, 16-4031) were administered i.p. at 100 µg/25gbw mouse twice per week for 8 weeks. Representative hematoxylin and eosin staining (H&E) and Pericardial inflammation score for focality and intensity of heart tissue from TKO mice treated with isotype control (IgG-Cont, n=3) or CD11b antibodies (n=3) every 3days at 100ug/20g mouse. At 1 day and 4 days after injection, peripheral blood was collected from the tail vein and estimated CD11b positive cells using flow cytometric analyzer (BD FACS. Canto-II). **(B) Resident microbes did not cause inflammatory myocarditis in Trex1 mice.** 4 weeks old WT and TKO mice were provided ampicillin (1 g/l), vancomycin (500 mg/l), neomycin trisulfate (1 g/l), and metronidazole (1 g/l) in drinking water for 8 weeks. Representative hematoxylin and eosin staining (H&E) of heart tissue, heart/body weight and inflammation score from WT (n=4) and TKO (n=4) mice treated with oral antibiotic cocktail for 8 weeks.




**Supplemental Fig. 3. Retrotransposon activity was not detected in either BMDM or BMDC isolated from TKO mice.** Total RNA was isolated in BMDM (**A**) and BMDC (**B**) from WT, TKO, and STKO and analyzed using NanoString technology. Normalized nCounts (left) of 19 retroviral elements and 3 innates immunity related genes were normalized to 3 housekeeping genes. Data are shown the mean of duplicates experiments.

•**mERV NanoString Codeset design.** The mERV NanoString Codeset is designed to detect expression of 18 genes from 9 murine endogenous retroviruses (mERVs) of various types and 8 murine cellular genes that are involved in innate immunity and inflammation. 3 house-keeping genes were also included for internal controls. The open reading frame sequences of all retroviral genes and GenBank RefSeq numbers of all cellular genes were submitted to NanoString Technologies Inc for probe design. Probe sequences were then reviewed and blasted against mouse genome to ensure probe uniqueness. Detailed probe sequences are available upon request.

•**NanoString nCounter Assay.** Total RNA was extracted from sample tissue or cells using RNeasy mini kit (Qiagen). 200ng of RNA were used in the NanoString nCounter assays which are performed at the Oncogenomics Core Facility, University of Miami. In brief, RNA or DNA was hybridized to the capture and reporter probes according to nCounter Gene Expression Assay Manual. Hybridized probes were then recovered with the NanoString Prep Station and immediately evaluated with the NanoString nCounter Digital Analyzer.






**Supplemental Fig. 4. Extracellular DNA by Neutrophil extracellular traps (NETs) in TKO neutrophil.** Mouse neutrophils were isolated from bone marrow of WT and TKO mice using percoll gradient method (Isolation of human and mouse neutrophils exvivo and in vitro). Neutrophils were seeded on glass coverslips (VWR, 89015-724), allowed to settle and treated with (5, 50 nM) for 6 hours. (**A**) Sytox Green and DAPI staining in WT and TKO neutrophils stimulated with 50 nM of phorbol myristate acetate (PMA). For DNA detection, 5uM Sytox green nucleic acid stain (Invitrogen) at final concentration of 5 uM was used. After staining, cells were mounted in anti-fade mounting solution (Invitrogen) and examined under Leica SP5 spectral confocal inverted microscope. (**B**) Quantitation of DNA release from activated neutrophils by PMA. To quantify extracellular DNA, isolated neutrophils from WT and TKO mice were seeded into 96-well plates and stimulated with PMA at concentrations between 5 and 50 nM for 24 hours. After 24 hrs, Sytox Green was added to the cells at a final concentration of 5 μM to detect extracellular DNA. Non-stimulated neutrophils were used a control. The plates were read in a fluorescence microplate reader with a filter setting of 485(excitation)/527(emission). (**C**) qPCR of Cxcl10 and Tnf in neutrophils same as (A).