Supplementary Material

AR-13, a celecoxib derivative, directly kills *Francisella in vitro* and aids clearance and mouse survival *in vivo*

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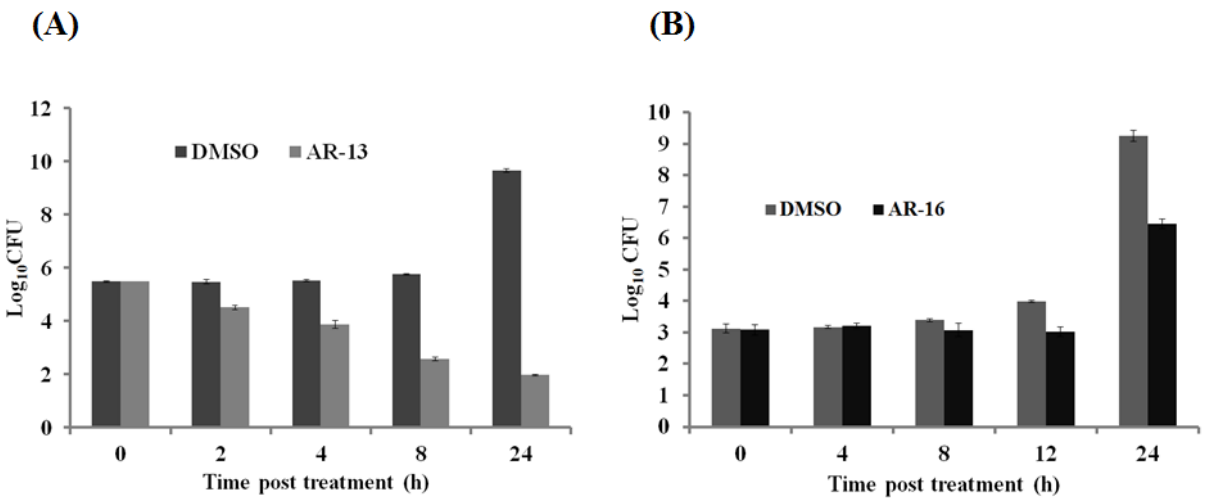
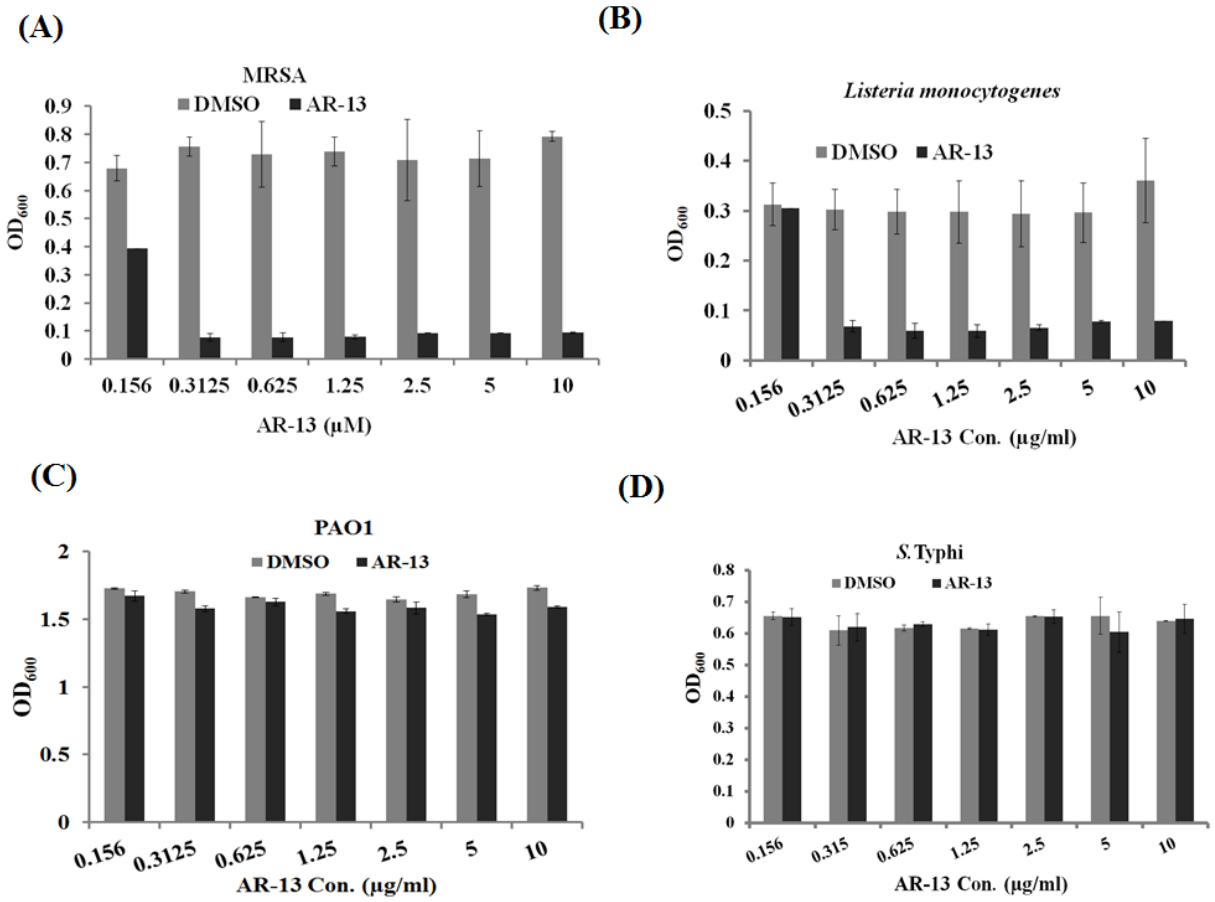
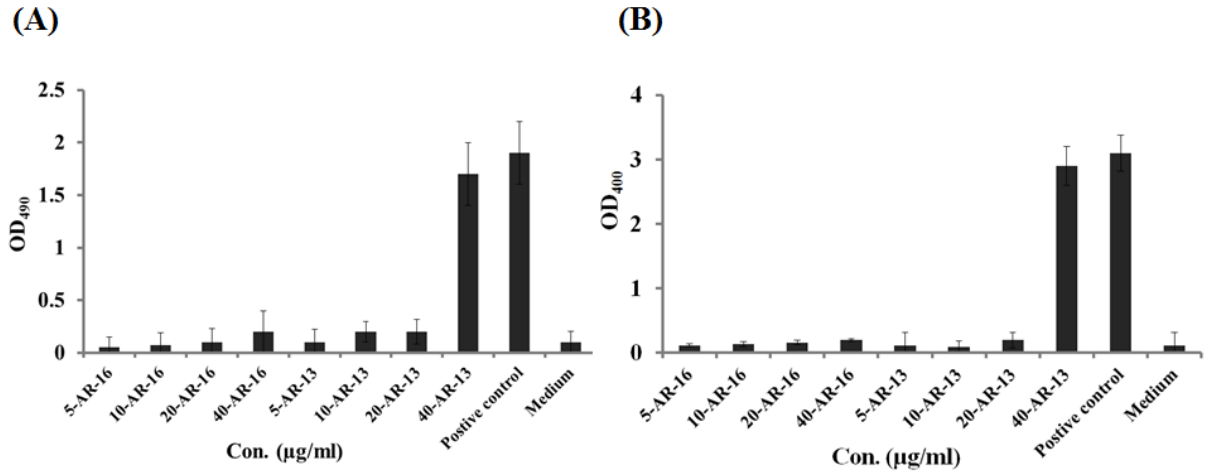


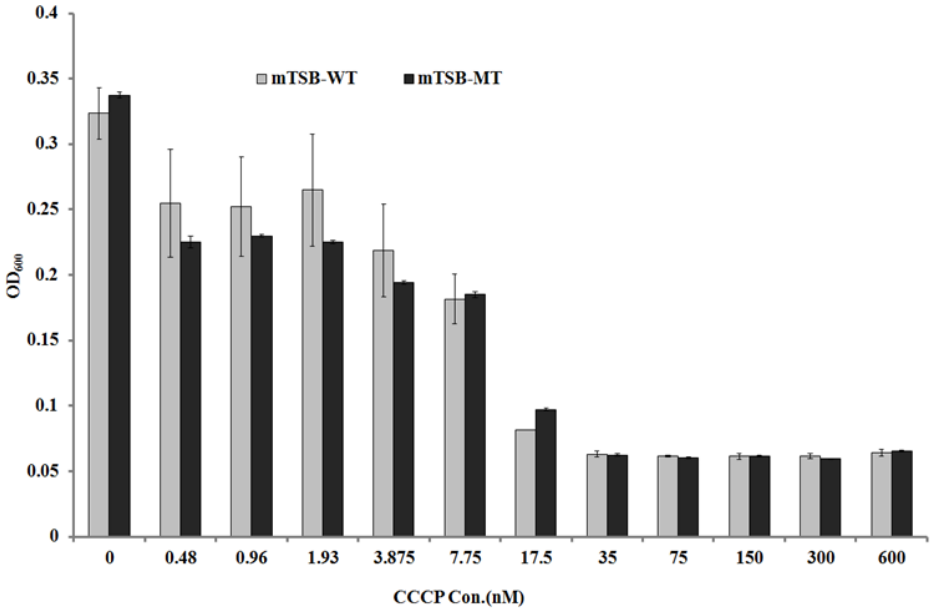
Supplementary Figure 1. Approximately 5-6x10^5 CFUs of LVS were incubated while shaking at 37°C in 1 ml mTSB containing 10 μg of AR-13 (A) or AR-16 (B). Viable bacteria were evaluated at different time-points by serial dilution and plating. Data are representative of three independent experiments, each performed in triplicate.



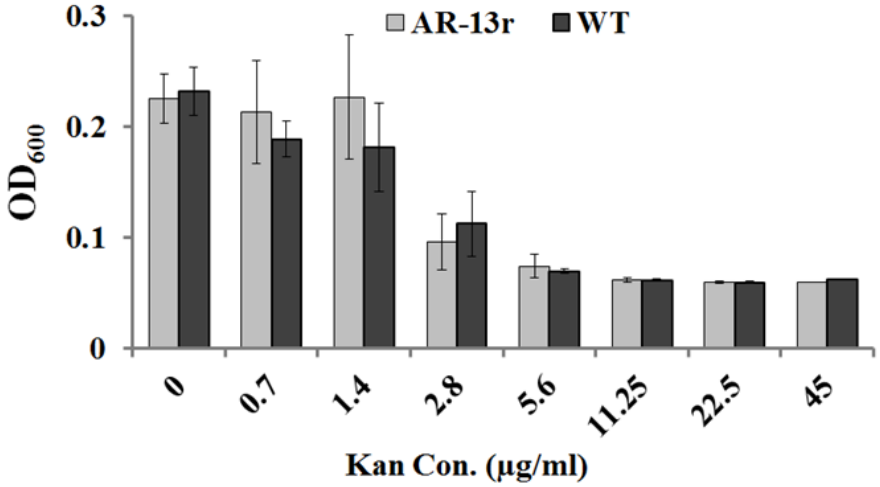
Supplementary Figure 2. Bacteria were grown in 2-fold serial dilutions of AR-13 in (A) mTSB (MRSA, strain JE2), (B) BHI (*L. monocytogenes,* strain 10403S), (C) LB (*P. aeruginosa* strain PAO1) and (D) *S.* Typhi Ty2. Optical densities at 600nm (OD_{600}) were measured by a plate reader at 24h post-inoculation. Two to three independent experiments were performed for each bacterium, with triplicate cultures in each experiment. Representative data are presented.



Supplementary Figure 3. Cytotoxicity of human monocyte-derived macrophages (hMDMs) cultured in the absence or presence of AR-13 or AR-16 for 24h (A) and 48h (B). Cytotoxicity was determined as LDH release measured at OD_{490}. A positive control (0.2% Triton X-100) was included. Experiments were repeated two times (each in triplicate) and the data from one experiment is presented.

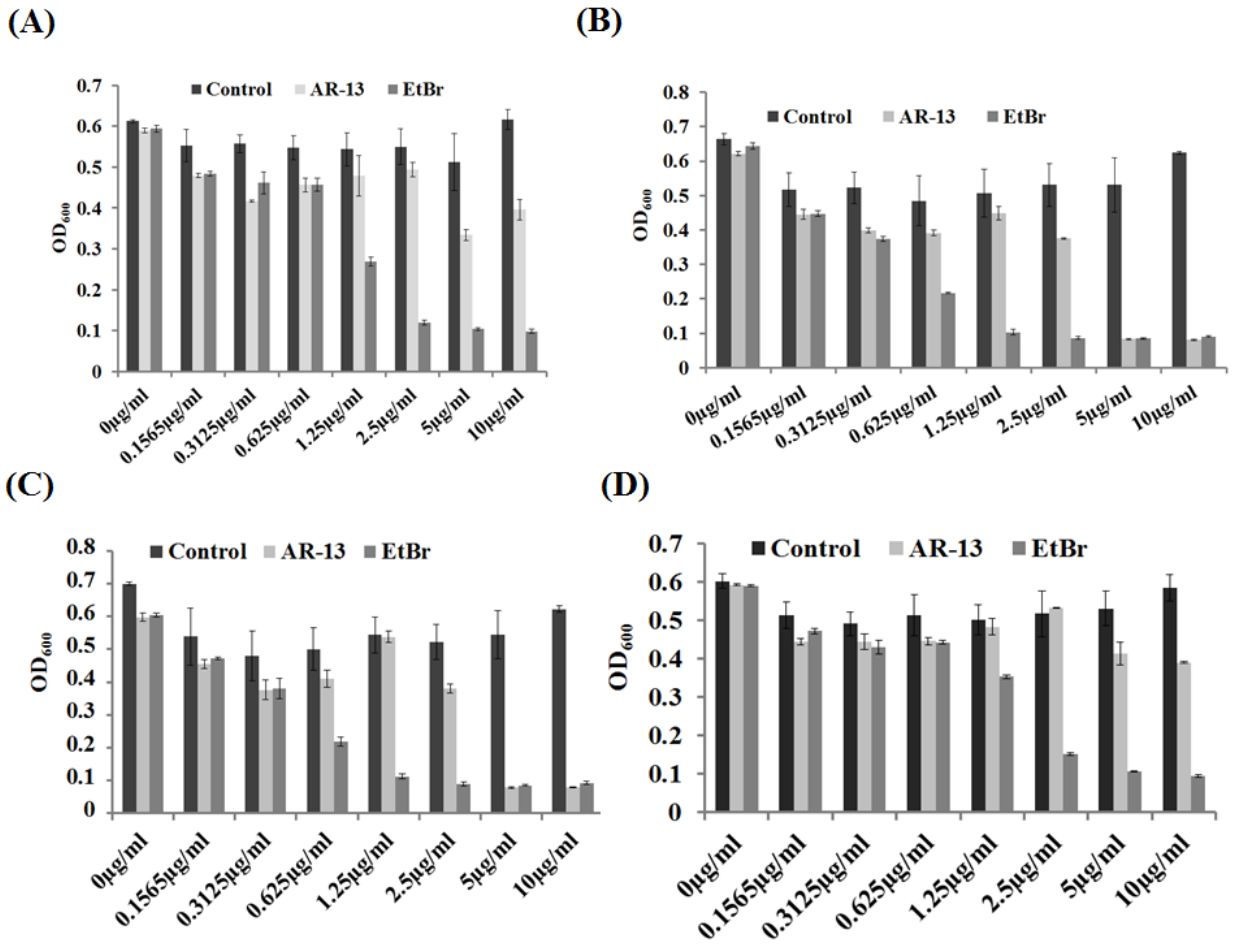


Supplementary Figure 4. Growth curve of a AR-13^r mutant (MT) and wild type LVS (WT) in varied concentrations of CCCP. LVS was grown in a 2-fold serial dilution of CCCP in mTSB. Optical densities at 600nm (OD_{600}) were measured by a plate reader at 18h post-inoculation. Experiments were repeated two times (each in triplicate) and the data from one experiment was presented.



Supplementary Figure 5. An AR-13^r mutant does not confer resistance to kanamycin. LVS was grown in 2-fold serial dilutions of kanamycin in mTSB. Optical densities at 600nm (OD_{600}) were

measured by a plate reader at 18h post-inoculation. Experiments were repeated two times (each in triplicate) and the data from one experiment was presented.



Supplementary Figure 6. Mutations in efflux pump genes but not an O-antigen synthesis gene (*wbtH*) confer AR-13 resistance in *F. novicida (Fn)*. Wild type *Fn*, together with efflux pump and *wbtH* mutants, were examined for sensitivity to AR-13 in mTSB; ethidium bromide was included as a control. (A) The growth of wild type *Fn* was partially inhibited by >5 μg of AR-13/ml and >1.25 μg of EtBr. Transposon insertions in (B) *tolC* (FTN_0779) and (C) *ftlC* (FTN_1703) increased susceptibility of these mutants to AR-13 (no growth was observed at 5 μg of AR-13/ml). (D) A *wbtH* (FTN_1421) mutant is only weakly affected by AR-13 concentrations of >5 μg of AR-13/ml. The experiment was performed 2-3 times in triplicate with at least three independent transposon mutants obtained from a BEI Resources library for each gene.