



**Fig. S1 IRE1 $\alpha$  inhibitors do not impact bacterial and PMN viability.**

(A) Isolated human neutrophils and buffy coat were stained with anti-CD15-FITC and anti-CD16-APC and analyzed by flow cytometry. Axenic growth of MRSA in tryptic soy broth in the presence of DMSO or IRE1 $\alpha$  inhibitors, 25  $\mu$ M 4 $\mu$ 8C (B) and 10  $\mu$ M KIRA6 (C). Results represent the average of  $n \geq 3$  independent experiments done in triplicate. (D) SYTOX Green Assay was performed on human neutrophils when left untreated or treated with 100 nM phorbol 12-myristate 13-acetate (PMA), 25  $\mu$ M 4 $\mu$ 8C and 10  $\mu$ M KIRA6 and DMSO control for 4h. Graph indicate mean  $\pm$  SEM of  $n \geq 3$  independent experiments. (E) CASPASE-3/7 activity of neutrophils treated with DMSO, 1  $\mu$ M Staurosporine (STS), 25  $\mu$ M 4 $\mu$ 8C or 10  $\mu$ M KIRA6 for 4h. CASPASE-3/7 activity was measured by flow cytometry using the CellEvent CASPASE-3/7 green flow cytometry assay kit (Thermo Fisher). Percent of CASPASE-3/7<sup>+</sup> cells was determined by gating against unstained cells. Graph shows the mean  $\pm$  SD from at least 3 independent experiments. *P* value was calculated using one-way ANOVA with Tukey's post-test for multiple comparisons. *P* value: \*\*< 0.01 and \*\*\*\*<0.0001.