

Figure S1. Despite utilising published protocols and a variety of optimisation steps, we found that prepared agar beads (A) showed significant diversity in size (B). Whilst the inoculation of βENaC mice resulted in consistent establishment of chronic infection (7 days post-inoculation), there was an unacceptable degree of variability in wild-type (C57BL6) animals (C). ○ represent individual data points

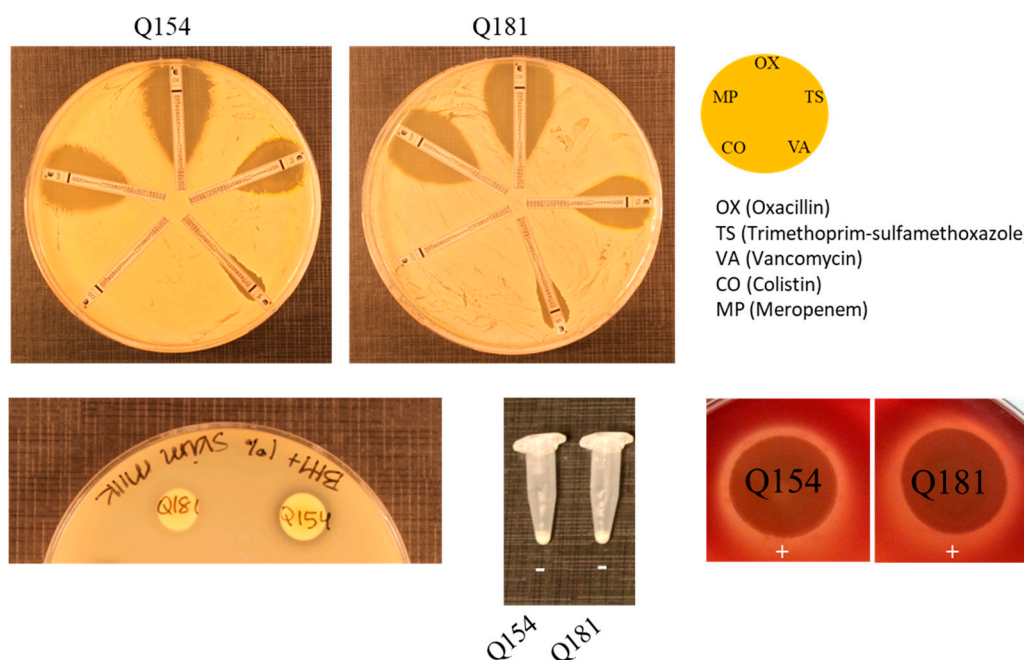


Figure S2. Phenotypic characterisation of *S. aureus* isolates.

Table S1; Characterisation of divergent clinical isolates of *S. aureus*.

Strain	Protease	Hemolytic (sheep blood)	Carotenoid pigment production	mecA gene	Antibiotic sensitivity				
					Oxacillin	Vancomycin	Colistin	Meropenem	Trimethoprim- sulfamethoxazole
Q154	+	+	-	-	0.23	7.3	>256	0.1	0.64
Q181	-	+	-	-	0.25	6	>256	0.06	0.29

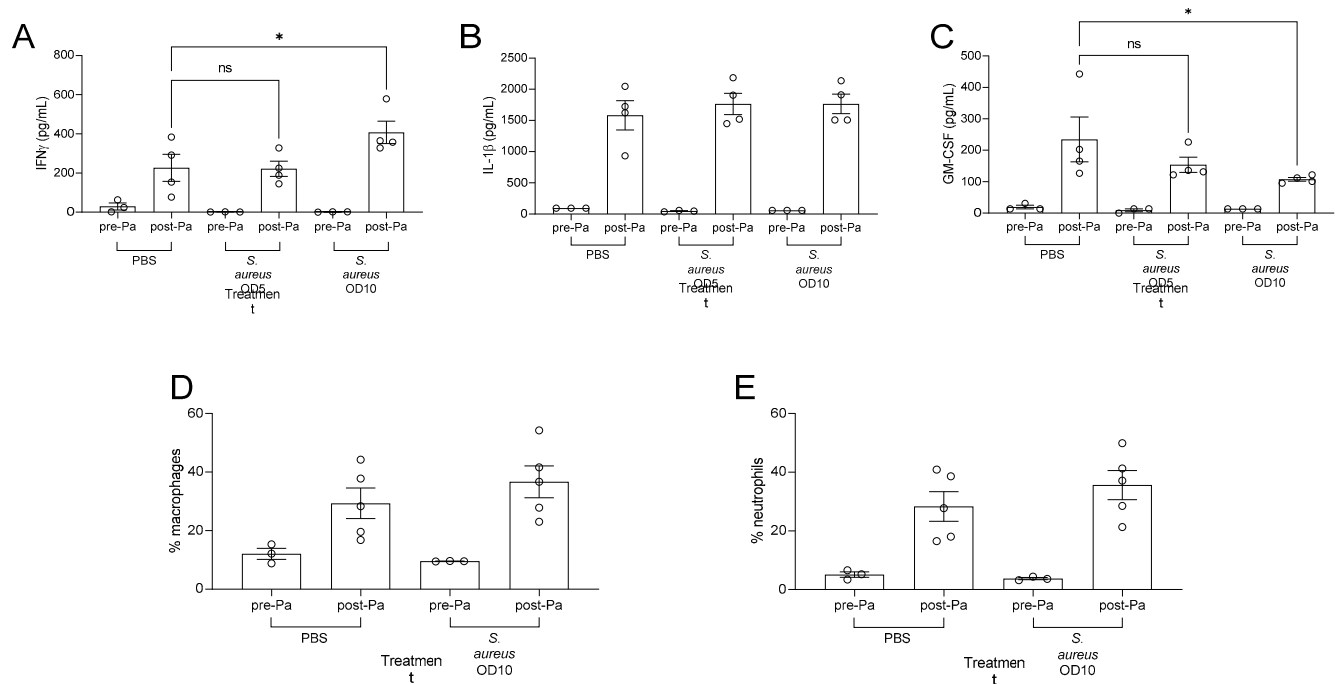


Figure S3. There was increased levels of IFN γ (A) with *S. aureus* pre-treatment, reduced G-CSF (C) and no difference in IL-1 β (B) – despite changes in cytokines and CFU, there is no significant difference in macrophages or neutrophils. \circ represent individual data points, * $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$.

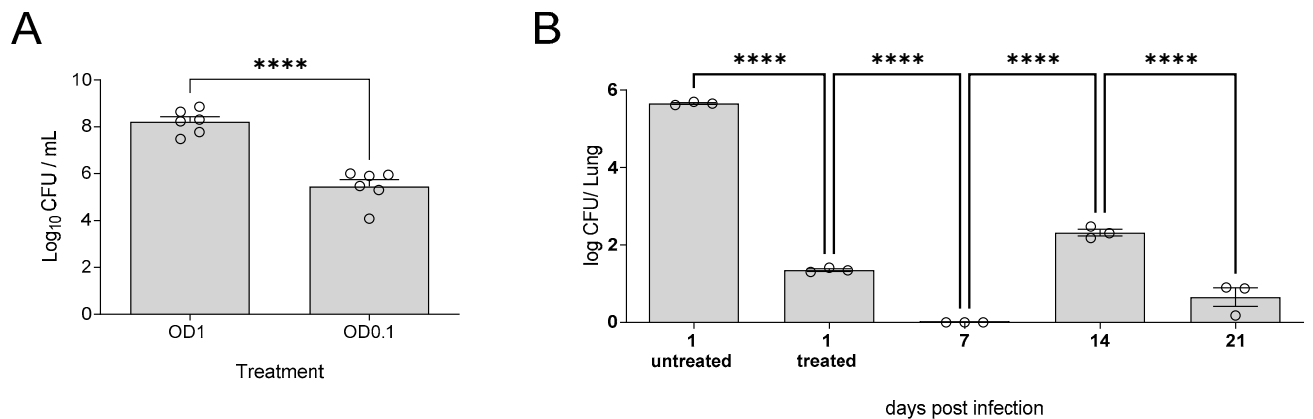


Figure S4. (A) Mice were infected intranasally with high (OD1 = $\sim 1 \times 10^6$) or low (OD0.1 = $\sim 1 \times 10^5$) dose PAO1; significantly less CFU were detected in lungs of the mice infected with the low dose. (B) After low dose infection, followed by 5 days of antibiotic treatment, complete clearance was achieved at days 7, whilst there was a bounce back at day 14; however, the level was not sustained at day 21. \circ represent individual data points, **** $p \leq 0.0001$.