

Supplemental figure 1. C5a specificity of calcium mobilization assay.

S. aureus Newman Δ Ecb Δ Efb was incubated with 30% human serum or buffer for 30 minutes at 37°C. Bacteria were centrifuged and C5a was detected in collected supernatants by calcium mobilization. Supernatants were added to Fluo-4-AM labeled U937-C5a receptor cells and the increase of intracellular calcium was measured by flow cytometry. Calcium mobilization was calculated by subtracting the 'fluorescence after stimulation' from the 'baseline fluorescence'. (In comparison to recombinant C5a: a fluorescence increase of 10 is approximately equal to 2x10⁻⁹ M rC5a, an increase of 30 \cong 1x10⁻⁸ M rC5a (data not shown)). No response was observed for untransfected U937 cells (U937-empty vector) or for U937-C5aR cells pre-treated with the C5aR antagonist CHIPS (10 µg/ml). Figures represent mean±S.E. of two independent experiments.



Supplemental Figure 2: Ecb and Efb block neutrophil influx during *S. aureus* pneumonia

Lungs of mice infected with PBS, $4x10^8$ cfu *S. aureus* Newman (WT) or its mutant $\Delta Ecb\Delta Efb$ via intranasal inoculation. Animals were sacrificed 6 hrs after challenge and formalin-fixed lung tissues were stained with H&E (two left columns) or peroxidase-labeled streptavidin-detection of myeloperoxidase (right column, brownish staining). Related to Figure 3.



Supplemental Figure 3: Bacterial loads in lung, spleen and liver.

Cohorts of 7 (WT) and 9 ($\Delta Ecb\Delta Efb$) mice were infected with 1.5x10⁷ cfu of *S. aureus* Newman (WT) or its mutant $\Delta Ecb\Delta Efb$ via intravenous inoculation. Bacterial loads in lung, spleen and liver 10 days after challenge.



Supplemental Figure 4: Ecb and Efb are required for abscess formation

H&E stained kidney sections of mice infected with 1.5×10^7 cfu of *S. aureus* Newman (WT) or its mutant $\Delta Ecb\Delta Efb$ via intravenous inoculation. Kidneys were analyzed 10 days after challenge. Kidney abscesses of mice infected with wild-type *S. aureus* Newman (WT#2 and #3) contain central populations of staphylococci surrounded by amorphous material. Abscesses of mice infected with the $\Delta Ecb\Delta Efb$ mutant ($\Delta Ecb\Delta Efb$ #2 and #3) contain large zones of intact neutrophils. Related to Figure 5.