SUPPLEMENTAL DATA

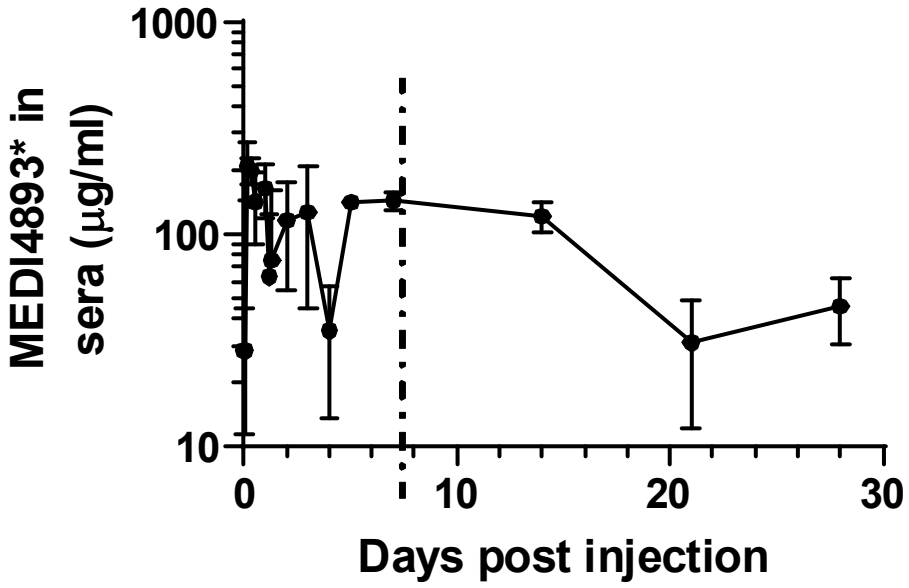

Figure S1. Pharmacokinetic data and half-life determination of the anti-AT mAb in mice. C57BL/6 mice (6-7 week-old) were injected i.p. with the anti-AT mAb (MEDI4893*; 14 mg/kg in 500 µL PBS). Blood was then collected (retro-orbital vein) at indicated time points between 0 and 28 days (n=3-5 mice/time point), and sera frozen at -80ºC. MEDI4893* was quantified by ELISA. Maxisorp 96 well plate (VWR) were coated with 1 µg/mL of sheep anti-human IgG (The Binding Site) in 100 µL of PBS. After overnight incubation at 4ºC, and 1 hour blocking at room temperature with PBS with BSA (2%) (Sigma), plates were washed with PBS with tween (0.1%), and then incubated with serial dilutions of mouse sera. MEDI4893* was used as to generate a standard curve. After a 1 hour incubation at room temperature, and 3 washes, goat anti-human IgG HRP-conjugated (Bethyl Laboratories) was added and incubated for 1 hour. After 3 washes, antibody binding was detected using 100 µL of SureBlue Reserve 3,3′,5,5′-tetramethylbenzidine (TMB) substrate (KPL), followed by neutralization with 100 µL of sulfuric acid (0.2 N). Absorbance was determined at 450 nm with an Envision plate reader (PerkinElmer). The terminal elimination half-life of 7.6 days (denoted as a vertical dotted line) was determined using a log-linear regression of the concentration data with the equation $\ln(2)/\lambda z$, where λz is the slope of the terminal portion of the natural log concentration-time curve, determined by linear regression of the data from at least the last three time points.

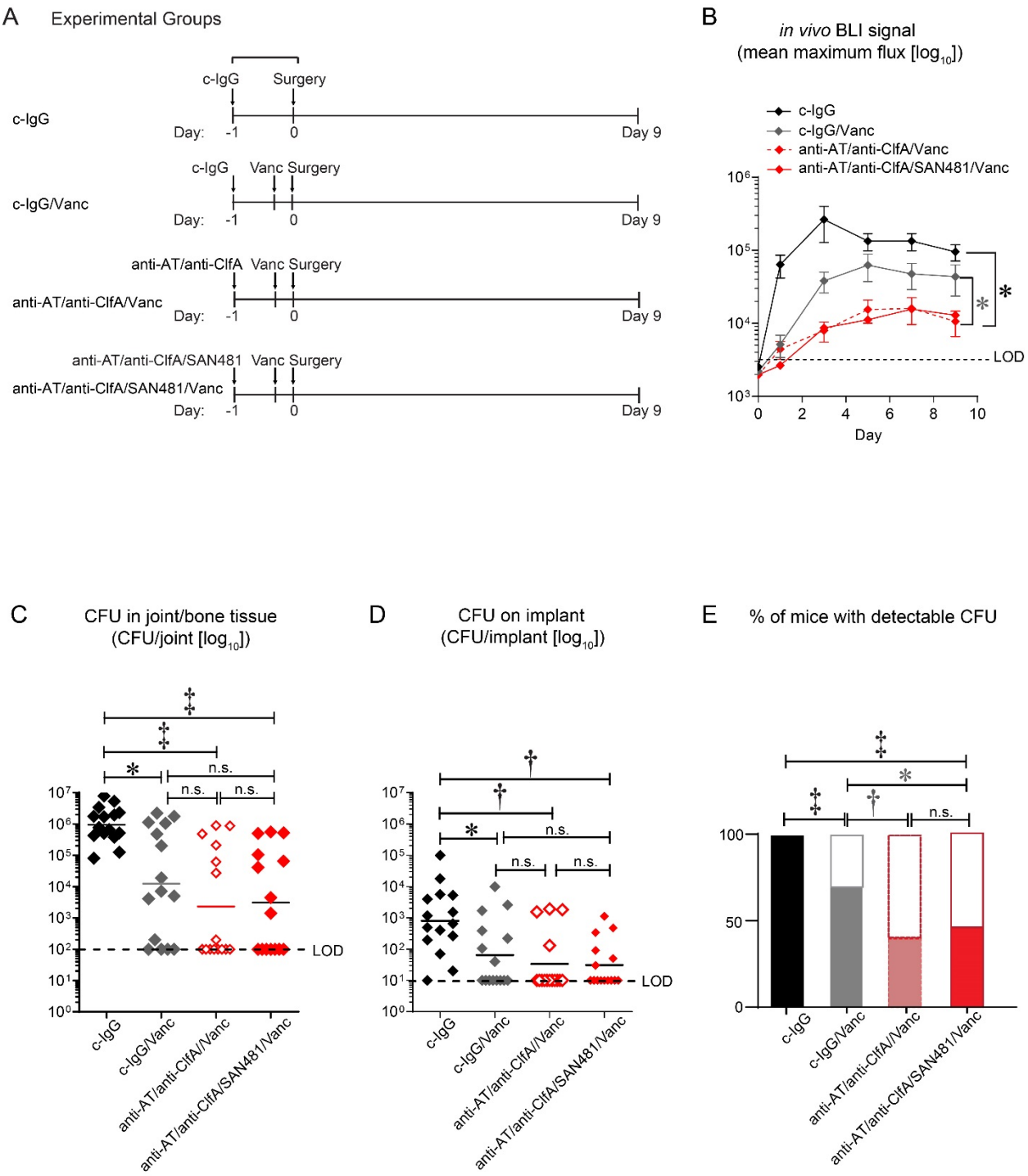

Figure S2. Comparing the per-operative efficacy of anti-AT/anti-ClfA/Vanc vs anti-AT/anti-ClfA/SAN481/Vanc in an orthopaedic SSI model. The mouse model of orthopaedic SSI with MRSA strain SAP231 was performed in C57BL/6 mice (n=15/group). (A) Timeline of preoperative administration in the experimental groups (there was no postoperative administration in this experiment): c-IgG (isotype control mAb), c-IgG/Vanc, anti-AT/anti-ClfA/Vanc, and anti-AT/anti-ClfA/SAN481/Vanc. (B) Mean maximum flux

(photons/s/cm^2/steradian) ± s.e.m. (logarithmic scale). LOD, limit of detection. * $P < 0.05$ (2-way ANOVA). (C and D) *ex vivo* CFU (geometric mean = horizontal bars) isolated from joint/bone tissue (C) and implants (D) from euthanized mice on day 9 (logarithmic scale). * $P < 0.05$, †$P<0.01$, ‡$P < 0.001$(Kruskal-Wallis test with 2-stage linear step-up procedure of Benjamini, Krieger and Yekutieli to correct for multiple comparisons). n.s., not significant. (E) Percentage of mice with (filled) or without (open) *ex vivo* CFU detected from tissue (C) or implant (D) specimens. * $P < 0.05$, †$P<0.01$, ‡ $P < 0.001$ (Fisher's exact test).

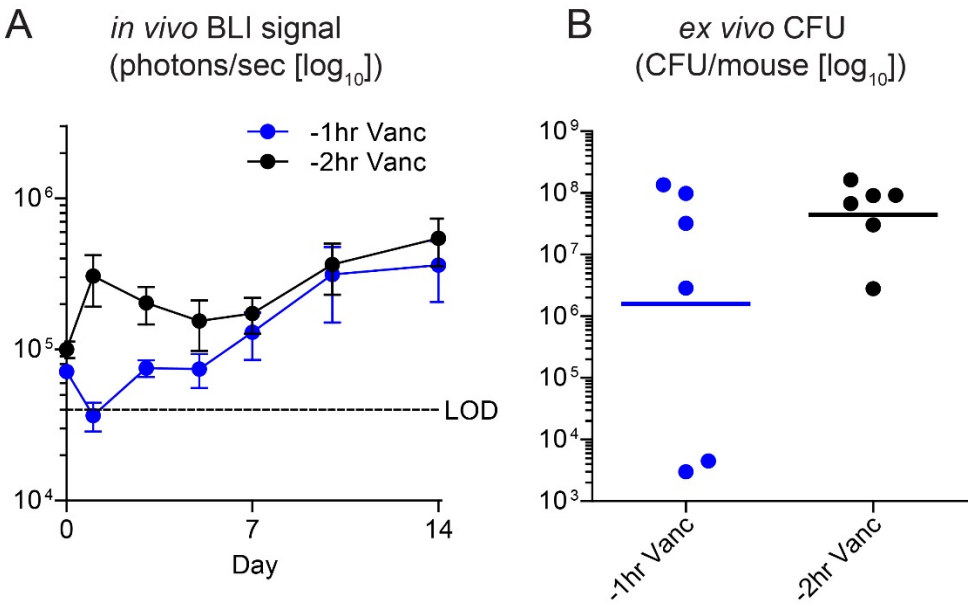

Figure S3. Effect of timing preoperative vancomycin administration in skin SSI model. The mouse model of skin SSI with MRSA strain USA300 LAC::*lux* was performed in diabetic TallyHo/JngJ mice (n=6/group). Preoperative vancomycin at 110 mg/kg i.v. was administered at either 1 hour (-1hr Vanc) or 2 hours (-2hr Vanc) prior to infection. (A) *In vivo* bioluminescence imaging was performed and data reported as mean total flux (photons/s) ± s.e.m. (logarithmic scale). LOD, limit of detection. (B) *ex vivo* CFU (geometric mean = horizontal bars) isolated from skin biopsies performed on euthanized mice on day 14 (logarithmic scale).