DNA Alignment (Optimized Region). The changed codons are indicated as red letters:

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Optimized   22 ATGGTATCTAAAGGAGAAGAATTATTTACTGGAGTTGTTCCTATTTTAGTTGAATTAGAT
Original    22 ATGGTGAGCAAGGGCGAGGAGCTGTTCACCGGGGTGGTGCCCATCCTGGTCGAGCTGGAC

Optimized   82 GGTGATGTTAATGGTCATAAATTTTCTGTTAGTGGTGAAGGAGAAGGTGATGCTACATAT
Original    82 GGCGACGTAAACGGCCACAAGTTCAGCGTGTCCGGCGAGGGCGAGGGCGATGCCACCTAC

Optimized  142 GGTAAATTAACATTAAAATTTATTTGTACTACAGGAAAATTACCAGTTCCATGGCCTACA
Original   142 GGCAAGCTGACCCTGAAGTTCATCTGCACCACCGGCAAGCTGCCCGTGCCCTGGCCCACC

Optimized  202 TTAGTAACTACATTAACATATGGTGTACAATGTTTTTCTCGTTATCCAGATCATATGAAA
Original   202 CTCGTGACCACCCTGACCTACGGCGTGCAGTGCTTCAGCCGCTACCCCGACCACATGAAG

Optimized  262 CAACATGATTTTTTTAAATCAGCAATGCCAGAAGGTTATGTACAAGAACGAACTATTTTT
Original   262 CAGCACGACTTCTTCAAGTCCGCCATGCCCGAAGGCTACGTCCAGGAGCGCACCATCTTC

Optimized  322 TTTAAAGATGATGGTAATTATAAAACTCGTGCTGAAGTAAAATTTGAAGGTGATACTTTA
Original   322 TTCAAGGACGACGGCAACTACAAGACCCGCGCCGAGGTGAAGTTCGAGGGCGACACCCTG

Optimized  382 GTGAATAGAATTGAATTAAAAGGTATAGATTTCAAAGAAGATGGTAATATTTTAGGTCAT
Original   382 GTGAACCGCATCGAGCTGAAGGGCATCGACTTCAAGGAGGACGGCAACATCCTGGGGCAC

Optimized  442 AAATTAGAATATAACTATAACAGTCATAATGTGTATATTATGGCTGATAAACAAAAAAAT
Original   442 AAGCTGGAGTACAACTACAACAGCCACAACGTCTATATCATGGCCGACAAGCAGAAGAAC

Optimized  502 GGTATTAAAGTTAACTTTAAAATACGTCATAATATAGAAGATGGAAGTGTTCAATTAGCT
Original   502 GGCATCAAGGTGAACTTCAAGATCCGCCACAACATCGAGGACGGCAGCGTGCAGCTCGCC

Optimized  562 GATCATTATCAACAAAATACACCAATAGGTGATGGTCCAGTTTTATTACCTGATAATCAT
Original   562 GACCACTACCAGCAGAACACCCCCATCGGCGACGGCCCCGTGCTGCTGCCCGACAACCAC

Optimized  622 TATTTAAGTACACAATCTGCATTATCAAAAGATCCAAATGAAAAACGAGATCATATGGTA
Original   622 TACCTGAGCACCCAGTCCGCCCTGAGCAAAGACCCCAACGAGAAGCGCGATCACATGGTC

Optimized  682 TTATTAGAATTTGTTACAGCAGCTGGTATAACTTTAGGAATGGATGAATTATATAAA
Original   682 CTGCTGGAGTTCGTGACCGCCGCCGGGATCACTCTCGGCATGGACGAGCTGTACAAG
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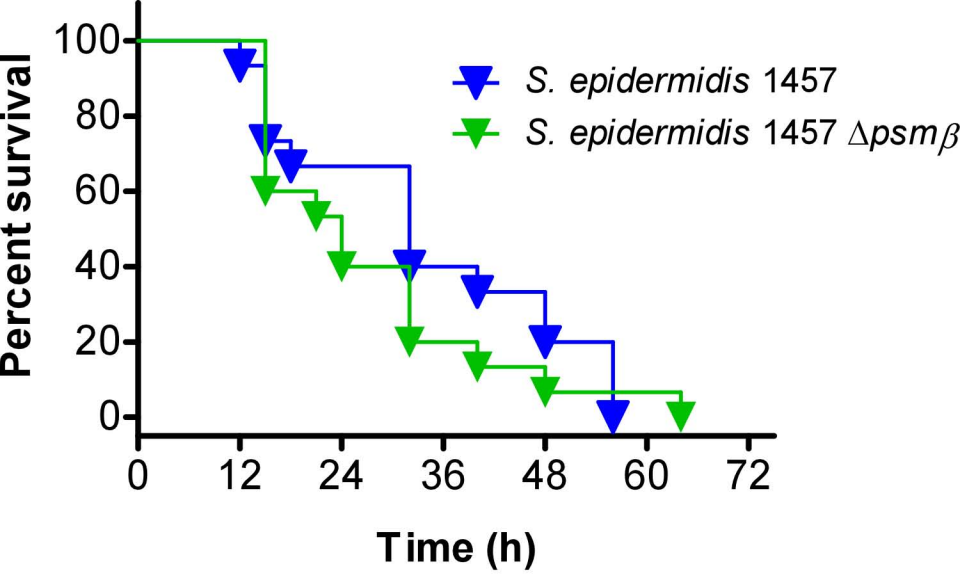
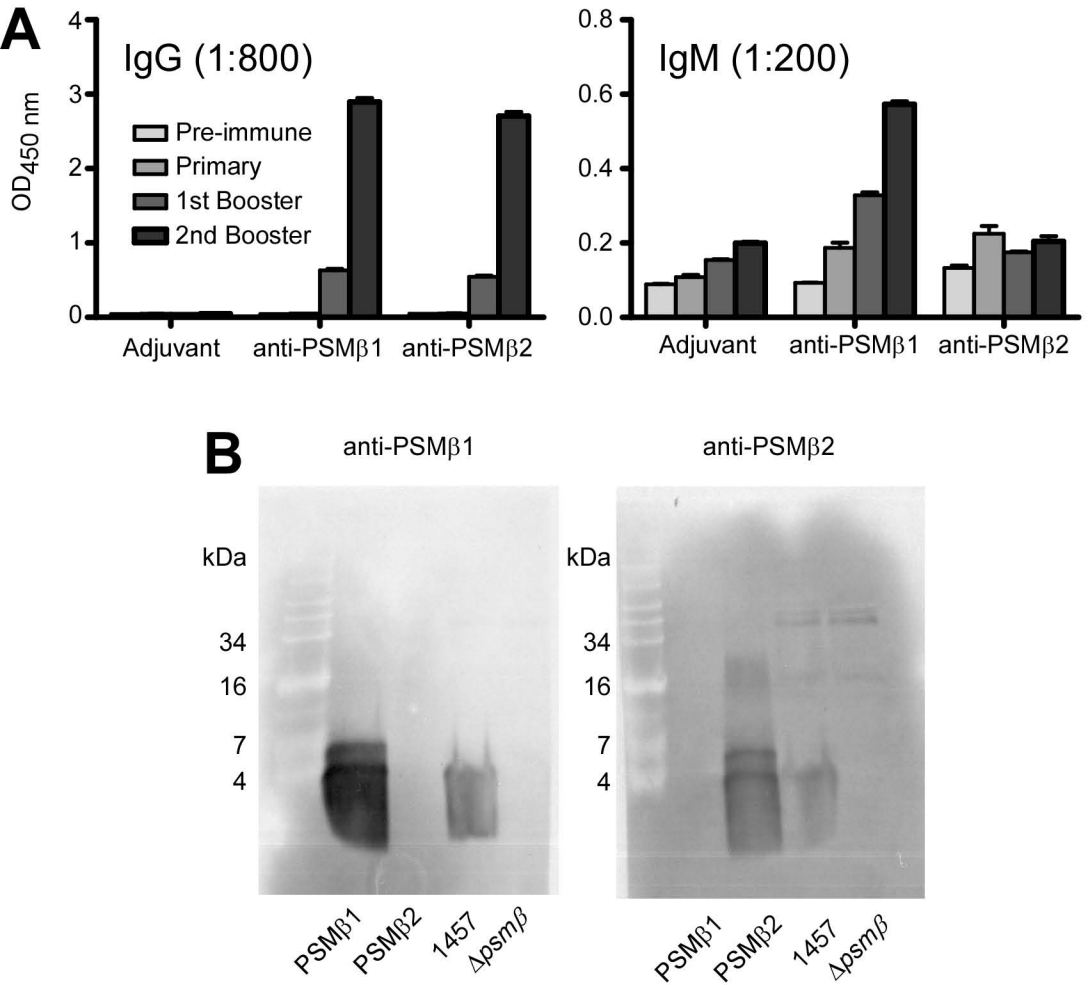
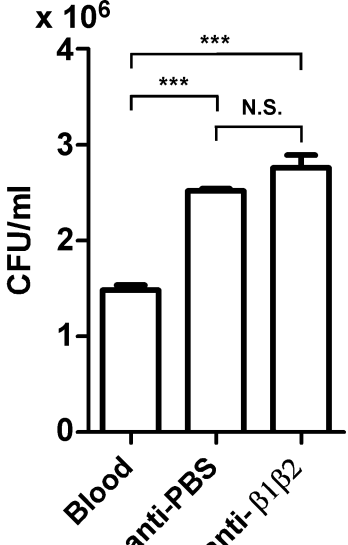
Supplemental Figure 1. Codon optimization for the *egfp* gene. The *egfp* gene was optimized for *Staphylococcus* codon usage and synthesized by Genescript Corp. The synthesized gene was cloned in the *Sma*I site of pUC57, excised via *Pst*I and *Hin*dIII, and cloned in pRB473. The final construct contains a Shine/Dalgarno sequence next to the *Pst*I site in front of the *egfp* ATG start codon: ctgcagaggaggtaagttata*atg*. To construct the *psmβ* promoter *egfp* fusion, the *psmβ* promoter was cloned in the *Eco*RI/*Bam*HI sites in front of the *egfp* gene, using the multiple cloning site of plasmid pRB473.



Supplemental Figure 2. Bacteremia model. Immune-compromised Nu/Nu B/C CRL female mice (Charles River Laboratories) were between 6 and 8 weeks of age at the time of use. *S. epidermidis* 1457 wild-type or isogenic *Δpsmβ* strains were grown to mid-exponential phase, washed once with sterile PBS, then resuspended in PBS at 1 x10^9 CFUs/100 µl. Each animal received 10^9 CFUs of live *S. epidermidis* 1457 wild-type or isogenic *Δpsmβ* strains in 100 µl sterile PBS by retro-orbital injection via the right eye. Control animals received sterile PBS only. After inoculation, mouse health and disease advancement were monitored every 3 h for the first 24 h, then every 8 h for up to 72 h. Mice were euthanized immediately if they showed signs of respiratory distress, mobility loss or inability to eat and drink. All surviving animals were euthanized at the end of the study.



Supplemental Figure 3. Anti-PSM antisera. Antisera were raised separately against PSMβ1 and PSMβ2 in mice. (A) Immunogenicity. ELISAs of mouse sera using IgG or IgM-specific horse radish peroxidase-labeled goat antibodies and PSMβ1- or PSMβ2-coated microtiter plates. (B) Specificity. Obtained sera were blocked with extracts from *S. epidermidis* Δ*psmβ* and purified using Protein G affinity columns. SDS-PAGE on a 16% Tricine gel with synthetic PSMβ1 and PSMβ2, and culture filtrates from *S. epidermidis* wild-type and Δ*psmβ* strains were used to analyze specificity of obtained antisera. Horseradish peroxidase conjugated goat anti-mouse IgG and enhanced chemoluminescence were used to visualize reactions.



Supplemental Figure 4. Opsonophagocytosis assay with anti-PSMβ antiserum. Dilutions of bacteria, in PBS, were opsonized with purified mouse antibodies against PBS or PSMβ1/PSMβ2 in a 1:1 ratio for 30 min at 37°C. Blood obtained from Female Nu/Nu B/C CRL mice was incubated for 60 min at 37°C with the opsonized bacteria (5 x 10^4 CFU) to a ratio of antibody:bacteria:blood at 1:1:16 in a total volume of 100 µl. Surviving bacteria were counted by spotting 400 µl (16 x 25 µl aliquots) onto TSB plates. N.S., not significant; ***, $p<0.001$; 1-way ANOVA with Bonferroni post-test.