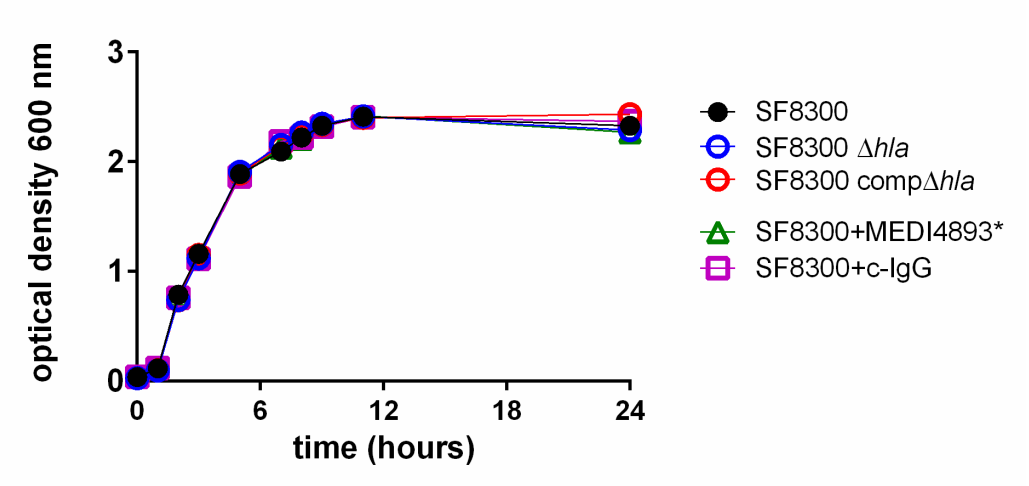
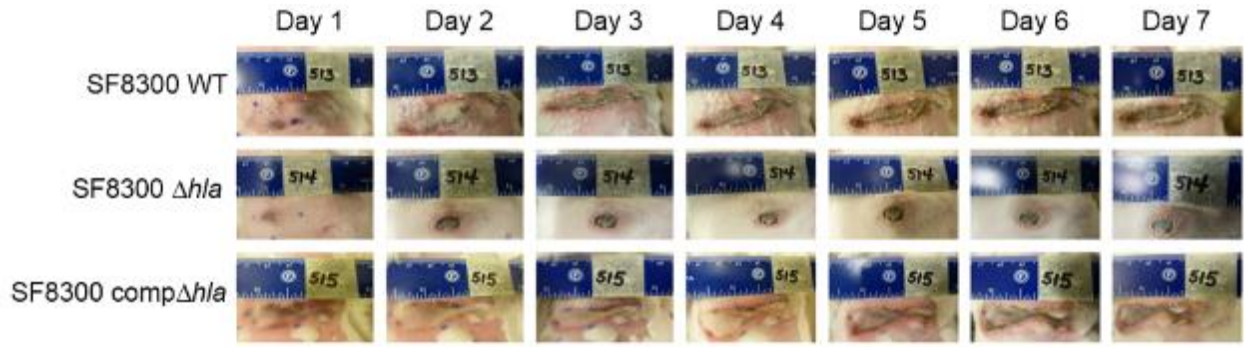
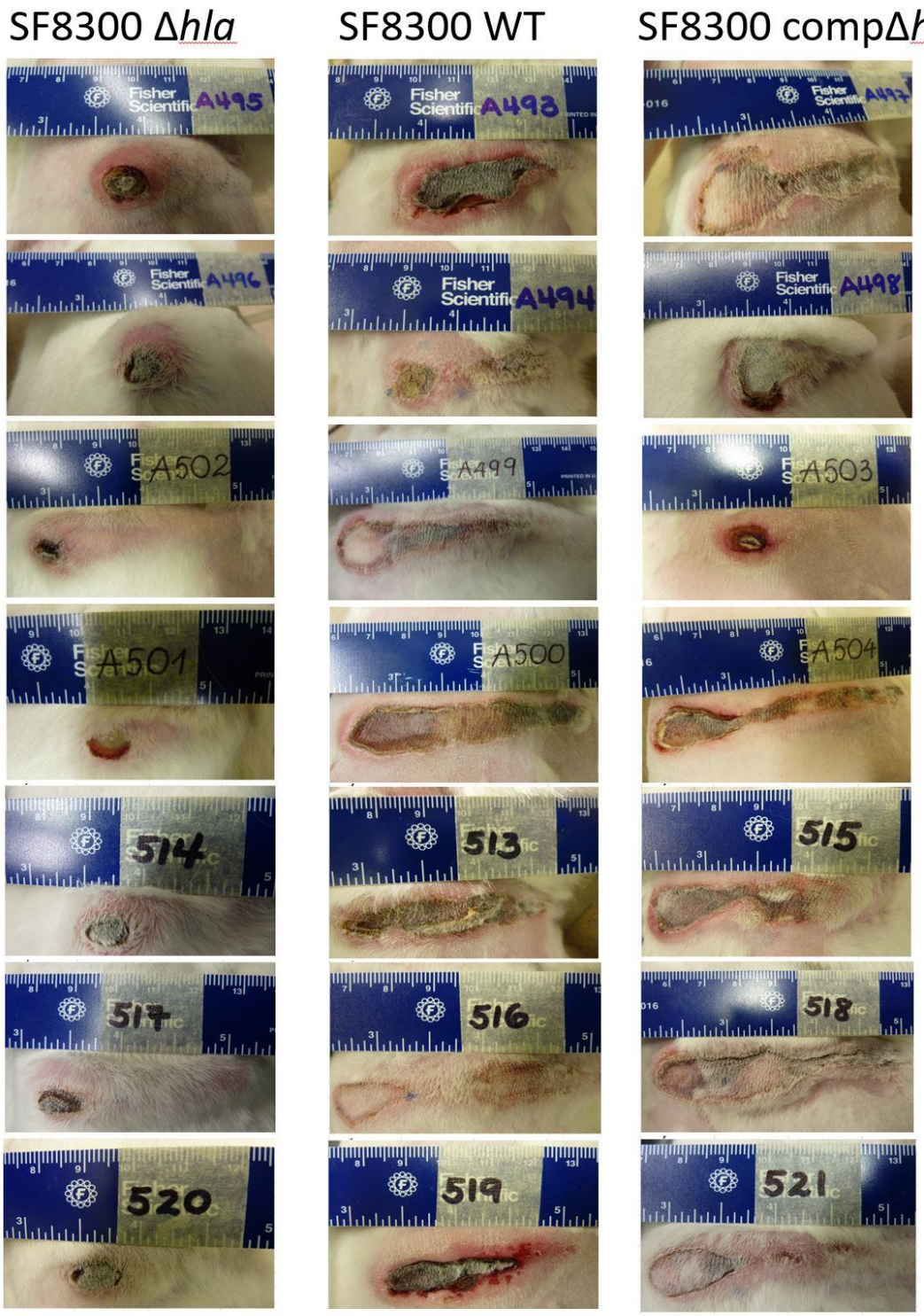


Supplemental Figure 1. Growth curves of SF8300 WT, Δ*hla*, and compΔ*hla* strains in tryptic soy broth (TSB), and growth curves of SF8300 WT in TSB containing 50 µg/mL of MEDI4893* or c-IgG.



Supplemental Figure 2. Representative gross images of dermonecrotic ulceration caused by SF8300 WT, Δ*hla*, and compΔ***hla* strains over the seven-day infection period.**



Supplemental Figure 3. Gross images of dermonecrotic ulceration caused by SF8300 WT, Δ*hla*, and compΔ***hla*** **strains on Day 7 post infection.**

Supplemental Table 1. Oligonucleotides used for construction of in-frame gene deletions using pKOR1 allelic replacement system (9, 16).

Oligo ID	Nucleotide sequence 5' to 3'
For in-frame deletion of gene encoding alpha-toxin (Hla)	
Hla-X1	GATTTATTATGTCTTAGGCTCTATTCC
Hla-X2	CCATTTATCTTTAGTATTGGTACCTTTCCATGTTGTTACTGAGCTGACTATACG
Hla-X3	CGTATAGTCAGCTCAGTAACAACATGGAAAGGTACCAATACTAAAGATAAATGG
Hla-X4	TTAGGATAATCGACGTAAGAAGAATC
Hla-X5	GGGG ACAAGTTTGTACAAAAAAGCAGGCT CTTTATTGTCCCATGATTAGTGTTC
Hla-X6	GGGG ACCACTTTGTACAAGAAAGCTGGGT GCATCATTTGTTGTTAATAATGGGAC
Hla-S1	CCCTCGAAATTGAAATGCTTC
Hla-S2	CCTCATATAGTGTCATGTTTAGTC
***For complementation of Δhla* mutation, primers Hla-X1, X4, X5, X5, S1, S2 above were used with X2c and X3c primers below.**	
Hla-X2c	CTCTTTTGTATCAATCGAATTTCTTGGGTAATAATCAGATATTTGAGCTACTTCATTATCAGG
Hla-X3c	CCTGATAATGAAGTAGCTCAAATATCTGATTATTACCCAAGAAATTCGATTGATACAAAAGAG

Supplemental Table 2. Pharmacokinetic parameters of linezolid in serum after a single subcutaneous dose of 25 mg/kg.

	25 mg/kg linezolid s.c.*
C_{max} (µg/mL)	16.0 ± 0.5
T_{max} (h)	0.75 ± 0.29
$t_{1/2}$ (h)	0.64 ± 0.05
$AUC_{0\ to\ \infty}$ (µg · h/mL)	26.3 ± 3.8

*values represent means of 4 animals ± standard deviation

Supplemental Table 3. Mean dermonecrosis area (±SEM) and multiply-adjusted *P*-values for rabbits challenged with SF8300 WT, Δ*hla*, compΔ*hla* (related to Figure 2A)

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Dermonecrosis area (mm^2) ± SEM							
SF8300 WT (n=7)	271±42	335±30	346±24	386±58	413±66	446±83	385±63
SF8300 Δ*hla* (n=7)	31±5	64±12	69±74	66±6	70±9	66±6	63±9
SF8300 compΔ*hla* (n=7)	278±64	385±103	360±74	397±82	394±83	376±65	385±69
Kruskal-Wallis followed by Dunn's test, multiplicity adjusted *P* values							
WT vs. Δ*hla*	0.006	0.010	0.019	0.020	0.015	0.012	0.007
compΔ*hla* vs. Δ*hla*	0.015	0.018	0.010	0.020	0.026	0.023	0.005
WT vs. compΔ*hla*	> 0.999	> 0.999	> 0.999	> 0.999	> 0.999	> 0.999	> 0.999

Supplemental Table 4. Mean dermonecrosis area (±SEM) and unpaired *t* test *P* values (two-sided) with Welch's correction for prophylaxis study with MEDI4893* and c-IgG (related to Figure 4A)

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Dermonecrosis area (mm^2) ± SEM							
c-IgG	237±48	355±59	366±71	349±73	324±69	325±64	299±69
MEDI4893*	26±3	33±3	34±4	35±8	34±5	34±4	31±4
Unpaired *t* test with Welch's correction, *P* values							
c-IgG vs. MEDI4893*	0.003	0.001	0.002	0.004	0.004	0.003	0.006

Supplemental Table 5. Mean dermonecrosis area (±SEM) and multiplicity-adjusted *P*-values for rabbits treated with linezolid and/or MEDI4893* at 2 h post-infection (related to Figure 5A)

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Dermonecrosis area (mm^2) ± SEM							
c-IgG	554±96	645±124	662±123	712±144	696±137	696±138	708±133
MEDI4893*	148±37	194±47	188±41	186±41	190±39	186±40	199±42
Linezolid	326±68	326±65	316±65	310±64	320±64	329±70	321±68
Linezolid + MEDI4893*	122±22	121±23	128±24	128±23	131±23	128±26	133±24
One-way ANOVA of log_{10} transformed data followed by Tukey's post test, multiplicity adjusted *P* values							
c-IgG vs. LZD	0.124	0.090	0.047	0.018	0.019	0.044	0.024
c-IgG vs. MEDI4893*	<0.001	0.001	<0.001	<0.001	<0.001	<0.001	<0.001
c-IgG vs. LZD + MEDI4893*	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
LZD vs. MEDI4893*	0.067	0.236	0.308	0.328	0.304	0.231	0.354
LZD vs. LZD + MEDI4893*	0.019	0.027	0.033	0.032	0.022	0.019	0.036
MEDI4893* vs. LZD + MEDI4893*	0.954	0.747	0.698	0.662	0.599	0.665	0.667