

Online Suppl. Table 1. Host-factors differentially regulate *saeR/S* targets

ID	Locus	Human PMNs	Human PMNs	α -Defensin	LL-37	H ₂ O ₂
		5 min	10 min	10 min	10 min	10 min
		USA300	USA300	USA300	USA300	USA300
SAUSA300_1992	<i>agrA</i>	0.61 +/- 0.4	0.86 +/- 0.16	0.92 +/- 0.12	0.93 +/- 0.04	1.21 +/- 0.06
SAUSA300_1308	<i>arlR</i>	0.76 +/- 0.23	0.59 +/- 0.01	0.97 +/- 0.01	0.79 +/- 0.04	1.09 +/- 0.2
SAUSA300_0835	<i>dltA</i>	1.3 +/- 0.79	0.56 +/- 0.13	1.12 +/- 0.08	1.28 +/- 0.2	1.08 +/- 0.31
SAUSA300_1058	<i>hla</i>	0.77 +/- 0.37	1.15 +/- 0.13	0.94 +/- 0.02	0.71 +/- 0.11	1.1 +/- 0.41
SAUSA300_2365	<i>hlgA</i>	24.65 +/- 12.98	71.86 +/- 19.15	17.32 +/- 5.23	0.69 +/- 0.09	1.05 +/- 0.17
SAUSA300_2366	<i>hlgB</i>	23.33 +/- 9.2	40.1 +/- 6.8	10.08 +/- 3.9	0.83 +/- 0.22	1.31 +/- 0.4
SAUSA300_2367	<i>hlgC</i>	7.08 +/- 1.11	14.39 +/- 3.19	7.51 +/- 2.5	0.7 +/- 0.14	1.03 +/- 0.16
SAUSA300_1974	<i>lukA</i>	4.35 +/- 2.96	17.59 +/- 0.28	4.46 +/- 0.66	0.78 +/- 0.55	1.03 +/- 0.59
SAUSA300_1768	<i>lukD</i>	0.58 +/- 0.34	0.75 +/- 0.14	0 +/- 0	0 +/- 0	0 +/- 0
SAUSA300_1381	<i>lukF-PVL</i>	0.7 +/- 0.13	0.94 +/- 0.23	1.53 +/- 0.11	0.88 +/- 0.07	1.12 +/- 0.23
SAUSA300_0032	<i>mecA</i>	0.73 +/- 0.25	0.68 +/- 0.03	0.91 +/- 0.08	0.97 +/- 0.1	1.16 +/- 0.11
SAUSA300_1708	<i>rot</i>	0.66 +/- 0.19	0.49 +/- 0.16	0.85 +/- 0.04	0.87 +/- 0.05	1 +/- 0.04
SAUSA300_0693	<i>saeP</i>	2.65 +/- 1.22	0.8 +/- 0.13	1.27 +/- 0.38	0.6 +/- 0.06	1.17 +/- 0.23
SAUSA300_0691	<i>saeR</i>	2 +/- 0.21	1.78 +/- 0.35	2.17 +/- 1.05	0.63 +/- 0.03	1.1 +/- 0.3
SAUSA300_0690	<i>saeS</i>	1.02 +/- 0.35	1.09 +/- 0.25	1.74 +/- 0.76	0.67 +/- 0.01	1.18 +/- 0.3
SAUSA300_2364	<i>sbi</i>	7.73 +/- 2.43	3.02 +/- 0.45	1.31 +/- 0.34	0.68 +/- 0.04	1.26 +/- 0.27
SAUSA300_1758	<i>splA</i>	0.86 +/- 0.12	1.59 +/- 0.75	1.96 +/- 0.31	0.85 +/- 0.03	1.13 +/- 0.28
SAUSA300_0401	<i>ssl7</i>	0.4 +/- 0.06	0.56 +/- 0.08	1.27 +/- 0.01	0.91 +/- 0.07	1.18 +/- 0.09

Gene expression in USA300 treated with the depicted stimulus was measured by QuantiGene 2.0 assays and normalized to *gyrB* transcript levels. Ratio of gene expression in stimulus-treated vs untreated *S. aureus* (time-matched) is shown as mean fold change +/- standard deviation of two separate experiments. 0 = Gene expression under limit of detection.

Online Suppl. Table 2. Host-factors differentially regulate *saeR/S* targets

ID	Locus	α -Defensin	Human PMNs	Mouse PMNs
		30 min	30 min	30 min
		USA300	USA300	USA300
SAUSA300_1992	<i>agrA</i>	1.23 +/- 0.28	0.38 +/- 0.01	1.03 +/- 0.47
SAUSA300_1308	<i>arlR</i>	1.58 +/- 0.46	0.4 +/- 0.08	0.92 +/- 0.2
SAUSA300_0835	<i>dltA</i>	2.16 +/- 0.64	0.36 +/- 0.1	0.6 +/- 0.12
SAUSA300_1058	<i>hla</i>	1.98 +/- 1.34	0.74 +/- 0.17	1.52 +/- 0.49
SAUSA300_2365	<i>hlgA</i>	61.41 +/- 19.07	103.94 +/- 28.11	187.88 +/- 25.04
SAUSA300_2366	<i>hlgB</i>	21.53 +/- 12.88	73.01 +/- 15.32	130.23 +/- 17.07
SAUSA300_2367	<i>hlgC</i>	12.04 +/- 7.41	35.06 +/- 3.57	72.6 +/- 10.73
SAUSA300_1974	<i>lukA</i>	24.03 +/- 16.01	1.7 +/- 0.01	4.06 +/- 0.55
SAUSA300_1768	<i>lukD</i>	0 +/- 0	0.71 +/- 0.02	1.16 +/- 0.13
SAUSA300_1381	<i>lukF-PVL</i>	3.74 +/- 0.21	1.82 +/- 0.46	1.37 +/- 0.14
SAUSA300_0032	<i>mecA</i>	1.33 +/- 0.33	0.63 +/- 0.04	1.03 +/- 0.19
SAUSA300_1708	<i>rot</i>	1.37 +/- 0.57	0.89 +/- 0.46	0.97 +/- 0.04
SAUSA300_0693	<i>saeP</i>	3.04 +/- 2.11	*	2.09 +/- 0.46
SAUSA300_0691	<i>saeR</i>	5.85 +/- 3.85	*	2.33 +/- 0.6
SAUSA300_0690	<i>saeS</i>	3.6 +/- 1.97	*	1.67 +/- 0.12
SAUSA300_2364	<i>sbi</i>	7.15 +/- 3.66	1.39 +/- 0.45	2.42 +/- 0.63
SAUSA300_1758	<i>splA</i>	3.82 +/- 2.38	1.52 +/- 0.95	2.43 +/- 0.1
SAUSA300_0401	<i>ssl7</i>	2.65 +/- 0.58	1.1 +/- 0.93	1.16 +/- 0.09

Gene expression in USA300 treated with the depicted stimulus was measured by QuantiGene 2.0 assays and normalized to *gyrB* transcript levels. Ratio of gene expression in stimulus-treated vs untreated *S. aureus* (time-matched) is shown as mean fold change +/- standard deviation of two separate experiments. 0 = Gene expression under the limit of detection; *Gene expression above limit of detection.

Online Suppl. Table 3. Skin environment promotes transcription of *saeR/S* targets

ID	Locus	USA300	USA300 Δ <i>saeR/S</i>	USA300 Δ <i>agr</i>
SAUSA300_1992	<i>agrA</i>	1.25 +/- 0.37	1.84 +/- 0.14	0 +/- 0
SAUSA300_1308	<i>arlR</i>	1.67 +/- 0.8	1.46 +/- 0.56	0.95 +/- 0.04
SAUSA300_0835	<i>dltA</i>	1.21 +/- 0.36	0.78 +/- 0.3	0.51 +/- 0.25
SAUSA300_1058	<i>hla</i>	6.4 +/- 4.19	0.79 +/- 1.11	5.08 +/- 1.44
SAUSA300_2365	<i>hlgA</i>	37.32 +/- 13.37	0.54 +/- 0.77	124.68 +/- 45.88
SAUSA300_2366	<i>hlgB</i>	18.39 +/- 2.14	0 +/- 0	115.78 +/- 6.72
SAUSA300_2367	<i>hlgC</i>	18.21 +/- 3.14	0.67 +/- 0.94	101.37 +/- 9.21
SAUSA300_1974	<i>lukA</i>	7.86 +/- 4.68	1.81 +/- 0.17	9.96 +/- 5.44
SAUSA300_1768	<i>lukD</i>	0 +/- 0	0 +/- 0	0 +/- 0
SAUSA300_1381	<i>lukF-PVL</i>	2.84 +/- 0.28	2.11 +/- 0.13	3.01 +/- 0.52
SAUSA300_0032	<i>mecA</i>	0.63 +/- 0.05	2.26 +/- 0.23	1.08 +/- 0.04
SAUSA300_1708	<i>rot</i>	3.45 +/- 0.46	2.82 +/- 1.38	0.47 +/- 0.17
SAUSA300_0693	<i>saeP</i>	1.52 +/- 0.18	3.12 +/- 1.85	4.13 +/- 1.1
SAUSA300_0691	<i>saeR</i>	1.35 +/- 0.63	0 +/- 0	2.36 +/- 0.52
SAUSA300_0690	<i>saeS</i>	1.28 +/- 0.26	0 +/- 0	1.99 +/- 0.23
SAUSA300_2364	<i>sbi</i>	0.82 +/- 0.37	0.4 +/- 0.57	2.14 +/- 0.23
SAUSA300_1758	<i>splA</i>	7.65 +/- 0.98	1.09 +/- 1.53	3.2 +/- 0.58
SAUSA300_0401	<i>ssl7</i>	3.95 +/- 1.67	2.5 +/- 0.93	6.41 +/- 4.24

Gene expression in USA300, USA300 Δ *saeR/S* and USA300 Δ *agr* was measured by QuantiGene 2.0 assays and normalized to *gyrB* transcript levels. Ratio of gene expression in strains from the skin abscess 8 hours post-infection vs bacteria grown at mid-exponential phase (strain-matched) is shown as mean fold change +/- standard deviation of two separate experiments. 0 = Gene expression under the limit of detection.