

Supplementary Materials: *Staphylococcus aureus* Pathogenicity in Cystic Fibrosis Patients—Results from an Observational Prospective Multicenter Study Concerning Virulence Genes, Phylogeny, and Gene Plasticity

Jonas Lange, Kathrin Heidenreich, Katharina Higelin, Kristina Dyck, Vanessa Marx, Christian Reichel, Willem van Wamel, Martijn den Reijer, Dennis Goerlich and Barbara C. Kahl

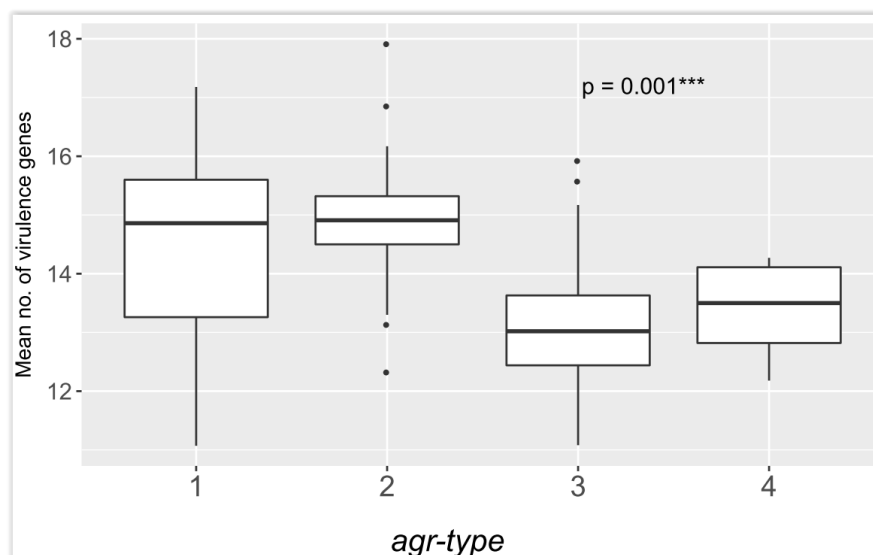


Figure S1. *Agr*-type vs. virulence gene count.

Table S1. *Spa*-types detected among the 3180 *S. aureus* isolates.

Number of <i>spa</i> -Types	<i>Spa</i> -Type	Frequency	Percent	Valid Percent	Cumulative Percent
	n.t.	6	0.2	0.2	0.2
1	t002	85	2.7	2.7	2.9
2	t003	21	0.7	0.7	3.5
3	t004	13	0.4	0.4	3.9
4	t005	29	0.9	0.9	4.8
5	t006	12	0.4	0.4	5.2
6	t008	117	3.7	3.7	8.9
7	t009	8	0.3	0.3	9.2
8	t010	2	0.1	0.1	9.2
9	t011	11	0.3	0.3	9.6
10	t012	149	4.7	4.7	14.2
11	t015	100	3.1	3.1	17.4
12	t017	15	0.5	0.5	17.9
13	t018	41	1.3	1.3	19.2
14	t019	21	0.7	0.7	19.8
15	t021	48	1.5	1.5	21.3
16	t022	13	0.4	0.4	21.7
17	t024	26	0.8	0.8	22.5

18	t026	61	1.9	1.9	24.5
19	t034	21	0.7	0.7	25.1
20	t040	4	0.1	0.1	25.3
21	t044	12	0.4	0.4	25.6
22	t045	5	0.2	0.2	25.8
23	t050	51	1.6	1.6	27.4
24	t056	60	1.9	1.9	29.3
25	t065	44	1.4	1.4	30.7
26	t068	1	0.0	0.0	30.7
27	t073	11	0.3	0.3	31.0
28	t076	1	0.0	0.0	31.1
29	t078	62	1.9	1.9	33.0
30	t081	22	0.7	0.7	33.7
31	t084	241	7.6	7.6	41.3
32	t085	11	0.3	0.3	41.6
33	t091	137	4.3	4.3	45.9
34	t094	4	0.1	0.1	46.1
35	t099	1	0.0	0.0	46.1
36	t100	8	0.3	0.3	46.4
37	t103	1	0.0	0.0	46.4
38	t105	4	0.1	0.1	46.5
39	t1050	19	0.6	0.6	47.1
40	t1057	2	0.1	0.1	47.2
41	t10605	6	0.2	0.2	47.4
42	t10606	2	0.1	0.1	47.4
43	t1070	2	0.1	0.1	47.5
44	t108	3	0.1	0.1	47.6
45	t116	18	0.6	0.6	48.1
46	t1201	1	0.0	0.0	48.2
47	t1203	3	0.1	0.1	48.3
48	t1211	24	0.8	0.8	49.0
49	t122	36	1.1	1.1	50.2
50	t1245	2	0.1	0.1	50.2
51	t1259	2	0.1	0.1	50.3
52	t12674	7	0.2	0.2	50.5
53	t12678	1	0.0	0.0	50.5
54	t12679	4	0.1	0.1	50.7
55	t12680	2	0.1	0.1	50.7
56	t12681	1	0.0	0.0	50.8
57	t127	37	1.2	1.2	51.9
58	t129	11	0.3	0.3	52.3
59	t1333	4	0.1	0.1	52.4
60	t1345	1	0.0	0.0	52.4
61	t136	8	0.3	0.3	52.7
62	t138	1	0.0	0.0	52.7
63	t1406	2	0.1	0.1	52.8
64	t1416	2	0.1	0.1	52.8
65	t144	7	0.2	0.2	53.1
66	t1451	28	0.9	0.9	53.9

67	t1491	1	0.0	0.0	54.0
68	t1492	2	0.1	0.1	54.0
69	t150	4	0.1	0.1	54.2
70	t1510	14	0.4	0.4	54.6
71	t153	14	0.4	0.4	55.0
72	t1541	1	0.0	0.0	55.1
73	t1544	1	0.0	0.0	55.1
74	t156	6	0.2	0.2	55.3
75	t1574	1	0.0	0.0	55.3
76	t1577	23	0.7	0.7	56.0
77	t159	33	1.0	1.0	57.1
78	t162	1	0.0	0.0	57.1
79	t164	5	0.2	0.2	57.3
80	t1652	8	0.3	0.3	57.5
81	t166	38	1.2	1.2	58.7
82	t1670	9	0.3	0.3	59.0
83	t1671	6	0.2	0.2	59.2
84	t1685	2	0.1	0.1	59.2
85	t1689	2	0.1	0.1	59.3
86	t169	1	0.0	0.0	59.3
87	t1707	7	0.2	0.2	59.6
88	t1709	1	0.0	0.0	59.6
89	t179	12	0.4	0.4	60.0
90	t185	17	0.5	0.5	60.5
91	t1858	2	0.1	0.1	60.6
92	t186	4	0.1	0.1	60.7
93	t189	11	0.3	0.3	61.0
94	t190	17	0.5	0.5	61.6
95	t193	2	0.1	0.1	61.6
96	t1978	13	0.4	0.4	62.0
97	t1991	20	0.6	0.6	62.7
98	t2065	3	0.1	0.1	62.8
99	t2080	21	0.7	0.7	63.4
100	t209	42	1.3	1.3	64.7
101	t211	16	0.5	0.5	65.3
102	t2133	2	0.1	0.1	65.3
103	t2164	5	0.2	0.2	65.5
104	t223	2	0.1	0.1	65.5
105	t227	1	0.0	0.0	65.6
106	t2275	1	0.0	0.0	65.6
107	t228	1	0.0	0.0	65.6
108	t230	2	0.1	0.1	65.7
109	t2309	1	0.0	0.0	65.7
110	t2351	1	0.0	0.0	65.8
111	t2375	1	0.0	0.0	65.8
112	t2383	20	0.6	0.6	66.4
113	t2398	4	0.1	0.1	66.5
114	t240	10	0.3	0.3	66.9
115	t2419	3	0.1	0.1	66.9

116	t2439	21	0.7	0.7	67.6
117	t2441	24	0.8	0.8	68.4
118	t246	2	0.1	0.1	68.4
119	t2509	17	0.5	0.5	69.0
120	t254	16	0.5	0.5	69.5
121	t2553	3	0.1	0.1	69.6
122	t258	11	0.3	0.3	69.9
123	t2666	8	0.3	0.3	70.2
124	t272	11	0.3	0.3	70.5
125	t275	5	0.2	0.2	70.7
126	t277	1	0.0	0.0	70.7
127	t2787	14	0.4	0.4	71.1
128	t279	16	0.5	0.5	71.6
129	t2802	16	0.5	0.5	72.1
130	t284	10	0.3	0.3	72.5
131	t2845	12	0.4	0.4	72.8
132	t289	1	0.0	0.0	72.9
133	t2919	4	0.1	0.1	73.0
134	t2949	1	0.0	0.0	73.0
135	t295	1	0.0	0.0	73.1
136	t3012	1	0.0	0.0	73.1
137	t304	4	0.1	0.1	73.2
138	t306	23	0.7	0.7	73.9
139	t308	3	0.1	0.1	74.0
140	t3258	1	0.0	0.0	74.1
141	t330	8	0.3	0.3	74.3
142	t331	18	0.6	0.6	74.9
143	t3331	2	0.1	0.1	74.9
144	t338	16	0.5	0.5	75.4
145	t346	56	1.8	1.8	77.2
146	t352	1	0.0	0.0	77.2
147	t359	12	0.4	0.4	77.6
148	t362	21	0.7	0.7	78.3
149	t363	1	0.0	0.0	78.3
150	t364	3	0.1	0.1	78.4
151	t3667	1	0.0	0.0	78.4
152	t370	2	0.1	0.1	78.5
153	t3745	14	0.4	0.4	78.9
154	t377	1	0.0	0.0	79.0
155	t390	2	0.1	0.1	79.0
156	t393	3	0.1	0.1	79.1
157	t3933	6	0.2	0.2	79.3
158	t394	7	0.2	0.2	79.5
159	t4069	1	0.0	0.0	79.6
160	t4096	1	0.0	0.0	79.6
161	t4228	2	0.1	0.1	79.7
162	t4325	17	0.5	0.5	80.2
163	t435	2	0.1	0.1	80.3
164	t4451	8	0.3	0.3	80.5

165	t447	4	0.1	0.1	80.6
166	t449	10	0.3	0.3	80.9
167	t4570	1	0.0	0.0	81.0
168	t466	1	0.0	0.0	81.0
169	t4870	1	0.0	0.0	81.0
170	t488	1	0.0	0.0	81.1
171	t491	6	0.2	0.2	81.3
172	t493	2	0.1	0.1	81.3
173	t4989	31	1.0	1.0	82.3
174	t499	14	0.4	0.4	82.7
175	t505	16	0.5	0.5	83.2
176	t5088	5	0.2	0.2	83.4
177	t509	6	0.2	0.2	83.6
178	t514	16	0.5	0.5	84.1
179	t5152	8	0.3	0.3	84.3
180	t5154	2	0.1	0.1	84.4
181	t521	3	0.1	0.1	84.5
182	t5210	2	0.1	0.1	84.6
183	t524	3	0.1	0.1	84.7
184	t5306	1	0.0	0.0	84.7
185	t539	8	0.3	0.3	84.9
186	t5430	13	0.4	0.4	85.3
187	t548	46	1.4	1.4	86.8
188	t550	4	0.1	0.1	86.9
189	t5520	1	0.0	0.0	86.9
190	t559	9	0.3	0.3	87.2
191	t5682	6	0.2	0.2	87.4
192	t5683	10	0.3	0.3	87.7
193	t5684	1	0.0	0.0	87.8
194	t5685	1	0.0	0.0	87.8
195	t5686	1	0.0	0.0	87.8
196	t5687	1	0.0	0.0	87.9
197	t5688	1	0.0	0.0	87.9
198	t5689	4	0.1	0.1	88.0
199	t5690	7	0.2	0.2	88.2
200	t571	25	0.8	0.8	89.0
201	t5721	3	0.1	0.1	89.1
202	t5758	3	0.1	0.1	89.2
203	t5759	10	0.3	0.3	89.5
204	t5760	4	0.1	0.1	89.7
205	t5761	1	0.0	0.0	89.7
206	t5775	1	0.0	0.0	89.7
207	t589	14	0.4	0.4	90.2
208	t5894	1	0.0	0.0	90.2
209	t591	11	0.3	0.3	90.5
210	t605	12	0.4	0.4	90.9
211	t617	6	0.2	0.2	91.1
212	t6172	1	0.0	0.0	91.1
213	t6191	1	0.0	0.0	91.2

214	t6192	1	0.0	0.0	91.2
215	t6193	9	0.3	0.3	91.5
216	t6194	8	0.3	0.3	91.7
217	t6195	5	0.2	0.2	91.9
218	t630	16	0.5	0.5	92.4
219	t6372	20	0.6	0.6	93.0
220	t6373	1	0.0	0.0	93.1
221	t6374	7	0.2	0.2	93.3
222	t6375	1	0.0	0.0	93.3
223	t6376	1	0.0	0.0	93.3
224	t645	3	0.1	0.1	93.4
225	t647	5	0.2	0.2	93.6
226	t676	10	0.3	0.3	93.9
227	t6762	2	0.1	0.1	94.0
228	t6763	1	0.0	0.0	94.0
229	t681	1	0.0	0.0	94.0
230	t686	1	0.0	0.0	94.1
231	t688	2	0.1	0.1	94.1
232	t693	5	0.2	0.2	94.3
233	t701	14	0.4	0.4	94.7
234	t7064	3	0.1	0.1	94.8
235	t7065	2	0.1	0.1	94.9
236	t7066	8	0.3	0.3	95.1
237	t7067	23	0.7	0.7	95.8
238	t712	4	0.1	0.1	96.0
239	t7170	1	0.0	0.0	96.0
240	t7267	1	0.0	0.0	96.0
241	t7271	2	0.1	0.1	96.1
242	t7272	1	0.0	0.0	96.1
243	t728	12	0.4	0.4	96.5
244	t746	1	0.0	0.0	96.5
245	t774	25	0.8	0.8	97.3
246	t779	1	0.0	0.0	97.4
247	t790	8	0.3	0.3	97.6
248	t796	1	0.0	0.0	97.6
249	t8027	1	0.0	0.0	97.7
250	t803	1	0.0	0.0	97.7
251	t837	4	0.1	0.1	97.8
252	t840	8	0.3	0.3	98.1
253	t884	5	0.2	0.2	98.2
254	t891	8	0.3	0.3	98.5
255	t909	1	0.0	0.0	98.5
256	t930	16	0.5	0.5	99.0
257	t950	3	0.1	0.1	99.1
258	t9883	1	0.0	0.0	99.2
259	t9884	10	0.3	0.3	99.5
260	t9886	7	0.2	0.2	99.7
261	t9887	1	0.0	0.0	99.7
262	t9888	1	0.0	0.0	99.7

263	t9889	1	0.0	0.0	99.8
264	t9894	5	0.2	0.2	99.9
265	t9896	1	0.0	0.0	100.0
266	t9897	1	0.0	0.0	100.0
Total		3180	100.0	100.0	

Table S2. Most prevalent *spa*-types among the 3180 isolates.

<i>Spa</i> -Type	Number of Isolates	Prevalence
t084	182	7.2%
t012	111	4.4%
t091	110	4.3%
t008	91	3.6%
t015	83	3.3%
t002	63	2.5%

Table S3. IgG levels against *S. aureus* antigens in patients vs. healthy controls and estimated effect on FEV₁%.

Antigen	Mean IgG Level All Patients ($\pm$ SE) ^a	Mean IgG Level Controls ($\pm$ SE) ^a	<i>p</i> Value ^{b,c}	Estimated Effect on FEV ₁ % ^d	<i>p</i> Value ^c
CHIPS	11492 ($\pm$ 220)	11019 ($\pm$ 349)	0.104	−0.00073	0.0185
ClfA	5168 ($\pm$ 237)	4302 ($\pm$ 436)	0.081	0.000514	0.1104
ClfB	4587 ($\pm$ 222)	4092 ($\pm$ 338)	0.3809	0.002079	<0.0001
ETA	3999 ($\pm$ 447)	2043 ($\pm$ 424)	0.1180	−0.00061	0.0033
ETB	613 ($\pm$ 113)	320 ($\pm$ 94)	0.0032	−0.00700	<0.0001
FnbpA	2922 ($\pm$ 201)	2534 ($\pm$ 300)	0.6167	0.000222	0.6310
FnbpB	967 ($\pm$ 79)	1327 ($\pm$ 215)	0.1306	−0.00199	0.1150
HIgB	13621 ($\pm$ 174)	9878 ($\pm$ 407)	<0.0001	−0.00109	0.0088
LukF	4079 ($\pm$ 133)	2718 ($\pm$ 243)	<0.0001	−0.00305	<0.0001
LukS	14097 ($\pm$ 133)	7134 ($\pm$ 524)	<0.0001	−0.00169	<0.0001
SasG	569 ($\pm$ 70)	636 ($\pm$ 132)	0.1847	0.001484	0.1590
SdrD	1084 ($\pm$ 80)	694 ($\pm$ 76)	0.0507	−0.00145	0.1950
SdrE	3139 ($\pm$ 201)	1992 ($\pm$ 221)	0.0253	−0.00179	<0.0001
SEA	3835 ($\pm$ 320)	3613 ($\pm$ 425)	0.2544	−0.00007	0.7599
SEC	7390 ($\pm$ 441)	8714 ($\pm$ 809)	0.1350	0.000269	0.1366
SED	1106 ($\pm$ 118)	1292 ($\pm$ 268)	0.0498	0.001490	0.0377
SEE	1333 ($\pm$ 183)	879 ($\pm$ 136)	0.8113	−0.00057	0.2779
SEG	2047 ($\pm$ 184)	1225 ($\pm$ 270)	0.0544	−0.00108	0.0264
SEH	2290 ($\pm$ 291)	2174 ($\pm$ 359)	0.0113	−0.00047	0.0986
TSST1	7981 ($\pm$ 487)	9076 ($\pm$ 646)	0.499	0.000148	0.3554

^a Significant difference of results between 182 patients and 53 healthy controls; ^b *p* values of difference between patient and controls groups (Mann–Whitney U test); ^c adjusted *p*-values (Bonferroni correction); and ^d IgG levels are modelled as continuous factors. Estimated effects are therefore interpreted as mean change in FEV₁% predicted.

Table S4 Primers for single and multiplex PCRs.

Virulence Gene	Primer	Sequence (5'–3')	Reference
<i>chp</i>	<i>chp</i> forward	TTTACTTTTGAACCGTTTCCTAC	[1]
	<i>chp</i> reverse	CGTCCTGAATTCTTAGTATGCATATTCATTAG	
<i>clf A</i>	<i>clfA</i> forward	ATGGGACAACGAAGTAGCA	[2]
	<i>clfA</i> reverse	GCTTCATCTTCAGAACCTG	
<i>clf B</i>	<i>clfB</i> forward	GTTATGGTGGTGGAAAGTGCTG	[2]
	<i>clfB</i> reverse	CGCTCTTATCTCCTGTTTCTGG	
<i>fnb A</i>	<i>fnbAB</i> forward	TAGGAACTGAAAATGGTCAC	[2]
	<i>fnbA</i> reverse	GAAGCAATCAGAAAACACTC	
<i>fnb B</i>	<i>fnbAB</i> forward	TAGGAACTGAAAATGGTCAC	[2]
	<i>fnbB</i> reverse	GAGTATGTAATTATTTCTTGG	
<i>sdr C</i>	<i>sdrC</i> forward	ACGACTATTAACCAAGAAC	[3]
	<i>sdrC</i> reverse	GTACTTGAAATAAGCGGTTG	
<i>sdr D</i>	<i>sdrD</i> forward	GGAAATAAAGTTGAAGTTTC	[3]
	<i>sdrD</i> reverse	ACTTTGTCATCAACTGTAAT	
<i>sdr E</i>	<i>sdrE</i> forward	CAGTAAATGTGTCAAAAGA	[3]
	<i>sdrE</i> reverse	TTGACTACCAGCTATATC	
<i>cna</i>	<i>cna</i> forward	AGTGGTTACTAATACTG	[3]
	<i>cna</i> reverse	CAGGATAGATTGGTTTA	
<i>cap</i>	<i>cap5</i> forward	GAAAGTGAACGATTAGTAGAA	[4]
	<i>cap5</i> reverse	GTACGAAGCGTTTTGATAGTT	
	<i>cap8</i> forward	GTGGGATTTTTGTAGCTTTT	
	<i>cap8</i> reverse	CGCCTCGCTATATGAACTAT	
<i>sas G</i>	<i>sasG</i> forward	GGGAACTCAACAAGAGGCAG	[5]
	<i>sasG</i> reverse	CAGAACGAGCTTTTCTAACC	
<i>sas H</i>	<i>sasH</i> forward	GTGTAATGGGATTATGGCAAG	[5]
	<i>sasH</i> reverse	CGTTGCTGTGTGAGTTGG	
<i>sea</i>	<i>sea-3</i> forward	CCTTTGGAAACGGTTAAAACG	[6]
	<i>sea-4</i> reverse	TCTGAACCTTCCCATCAAAAAC	
<i>seb</i>	<i>seb-1</i> forward	TCGCATCAAACTGACAAACG	[6]
	<i>seb-4</i> reverse	GCAGGTACTCTATAAGTGCCTGC	
<i>sec</i>	<i>sec-3</i> forward	CTCAAGAACTAGACATAAAAGCTAGG	[6]
	<i>sec-4</i> reverse	TCAAAATCGGATTAACATTATCC	
<i>sed</i>	<i>sed-3</i> forward	CTAGTTTGGTAATATCTCCTTTAAACG	[6]
	<i>sed-4</i> reverse	TTAATGCTATATCTTATAGGGTAAACATC	
<i>see</i>	<i>see-2</i> forward	TAACCTACCGTGGACCCTTC	[6]
	<i>see-3</i> reverse	CAGTACCTATAGATAAAGTTAAAACAAGC	
<i>eta</i>	<i>eta-3</i> forward	CTAGTGCATTTGTTATTCAAGACG	[6]
	<i>eta-4</i> reverse	TGCATTGACACCATAGTACTTATTC	
<i>etb</i>	<i>etb-3</i> forward	ACGGCTATATACATTCAATTCAATG	[6]
	<i>etb-4</i> reverse	AAAGTTATTCAATTAATGCACTGTCTC	
<i>tst</i>	<i>tst-3</i> forward	AAGCCCTTTGTTGCTTGCG	[6]
	<i>tst-6</i> reverse	ATCGAACTTTGGCCCATACTTT	
<i>seg</i>	<i>seg-1</i> forward	AATGCTCAACCCGATCCTA	[7]
	<i>seg-4</i> reverse	CTTCCTTCAACAGGTGGAGAC	

seh	<i>seh</i> -1 forward	TTAGAAATCAAGGTGATAGTGGC	[7]
	<i>seh</i> -2 reverse	TTTTGAATACCATCTACCCAAAC	
sei	<i>sei</i> -1 forward	GCCACTTTATCAGGACAATACTT	[7]
	<i>sei</i> -2 reverse	AAAACCTTACAGGCAGTCCATCTC	
sej	<i>sej</i> -1 forward	CTCCCTGACGTTAACTACTAATAA	[7]
	<i>sej</i> -2 reverse	TTGTCTGGATATTGACCTATAACATT	
agr	<i>agr</i> SA-KON1 forward	ATGCACATGGTGCACATGC	[8]
	<i>agr</i> SA1-2 reverse	GTCACAAGTACTATAAGCTGCGAT	
	<i>agr</i> SA2-2 reverse	TATTACTAATTGAAAAGTGCCATAGC	
	<i>agr</i> SA3-2 reverse	GTAATGTAATAGCTTGTATAATAATACCCAG	
	<i>agr</i> SA4-2 reverse	CGATAATGCCGTAATACCCG	
pvl	<i>pvl</i> -1 forward	ATCATTAGGTAAAATGTCTGGACATGATCCA	[9]
	<i>pvl</i> -2 reverse	GCATCAASTGTATTGGATAGCAAAAAGC	
hlg	<i>hlg</i> -1 forward	GCCAATCCGTTATTAGAAAATGC	[9]
	<i>hlg</i> -2 reverse	CCATAGAAGTAGCAACGGAT	
eap	<i>eap</i> -CON1 forward	TACTAACGAAGCATCTGCC	[10]
	<i>eap</i> -CON2 reverse	TTAAATCGATATCACTAATAACCTC	
emp	<i>emp</i> -1 forward	AATAATCGCGTGAATGTAG	[11]
	<i>emp</i> -2 reverse	CGTAGTAATGAAGTGGTGGT	

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