Supplementary File

Network analysis for identifying potential anti-virulence targets from whole transcriptome of *Pseudomonas aeruginosa* and *Staphylococcus aureus* exposed to certain anti-pathogenic polyherbal formulations

Feny Ruparel, Siddhi Shah, Jhanvi Patel, Nidhi Thakkar, Gemini Gajera, Vijay Kothari*

Institute of Science, Nirma University, Ahmedabad, India
***Correspondence:** vijay.kothari@nirmauni.ac.in

Table S1. List of down regulated genes in *Panchvalkal* exposed *P. aeruginosa* satisfying the dual criteria of log fold-change ≥2 and FDR≤0.01

No.	Feature ID/ Gene	Codes for	log fold change	FDR
1	PA0521	Nitric oxide reductase NorE protein	8.76	2.34E-10
2	PA4962	Inner membrane protein	8.40	0.0001
3	PA2182	Hypothetical protein	7.75	0.001
4	PA2607	tRNA 2-thiouridine synthesizing protein B	6.75	0.003
5	PA2980	Hypothetical protein	5.88	7.77E-05
6	*norB*	Nitric oxide reductase subunit B	5.44	0
7	*norC*	Nitric oxide reductase subunit B	5.04	0
8	PA1827	3-oxoacyl-[acyl-carrier protein] reductase	4.52	3.77E-06
9	PA1013.1	tRNA-Ser	4.50	0.002
10	*atuE*	Isohexenylglutaconyl-CoA hydratase	4.50	0.009
11	PA1492	Hypothetical protein	4.20	0.001
12	PA2085	Ring-hydroxylating dioxygenase small subunit	4.16	0.01
13	*nosL*	Copper chaperone NosL	4.15	1.82E-05
14	PA0525	Nitric oxide reductase NorD protein	4.14	0
15	PA5071	16S ribosomal RNA methyltransferase RsmE	3.57	0.001
16	PA2146	Hypothetical protein	3.53	0.001
17	*nosY*	Cu-processing system permease protein	3.46	0.002
18	PA3377	Alpha-D-ribose 1-methylphosphonate 5-phosphate C-P lyase	3.45	0.0002
19	PA1211	Hypothetical protein	3.40	0.01
20	PA0818	Hypothetical protein	3.30	0.004
21	PA3033	Hypothetical protein	3.25	0.0005
22	*kynB*	Arylformamidase (kynurenine formamidase)	3.15	0.0001
23	PA5196	Hypothetical protein	3.14	0.005
24	PA5181.1	P34	3.11	0.001
25	*nuoI*	NADH-quinone oxidoreductase subunit I	3.08	2.73E-08
26	PA4702	Hypothetical protein	3.04	1.11E-09
27	*algE*	Alginate production protein	3.00	0.003
28	PA0526	Hypothetical protein	2.95	0
29	PA2180	Hypothetical protein	2.94	0.004
30	*nirQ*	Nitric oxide reductase NorQ protein	2.91	0
31	PA3493	Electron transport complex protein RnfG |	2.80	3.64E-05
32	*nirS*	Heme d1 biosynthesis protein	2.78	0
33	*infA*	Translation initiation factor IF-1	2.73	4.90E-06
34	PA1879	Hypothetical protein	2.71	1.94E-05

No.	**Feature ID/ Gene**	**Codes for**	**log fold change**	**FDR**
35	PA0270	Hypothetical protein	2.70	0.002
36	PA4466	Phosphoryl carrier protein	2.68	9.20E-06
37	PA0806	Hypothetical protein	2.68	0.006
38	*rluA*	Ribosomal large subunit pseudouridine synthase A	2.66	0.001
39	PA2506	Hypothetical protein	2.66	0.01
40	*lldD*	L-lactate dehydrogenase	2.65	4.74E-05
41	PA2570.1	tRNA-Leu	2.63	0.008
42	PA2433	Hypothetical protein	2.62	1.35E-09
43	*pcaC*	4-carboxymuconolactone decarboxylase	2.62	0.001
44	*pilE*	Type IV pilus assembly protein	2.62	0.001
45	PA2754a	Hypothetical protein	2.59	0.005
46	PA0682	HxcX atypical pseudopilin	2.55	0.001
47	*pscL*	Type III secretion protein L	2.55	0.01
48	PA2602	Hypothetical protein	2.54	0.006
49	*pcaH*	Protocatechuate 3,4-dioxygenase	2.54	0.006
50	PA3580	Cys-tRNA(Pro)/Cys-tRNA(Cys) deacylase	2.48	5.39E-09
51	PA5535	Hypothetical protein	2.44	3.13E-08
52	PA0179	Two-component system, chemotaxis family, response regulator CheY	2.43	5.44E-06
53	PA1312	Transcriptional regulator	2.42	0.0005
54	PA0431	Hypothetical protein	2.42	0.005
55	PA2039	Hypothetical protein	2.42	0.01
56	PA5115	Hypothetical protein	2.40	0.005
57	*gntR*	Transcriptional regulator GntR	2.37	4.44E-16
58	PA2162	(1->4)-alpha-D-glucan 1-alpha-D-glucosylmutase	2.37	1.51E-05
59	PA3274	Hypothetical protein	2.36	9.66E-05
60	PA3275	Small multidrug resistance family-3 protein	2.36	0.001
61	PA2150	DNA end-binding protein Ku	2.35	0.0006
62	*narH*	Respiratory nitrate reductase beta chain	2.34	2.12E-05
63	PA2136	Hypothetical protein	2.33	0.0003
64	*nadE*	NH3-dependent NAD synthetase	2.32	0.004
65	PA4171	Protease I	2.31	0.003
66	PA0924	Hypothetical protein	2.29	1.81E-09
67	PA3880	Hypothetical protein	2.28	0.0007
68	PA0544	Hypothetical protein	2.27	2.71E-08
69	PA3450	Antioxidant protein	2.25	0.006
70	PA0522	Hypothetical protein	2.25	0.01
71	PA0952	Hypothetical protein	2.20	7.23E-05
72	PA5155	Polar amino acid transport system permease protein	2.20	0.01
73	PA0830	Hypothetical protein	2.19	2.18E-14
74	PA1093	Flagellar protein FlaG	2.19	0.008551
75	PA4064	Putative ABC transport system ATP-binding protein	2.18	0.007
76	*cueR*	Copper efflux regulator	2.15	0.0002
77	PA0942	Transcriptional regulator	2.14	0
78	PA0515	Heme d1 biosynthesis protein NirD	2.14	8.23E-05
79	PA1020	Acyl-CoA dehydrogenase	2.14	0.007
80	PA4921	Hypothetical protein	2.12	0.0001
81	PA1763	Hypothetical protein	2.12	0.001
82	*glpD*	Glycerol-3-phosphate dehydrogenase	2.10	1.14E-12
83	PA0121	Hypothetical protein	2.10	2.00E-05

No.	**Feature ID/ Gene**	**Codes for**	**log fold change**	**FDR**
84	PA3172	Phosphoglycolate phosphatase	2.09	6.52E-05
85	PA3859	Phospholipase/carboxylesterase	2.09	0.0005
86	*moeA1*	Molybdopterin molybdotransferase	2.08	1.48E-06
87	*braZ*	Branched-chain amino acid:cation transporter	2.08	0.0002
88	PA0218	Transcriptional regulator	2.08	0.0003
89	PA3016	Hypothetical protein	2.08	0.0009
90	PA4357	Ferrous iron transport protein C	2.06	1.11E-12
91	PA3224	Hypothetical protein	2.06	6.11E-07
92	PA1221	Hypothetical protein	2.06	0.002
93	PA3459	Asparagine synthase	2.05	0
94	PA0665	Iron-sulfur cluster insertion protein	2.05	9.64E-12
95	PA0443	Nucleobase:cation symporter-1, NCS1 family	2.05	0.01
96	PA0828	Transcriptional regulator	2.04	0.0009
97	PA1015	Transcriptional regulator	2.04	0.004
98	PA3913	Putative protease	2.03	1.03E-05
99	PA1057	Multicomponent K+:H+ antiporter subunit E	2.03	0.01
100	*ohrR*	Transcriptional regulator	2.03	0.01
101	PA0177	Purine-binding chemotaxis protein CheW	2.03	0.01
102	PA3847	Hypothetical protein	2.03	0.01
103	PA1470	3-oxoacyl-[acyl-carrier protein] reductase	2.02	0.003
104	PA0911	Hypothetical protein	2.02	0.01
105	PA3070	MoxR-like ATPase	2.01	5.10E-07

Genes are arranged in decreasing order of Fold Change.

Table S2. Node degree score of the genes mentioned in Table S1

No.	Gene ID/ Symbol	Identifier	Node degree
1	*nirS*	208964.PA0519	11
2	*norB*	208964.PA0524	11
3	PA0525	208964.PA0525	10
4	*nirQ*	208964.PA0520	10
5	*norC*	208964.PA0523	10
6	*nosL*	208964.PA3396	10
7	PA0521	208964.PA0521	9
8	*nosY*	208964.PA3395	9
9	PA3913	208964.PA3913	8
10	PA0515	208964.PA0515	6
11	PA0522	208964.PA0522	6
12	PA2146	208964.PA2146	6
13	*narH*	208964.PA3874	6
14	*anvM*	208964.PA3880	5
15	PA0177	208964.PA0177	3
16	PA1763	208964.PA1763	3
17	PA2180	208964.PA2180	3
18	PA3274	208964.PA3274	3
19	*ku*	208964.PA2150	3
20	*nadE*	208964.PA4920	3
21	PA0828	208964.PA0828	2
22	*algE*	208964.PA3544	2
23	*moeA1*	208964.PA3914	2
24	*nuoI*	208964.PA2644	2
25	*pcaH*	208964.PA0153	2
26	PA0179	208964.PA0179	1
27	PA0544	208964.PA0544	1
28	PA0682	208964.PA0682	1
29	PA0830	208964.PA0830	1
30	PA0924	208964.PA0924	1
31	PA0952	208964.PA0952	1
32	PA1015	208964.PA1015	1
33	PA1020	208964.PA1020	1
34	PA1211	208964.PA1211	1
35	PA1221	208964.PA1221	1
36	PA1470	208964.PA1470	1
37	PA1827	208964.PA1827	1
38	PA2136	208964.PA2136	1
39	PA2433	208964.PA2433	1
40	PA3016	208964.PA3016	1
41	PA3224	208964.PA3224	1
42	PA3450	208964.PA3450	1
43	PA3859	208964.PA3859	1
44	PA5071	208964.PA5071	1
45	*choE*	208964.PA4921	1
46	*erpA*	208964.PA0665	1
47	*glpD*	208964.PA3584	1
48	*infA*	208964.PA2619	1
49	*kynB*	208964.PA2081	1
50	*pcaC*	208964.PA0232	1
51	*pscL*	208964.PA1725	1
52	*rluA*	208964.PA3246	1

Rest 48 genes with node degree score ‘zero’ are not listed.

Table S3. Top ten cytoHubba ranked genes from among the top-13 in Table S2

No.	Gene ID	Gene Name	Number of methods ranking this protein among top 10	Names of 12 ranking methods of CytoHubba and rank score provided by them											
				Degree	MNC	DMNC	MCC	Bottleneck	EcCentricity	Closeness	Radiality	Betweenness	Stress	CC	EPC
1	PA0525	*norD*	12	10	10	0.71829	7200	2	0.325	11	1.35417	3.28571	18	0.8	5.793
2	PA0520	*nirQ*	12	10	10	0.71829	7200	1	0.325	11	1.35417	3.28571	18	0.8	5.68
3	PA3395	*nosY*	12	9	9	0.69213	5772	1	0.325	10.5	1.3	3.18571	14	0.80556	5.559
4	PA3396	*nosL*	11	10	10	0.63848	5784	3	0.325	11	1.35417	7.01905	26	-	5.69
5	PA0521	*norE*	11	9	9	0.73986	6480	-	0.325	10.5	1.3	1.66667	10	0.86111	5.492
6	PA0519	*nirS*	10	11	11	-	6498	2	0.325	11.5	1.48033	13.4	38	-	5.84
7	PA0524	*norB*	10	11	11	0.64479	7206	-	0.325	11.5	1.48033	9.11905	34	-	5.917
8	PA0523	*norC*	9	10	10	0.71829	7200	-	-	11	1.35417	3.28571	18	-	5.572
9	PA0522	Hypothetical protein	10	6	6	0.713237	720	1	0.325	9	1.1375			1	4.708
10	PA3913	*UbiU*	10	7	7	0.621988	726	-	-	9.5	1.191667	1.9	8	0.809524	4.88

"-": This method did not rank the shown protein among top 12.

MNC: Maximum Neighborhood Component; DMNC: Density of Maximum Neighborhood Component; MCC: Maximal Clique Centrality; CC: Clustering Co-efficient; EPC: Edge Percolated Component

TableS4. List of up regulated genes in *Panchvalkal* exposed *P. aeruginosa* satisfying the dual criteria of log fold-change ≥2 and FDR≤0.01

No.	Feature ID/Gene	Codes for	log fold change	FDR
1	*mexC*	Membrane fusion protein, multidrug efflux system	16.82	0
2	PA2139	Pseudogene	15	0.01
3	PA3441	Molybdopterin-binding protein	10	0.006
4	PA5328	Mono-heme cytochrome C	8	0.01
5	PA2161	Hypothetical protein	7.22	4.16E-06
6	*oprJ*	Outer membrane protein, multidrug efflux system	6.91	0
7	PA3383	Phosphonate transport system substrate-binding protein	6.33	0.0006
8	PA0700	Hypothetical protein	5.8	0.003
9	PA2565	Hypothetical protein	5.74	0
10	PA0909	Hypothetical protein	5.4	0.005
11	*napB*	Cytochrome c-type protein	5.26	1.12E-13
12	PA2090	Hypothetical protein	5.11	0.0004
13	*hpcD*	5-carboxymethyl-2-hydroxymuconate isomerase	4.8	0.01
14	PA2285	Hypothetical protein	4.8	1.55E-05
15	PA3566	Hypothetical protein	4.75	0.001
16	PA0695	Hypothetical protein	4.42	0.005
17	PA1107	Diguanylate cyclase	4.21	0
18	*mexD*	Multidrug efflux pump	4.15	0
19	PA2364	Type VI secretion system protein	4.03	1.29E-12
20	*coaB*	Phage coat protein B	4	0.01
21	PA3442	Sulfonate transport system ATP-binding protein	4	0.004
22	PA4866	Phosphinothricin acetyltransferase	4	0.002
23	PA1231	Hypothetical protein	3.93	0.0002
24	PA4172	Exodeoxyribonuclease III	3.93	5.00E-07
25	PA0640	Bacteriophage protein	3.55	1.84E-07
26	PA2499	Deaminase	3.53	0.002
27	PA1352	Hypothetical protein	3.51	1.34E-05
28	*ospR*	Transcriptional regulator	3.43	0
29	*cdhA*	Carnitine 3-dehydrogenase	3.42	0.002
30	PA4908	Ornithine cyclodeaminase	3.31	1.18E-06
31	PA5391	Hypothetical protein	3.21	0.0008
32	PA2307	NitT/TauT family transport system permease protein	3.18	8.69E-05
33	PA5135	Hypothetical protein	2.97	9.42E-06

No.	Feature ID/Gene	Codes for	log fold change	FDR
34	PA2933	large subunit ribosomal protein L6 (rplF; 50S ribosomal protein L6)	2.96	0.0004
35	PA3235	Hypothetical protein	2.96	1.62E-10
36	PA4290	Methyl-accepting chemotaxis protein	2.96	0
37	PA0384	Hypothetical protein	2.92	0.01
38	PA3287	Hypothetical protein	2.92	5.20E-14
39	PA0848	Peroxiredoxin (alkyl hydroperoxide reductase subunit C)	2.9	2.08E-09
40	PA1021	enoyl-CoA hydratase	2.88	0.0007
41	PA2916	Hypothetical protein	2.86	0.009
42	PA0638	Bacteriophage protein	2.84	8.11E-06
43	PA0633	Hypothetical protein	2.84	1.29E-10
44	*msuE*	FMN reductase	2.75	0.01
45	PA0623	Bacteriophage protein	2.74	9.84E-08
46	*soxG*	Sarcosine oxidase	2.73	0.002
47	PA0814	Hypothetical protein	2.71	0.01
48	PA2666	6-pyruvoyltetrahydropterin/6-carboxytetrahydropterin synthase	2.7	0.009
49	PA3431	Hypothetical protein	2.7	0.009
50	PA5431	GntR family transcriptional regulator	2.67	1.41E-08
51	PA0941	Hypothetical protein	2.66	0.01
52	PA3757	GntR family transcriptional regulator	2.64	0.01
53	PA2679	Hypothetical protein	2.61	0
54	PA1343	Bacteriophage protein	2.59	1.03E-08
55	*mraY*	Phospho-N-acetylmuramoyl-pentapeptide-transferase	2.59	1.92E-10
56	PA0622	Bacteriophage protein	2.59	3.12E-11
57	PA0185	Sulfonate transport system permease protein	2.55	1.45E-06
58	PA1260	Polar amino acid transport system substrate-binding protein	2.5	0.01
59	PA4596	Transcriptional regulator	2.5	3.21E-09
60	PA3606	DTW domain-containing protein	2.47	0.0001
61	PA1977	Hypothetical protein	2.47	1.73E-05
62	*hutU*	Urocanate hydratase	2.46	0
63	*mdcC*	Malonate decarboxylase delta subunit	2.45	0.009
64	*hasD*	ATP-binding cassette, subfamily C, bacterial exporter for protease/lipase	2.45	5.11E-08
65	*gloA2*	Lactoylglutathione lyase	2.44	0.01
66	*betT1*	Choline/glycine/proline betaine transport protein	2.44	0.0009
67	*pslK*	Polysaccharide biosynthesis protein PslK	2.44	2.46E-05

No.	Feature ID/Gene	Codes for	log fold change	FDR
68	PA2122	Hypothetical protein	2.43	0.0002
69	*ahpC*	Peroxiredoxin (alkyl hydroperoxide reductase subunit C)	2.43	0
70	PA3412	Hypothetical protein	2.42	0.01
71	PA3938	Taurine transport system substrate-binding protein	2.41	0.002
72	PA1038	Hypothetical protein	2.4	0.005
73	PA1958	Nicotinamide mononucleotide transporter	2.39	0.0004
74	PA5377	Glycine betaine/proline transport system permease protein	2.39	0.0002
75	PA4093	Hypothetical protein	2.37	0.009
76	PA1518	5-hydroxyisourate hydrolase	2.36	0.01
77	*ureD*	Urease accessory protein	2.35	0.003
78	PA0118	Hypothetical protein	2.33	0.01
79	*mtlD*	Mannitol 2-dehydrogenase	2.32	0.01
80	PA5033	Hypothetical protein	2.32	0.001
81	PA3453	Hypothetical protein	2.32	1.43E-07
82	PA2352	Glycerophosphoryl diester phosphodiesterase	2.3	0.0008
83	PA3534	Oxidoreductase	2.3	1.04E-06
84	PA0962	Starvation-inducible DNA-binding protein	2.28	4.83E-09
85	*hcnA*	Hydrogen cyanide synthase	2.27	0.01
86	*mobA*	Molybdenum cofactor guanylyltransferase	2.27	0.01
87	PA2111	Hypothetical protein	2.26	6.66E-16
88	PA1922	Outer membrane receptor for ferrienterochelin and colicins	2.25	0.01
89	PA4790	S-adenosylmethionine-dependent methyltransferase	2.25	0.006
90	PA0647	Hypothetical protein	2.25	0.001
91	PA4578	Hypothetical protein	2.25	6.67E-08
92	PA4280.5	16S ribosomal RNA	2.25	0
93	*acsA*	Acetyl-CoA synthetase	2.24	0
94	PA4508	Lrp/AsnC family transcriptional regulator, leucine-responsive regulatory protein	2.22	0.002
95	PA0098	3-oxoacyl-[acyl-carrier-protein] synthase I	2.21	0.003
96	PA4651	Fimbrial chaperone protein	2.19	0.001
97	*xcpT*	Type II secretion system protein G	2.17	0.002
98	PA2555	Acetyl-CoA synthetase	2.17	8.88E-16
99	PA0817	Hypothetical protein	2.16	0.01
100	PA2375	Hypothetical protein	2.15	0.003
101	*masA*	Enolase-phosphatase E1	2.15	2.30E-11
102	PA2826	Glutathione peroxidase	2.14	1.89E-07
103	PA5445	Succinyl-CoA:acetate CoA-transferas	2.13	4.02E-09
104	PA0630	Hypothetical protein	2.11	0.009

No.	Feature ID/Gene	Codes for	log fold change	FDR
105	*panD*	Aspartate 1-decarboxylase	2.1	0.006
106	PA0557	Hypothetical protein	2.1	0.0009
107	*cyoA*	Cytochrome o ubiquinol oxidase subunit II	2.09	0.003
108	PA0306	Transcriptional regulator	2.07	3.45E-05
109	*oprH*	oprH; PhoP/Q and low Mg2+ inducible outer membrane protein H1	2.06	0
110	PA2293	Hypothetical protein	2.05	0.007
111	PA3694	Hypothetical protein	2.05	0.007
112	PA3294	Type VI secretion system secreted protein VgrG	2.05	0.0002
113	*rpmD*	Large subunit ribosomal protein L30	2.05	4.80E-09
114	PA3289	Hypothetical protein	2.04	0.0009
115	PA5539	GTP cyclohydrolase I	2.03	0.01
116	PA0864	Transcriptional regulator	2.03	0.01
117	PA3420	Transcriptional regulator	2.03	2.15E-06
118	PA3568	Propionyl-CoA synthetase	2.03	2.01E-09
119	*ampDh3*	N-acetylmuramoyl-L-alanine amidase	2.02	0.008
120	PA3332	Hypothetical protein	2	0.01
121	PA3882	Hypothetical protein	2	0.006
122	PA4824	Hypothetical protein	2	0.002
123	PA4612	Hypothetical protein	2	4.55E-07

Genes are arranged in decreasing order of Fold Change.

Table S5. Node degree score of the genes mentioned in Table S4

No.	Gene ID / Symbol	Identifier	Node degree
1	PA0185	208964.PA0185	5
2	PA0630	208964.PA0630	5
3	PA3938	208964.PA3938	5
4	*ssuB1*	208964.PA3442	5
5	PA2090	208964.PA2090	4
6	PA3287	208964.PA3287	4
7	*acsA*	208964.PA0887	4
8	*ahpC*	208964.PA0139	4
9	*ampDh3*	208964.PA0807	4
10	*msuE*	208964.PA2357	4
11	*oprJ*	208964.PA4597	4
12	PA0622	208964.PA0622	3
13	PA0695	208964.PA0695	3
14	PA0817	208964.PA0817	3
15	PA0848	208964.PA0848	3
16	PA0909	208964.PA0909	3
17	PA2555	208964.PA2555	3
18	PA3383	208964.PA3383	3
19	PA3568	208964.PA3568	3
20	PA4596	208964.PA4596	3
21	PA4612	208964.PA4612	3
22	PA4824	208964.PA4824	3
23	PA5445	208964.PA5445	3
24	*mexC*	208964.PA4599	3
25	*mexD*	208964.PA4598	3
26	*oprH*	208964.PA1178	3
27	PA0557	208964.PA0557	2
28	PA0623	208964.PA0623	2
29	PA1107	208964.PA1107	2
30	PA1260	208964.PA1260	2
31	PA2307	208964.PA2307	2
32	PA2826	208964.PA2826	2
33	PA5539	208964.PA5539	2
34	*cdhA*	208964.PA5386	2
35	*hcnA*	208964.PA2193	2
36	*mdcC*	208964.PA0210	2
37	*napB*	208964.PA1173	2
38	PA0098	208964.PA0098	1

No.	**Gene ID / Symbol**	**Identifier**	**Node degree**
39	PA0633	208964.PA0633	1
40	PA0640	208964.PA0640	1
41	PA0700	208964.PA0700	1
42	PA1021	208964.PA1021	1
43	PA1343	208964.PA1343	1
44	PA1922	208964.PA1922	1
45	PA2139	208964.PA2139	1
46	PA2161	208964.PA2161	1
47	PA2285	208964.PA2285	1
48	PA2364	208964.PA2364	1
49	PA2375	208964.PA2375	1
50	PA2666	208964.PA2666	1
51	PA2679	208964.PA2679	1
52	PA3235	208964.PA3235	1
53	PA3420	208964.PA3420	1
54	PA3441	208964.PA3441	1
55	PA3694	208964.PA3694	1
56	PA3882	208964.PA3882	1
57	PA5328	208964.PA5328	1
58	*hutU*	208964.PA5100	1
59	*ospR*	208964.PA2825	1
60	*pitA*	208964.PA4866	1
61	*pslK*	208964.PA2241	1
62	*ureD*	208964.PA4864	1

Rest 58 genes with node degree score ‘zero’ are not listed.

Table S6. Top fourteen cytoHubba ranked genes from among the top-26 in Table S5

No.	**Gene ID**	**Gene Name**	**Number of methods ranking this protein among top 10**	**Names of 12 ranking methods of CytoHubba and rank score provided by them**											
				Degree	**MNC**	**DMNC**	**MCC**	**Bottleneck**	**EcCentricity**	**Closeness**	**Radiality**	**Betweenness**	**Stress**	**CC**	**EPC**
1	PA2357	*msuE, slfA*	11	4	3	0.46346	7	6	0.10256	5.333333	1.27473	9	18	-	5.113
2	PA3442	*ssub1*	10	4	4	0.47366	12	1	-	5.083333	1.18681	0.5	2	-	5.131
3	PA0185	*atsB*	9	4	4	0.47366	12	-	-	5.083333	1.18681	0.5	2	-	5.124
4	PA3938	*tauA*	8	4	-	-	7	2	-	5.333333	1.27473	9	18	-	5.101
5	PA4597	oprJ	11	4	3	0.46346	7	2	0.19231	4	0.52885	6	6	-	3.575
6	PA4599	mexC	11	3	3	0.46346	6	1	-	3.5	0.48077	0	0	1	3.436
7	PA0630		10	4	4	-	8	1	0.19231	4	0.52885	2	4	-	3.827
8	PA0807	ampDh3	10	4	4	-	8	2	0.19231	4	0.52885	2	4	-	3.835
9	PA2090		9	4	4	0.47366	12	-	-	5.083333	1.18681	0.5	2	-	5.094
10	PA3287		9	3		0.46346	6	1	-	-	-	0	0	1	3.456
11	PA4596		9	3	3	0.46346	6	1	-	3.5	0.48077	-	-	1	3.456
12	PA5445		9	3	3	0.46346	6	1	0.15385	-	-	0	0	1	-
13	PA2555		7	3	3	0.46346	6	1	0.15385	-	-	-	-	1	-
14	PA3383		7	-	-	-	-	3	0.153846	5	1.27473	20.5	34	-	4.629

"-": This method did not rank the shown protein among top 12.

MNC: Maximum Neighborhood Component; DMNC: Density of Maximum Neighborhood Component; MCC: Maximal Clique Centrality; CC: Clustering Co-efficient; EPC: Edge Percolated Component

Table S7. List of DEG in Herboheal-exposed *S. aureus* satisfying the dual criteria of log fold-change ≥2 and FDR≤0.01

No.	Feature ID/ Gene	Codes for	log fold change	FDR	Up- or down-regulation
1	*sarT*	HTH-type transcriptional regulator SarT	18.00	0.005	↑
2	SAFDA_1030	Alpha-hemolysin	17.35	0	↓
3	SAFDA_1326	Hypothetical protein	11.00	0.003	↓
4	SAFDA_0523	Hypothetical protein	10.00	0.006	↓
5	SAFDA_0033	Hypothetical protein	8.50	0.01	↑
6	*hlgA*	Gamma-hemolysin component A precursor	7.16	2.45E-14	↓
7	SAFDA_1218	Sensor histidine kinase	6.91	8.32E-07	↓
8	SAFDA_1829	Truncated beta-hemolysin	6.75	0.003	↓
9	SAFDA_0271	Pyrimidine nucleoside transporter (nupC)	6.16	2.27E-06	↑
10	SAFDA_1022	Fibrinogen binding-related protein	6.00	6.10E-05	↓
11	SAFDA_1441	Competence protein ComGA	6.00	0.007	↑
12	SAFDA_2337	Hypothetical protein	5.87	0	↓
13	*hlgB*	Gamma-hemolysin component B precursor	5.83	4.33E-15	↓
14	SAFDA_0231	Hypothetical protein	5.50	0.01	↑
15	SAFDA_1217	ABC transporter permease	5.44	0.0002	↓
16	*acuA*	Acetoin utilization protein	4.80	0.01	↓
17	*icaR*	Intercellular Adhesin Locus Regulator	4.80	0.01	↓
18	*ureA*	Urea catabolic process	4.80	0.01	↑
19	SAFDA_0372	Hypothetical protein	4.67	0.001	↓
20	SAFDA_1187	Hypothetical protein	4.60	0.007	↑
21	*saeP*	Auxillary protein	4.26	1.77E-07	↓
22	SAFDA_0127	Hypothetical protein	4.25	0.004	↑
23	SAFDA_2543	Hypothetical protein	4.13	2.77E-06	↑
24	*saeR*	two-component system, OmpR family, response regulator	4.10	1.68E-07	↓
25	SAFDA_0843	HAD superfamily hydrolase	4.00	0.0006	↓
26	*glpQ*	Glycerophosphoryldiesterphosphodiesterase	3.85	0.0009	↓
27	*dapB*	4-hydroxy-tetrahydrodipicolinate reductase	3.71	0.01	↓
28	*ureD*	urease accessory protein	3.66	6.33E-05	↑
29	SAFDA_1182	Phage repressor	3.64	0.004	↓

No.	Feature ID/ Gene	Codes for	log fold change	FDR	Up- or down-regulation
30	*hlgC*	Gamma-hemolysin component C precu	3.63	4.79E-08	↓
31	*modC*	molybdenum transport protein	3.57	1.41E-05	↑
32	SAFDA_1138	50S ribosomal protein L7	3.54	0.002	↓
33	*saeS*	Two-component system, OmpR family, sensor histidine kinase	3.47	3.31E-10	↓
34	*secG*	Preproteintranslocase subunit	3.44	0.001	↓
35	*splA*	Serine protease	3.44	0.001	↓
36	*sbi*	Immunoglobulin G-binding protein Sbi	3.43	1.02E-09	↓
37	SAFDA_0853	Hypothetical protein	3.38	0.003	↓
38	SAFDA_0003	S4 region YaaA family protein	3.33	0.002	↓
39	SAFDA_1229	Hypothetical protein	3.33	0.01	↓
40	*trpA*	Tryptophan synthase alpha chain	3.33	0.01	↑
41	SAFDA_1219	Two-component response regulator	3.26	6.13E-06	↓
42	SAFDA_0085	Hypothetical protein	3.22	0.001	↑
43	SAFDA_0794	Hypothetical protein	3.22	0.001	↑
44	SAFDA_0277	Hypothetical protein	3.18	0.002	↑
45	SAFDA_1494	HAD superfamily hydrolase	3.14	0.005	↓
46	SAFDA_1538	Hypothetical protein	3.13	0.004	↑
47	SAFDA_0193	Hypothetical protein	3.05	0	↓
48	SAFDA_0562	Hydrolase	2.93	0.007	↓
49	SAFDA_1410	Hypothetical protein	2.93	2.62E-07	↓
50	SAFDA_2187	Phosphosugar-binding transcriptional regulator	2.92	0.01	↑
51	SAFDA_t0025	tRNA-Cys	2.88	0.007	↓
52	*spsB*	signal peptidase I	2.88	0.007	↓
53	SAFDA_0228	Choloylglycine hydrolase	2.87	0.007	↑
54	*glpP*	Glycerol uptake operon antiterminator regulatory protein	2.85	0.01	↑
55	*lukG*	leukocidin/hemolysin toxin family protein	2.80	9.14E-06	↓
56	SAFDA_2043	Hypothetical protein	2.78	6.55E-10	↓
57	SAFDA_r0007	5S ribosomal RNA	2.71	0	↑
58	*coaE*	dephospho-CoA kinase	2.71	0.0008	↑
59	SAFDA_0232	Hypothetical protein	2.71	0.01	↑
60	*pnp*	Polyribonucleotide nucleotidyltransferase	2.71	4.39E-08	↑
61	SAFDA_2297	Hypothetical protein	2.66	0.01	↑
62	SAFDA_2405	MmpL efflux pump	2.66	9.41E-09	↑

No.	Feature ID/ Gene	Codes for	log fold change	FDR	Up- or down-regulation
63	SAFDA_0565	Alpha/beta fold family hydrolase	2.66	6.40E-11	↑
64	SAFDA_2223	ABC transporter permease	2.64	0.01	↑
65	SAFDA_0423	Orn Lys Arg decarboxylase family protein	2.63	1.62E-08	↑
66	SAFDA_2221	Hypothetical protein	2.63	0.008	↑
67	*tagX*	glycosyltransferase	2.58	0.002	↓
68	*sraP*	Serine-rich adhesin for platelets	2.55	7.48E-10	↑
69	SAFDA_2160	Transcription regulator	2.55	0.0003	↑
70	SAFDA_0932	Hypothetical protein	2.53	1.10E-05	↓
71	SAFDA_1828	Truncated cell surface protein map-w	2.52	7.00E-07	↓
72	*saeQ*	transmembrane protein	2.47	0.001	↓
73	*drm*	Phosphopentomutase	2.45	0	↑
74	SAFDA_0392	Cobalamin synthesis protein	2.45	0.01	↑
75	SAFDA_2310	Amino acid transporter	2.43	0.008	↑
76	SAFDA_2453	2-dehydropantoate 2-reductase	2.43	0.002	↑
77	*sarA*	Transcriptional regulator SarA	2.43	2.11E-07	↑
78	SAFDA_1135	Hypothetical protein	2.43	0.003	↓
79	*nreA*	NreA protein; GAF domain containing protein	2.41	0.005	↓
80	*gcvH*	Glycine cleavage system H protein	2.33	0.0004	↓
81	*sdaAB*	L-serine dehydratase	2.32	0.006	↓
82	*recQ_1*	ATP-dependent DNA helicase RecQ	2.32	4.68E-06	↑
83	SAFDA_2273	Polar amino acid ABC transporter ATPase	2.31	0.003	↓
84	*icaA*	intercellular adhesion (ica) locus	2.30	0.009	↑
85	SAFDA_0225	Ribose transcriptional repressor RbsR	2.28	0.001	↑
86	SAFDA_2537	Lipoprotein, putative	2.26	0.01	↑
87	*rpsO*	Small subunit ribosomal protein S15	2.26	9.03E-06	↓
88	SAFDA_1759	Sugar ABC transporter ATPase	2.26	2.72E-07	↓
89	SAFDA_0987	Hypothetical protein	2.25	0.009	↓
90	SAFDA_2261	Transcriptional regulator NirR	2.25	0.009	↓
91	SAFDA_0998	Iron-regulated heme-iron binding protein	2.25	0.001	↑
92	SAFDA_1045	HAD superfamily hydrolase	2.25	0.009	↑
93	*xerC*	Integrase/recombinase	2.24	0.005	↓
94	SAFDA_2230	Glycosylglycerophosphatetransferase involvedin teichoic acid biosynthesis	2.22	0.003	↑

No.	Feature ID/ Gene	Codes for	log fold change	FDR	Up- or down-regulation
95	*pheT*	Phenylalanine--tRNA ligase beta subunit	2.22	1.75E-07	↑
96	SAFDA_2057	Alcohol dehydrogenase	2.21	5.04E-08	↑
97	SAFDA_0091	Major facilitator transporter	2.21	6.48E-14	↑
98	*tcaB*	teicoplanin-associated operon	2.20	0.001	↑
99	*dra*	Deoxyribose phosphate aldolase	2.19	5.62E-11	↑
100	SAFDA_1716	Hypothetical protein	2.18	0.006	↓
101	*Dps*	General stress protein 20U	2.17	0	↓
102	SAFDA_2462	Hypothetical protein	2.14	0.007	↑
103	SAFDA_0189	ABC transporter substrate-binding protein	2.11	0.009	↑
104	*Geh*	Glycerol ester hydrolase	2.11	6.59E-06	↓
105	*rpoE*	Probable DNA-directed RNA polymerase subunit delta	2.10	0.001	↑
106	SAFDA_1657	Aesenical pump membrane protein	2.10	0.005	↑
107	*rpsB*	Small subunit ribosomal protein S2	2.09	3.60E-11	↓
108	SAFDA_2315	M42 glutamylaminopeptidase, cellulose	2.04	4.16E-10	↑
109	*ureC*	Urease subunit alpha	2.03	0.0008	↑
110	*mviM*	putative oxidoreductase	2.02	0.01	↑
111	SAFDA_1331	Major facilitator superfamily permease	2.02	0.01	↑
112	*dapA*	4-hydroxy-tetrahydrodipicolinate synthase	2.01	0.001	↑
113	SAFDA_2229	L-lactate permease	2.00	3.68E-09	↓

Genes are arranged in decreasing order of Fold Change.

Table S8. Node degree score of up-down regulated genes mentioned in Table S7

No.	Gene symbol	Identifier	Node degree
1	*sbi*	1280.SAXN108_2673	7
2	*saeR*	1280.SAXN108_0774	6
3	*hlgB*	1280.SAXN108_2677	5
4	*hlgC*	1280.SAXN108_2676	5
5	*pheT*	1280.SAXN108_1134	5
6	*saeS*	1280.SAXN108_0773	5
7	*sarA*	1280.SAXN108_0683	5
8	*icaA*	1280.SAXN108_2939	4
9	*splA*	1280.SAXN108_1846	4
10	*lip2*	1280.SAXN108_0305	3
11	*pnp*	1280.SAXN108_1278	3
12	*rpsB*	1280.SAXN108_1258	3
13	*rpsO*	1280.SAXN108_1277	3
14	*icaR*	1280.SAXN108_2938	2
15	*ureA*	1280.SAXN108_2536	2
16	*ureC*	1280.SAXN108_2538	2
17	*ureD*	1280.SAXN108_2542	2
18	*coaE*	1280.SAXN108_1714	1
19	*dapA*	1280.SAXN108_1411	1
20	*dapB*	1280.SAXN108_1412	1
21	*sarT*	1280.SAXN108_2745	1
22	*tagX*	1280.SAXN108_0708	1
23	*trpA*	1280.SAXN108_1389	1

Rest 5 genes with node degree score ‘zero’ are not listed.

Table S9. Top twelve cytoHubba ranked genes from among the top-13 in Table S8

No.	Gene ID	Gene Name	Number of methods ranking this protein among top 10	Names of 12 ranking methods of CytoHubba and rank score provided by them											
				Degree	MNC	DMNC	MCC	Bottleneck	EcCentricity	Closeness	Radiality	Betweenness	Stress	CC	EPC
1	SAXN108_0683	*sarA*	11	4	3	0.46346306	7	1	0.346154	6	2.076923	7.4	18	-	4.534
2	SAXN108_2673	*sbi*	12	7	7	0.40246305	38	4	0.346154	7.5	2.336538	13.266667	28	0.52381	5.374
3	SAXN108_1846	*splA*	11	4	4	-	8	1	0.346154	6	2.076923	2.8	8	0.666667	4.527
4	SAXN108_0774	*saeR*	11	5	5	0.51861011	30	-	0.346154	6.5	2.163462	2.1333333	8	0.8	4.973
5	SAXN108_0773	*saeS*	11	5	5	0.51861011	30	-	0.346154	6.5	2.163462	2.1333333	8	0.8	4.943
6	SAXN108_2677	*hlgB*	11	5	5	0.51861011	30	1	-	6.333333	2.076923	1.3333333	4	0.8	4.876
7	SAXN108_2676	*hlgC*	11	5	5	0.51861011	30	1	-	6.333333	2.076923	1.3333333	4	0.8	4
8	SAXN108_1278	*pnp*	11	3	3	0.46346306	6	1	0.307692	3	0.512821	0	0	1	-
9	SAXN108_0305	*lip2*	8	3	-	-	-	2	0.346154	5.5	1.990385	4.6	12	-	3.953
10	SAXN108_1134	*pheT*	7	3	3	0.46346306	6	1	0.307692	-	-	-	-	1	-
11	SAXN108_1277	*rpsO*	7	-	3	0.46346306	6	1	0.307692	-	-	-	-	1	2.315
12	SAXN108_2939	*icaA*	6	-	-	-	-	1	-	4.666667	1.730769	1	2	-	3.092

"-": This method did not rank the shown protein among top 12.

NC: Maximum Neighborhood Component; DMNC: Density of Maximum Neighborhood Component; MCC: Maximal Clique Centrality; CC: Clustering Co-efficient; EPC: Edge Percolated Component