Table S1:

DNA sequences of primers used for constructing recombinant proteins and GAS mutants in the present study.

Primer	Name	Sequence	Restriction sites
1	GBSPy19-F	CTGTA**CTCGAG**GAGGATTTAAGTACTAAGATTGC	*Xho*I
2	GBSPy19-R	AAA**GGATCC**GTTAGTGTGGATAAATAAATGTAACAC	*Bam*HI
3	GB19Bam-UpNt	TCA**GGATCC**AGCGTTACAGGCTCAAGTAAG	*Bam*HI
4	GB19Hin-UpCt	TTT**AAGCTT**TCGCACCTACCATCGGCGTTG	*Hind*III
5	GB19Nco-DnNt	AAAT**CCATGG**CTCCTTGGGCAGGAAA	*Nco*I
6	GB19Pst-DnCt	TGA**CTGCAG**TTCAGCACTAGCACGC	*Pst*I
7	upNt-Pr3	GTCTAAGACGTTGGGGGAT	
8	dnCt-Pr6	GCCGTAGTAAGGCATCAC	
9	aad9-F	TTGGATCAGGAGTTGAGAGTGGAC	
10	aad9-R	GCCACTGCATTTCCCGCAATATCT	
11	GB19C55-F	CTC**GGATCC**GTGGGCACTGAGTATGCCTATGG	*Bam*HI
12	GB19C55-R	CCG**AAGCTT**ATTAAGTTGTAGCTGCTCCGAGGG	*Hind*III
13	GB19PDCHin-F	TTCA**AAGCTT**GAAGGATAAGGTGTCTGAGTGAAG	*Hind*III
14	GB19PDCKpn-R	AAC**GGTACC**GTCAATACTCTCAGAACTATTCC	*Kpn*I
15	AMB93SPy19RN-F	TCCC**CCCGGG**ATGAAAAAAAGAATTTTATCAGC	*Xma*I
16	AMB94SPy19RN-R	CGG**GGTACC**TTAGTGTGGATAAATAAATGTAAC	*Kpn*I

Bold underlined letters indicate the restriction enzyme sites.

Table S2: Strains used in the present study: (two-pages)

Strain	**Characteristic/Description**	**Reference/source**
E. coli XL1-blue	F'::Tn10*proA+B+lacIq* Δ*(lacZ)M15/recA1endA1 gyrA96(Nal r)thi hsdR17* (rk- mk+) *glnV44 relA1 lac*	Stratagene
E. coli BL21(DE3)pLysS	*E.coli* B F$^-$*dcm ompT hsdS*($r_B^-m_B^-$)*gal* λ(DE3)[pLysS Cam^r]	Novagen
E. coli MC1061	F'*araD139* Δ*(ara-leu)7696* Δ*(lac)X74 galU galK hadR2*(rk- mk+) *mcrB1 rpsL* (Str+)	From: Craig Rubens (1)
Streptococcus pyogenes SF370	Wild-type strain	ATCC 700294 (2)
Staphylococcus aureus RN4220	A derivative RN450 (ATCC8325-4) a Toxic-shock syndrome exotoxin-negative indicator strain	From Barry Kreisworth, PHRI (3)
Plasmid		
pET14B	Vector used for making recombinant protein with His-tag at the N-terminal- *AmpR*	Novagen
pFW5	Suicide plasmid containing Spectinomycin^R (aad9 resistance marker- *Spc*^{R}) flanked by multiple cloning site (MCS-I) and MCS-II for constructing GAS mutant	Podbielski et al (4) Jin and Pancholi (5)
pDC123	Plasmid used for complementation experiments-Chloramphenicol^R (*Chl*^{R})	From: Craig Rubens (1)
pCN40tet	pCN40 (*E.coli-S. aureus* shuttle vector) with ermC gene replaced by tet(M) from pCN36Plasmid used for complementing *Staphylococcus aureus- tetracycline(Tet*^{R}*)*	Charpentier et al (6) Beltramini et al (7).
pET14B-*cdhA*	pET14B plasmid with *spy0019/cdhA* insert without signal sequence	This study
pFW5-up19Ntct-1	pFW5 with upstream flanking region (930bp) in MCS-I(*Bam*H1 and *Hind*III)	This study
pFW5-dn19Ntct-2	pFW5 with downstream flanking region (774bp) in MCS-II(*Nco*I and *Pst*I)	This study
pFW5ΔcdhA	pFW5 with flanking up and down stream regions (930bp and 774bp) in MCS-I and –II respectively	This study
pFWCdhAΔC55	pFW5 with 1075bp (157-1231) insert of *cdhA* in MCS-I	This study
pDC123-cdhA	pDC123 plasmid with cdhA insert between *Hind*III and *Kpn*I	This study
pCN49-cdhA	pCN49tet plasmid with cdhA insert between *Xma*I and *Kpn*I	This study
Mutant strains		
XL-1-cdhA	XL-1 blue *E. coli* containing pET14B-*cdhA* plasmid	This study

	Amp^R	
BL21-cdhA	BL21(DE3)pLysS *E. coli* containing pET14B-*cdhA* plasmid and expressing CdhA without its signal sequence. *Amp^R*	This study
M1ΔSTK	M1 SF370 lacking SPy1625 (SP-STK[eukaryotic-type serine/threonine kinase]) *$Spectinomycin^R$ (Spc^R)*	Jin and Pancholi (5)
M1ΔSTK::*cdhA*	M1ΔSTK complemented with wild-type *cdhA*- *Spc^R and ChloramphenicolR(Chl^R)*	This study
M1ΔCdhA	M1 SF370 lacking *cdhA*- *Spc^R*	This study
M1CdhAΔC55	M1 SF370 expressing truncated CdhA without the C-terminal 55 residues that contributes to the catalytic site of the CHAP-domain- *Spc^R*	This study
M1ΔCdhA::*cdhA*	M1ΔCdhA mutant complemented with the wild-type *cdhA*- *Spc^R-Chl^R*	This study
M1-WT::*cdhA*	Wild-type M1 complemented with *cdhA* resulting in over expression of CdhA-*Chl^R*	This study
RN4220::*cdhA*	Wild-type RN4220 complemented with *cdhA* resulting in over expression of CdhA-*tet^R*	This study

*References for Table S2

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4. Podbielski A, Spellerberg B, Woischnik M, Poh B, Lutticken, R. (1996) Novel series of plasmid vectors for gene inactivation and expression analysis in group A streptococci (GAS). Gene 177: 137-147.

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6. Charpentier E, Anton A I, Barry P, Alfonso B, Fang Y, Novick R P (2004) Novel cassette-based shuttle vector system for Gram-positive bacteria. Appl Environ Microbiol 70: 6076-6085.

7. Beltramini A M, Mukhopadhyay C D, Pancholi V (2009) Modulation of cell wall structure and antimicrobial susceptibility by a *Staphylococcus aureus* eukaryotic-like serine/threonine kinase and phosphatase. Infect Immun 77: 1406-1416.

Table S3 : Primers sequences used for qRT-PCR assays in the present study.

Gene ORF	**Gene Symbol**	**Sequence**	
		Forward	**Reverse**
SPy1152	*gyrA*	TTCGTATGGCTCAGTGGTTTAGTT	CTGGTTCTCTTTCGCTTCCATCGT
SPy1962	*ProS*	GGGTGGTTCTTGACAAGTCTATTGCG	TTCTGCCAAGGCATCTTCAGCA
SPy0019	*cdhA/sibA*	TCTTGTAAGTGGTGTTACCCTCGG	GCGCCTCAAGTTCTGTATTTCTTGCG
SPy0136	*unknown*	TTGGGACGGTACAGTTCGTTCTGA	AGTGTGTGATTGACGGCCATAGGT
SPy0148	*ntpI*	GCCATCGACAACAAGCAGCTCAAA	AGGAATCGTTCCAACTCTTGCCGA
SPy0167	*slo*	AGCTCCGCCACTCTTTGTGAGTAA	CTCTGCAGCATCTCCTCC
SPy0252	*PTS*	AAATGCTCAAAGATGCTGGCGTCC	TGGTCACCACCTTGACCATTAGCA
SPy0711	*speC*	AAGCGGCAGAATCGAAATTGGCAC	TCTAGTCCCTTCATTTGGTGAGTC
SPy0712	*mf2*	GCAATGACAGCCTGGCTAAACACA	TCGAGGCACTACTTCATTGCCACT
SPy0738	*sagA*	GCTGCTGTTGCTGCTGTACTACTT	GCGTATAACTTCCGCTACCACCTT
SPy0855	*PTS*	GCCATTTGTTATTGGTGGCGGGAT	AGCTGATCATTTGGCACACCAAGC
SPy1058	*PTS*	GACCAAAGAGTTAAATGCGCCGCT	CTTGTCTTTGGCGCGTGGATCATT
SPy1294	*malB*	TTCCTTTGAATCAGGACCGTGGGA	TTTAGCTGGTGCTTGGTTGACTGC
SPy1357	*grab*	ACTCACCTATCGAACAGCCTCGAA	GCGTCTGTTTGATCCGCTAATGCT
SPy1917	*lacE*	TTACCATGGGTGGTACTGGTGCAA	CTGATGCACGTCCAATGGCTTTGT
SPy1983	*scl*	AAATCTGGAATCAAGGGAGACCGTGG	TTTCACCGCGTTCACCGGTTTCA
SPy2018	*emm1*	TTAGCGATAGACCAAGCGAGTCAG	GCTTTGACGACTTGCGTCTGAGAT
SPy2019	*mga*	GACCTTTCACGCTTGTTTCACCTC	GTGACGCTGAGATTGAGCCTGATT
SPy2039	*speB*	TTCTGCAGGTAGCTCTCGTGTTC	TCGATAACAAAGGCATGTCCGCC
SPy2200	*hasA*	GCCACATGACTATAAAGTTGCTGCTG	TTGACAAGGGAACGGTGAACGA

Table S4: Microarray-based differential gene expression analysis for M1ΔCdhA vs the wild-type M1-SF370 (GSE#15546).

ORF# M1-SF370	*Gene*	Functional category	Log$_2$-fold change (M1ΔCdhA vs M1-WT) ¶	P value*
		Amino acid transport and metabolism		
SPy0184	*opuABC*	putative glycine-betaine binding permease protein	2.05640	0.00598
SPy1541	*arcC*	putative carbamate kinase	-3.4416	0.00153
SPy1542	-	putative Xaa-His dipeptidase	-3.29318634	0.00626
SPy1544	*arcB*	putative ornithine transcarbamylase	-2.93909102	0.02302
SPy1547	*sagP (arcA)*	streptococcal antitumor protein (possible arginine deiminase)	-2.75651843	0.02362
SPy2189	*sdhB*	putative L-serine dehydratase beta subunit	-1.63081526	0.00773
SPy2190	*sdhA*	putative L-serine dehydratase alpha subunit	-1.78756811	0.0179
		Carbohydrate transport and metabolism		
SPy0146	-	putative regulatory protein	-3.10918311	0.00079
SPy0255	-	putative regulatory protein	-3.58895686	0.00364
SPy1057	-	Hypothetical protein	-2.58079205	0.03288
SPy1058	-	putative phosphotransferase system (PTS), enzyme II component B	-2.95458551	0.00816
SPy1059	-	putative phospotransferase system (PTS), enzyme II, component C	-2.67254237	0.01141
SPy1060	-	putative phospotransferase system (PTS), enzyme II component D	-2.16720074	0.03663
SPy1292	*malM*	putative 4-alpha-glucanotransferase	-2.3532552	0.04502
SPy1294	-	putative maltose/maltodextrin-binding protein	-2.08709915	0.05454
SPy1301	*malC*	maltodextrin transport system permease	-2.72742748	0.02236
SPy1304	*amyB*	putative cyclomaltodextrinase	-2.58349588	0.01888
SPy1707	*lacB.1*	putative galactose-6-phosphate isomerase	-2.80990347	0.00963
SPy1708	*lacA.1*	putative galactose-6-phosphate isomerase	-2.88753155	0.00565
		Cell envelope biogenesis, outer		

		membrane		
SPy2201	*hasB*	UDP-glucose 6-dehydrogenase	-5.83464339	1.08E-11
SPy2202	*hasC*	UDP-glucose pyrophosphorylase	-4.7896666	5.12E-06
		Cell motility and secretion		
SPy0857	*mur1.2*	putative peptidoglycan hydrolase	1.775223248	0.04556
		DNA replication, recombination and repair		
SPy1563	-	conserved hypothetical protein	-2.0734014	0.02289
		Energy production and conversion		
SPy0149	*ntpK*	V-type Na+ -ATPase subunit K	-2.36833651	0.0096
SPy0150	*ntpE*	putative V-type Na+ -ATPase subunit E	-2.83273618	0.00809
SPy0154	*ntpA*	putative V-type Na+ -ATPase alpha subunit	-3.07025116	0.00224
SPy0155	*ntpB*	putative V-type Na+ -ATPase subunit B	-2.79904425	0.03036
SPy0157	*ntpD*	putative V-type Na+ -ATPase subunit D	-2.89979146	0.00292
		Function unknown		
SPy0019	-	putative secreted protein/ CdhA/sibA	-3.72812322	0.00025
SPy0136	-	hypothetical protein	-3.80404194	0.00027
SPy0166	-	hypothetical protein	-3.09748473	0.0004
SPy0170	-	hypothetical protein	-4.80814656	1.55E-05
SPy0256	-	hypothetical protein	-2.4527254	0.00655
SPy0428	-	conserved hypothetical protein	-3.35991921	0.00024
SPy0430	-	hypothetical protein	-3.6328223	2.23E-05
SPy0433	-	hypothetical protein	-2.62327812	9.64E-05
SPy0435	-	hypothetical protein	-2.79926332	0.0008
SPy0437	-	hypothetical protein	-1.38948653	0.0458
SPy0743	-	hypothetical protein	-1.37395731	0.05468
SPy0861	-	hypothetical protein	-2.24634217	0.00658
SPy1017	-	hypothetical protein	1.708325383	0.02793
SPy1543	-	conserved hypothetical protein	-3.33026296	0.00269

SPy1562	-	conserved hypothetical protein	-3.06442454	0.00091
SPy1564	-	conserved hypothetical protein	-2.44132327	0.00335
SPy1565	-	conserved hypothetical protein	-2.9655306	0.00187
SPy1686	-	hypothetical protein	1.562696323	0.03546
SPy1710	-	putative PTS system, enzyme IIB component	-2.00494928	0.02123
SPy1832	-	hypothetical protein	-1.53364716	0.02572
SPy1985	-	hypothetical protein	-1.9194945	0.03479
		General function prediction only		
SPy0742	-	hypothetical protein	-1.5674321	0.04718
		Lipid metabolism		
SPy1718	-	putative esterase	-2.13943137	0.01467
		Posttranslational modification, protein turnover, chaperones		
SPy0416	*prtS*	putative cell envelope proteinase	-2.92746688	0.00015
		Signal transduction		
SPy1062	-	putative two-component response regulator	-2.24109495	0.02052
		Transcription		
SPy1546	-	hypothetical protein	-2.78005908	0.01756
		Virulence factors		
SPy0165	*nga*	NAD glycohydrolase precursor	-4.70774684	2.27E-06
SPy0167	*slo*	streptolysin O precursor	-3.74007054	7.33E-05
SPy0711	*speC*	pyrogenic exotoxin C precursor, phage associated	1.784534856	0.0182
SPy0712	*mf2*	putative DNase (mitogenic factor), phage	1.66593819	0.00257
SPy1302	*amyA*	putative cyclomaltodextrin glucanotransferase	-2.74293186	0.02244
SPy1357	*grab*	protein GRAB (protein G-related ?2M-binding protein)	1.860433621	0.02545
SPy1983	*scl*	collagen-like surface protein	-5.45831621	5.50E-06
SPy2016	*sic*	inhibitor of complement-mediated lysis	-3.76662345	0.00078

SPy2018	*emm1*	M protein type 1	-4.16572585	0.00012
SPy2039	*speB*	pyrogenic exotoxin B	-3.59998351	0.00128
SPy2043	*mf*	mitogenic factor	-2.25560173	0.02301
SPy2200	*hasA*	hyaluronate synthase	-7.19307349	6.59E-13

¶-- Microarray analysis and Log$_2$-fold changes were derived from 11 independent experiments including dye-swap experiments as described in Material Methods using the CARMAweb software.

***--** Differential gene expression value, $\pm$ Log$_2$$\geq$1 fold change with $p \leq 0.05$, was treated as significant change.

-Open reading frame (ORF) numbers are based on the genome sequence data of type M1 GAS strain SF370 (2).

OPR # in bold letters are also found in M1CdhADC55 mutant (Table-S2)

Table S5. Microarray-based differential gene expression analysis for M1CdhAΔC55 vs M1SF-370 (GSE# 15598).

ORF# (M1-SF370)	***Gene***	**Functional category and Product**	**Log$_2$-fold change M1CdhADC55 vs.M1SF370¶**	***P* Value***
		Amino acid transport and metabolism		
SPy0257	*nanH*	putative acylneuraminate lyase	-2.25493	0.042168
SPy1217	-	putative glycine cleavage system H protein	-1.58447	0.040303
SPy1541	*arcC*	putative carbamate kinase	-4.36467	7.71E-06
SPy1542	-	putative Xaa-His dipeptidase	-5.34734	1.97E-08
SPy1544	*arcB*	putative ornithine transcarbamylase	-4.76064	1.63E-06
SPy1547	*sagP (arcA)*	streptococcal antitumor protein (possible arginine deiminase)	-4.46374	1.23E-06
SPy2190	*sdhA*	putative L-serine dehydratase alpha subunit	-1.83436	0.013469
		Carbohydrate transport and metabolism		
SPy0146	-	putative regulatory protein	-2.70835	0.0014
SPy0251	-	putative N-acetylmannosamine-6-P epimerase	-2.87709	0.003248
SPy0252	-	putative sugar transporter sugar binding lipoprotein	-2.93048	0.000724
SPy0254	-	sugar transport system (permease)	-2.40877	0.00528
SPy0442	-	putative glycerol-3-phosphate transporter	-2.10287	0.008705
SPy0854	*fruB*	putative fructose-1-phosphate kinase	-3.43612	4.05E-05
SPy1057	-	hypothetical protein	-4.92344	4.41E-08
SPy1058	-	putative phosphotransferase system (PTS), enzyme II component B	-4.48982	1.10E-06
SPy1059	-	putative phospotransferase system (PTS), enzyme II, component C	-4.35334	1.11E-06
SPy1060	-	putative phospotransferase system (PTS), enzyme II component D	-3.52878	9.14E-05
SPy1292	*malM*	putative 4-alpha-glucanotransferase	-3.11974	0.00104
SPy1294	-	putative maltose/maltodextrin-binding protein	-3.50005	0.00015
SPy1295	*malF*	putative maltose/maltodextrin ABC transport system (permease)	-3.02496	0.004624

SPy1296	*malG*	putative maltose/maltodextrin ABC transport system (permease)	-1.82093	0.023356
SPy1299	*malD*	putative maltodextrin transport system permease	-2.53865	0.00837
SPy1301	*malC*	maltodextrin transport system permease	-3.62747	6.60E-05
SPy1304	*amyB*	putative cyclomaltodextrinase	-3.96239	3.67E-05
SPy1306	*malX*	maltose/maltodextrin-binding protein	-3.63956	0.001779
SPy1503	-	putative phosphomannomutase	-2.00506	0.00482
SPy1704	*lacD.1*	putative tagatose 1,6-diphosphate aldolase	-2.07113	0.018109
SPy1707	*lacB.1*	putative galactose-6-phosphate isomerase	-3.03622	0.001591
SPy1708	*lacA.1*	putative galactose-6-phosphate isomerase	-2.45743	0.008592
SPy1709	-	putative PTS system, enzyme IIC component	-2.82759	0.003145
SPy1711	-	putative PTS system, enzyme IIA component	-2.49478	0.010317
SPy1922	*lacB.2*	putative galactose-6-phosphate isomerase (B subunit)	-1.7812	0.036192
SPy1923	*lacA.2*	galactosidase acetyltransferase	-2.52042	0.011223
SPy1973	*dexB*	dextran glucosidase	-2.20939	0.006815
SPy2096	*dexS*	putative dextran glucosidase	-1.6257	0.037289
		Cell envelope biogenesis, outer membrane		
SPy**2201**	*hasB*	UDP-glucose 6-dehydrogenase	-4.53654	9.53E-07
SPy**2202**	*hasC*	UDP-glucose pyrophosphorylase	-3.8781	9.81E-05
		Cell motility and secretion		
SPy1976	*msmK*	multiple sugar-binding ABC transport system (ATP-binding protein)	-2.61871	0.000912
		Coenzyme metabolism		
SPy1063	-	putative periplasmic-iron-binding protein	-2.00402	0.007379
SPy1214	*lplA*	putative lipoate-protein ligase	-1.58223	0.026625
SPy1220	-	conserved hypothetical protein	-1.52459	0.02995
		DNA replication, recombination and repair		
SPy1563	-	conserved hypothetical protein	-2.17083	0.00679
		Energy production and conversion		
SPy0148	*ntpI*	V-type Na+ -ATPase subunit I	-3.78279	4.95E-05

SPy0149	*ntpK*	V-type Na+ -ATPase subunit K	-3.76487	4.38E-05
SPy0150	*ntpE*	putative V-type Na+ -ATPase subunit E	-4.07994	3.00E-05
SPy0151	*ntpC*	putative V-type Na+ -ATPase subunit C	-3.7906	8.06E-05
SPy0154	*ntpA*	putative V-type Na+ -ATPase alpha subunit	-3.8587	5.44E-05
SPy0155	*ntpB*	putative V-type Na+ -ATPase subunit B	-4.13006	1.78E-05
SPy0157	*ntpD*	putative V-type Na+ -ATPase subunit D	-3.74782	2.40E-05
SPy1218	-	conserved hypothetical protein	-1.92363	0.010479
SPy1849	*pfl*	putative pyruvate formate-lyase	-2.32763	0.002428
SPy2049	*pflD*	putative pyruvate formate-lyase 2	-1.44584	0.051227
		Function unknown		
SPy0019	-	putative secreted protein—CdhA/SibA	1.76572	0.012404
SPy0136	-	hypothetical protein	-2.4309	0.014809
SPy0147	-	hypothetical protein	-3.60598	0.000571
SPy0170	-	hypothetical protein	-3.225	0.001498
SPy0256	-	hypothetical protein	-2.98326	0.000944
SPy0430	-	hypothetical protein	-2.8642	0.002072
SPy0433	-	hypothetical protein	-1.89022	0.020243
SPy0435	-	hypothetical protein	-1.54147	0.050185
SPy0739	*sagB*	streptolysin S associated ORF	-2.97651	0.00026
SPy0740	*sagC*	streptolysin S associated ORF	-2.77969	0.001431
SPy0741	-	hypothetical protein	-2.66414	0.001328
SPy0743	-	hypothetical protein	-2.44239	0.003764
SPy0861	-	hypothetical protein	-2.34387	0.033703
SPy1216	-	hypothetical protein	-1.99825	0.011072
SPy1298	*malA*	putative maltodextrose utilization protein	-2.15022	0.016366
SPy1543	-	conserved hypothetical protein	-4.54638	5.13E-07
SPy1562	-	conserved hypothetical protein	-1.97883	0.006385
SPy1565	-	conserved hypothetical protein	-2.31821	0.002193
SPy1680	-	putative transcriptional regulatory protein	-1.6107	0.020366

SPy1710	-	putative PTS system, enzyme IIB component	-2.48215	0.011916
SPy1985	-	hypothetical protein	-2.13957	0.007286
SPy2066	-	putative dipeptidase	-1.73751	0.024801
SPy2191	-	hypothetical protein	1.753186	0.017852
		General function prediction only		
SPy0044	*adhA*	putative alcohol dehydrogenase I	-3.09639	0.00021
SPy0519	-	conserved hypothetical protein	-1.645	0.046764
SPy0742	-	hypothetical protein	-2.87017	0.000685
SPy0745	*sagH*	ABC transporter (ATP-binding protein) - streptolysin S associated ORF	-2.57412	0.001301
SPy0746	-	putative ABC transporter (ATP-binding protein)	-2.14013	0.002678
SPy0747	-	conserved hypothetical protein	-1.95705	0.010762
SPy1113	-	putative acid phosphatase (class B)	-1.7422	0.028163
SPy1567	-	conserved hypothetical protein	-1.73871	0.012842
SPy1693	-	putative reductase / dehydrogenase	-1.31522	0.039902
		Lipid metabolism		
SPy1751	*fabK*	putative trans-2-enoyl-ACP reductase II	1.255345	0.04672
SPy0022	*plsX*	putative fatty acid/phospholipid synthesis protein	1.398864	0.035703
SPy1753	*acpP*	putative acyl carrier protein	1.482747	0.041113
		Nucleotide transport and metabolism		
SPy0830	*pyrR*	putative pyrimidine regulatory protein	1.680411	0.025495
SPy0832	*pyrB*	putative aspartate transcarbamoylase	1.811749	0.014822
SPy0900	*pyrF*	putative orotidine-5'-decarboxylase PyrF	2.225126	0.008888
		Posttranslational modification, protein turnover, chaperones		
SPy0379	*pflC*	putative pyruvate-formate lyase activating enzyme	-1.73878	0.028716
SPy0416	*prtS*	putative cell envelope proteinase	-2.13093	0.003128
		Secondary metabolites biosynthesis, transport and catabolism		
SPy0744	-	Putative ABC transporter (ATP-binding protein)	-2.74699	0.000836
		Signal transduction mechanisms		

SPy1061	-	putative two-component sensor histidine kinase	-2.43915	0.005105
		Transcription		
SPy0853	-	putative transcriptional repressor	-3.96736	8.99E-07
SPy1062	-	putative two-component response regulator	-2.2121	0.024562
SPy1546	-	hypothetical protein	-4.67337	1.47E-06
		Translation		
SPy0145	-	conserved hypothetical protein	-1.61106	0.024883
SPy1613	-	conserved protein - function unknown	-1.60667	0.021384
		Virulence genes		
SPy0711	*speC*	pyrogenic exotoxin C precursor, phage associated	1.64463	0.032466
SPy0712	*mf2*	putative DNase (similar to mitogenic factor), phage associated	1.652306	0.026745
SPy0738	*sagA*	streptolysin S associated protein	-2.45486	0.004107
SPy1302	*amyA*	putative cyclomaltodextrin glucanotransferase	-3.63063	4.88E-05
SPy1436	*mf3*	putative deoxyribonuclease	2.130089	0.008555
SPy1983	*scl*	collagen-like surface protei	-4.48531	3.10E-06
SPy2018	*emm1*	M protein type 1	-2.90199	0.000887
SPy2043	*mf*	mitogenic factor	-1.67711	0.021443
SPy2200	*hasA*	hyaluronate synthase	-4.61878	4.43E-06

¶-- Microarray analysis and Log$_2$-fold changes were derived from 7 independent experiments including dye-swap experiments using the CARMAweb software as described in Materials and Methods .

*****-- Differential gene expression value, $\pm$ Log$_2 \geq 1$ fold change with $p \leq 0.05$, was treated as significant change.

-Open reading frame (ORF) numbers are based on the genome sequence data of type M1 GAS strain SF370 (2).

OPR # in bold letters are also found in M1ΔCdhA mutant (Table S1).

Table S6: Comparison of expression profiles of 18 relevant genes in M1ΔCdhA by qRT-PCR and by microarray analyses.

Gene	Log2 fold change (M1ΔCdhA)	
	Microarray	qRT-PCR
SPy0019	-3.73	-13.636948
SPy0136	-3.8	-2.2155798
SPy0148	-2.35	-7.062746
SPy0167	-3.74	0.61447428
SPy0252	-1.46	-7.4752142
SPy0711	1.78	-6.22
SPy0712	1.67	-8.28
SPy0738	-1.4	-3.88
SPy0855	-0.81	-7.57
SPy1057	-2.95	-0.549
SPy1294	-2.09	-4.54
SPy1357	1.86	-3.6
SPy1917	-1.37	-9.16
SPy1983	-5.46	-8.69
SPy2018	-4.17	-5.4
SPy2019	-1.24	-1.2
SPy2039	-3.6	-4.0
SPy2200	-7.19	-3.0

Gene	Log2 fold change (M1CdhAΔC55)	
	Microarray	qRT-PCR
SPy0019	1.76	-0.29
SPy0136	-2.43	0.34
SPy0148	-3.78	-2.32
SPy0167	-0.78	-1.55
SPy0252	-2.93	-3.32
SPy0711	1.64	0.76
SPy0712	1.65	-0.69
SPy0738	-2.45	-1.56
SPy0855	-1.64	-1.12
SPy1057	-4.48	-2.36
SPy1294	-3.5	-9.96
SPy1357	1.05	-6.646
SPy1917	-1.56	-2.74
SPy1983	-4.48	-1.09
SPy2018	-2.9	-1.0
SPy2019	-0.35	-1.61
SPy2039	-0.62	-4.54
SPy2200	-4.6	-4.35