

Supplemental material

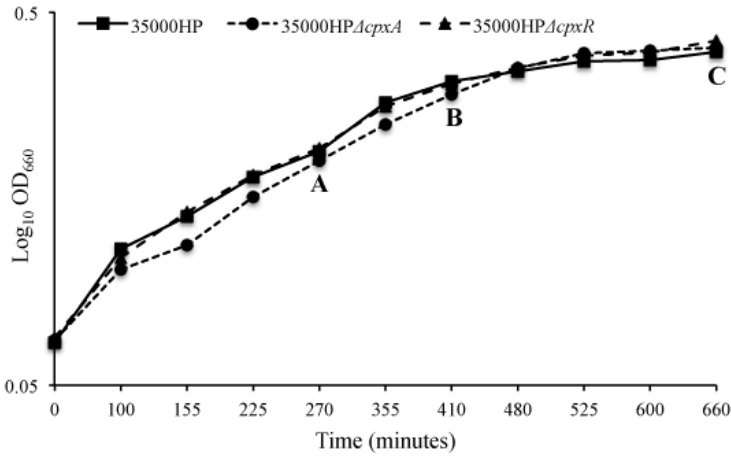
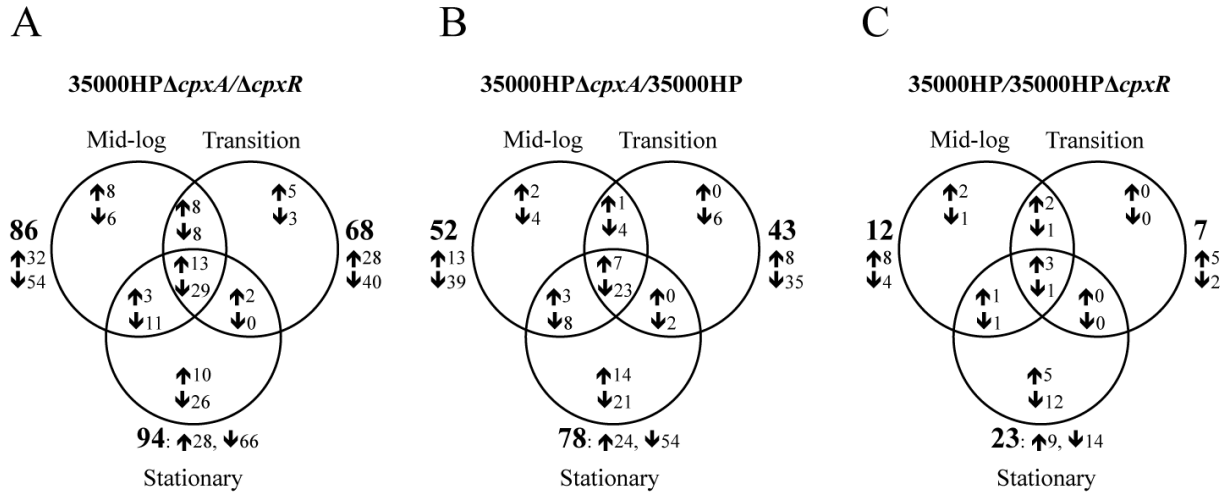


Figure S1. Growth kinetics of 35000HP, 35000HPΔcpxA, and 35000HPΔcpxR in GC broth. Growth kinetics was determined by measuring the optical density at 660 nm (OD₆₆₀) at different time points following inoculation from overnight cultures. A, B, and C indicate the time points at which bacteria were harvested for RNA isolation in the mid-log, transition, and stationary growth phases, respectively.



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14 **Figure S2.** Venn diagram showing the number of genes or operons differentially regulated by

15 the Cpx 2CST at different phases of growth. (A) 35000HPΔ*cpxA* compared to 35000HPΔ*cpxR*;

16 (B) 35000HPΔ*cpxA* compared to 35000HP; and (C) 35000HP compared to 35000HPΔ*cpxR*. The

17 up- and downregulated genes or operons are indicated by up (↑) and down (↓) arrows,

18 respectively. The total number of genes or operons differentially regulated in different phases of

19 growth is indicated in bold outside the Venn diagram.

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30 TABLE S1. Primers used in this study

Primer (gene)	5' to 3' sequence ^a
Primers used for qRT-PCR	
P1 (<i>dnaE</i> F)	AACGTTACCTTCAGCAAGCGGTTT
P2 (<i>dnaE</i> R)	GGCGTTTGGGATCGTCGAGTGTAT
P3 (<i>ccmD</i> F)	CGCAGATTCTTTTGGCATGGGA
P4 (<i>ccmD</i> R)	CTCGGTAAGACAACCAAATTAGCCC
P5 (<i>dsrA</i> F)	ATTACAACAATGGCTCAGCAGCCG
P6 (<i>dsrA</i> R)	ACCGCCTTCATTAGACCAAGTCCA
P7 (<i>fimA</i> F)	ATATCAGCTATGGCTGCTCCTCCA
P8 (<i>fimA</i> R)	CCGCTGCAGTTTGCCTAAAATCAA
P9 (<i>fis</i> F)	CAATGCTGAATGCACAAGCACAGC
P10 (<i>fis</i> R)	ATCGTTGCCGCACGGGTTTGATTA
P11 (<i>flp1</i> F)	GGCTTAATTGCAGTCGCAGTTGCT
P12 (<i>flp1</i> R)	GTGCCATTAGCGCTACTTATACCAG
P13 (<i>HD0182</i> F)	AATTGCCTTATCCAAACAGGCGGG
P14 (<i>HD0182</i> R)	TCTAATCTACCCGCCATACCGTCA
P15 (<i>HD0430</i> F)	AAATAGACCGCTTGTTACGCAAAA
P16 (<i>HD0430</i> R)	ATGCACCAATFCAATACCGCCTTG
P17 (<i>HD1123</i> F)	TTAGCCACGGTTGCGATTCTTCT
P18 (<i>HD1123</i> R)	CGCTGATGAAGCGGCTAATAACTC
P19 (<i>HD1278</i> F)	AGGTGTTCTAGTCGGTGTGCTTGA
P20 (<i>HD1278</i> R)	ACGCCAGTCTTCATAATTGCTGC
P21 (<i>HD1577</i> F)	TAAATCAAGCGCTCGCACCGAAAC
P22 (<i>HD1577</i> R)	AAACACACATTGTGGCGTGCCTTC
P23 (<i>HD1667</i> F)	CTGTACGACTCAAGCATGCGGTTT
P24 (<i>HD1667</i> R)	ATCTGGGCTAATGCCAAGCACAAAC
P25 (<i>lspB</i> F)	AGCTAGAGCGGCTGACCCATTAAA
P26 (<i>lspB</i> R)	GTGAGAAAATTGCTCCGCTTTGGCT
P27 (<i>momp</i> F)	ACAGGAAGCTGCACAGGTGTTAGA
P28 (<i>momp</i> R)	ATCACTTGGATTGCTGGTGTCCG
P29 (<i>ompA2</i> F)	GGTTGGGCAAGTTCCATAGAGGT
P30 (<i>ompA2</i> R)	ACCTAATTCAGCCGCTAAACCTGC
P31 (<i>tadA</i> F)	AATCAATGCCTTGCCTATGCGTCC
P32 (<i>tadA</i> R)	TGTATTGGCGTGCAGGGTAGACAT
P33 (<i>tadD</i> F)	AAATCACCGGTTCCACCGGCTAAA
P34 (<i>tadD</i> R)	TGAGATCGGCACGATACATGGCAA
P35 (<i>waaA</i> F)	CCGGCAACACATTCCGTTATCAT
P36 (<i>waaA</i> R)	AGGTTGCCAGCAGTGGTTAATTGC
Primers used for generating the reporter constructs	
P37 (<i>fimA</i> F)	ATACCTAGATCTTTTGAACCTTCAAGTAATCAC
P38 (<i>fimA</i> R)	AGGCGTAGATCTTTTACCTCTATAATTTAAG
P39 (<i>fis</i> F)	GGGCCTAGATCTTAATTTTTTTAATTTGTCG
P40 (<i>fis</i> R)	AGCTATAGATCTATTACCTCTCTACATAAGT
P41 (<i>HD0182</i> F)	ATATCTAGATCTCCGTAAGTTAGTAATGGGAT
P42 (<i>HD0182</i> R)	ATACCTAGATCTTTTTCGGAGGAATACTAGTT
P43 (<i>HD0430</i> F)	ATATATAGATCTAGCGCGACTCCTCCTATAAT
P44 (<i>HD0430</i> R)	ATACCTAGATCTTTATGGCTGTTACTCCCCAA
P45 (<i>HD1123</i> F)	AGGGCTAGATCTTTGCCATTTAACCTTCTAA
P46 (<i>HD1123</i> R)	AGGCCTAGATCTTGTCTCTCCTATATCAATA
P47 (<i>HD1278</i> F)	ATATATAGATCTTATCTTGAGGGGGTAGTGTC
P48 (<i>HD1278</i> R)	AGCCCTAGATCTAATTACTTGTAAGCAAGTAT
P49 (<i>gfp</i> R)	CCTTACCCTCTCCACTGACAG
Primers used for site directed mutagenesis	
P50 (<i>lspB</i> F1)	CAGAAATTTTATGTAAACTGTGTACTCTTAAGTGAATAATGTATATTTAGGCTCAATTTGTTCAG
P51 (<i>lspB</i> R1)	CTGAACAAAATTGAGCCATAAATATACATTAATTTCACTTAAAGAGTACACAGTTTACATAAAAAATTTCTG
P52 (<i>lspB</i> F2)	TAAAGCGGTTTATCTTATGGATAAAAATCAGAAATTTTTTATTGAAACTGTGTACTCTTAAGGTAA
P53 (<i>lspB</i> R2)	TTACCTTAAAGAGTACACAGTTTCAATAAAAAATTTCTGATTTTATCCATAAGATAAACCGCTTTA
P54 (<i>lspB</i> F3)	GTAAATTTCTTCAAAAAATGTGATCAATACCACAAATATTTGTAAAGCGGTTTATCTTATGGAT
P55 (<i>lspB</i> R3)	ATCCATAAGATAAACCGCTTTACAAAAATTTGTGGTATTGATCACATTTTGAAGAAATTTAC
P56 (<i>lspB</i> F4)	TTTCAAAGAATATCGTAAGCATAGCGTAATTTGTAAAATCGCCAAGTAAATTTCTTCAAAAAATG
P57 (<i>lspB</i> R4)	CATTTTTGAAGAAATTTACTTGGCGATTTACAAAATTACGCTATGCTTACGATATCTTTGAAA

31 Underlining indicates regions corresponding to restriction enzyme sites as mentioned in the text. *H. ducreyi* sequences are from GenBank

32 accession no. AE017143.

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34 TABLE S2. Summary of RNA-Seq read statistics

Bacterial strain	Growth phase	Biological replicate	Total reads	Aligned reads	% aligned reads	Average coverage/nt	Intergenic reads	% intergenic reads	Sense strand reads	Antisense strand reads
35000HP	Mid-log	R1	15,225,615	15,073,797	99.0	3.9	1,332,736	20.1	3,264,403	3,350,554
		R2	15,994,477	15,846,186	99.1	7.4	3,491,752	27.6	6,195,035	6,436,339
		R3	26,414,698	26,163,706	99.1	4.3	1,327,928	18.0	3,651,612	3,705,336
		R4	17,086,644	16,960,609	99.3	16.5	8,253,170	29.4	13,885,614	14,194,592
	Transition	R1	4,945,592	4,884,640	98.8	8.9	3,360,974	22.3	7,410,574	7,663,223
		R2	4,833,762	4,782,216	98.9	9.3	3,527,705	22.3	7,845,956	8,000,230
		R3	10,599,323	10,502,085	99.1	15.4	8,488,500	32.4	12,870,827	13,292,879
		R4	7,714,771	7,648,797	99.1	10.0	3,299,502	19.5	8,434,645	8,525,964
	Stationary	R1	6,680,671	6,614,957	99.0	2.9	1,442,949	29.5	2,387,167	2,497,473
		R2	12,843,688	12,631,374	98.3	2.8	1,228,311	25.7	2,357,938	2,424,278
		R3	7,418,648	7,356,948	99.2	6.2	3,443,581	32.8	5,174,345	5,327,740
		R4	28,370,833	28,080,206	99.0	4.5	2,028,504	26.5	3,779,182	3,869,615
35000HP <i>ΔcpxA</i>	Mid-log	R1	23,701,121	23,431,345	98.9	2.7	1,122,811	24.4	2,260,436	2,334,841
		R2	11,294,894	11,176,809	99.0	2.4	948,721	23.4	1,997,816	2,064,140
		R3	37,710,211	37,355,686	99.1	11.1	3,760,224	19.9	9,389,962	9,550,623
		R4	24,539,401	24,349,187	99.2	7.4	3,110,643	24.9	6,206,546	6,305,878
	Transition	R1	6,400,616	6,323,760	98.8	13.8	7,139,648	30.5	11,416,196	12,015,149
		R2	7,313,102	7,230,976	98.9	6.6	2,955,641	26.4	5,531,784	5,645,025
		R3	18,280,426	18,108,138	99.1	22.0	12,731,210	34.1	18,339,026	19,016,660
		R4	3,733,851	3,704,868	99.2	14.3	6,091,105	25.0	12,071,598	12,277,589
	Stationary	R1	4,649,206	4,595,277	98.8	3.7	1,767,470	27.9	3,093,621	3,230,139
		R2	4,106,577	4,061,956	98.9	4.3	2,140,229	29.6	3,563,903	3,667,073
		R3	19,075,447	18,940,585	99.3	10.7	4,382,836	24.2	8,962,292	9,145,846
		R4	12,620,310	12,512,424	99.1	2.2	983,125	26.5	1,830,191	1,874,677
35000HP <i>ΔcpxR</i>	Mid-log	R1	7,529,543	7,415,285	98.5	9.4	3,234,370	20.2	7,884,019	8,097,723
		R2	9,435,946	9,327,867	98.9	4.3	1,183,968	16.4	3,583,428	3,655,197
		R3	39,280,869	38,932,499	99.1	1.5	453,653	18.2	1,243,118	1,251,528
		R4	2,822,036	2,795,224	99.1	6.0	1,829,008	17.8	5,111,306	5,153,895
	Transition	R1	4,129,785	4,068,495	98.5	4.4	2,052,319	27.7	3,638,832	3,776,453
		R2	9,096,015	8,979,203	98.7	5.5	1,772,443	19.0	4,620,284	4,707,583
		R3	17,397,320	17,197,130	98.8	22.9	8,156,124	20.9	19,323,048	19,609,451
		R4	30,820,745	30,490,928	98.9	1.6	743,131	26.6	1,391,673	1,403,551
	Stationary	R1	16,185,039	15,981,742	98.7	2.4	1,123,266	27.6	1,998,573	2,069,922
		R2	7,312,017	7,238,625	99.0	5.3	2,526,528	28.1	4,421,590	4,557,613
		R3	2,519,648	2,494,646	99.0	10.1	4,446,631	25.9	8,509,360	8,687,770
		R4	10,362,439	10,265,201	99.1	17.9	6,562,677	21.5	15,144,383	15,346,545

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40 TABLE S3. Individual genes differentially expressed in 35000HPΔ*cpxA* compared to
 41 35000HPΔ*cpxR* at different phases of growth classified based on their functional categories

Gene ID	Gene name or homolog	Mid-log		Transition		Stationary	
		Fold	P-value	Fold	P-value	Fold	P-value
Amino acid biosynthesis							
HD0564	<i>aspA</i> , aspartate amonia-lyase			2.3	4.05E-04		
HD0577	<i>seld</i> , selenide, water dikinase	-2.0	1.94E-10	-2.5	7.78E-05	-2.2	2.49E-26
HD0890	<i>argC</i> , N-acetyl-gamma-glutamyl-phosphate reductase					2.3	1.07E-28
HD0896	<i>cysK</i> , O-acetylserine sulfhydrylase	-8.0	8.27E-70	-8.1	2.73E-17	-7.2	1.54E-147
Cell surface structures and associated proteins							
<u>Lipooligosaccharide biosynthesis</u>							
HD0454	<i>waaA</i> , 3-deoxy-D-manno-octulosonic-acid transferase					2.1	6.84E-24
HD0653	<i>waaF</i> , ADP-heptose-LPS heptosyltransferase II					-2.3	1.55E-31
HD1666	D,D-heptose 1,7-bisphosphate phosphatase	-2.2	3.33E-12			-4.3	7.10E-88
<u>Outer membrane proteins</u>							
HD0045	<i>momp</i> , major outer membrane protein	2.0	7.15E-11			17.9	2.46E-290
HD0046	<i>ompA2</i> , major outer membrane protein, OmpA2	-20.1	3.15E-129	-13.4	2.84E-24	-30.5	NS
HD0047	No known homolog	-5.8	6.71E-21	-7.5	1.92E-14	-9.9	4.45E-61
HD0048	No known homolog	-2.7	1.35E-10	-3.9	2.64E-08	-5.2	3.58E-51
HD0646	Outer membrane receptor protein, iron transport	-2.4	1.04E-15				
HD0746	<i>dltA</i> , Endo-1,4-beta-xylanase A			2.4	2.25E-04		
HD0769	<i>dsrA</i> , serum resistance protein DsrA	-17.7	7.84E-121	-10.5	8.36E-21	-40.4	NS
HD1017	24 kDa outer membrane protein; MipA protein	-3.9	7.80E-31	-3.0	4.10E-06	-5.7	1.97E-108
HD1078	<i>ompP1</i> , outer membrane protein P1					-2.3	3.73E-32
HD1155	<i>lspB</i> , large supernatant protein exporter	-10.7	9.68E-80	-5.7	8.47E-13		
HD1156	<i>lspA2</i> , large supernatant protein 2					-2.9	6.52E-51
HD1170	<i>ompP4</i> , outer membrane protein P4					-2.1	1.86E-24
HD1278	Serine protease	-4.2	4.57E-37	-2.9	5.36E-06	-3.7	1.03E-72
HD1280	Serine protease-like protein	-3.7	1.94E-31	-2.4	1.29E-04	-2.6	3.60E-42
HD1326	<i>hhdB</i> , hemolysin activation/secretion protein	-9.7	3.88E-81	-6.2	6.75E-14	-20.1	3.07E-290
HD1327	<i>hhdA</i> , hemolysin	-3.5	3.21E-29	-2.7	1.61E-05	-3.1	9.08E-54
HD1433	<i>ompP2A</i> , outer membrane protein P2-like protein	-12.2	6.76E-96	-8.0	3.96E-17	-9.8	9.08E-194
HD1435	<i>ompP2B</i> , outer membrane protein P2-like protein	5.7	8.19E-53	3.0	3.61E-06	13.1	1.33E-240
HD1856	Possible outer membrane protein	-8.5	1.86E-72	-6.3	3.91E-14	-5.2	2.16E-102
HD1920	<i>ncaA</i> , Membrane protein: NcaA class II	-6.7	6.28E-61	-5.1	1.57E-11	-8.8	4.53E-179
HD2017	Rare lipoprotein A	2.4	3.84E-15	2.7	2.13E-05		
HD2025	<i>hgbA</i> , hemoglobin-binding protein HgbA	-2.8	4.83E-21	-2.3	2.68E-04	-3.3	6.55E-61
<u>Sialyltransferases</u>							
HD0685	<i>neuA</i> , acylneuraminate cytidyltransferase			2.4	1.28E-04	2.2	1.88E-27
HD0686	<i>lst</i> , lipooligosaccharide sialyltransferase			2.3	3.26E-04	2.3	6.18E-30
<u>Type I fimbriae</u>							
HD0281	<i>fimA</i> , fimbrial major pilin protein	16.0	6.27E-114	15.6	1.50E-26	9.8	2.90E-192
HD0282	<i>fimB</i> , fimbrial structural subunit	6.4	2.68E-57	6.6	1.08E-14	3.5	3.92E-61
HD0283	<i>fimC</i> , fimbrial outer membrane usher protein	3.1	2.40E-24	2.6	3.93E-05	2.4	4.20E-34
HD0284	<i>fimD</i> , periplasmic fimbrial chaperone	3.9	1.19E-33	2.8	1.48E-05		
HD0285	Minor fimbrial subunit	3.7	1.88E-30	3.0	3.52E-06	2.2	6.03E-25
<u>Type IVa pili/type II secretion/competence</u>							
HD0182	Prepilin peptidase dependent protein A					-20.1	4.19E-264
HD0183	Prepilin peptidase dependent protein B					-19.4	6.27E-265
HD0184	No known homolog					-9.0	8.18E-168
HD0185	Prepilin peptidase dependent protein C					-7.0	5.25E-120
HD0209	<i>comF</i> , competence protein F					-2.7	3.84E-38
HD0318	Fimbrial biogenesis and twitching motility protein					-3.9	2.46E-72
HD0427	<i>comA</i> , competence protein A-like protein					-10.8	1.70E-172
HD0428	Tfp pilus assembly protein ComA					-14.0	1.14E-176
HD0429	No known homolog					-13.2	2.50E-97
HD0430	No known homolog					-13.9	2.53E-126
HD0431	No known homolog					-10.3	1.95E-98

Gene ID	Gene name or homolog	Mid-log		Transition		Stationary	
		Fold	P-value	Fold	P-value	Fold	P-value
HD0432	No known homolog					-9.7	3.43E-145
HD0433	Pilus assembly protein PilT/ComD					-11.2	9.54E-157
HD0434	<i>comE</i> , competence protein E/protein transport protein					-3.6	1.02E-66
HD0650	DNA uptake protein ComEA/type II secretion protein					-5.1	2.55E-104
HD0732	<i>radC</i> , DNA repair protein RadC					-5.2	2.21E-66
HD1123	Prepilin peptidase dependent protein D	-3.0	4.04E-15			-54.0	NS
HD1124	<i>hofB</i> , protein transport protein HofB, pili/fimbriae	-2.2	5.29E-12			-28.2	NS
HD1125	<i>hofC</i> , pili/fimbriae biogenesis protein					-5.7	2.65E-114
HD1126	Fimbrial leader peptidase HopD					-3.6	4.89E-58
HD1256	<i>rec2</i> , recombination protein 2					-10.2	7.32E-195
HD1888	<i>smf</i> , DNA processing chain A					-3.3	1.24E-51
HD1921	<i>recG</i> , ATP-dependent DNA helicase RecG	-3.4	5.34E-27	-3.4	2.20E-07	-2.5	9.83E-34
HD1985	DNA transformation protein, T(foX)/Sxy	-7.9	2.05E-68	-5.9	2.34E-13	-9.5	4.94E-183
Flp pili and associated proteins							
HD1298	<i>tadG</i> , tight adherence protein G	-2.6	1.99E-18			-2.8	1.08E-46
HD1299	<i>tadF</i> , tight adherence protein F	-3.1	1.14E-23	-2.0	2.22E-03	-3.7	3.04E-67
HD1300	<i>tadE</i> , tight adherence protein E	-2.8	1.50E-20	-2.0	2.47E-03	-3.0	1.88E-47
HD1301	<i>tadD</i> , tight adherence protein D	-3.5	2.16E-28	-2.2	6.00E-04	-6.0	1.12E-125
HD1302	<i>tadC</i> , tight adherence protein C	-3.9	5.14E-33	-2.4	2.18E-04	-6.0	1.14E-124
HD1303	<i>tadB</i> , tight adherence protein B	-4.0	8.16E-34	-2.4	2.35E-04	-9.6	2.71E-183
HD1304	<i>tadA</i> , tight adherence protein A	-3.5	5.90E-29	-2.4	1.80E-04	-9.4	5.06E-188
HD1305	<i>flp</i> operon protein D	-3.4	2.37E-27	-2.3	3.73E-04	-9.7	2.35E-190
HD1306	<i>rcpB</i> , rough colony protein B	-3.7	1.55E-30	-2.6	6.05E-05	-13.4	5.44E-233
HD1307	<i>rcpA</i> , rough colony protein A	-3.5	1.87E-29	-2.6	3.52E-05	-10.1	1.38E-197
HD1308	<i>flp</i> operon protein C	-3.9	1.72E-33	-2.9	7.36E-06	-12.4	4.41E-227
HD1309	<i>flp</i> operon protein B	-6.9	1.28E-60	-3.7	3.06E-08	-27.7	NS
HD1310	<i>flp3</i> , <i>flp</i> operon protein Flp3	-8.1	3.49E-69	-3.8	2.19E-08	-36.2	NS
HD1311	<i>flp2</i> , <i>flp</i> operon protein Flp2	-7.0	1.24E-58	-3.6	6.17E-08	-32.0	NS
HD1312	<i>flp1</i> , <i>flp</i> operon protein Flp1	-6.7	1.77E-55	-3.6	5.95E-08	-35.0	NS
Cell wall biosynthesis and remodeling							
HD0687	<i>rmlB</i> , dTDP-D-glucose 4,6-dehydratase			2.1	1.84E-03		
HD1400	Soluble lytic murein transglycosylase	2.4	4.03E-15	2.1	9.55E-04	2.5	3.03E-38
HD2016	<i>dacA</i> , D-alanyl-D-alanine carboxypeptidase fraction A	2.3	6.07E-14	2.2	7.35E-04		
Cofactor biosynthesis							
HD1389	<i>moaE</i> , molybdopterin converting factor subunit 2	-2.6	3.78E-17	-2.5	7.38E-05	-2.5	6.86E-34
HD1390	<i>moaD</i> , molybdopterin synthase small subunit	-3.1	1.20E-21	-2.5	1.01E-04	-2.5	4.00E-30
HD1391	<i>moaC</i> , molybdenum cofactor biosynthesis protein C	-3.1	7.95E-23	-2.8	1.42E-05	-2.7	7.77E-39
HD1392	<i>moaA</i> , molybdenum cofactor biosynthesis protein A	-3.0	3.90E-22	-2.2	9.72E-04	-2.8	1.59E-45
HD1480	<i>bioD</i> , dithiobiotin synthetase					-2.5	7.05E-37
HD1495	Putative dithiobiotin synthetase	-2.1	9.84E-12			-2.3	8.28E-29
HD1874	<i>ubiF</i> , 2-octaprenyl-3-methyl-6-methoxy-1,4-benzoquinol benzoquinol hydroxylase					-3.5	1.59E-65
Degradation/assimilation/utilization							
HD1857	<i>ulaD</i> , 3-keto-L-gulonate-6-phosphate decarboxylase	-3.0	1.03E-21	-3.2	1.03E-06	-2.0	8.93E-20
DNA replication, recombination, and repair							
HD0908	<i>tnpR</i> , transposon gamma-delta resolvase	-3.0	7.43E-19	-2.5	1.39E-04		
Fatty acid biosynthesis							
HD0181	<i>fabA</i> , 3-hydroxydecanoyl-ACP dehydratase					3.6	2.60E-63
Generation of precursor metabolites and energy							
HD0003	F0F1 ATP synthase subunit I	-3.0	3.69E-22	-2.3	4.82E-04	-7.6	2.50E-154
HD0004	<i>atpB</i> , ATP synthase F0F1 subunit A	-2.5	1.61E-16	-2.2	8.04E-04	-4.8	9.22E-100
HD0005	<i>atpE</i> , ATP synthase F0F1 subunit C	-2.2	4.38E-13			-4.8	1.47E-98
HD0006	<i>atpF</i> , ATP synthase F0F1 subunit B	-2.1	1.34E-11			-4.6	1.55E-94
HD0007	<i>atpH</i> , ATP synthase F0F1 subunit delta	-2.0	1.34E-10			-4.6	1.44E-95
HD0008	<i>atpA</i> , ATP synthase F0F1 subunit alpha					-4.1	5.00E-85
HD0009	<i>atpG</i> , ATP synthase F0F1 subunit gamma	-2.0	1.02E-10			-4.4	4.38E-91
HD0010	<i>atpD</i> , ATP synthase F0F1 subunit beta					-2.9	2.10E-49

Gene ID	Gene name or homolog	Mid-log		Transition		Stationary	
		Fold	P-value	Fold	P-value	Fold	P-value
HD0011	<i>atpC</i> , ATP synthase F0F1 subunit epsilon					-2.0	1.58E-20
Anaerobic respiration							
HD0084	<i>lldD</i> , L-lactate dehydrogenase	-5.9	1.57E-53	-4.3	1.04E-09	-9.8	4.74E-196
HD0261	NAD-dependent epimerase/dehydratase family protein					2.2	4.08E-28
HD0344	<i>nrfA</i> , cytochrome c552	-3.4	6.41E-27	-3.0	2.34E-06	-2.2	3.33E-24
HD0347	<i>nrfB</i> , cytochrome c nitrite reductase	-3.1	5.99E-22	-3.1	1.40E-06	-2.0	5.76E-17
HD0349	<i>nrfC</i> , nitrate reductase, Fe-S protein	-2.8	1.15E-18	-2.6	5.11E-05		
HD0350	<i>nrfD</i> , nitrate reductase, transmembrane protein	-2.2	3.16E-12				
HD0589	Beta-propeller domain of methanol dehydrogenase	-2.5	7.73E-16	-2.4	2.01E-04		
HD1110	<i>fdhE</i> , formate dehydrogenase accessory protein FdhE	4.1	6.38E-36	2.9	5.07E-06	3.1	7.78E-55
HD1393	<i>torY</i> , cytochrome c-type protein TorY	-2.7	1.17E-18	-2.7	2.54E-05	-2.7	6.28E-41
HD1394	<i>torZ</i> , TMAO reductase 2	-2.6	1.23E-18	-2.5	1.09E-04	-2.5	4.61E-37
HD1456	<i>ackA</i> , acetate kinase					-2.4	1.10E-33
HD1815	Dissimilatory sulfite reductase	3.3	6.93E-25	2.4	1.38E-04		
HD1986	<i>fumC</i> , fumarate hydratase	-2.2	4.15E-13			-3.6	7.75E-70
Hypothetical proteins							
HD0055	Hypothetical protein	2.0	2.62E-05	2.1	3.24E-03		
HD0083	Hypothetical protein			-2.2	1.24E-03		
HD0101	Hypothetical protein	2.3	5.35E-06				
HD0104	Hypothetical protein			2.1	4.75E-03		
HD0106	Hypothetical protein	2.7	1.07E-04				
HD0180	Hypothetical protein					2.4	1.34E-22
HD0286	Hypothetical protein	3.2	2.36E-25	2.8	1.56E-05		
HD0352	Hypothetical protein					2.1	1.79E-06
HD0590	Conserved hypothetical protein	-2.3	1.27E-13	-2.1	1.88E-03		
HD0805	Conserved hypothetical protein	-7.5	1.08E-66	-6.5	1.68E-14	-7.6	3.24E-158
HD0909	Hypothetical protein	-2.1	8.79E-11			-2.0	1.86E-21
HD0953	Hypothetical protein	2.3	3.23E-14				
HD1000	Hypothetical protein					2.5	1.01E-21
HD1060	Hypothetical protein	2.1	4.26E-12	2.0	2.12E-03		
HD1151	Hypothetical protein	-3.5	5.24E-20	-2.2	1.65E-03	-3.1	4.57E-16
HD1252	Hypothetical protein	-2.3	1.31E-09			-2.7	1.13E-11
HD1313	Hypothetical protein	-3.2	7.64E-16	-2.6	1.42E-04	-7.4	3.08E-81
HD1314	Hypothetical protein					3.4	7.48E-11
HD1432	Hypothetical protein	-4.7	1.88E-41	-3.6	8.14E-08	-8.6	1.00E-170
HD1434	Hypothetical protein	4.5	6.30E-40	3.1	1.95E-06	11.2	1.65E-202
HD1439	Hypothetical protein	-2.5	4.91E-16	-2.4	2.36E-04	-2.6	1.03E-38
HD1449	Hypothetical protein	2.1	1.78E-10	2.1	1.61E-03		
HD1502	Hypothetical protein	-2.9	5.48E-15	-3.2	1.78E-06		
HD1515	Hypothetical protein					-2.8	2.21E-39
HD1522	Hypothetical protein	-2.7	1.33E-03				
HD1523	Hypothetical protein	-2.5	1.27E-02				
HD1640	Hypothetical protein	5.6	4.30E-51	5.9	2.82E-13	9.9	4.20E-196
HD1899	<i>slyX</i> , SlyX family protein	-4.5	1.12E-39	-3.0	2.52E-06	-9.9	2.36E-188
HD2037	Conserved hypothetical protein	-2.2	4.12E-12			-2.1	3.56E-22
Lipid biosynthesis							
HD1253	<i>dggA</i> , diacylglycerol kinase	-2.0	4.06E-09				
Membrane transport/uptake							
HD0025	<i>dcuBI</i> , anaerobic C4-dicarboxylate transporter	4.5	3.11E-40	2.5	1.04E-04	2.5	9.61E-37
HD0312	<i>dppB</i> , dipeptide transport system permease			2.0	2.11E-03	2.0	2.89E-18
HD0313	<i>dppC</i> , dipeptide transport system permease	2.1	2.38E-10				
HD0614	<i>kefB</i> , glutathione-regulated K ⁺ -efflux system protein					2.6	2.19E-40
HD0766	<i>manZ</i> , PTS system mannose-specific transporter subunit subunit IID					2.0	1.55E-21
HD0770	HlyC/CorC family transporter with CBS domain			-2.1	1.33E-03		
HD0790	<i>ccmD</i> , heme exporter protein D					-2.2	1.24E-11
HD1018	<i>macA</i> , macrolide-specific efflux protein	-2.8	2.01E-20				

Gene ID	Gene name or homolog	Mid-log		Transition		Stationary	
		Fold	P-value	Fold	P-value	Fold	P-value
HD1019	<i>macB</i> , macrolide-specific ABC-type efflux carrier	-2.1	1.55E-11				
HD1074	<i>potD2</i> , spermidine/putrescine-binding protein	2.9	2.21E-21	2.3	2.44E-04	2.2	4.51E-30
HD1109	Oxalate/formate antiporter	9.9	8.56E-84	6.9	2.51E-15	7.6	3.38E-159
HD1146	<i>glpF</i> , glycerol uptake facilitator protein	4.5	5.29E-39	2.0	2.11E-03	3.3	2.39E-53
HD1150	<i>glpT</i> , glycerol 3-phosphate transporter	-2.4	1.20E-14	-2.4	2.06E-04		
HD1512	acriflavine resistance protein	2.2	7.34E-13				
HD1639	Major facilitator superfamily transporter	2.0	8.29E-11			4.7	3.10E-99
HD1814	Transporter/inner membrane protein YccA	3.3	5.19E-27	3.7	4.31E-08		
HD1859	PTS system enzyme II-A permease	-3.5	1.37E-26	-3.5	1.58E-07	-3.3	1.13E-46
HD1860	<i>ulaA</i> , PTS system ascorbate-specific transporter subunits subunits IICB	-2.8	3.14E-20	-3.2	9.04E-07		
Nucleoside and nucleotide metabolism							
HD0888	<i>deoC</i> , deoxyribose-phosphate aldolase					2.6	2.15E-40
HD0889	<i>deoD</i> , purine nucleoside phosphorylase					2.5	4.58E-36
HD1029	Nucleotidase	-2.0	2.38E-10			-5.9	1.64E-125
HD1424	<i>purD</i> , phosphoribosylaminoimidazole carboxylase	2.1	1.96E-11				
HD1503	<i>guaB</i> , inosine 5'-monophosphate dehydrogenase	-2.4	1.76E-15	-2.6	3.49E-05		
Phage-associated proteins							
HD0111	Mu-like phage C protein					2.0	4.46E-12
HD1533	Phage related DNA-binding protein			-2.8	7.47E-04		
Protein folding and degradation							
HD1900	<i>fkpA</i> , FKBP-type peptidylprolyl isomerase	-2.5	3.06E-16	-2.1	1.19E-03	-4.4	9.11E-93
Regulation and cell signaling							
HD0262	<i>argR</i> , arginine repressor ArgR	2.3	8.91E-13			3.4	2.54E-56
HD0280	Putative GrlR family protein	13.8	3.27E-101	16.7	2.05E-27	8.8	3.32E-152
HD0449	<i>fis</i> , DNA-binding protein Fis					-2.4	1.31E-31
HD0591	LemA protein; GacS homolog	-3.5	5.92E-29	-2.9	4.84E-06	-2.5	2.94E-35
HD0665	LysM domain/BON superfamily protein	2.0	8.17E-11	2.0	2.48E-03	2.5	7.09E-38
HD0738	<i>crp</i> , cAMP-regulatory protein	2.2	9.03E-13	2.1	1.00E-03	3.2	1.28E-58
HD0910	<i>hicB</i> , HicB protein					-2.3	3.54E-32
HD0911	<i>hicA</i> , HicA protein					-2.2	1.20E-27
HD1028	<i>gcvA</i> , DNA-binding transcriptional activator GcvA	-2.1	8.59E-12			-7.1	6.51E-150
HD1096	DNA-binding helix-turn-helix protein	-2.7	1.58E-16			-3.0	3.16E-40
HD1641	<i>purR</i> , DNA-binding transcriptional repressor PurR	-2.1	7.42E-11			-2.8	1.11E-43
Stress survival							
HD0848	<i>sodC</i> , superoxide dismutase (Cu-Zn)					-2.8	2.79E-45
HD1366	<i>cspC</i> , cold shock-like protein CspC			2.6	4.56E-05		
HD1366	<i>cspD</i> , cold shock-like protein CspD	2.1	5.66E-11				
HD1667	<i>bcp</i> , thioredoxin-dependent thiol peroxidase	-2.0	1.65E-10			-3.0	6.66E-50
HD1754	<i>ftnA</i> , ferritin					-2.1	7.13E-26
HD1784	<i>groEL</i> , molecular chaperone GroEL	2.6	1.41E-17				
HD1785	<i>groES</i> , co-chaperonin GroES	2.6	1.32E-17				
Translation							
HD0226	<i>miaB</i> , (dimethylallyl)adenosine tRNA methylthiotransferase					-2.3	3.60E-29
HD0319	<i>rlmN</i> , rRNA large subunit methyltransferase N					-7.5	5.12E-156
HD0448	<i>dusB</i> , tRNA-dihydrouridine synthase B					-2.9	1.91E-47
HD1257	<i>queA</i> , S-adenosylmethionine:tRNA ribosyltransferase-isomerase					-4.6	6.49E-92
HD1407	<i>efp</i> , elongation factor P					-2.3	5.54E-32
HD1664	tRNA/rRNA methyltransferase					-2.2	3.71E-26
HD1665	<i>queF</i> , 7-cyano-7-deazaguanine reductase					-5.3	4.66E-112

42 NS indicates genes that are statistically not significant in the stationary growth phase but 25-fold or higher differentially expressed and statistically significant in mid-
43 log and/or transition growth phases.

44

45 TABLE S4. Individual genes differentially expressed in 35000HPΔ*cpxA* compared to 35000HP
 46 at different phases of growth classified based on their functional categories.

Gene ID	Gene name or homolog	Mid-log		Transition		Stationary	
		Fold	P-value	Fold	P-value	Fold	P-value
Amino acid biosynthesis							
HD0890	<i>argC</i> , N-acetyl-gamma-glutamyl-phosphate reductase					2.1	3.85E-17
HD0891	<i>argB</i> , acetylglutamate kinase					2.1	8.01E-17
HD0896	<i>cysK</i> , O-acetylserine sulfhydrylase	-5.6	4.65E-26	-5.2	1.16E-12	-5.7	1.60E-89
Cell surface structures and associated proteins							
HD0653	<i>waaF</i> , ADP-heptose-LPS heptosyltransferase II					-2.3	7.81E-24
HD1666	D,D-heptose 1,7-bisphosphate phosphatase	-2.1	2.57E-06			-3.6	1.30E-51
Outer membrane proteins							
HD0045	<i>momp</i> , major outer membrane protein					7.2	1.69E-114
HD0046	<i>ompA2</i> , major outer membrane protein, OmpA2	-12.4	3.91E-49	-8.1	1.39E-18	-25.6	1.14E-259
HD0047	No known homolog	-4.0	1.17E-09	-4.4	1.73E-09	-7.5	2.57E-36
HD0048	No known homolog	-2.0	1.69E-04	-2.7	2.50E-05	-3.8	3.94E-26
HD0646	Outer membrane receptor protein, iron transport	-2.4	2.27E-08				
HD0651	<i>oapA</i> , opacity associated protein A					-2.2	6.70E-23
HD0652	<i>oapB</i> , opacity associated protein B					-2.0	5.09E-17
HD0746	<i>dltA</i> , Endo-1,4-beta-xylanase A					-2.8	1.83E-35
HD0769	<i>dsrA</i> , serum resistance protein DsrA	-18.0	4.46E-61	-12.5	5.41E-25	-27.4	3.17E-268
HD1017	24 kDa outer membrane protein; MipA protein	-2.3	4.88E-07			-3.9	1.08E-50
HD1078	<i>ompP1</i> , outer membrane protein P1					-2.7	5.89E-33
HD1155	<i>lspB</i> , large supernatant protein exporter	-3.8	6.44E-16	-2.0	1.64E-03	-15.4	2.46E-171
HD1278	Serine protease	-2.6	6.82E-10	-2.2	3.22E-04	-3.0	1.76E-38
HD1280	Serine protease-like protein	-2.6	2.40E-09			-2.4	4.69E-27
HD1326	<i>hhdB</i> , hemolysin activation/secretion protein	-5.3	1.78E-24	-3.6	2.06E-08	-16.9	3.97E-190
HD1327	<i>hhdA</i> , hemolysin	-2.5	1.10E-08	-2.0	1.32E-03	-2.4	2.35E-26
HD1433	<i>ompP2A</i> , outer membrane protein P2-like protein	-8.8	2.17E-38	-5.8	6.06E-14	-11.2	2.17E-160
HD1435	<i>ompP2B</i> , outer membrane protein P2-like protein	5.0	1.73E-23	3.3	1.76E-07	15.9	4.02E-202
HD1856	Possible outer membrane protein	-6.5	1.03E-29	-4.6	2.98E-11	-5.5	2.34E-83
HD1920	<i>ncaA</i> , NcaA class II	-6.0	4.56E-28	-3.7	6.90E-09	-7.2	4.97E-114
HD2025	<i>hgbA</i> , hemoglobin-binding protein HgbA	-2.5	3.67E-09	-2.2	4.07E-04	-2.6	3.34E-31
Type I fimbriae							
HD0281	<i>fimA</i> , fimbrial major pilin protein	8.9	5.45E-39	8.7	1.54E-19	9.9	3.29E-144
HD0282	<i>fimB</i> , fimbrial structural subunit	4.7	1.03E-21	4.6	2.66E-11	3.1	2.01E-38
HD0283	<i>fimC</i> , fimbrial outer membrane usher protein	2.6	1.11E-09	2.1	7.36E-04	2.4	1.04E-25
HD0284	<i>fimD</i> , periplasmic fimbrial chaperone	3.1	5.07E-13	2.2	5.86E-04		
HD0285	Minor fimbrial subunit	3.0	3.31E-12	2.3	1.44E-04	2.1	4.45E-17
Type IVa pili/type II secretion/competence							
HD0182	Prepilin peptidase dependent protein A					-2.2	1.02E-16
HD0183	Prepilin peptidase dependent protein B					-2.3	7.18E-18
HD0428	Tfp pilus assembly protein ComA					-2.0	5.90E-10
HD0433	Pilus assembly protein PilT/ComD					-2.0	9.21E-11
HD1123	Prepilin peptidase dependent protein D					-4.3	1.45E-41
HD1124	<i>hofB</i> , protein transport protein, pili/fimbrial protein					-2.6	6.27E-28
HD1921	<i>recG</i> , ATP-dependent DNA helicase RecG	-2.1	1.47E-06			-2.3	9.34E-23
HD1985	DNA transformation protein, T(foX)/Sxy	-3.4	1.79E-14	-2.8	4.35E-06	-6.6	1.08E-100
Flp pili and associated proteins							
HD1298	<i>tadG</i> , tight adherence protein G	-2.1	1.44E-06			-2.1	1.83E-19
HD1299	<i>tadF</i> , tight adherence protein F	-2.5	1.04E-08	-2.0	1.93E-03	-2.7	3.16E-31
HD1300	<i>tadE</i> , tight adherence protein E	-2.3	8.50E-08			-2.5	2.90E-25
HD1301	<i>tadD</i> , tight adherence protein D	-2.8	1.18E-10			-4.8	7.49E-75
HD1302	<i>tadC</i> , tight adherence protein C	-3.1	1.25E-12	-2.1	1.22E-03	-5.2	2.08E-80
HD1303	<i>tadB</i> , tight adherence protein B	-2.8	9.05E-11			-6.9	1.04E-104
HD1304	<i>tadA</i> , tight adherence protein A	-2.5	5.48E-09			-6.9	8.87E-109
HD1305	<i>flp</i> operon protein D	-2.5	9.74E-09			-7.3	1.02E-113
HD1306	<i>rcpB</i> , rough colony protein B	-2.7	6.47E-10	-2.1	9.11E-04	-10.3	8.06E-147
HD1307	<i>rcpA</i> , rough colony protein A	-2.5	3.42E-09	-2.2	4.11E-04	-8.0	2.74E-123

Gene ID	Gene name or homolog	Mid-log		Transition		Stationary	
		Fold	P-value	Fold	P-value	Fold	P-value
HD1308	<i>flp</i> operon protein C	-2.8	7.19E-11	-2.4	1.17E-04	-9.3	4.16E-139
HD1309	<i>flp</i> operon protein B	-4.6	7.34E-21	-2.8	4.43E-06	-21.8	2.19E-235
HD1310	<i>flp3</i> , <i>flp</i> operon protein Flp3	-5.1	3.57E-23	-2.8	4.51E-06	-32.9	5.37E-287
HD1311	<i>flp2</i> , <i>flp</i> operon protein Flp2	-4.0	3.12E-17	-2.6	1.64E-05	-28.3	2.27E-248
HD1312	<i>flp1</i> , <i>flp</i> operon protein Flp1	-4.1	1.30E-17	-2.6	2.65E-05	-31.3	7.18E-256
Cofactor biosynthesis							
HD1389	<i>moaE</i> , molybdopterin converting factor subunit 2	-2.3	1.25E-07	-2.5	6.38E-05	-2.4	3.47E-24
HD1390	<i>moaD</i> , molybdopterin synthase small subunit	-2.7	1.33E-09	-2.3	1.50E-04	-2.5	1.11E-23
HD1391	<i>moaC</i> , molybdenum cofactor biosynthesis protein C	-2.7	1.03E-09	-2.5	4.33E-05	-2.8	1.38E-31
HD1392	<i>moaA</i> , molybdenum cofactor biosynthesis protein A	-2.5	9.82E-09	-2.1	7.85E-04	-3.2	9.72E-43
HD1495	Putative dithiobiotin synthetase	-2.3	1.54E-07			-2.4	1.66E-23
Degradation/assimilation/utilization							
HD1857	<i>ulaD</i> , 3-keto-L-gulonate-6-phosphate decarboxylase	-2.8	8.64E-11	-2.9	3.07E-06		
DNA replication, recombination, and repair							
HD0908	<i>tnpR</i> , transposon gamma-delta resolvase	-2.0	1.75E-05				
Fatty acid biosynthesis							
HD0181	<i>fabA</i> , 3-hydroxydecanoyl-ACP dehydratase					2.3	1.61E-22
Generation of precursor metabolites and energy							
HD0003	F0F1 ATP synthase subunit I	-2.1	5.02E-06			-6.5	1.48E-101
HD0004	<i>atpB</i> , ATP synthase F0F1 subunit A					-3.9	1.21E-57
HD0005	<i>atpE</i> , ATP synthase F0F1 subunit C					-3.6	1.29E-50
HD0006	<i>atpF</i> , ATP synthase F0F1 subunit B	-2.0	7.95E-06			-3.4	3.58E-48
HD0007	<i>atpH</i> , ATP synthase F0F1 subunit delta					-3.4	1.67E-46
HD0008	<i>atpA</i> , ATP synthase F0F1 subunit alpha					-2.9	3.83E-38
HD0009	<i>atpG</i> , ATP synthase F0F1 subunit gamma					-2.9	3.35E-37
Anaerobic respiration							
HD0084	<i>lldD</i> , L-lactate dehydrogenase	-9.5	6.46E-41	-7.8	4.59E-18	-11.6	1.58E-165
HD0261	NAD-dependent epimerase/dehydratase family protein					2.0	8.73E-18
HD0344	<i>nrfA</i> , cytochrome c552	-2.3	1.47E-07	-2.4	1.21E-04	-2.7	9.42E-30
HD0347	<i>nrfB</i> , cytochrome c nitrite reductase	-2.1	4.72E-06	-2.5	6.40E-05	-2.4	2.89E-19
HD0349	<i>nrfC</i> , nitrate reductase, Fe-S protein	-2.0	8.76E-06	-2.2	5.11E-04		
HD0589	Beta-propeller domain of methanol dehydrogenase	-2.8	1.94E-10	-2.2	5.08E-04		
HD1110	<i>fdhE</i> , formate dehydrogenase accessory protein FdhE	3.3	5.44E-14	2.5	3.29E-05	3.8	1.73E-56
HD1393	<i>torY</i> , cytochrome c-type protein TorY	-2.2	7.22E-07	-2.3	1.58E-04	-2.4	1.18E-24
HD1394	<i>torZ</i> , TMAO reductase 2			-2.2	3.47E-04	-2.0	6.33E-18
HD1986	<i>fumC</i> , fumarate hydratase					-3.0	1.14E-39
Hypothetical proteins							
HD0099	Hypothetical protein					2.5	3.36E-02
HD0149	Hypothetical protein					2.2	2.47E-03
HD0286	Hypothetical protein	2.6	2.74E-09	2.2	5.27E-04		
HD0590	Conserved hypothetical protein	-2.5	1.07E-08				
HD0805	Conserved hypothetical protein	-6.1	1.98E-28	-4.3	2.24E-10	-6.7	3.36E-106
HD0909	Hypothetical protein					-2.1	1.12E-17
HD1060	Hypothetical protein					-2.4	4.21E-27
HD1151	Hypothetical protein	-2.3	2.65E-06	-2.8	6.35E-06	-2.1	4.07E-06
HD1252	Hypothetical protein					-2.3	1.11E-06
HD1313	Hypothetical protein	-2.1	4.05E-05	-2.1	2.31E-03	-6.3	2.91E-55
HD1314	Hypothetical protein					6.7	2.26E-11
HD1316	<i>sana</i> , SanA protein					2.5	1.64E-08
HD1409	Hypothetical protein					-2.2	2.96E-21
HD1432	Hypothetical protein	-3.5	6.60E-15	-2.8	6.50E-06	-8.9	2.45E-132
HD1434	Hypothetical protein	4.1	1.97E-18	2.9	3.14E-06	14.3	7.80E-169
HD1471	Hypothetical protein					-2.0	6.90E-15
HD1502	Hypothetical protein			-2.1	1.22E-03	-2.1	2.29E-13
HD1515	Hypothetical protein					-2.6	1.81E-26
HD1526	Hypothetical protein			-2.4	4.69E-04		
HD1534	Hypothetical protein			-2.8	3.27E-04		
HD1537	Hypothetical protein					-2.7	2.24E-07

Gene ID	Gene name or homolog	Mid-log		Transition		Stationary	
		Fold	P-value	Fold	P-value	Fold	P-value
HD1577	Hypothetical protein					6.4	3.54E-04
HD1640	Hypothetical protein	4.4	3.87E-20	3.9	2.04E-09	7.8	2.78E-122
HD1899	<i>slyX</i> , SlyX family protein	-4.0	1.21E-17	-2.8	4.57E-06	-8.4	5.94E-125
Lipid biosynthesis							
HD1253	<i>dgkA</i> , diacylglycerol kinase	-2.0	1.78E-05			-2.0	1.95E-12
Membrane transport/uptake							
HD0025	<i>dcuB1</i> , anaerobic C4-dicarboxylate transporter	2.1	2.07E-06				
HD0313	<i>dppB</i> , dipeptide transport system permease					2.3	3.16E-19
HD0489	Putative sulfate transport protein CysZ	2.3	3.76E-03				
HD0766	<i>manZ</i> , PTS system mannose-specific transporter subunit II					2.3	7.25E-21
HD0767	<i>manY</i> , mannose-specific PTS system IIC component					2.0	2.00E-16
HD0768	<i>manX</i> , mannose-specific phosphotransferase IIAB					2.1	5.03E-18
HD1018	<i>macA</i> , macrolide-specific efflux protein	-2.0	8.26E-06				
HD1109	Oxalate/formate antiporter	6.9	6.84E-32	4.4	1.34E-10	7.9	6.49E-124
HD1146	<i>glpF</i> , glycerol uptake facilitator protein	3.2	1.69E-13			3.0	2.88E-35
HD1150	<i>glpT</i> , glycerol 3-phosphate transporter	-2.0	5.15E-06	-2.7	1.03E-05		
HD1639	Major facilitator superfamily transporter	2.1	2.60E-06			5.3	5.76E-86
HD1859	PTS system enzyme II-A permease	-3.1	3.13E-12	-3.2	3.69E-07	-2.8	1.97E-27
HD1860	<i>ulaA</i> , PTS system ascorbate-specific transporter subunits IICB	-2.3	1.19E-07	-2.9	2.48E-06		
HD0614	<i>kefB</i> , glutathione-regulated K ⁺ -efflux system protein					2.5	6.36E-28
Nucleoside and nucleotide metabolism							
HD0888	<i>deoC</i> , deoxyribose-phosphate aldolase					2.5	7.40E-27
HD0889	<i>deoD</i> , purine nucleoside phosphorylase					2.3	1.43E-22
HD1029	nucleotidase	-2.5	5.42E-09			-4.3	5.15E-67
Phage-associated proteins							
HD1525	<i>gam</i> , mu-phage host-nuclease inhibitor protein			-2.6	9.84E-05		
HD1530	Putative phage-associated protein			-2.2	1.12E-03		
HD1532	Putative phage-associated protein			-2.5	9.49E-05		
HD1533	Phage related DNA-binding protein			-3.5	4.35E-06		
HD1538	Putative phage-related DNA-binding protein			-2.2	1.46E-03	-2.6	1.61E-09
Protein folding and degradation							
HD1900	<i>jkpA</i> , FKBP-type peptidylprolyl isomerase	-2.4	2.54E-08			-3.2	7.15E-45
Regulation and cell signaling							
HD0262	<i>argR</i> , arginine repressor ArgR	2.0	1.35E-05			3.0	3.56E-35
HD0280	Putative GrlR family protein	9.5	5.83E-41	9.0	4.63E-20	8.9	1.87E-114
HD0591	LemA protein; GacS homolog	-4.1	8.62E-19	-2.7	1.44E-05	-3.8	5.85E-56
HD0738	<i>crp</i> , cAMP-regulatory protein					2.5	1.31E-27
HD0910	<i>hicB</i> , HicB protein					-2.6	3.96E-30
HD0911	<i>hicA</i> , HicA protein					-2.6	5.99E-31
HD1028	<i>gcvA</i> , DNA-binding transcriptional activator GcvA	-2.5	5.31E-09			-5.1	6.74E-82
HD1096	DNA-binding helix-turn-helix protein					-2.6	8.15E-24
HD1524	Transcriptional activator PerC domain protein			-3.8	3.90E-06		
HD1641	<i>purR</i> , DNA-binding transcriptional repressor PurR					-2.8	3.68E-33
Stress survival							
HD0848	<i>sodC</i> , superoxide dismutase (Cu-Zn)					-2.4	8.85E-26
HD1667	<i>bcp</i> , thioredoxin-dependent thiol peroxidase					-2.3	4.80E-24
Translation							
HD0448	<i>dusB</i> , tRNA-dihydrouridine synthase B					-2.3	6.25E-24
HD1665	<i>queF</i> , 7-cyano-7-deazaguanine reductase					-4.8	2.71E-75

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51 TABLE S5. Individual genes differentially expressed in 35000HP Δ *cpxR* compared to 35000HP
 52 at different phases of growth classified based on their functional categories

Gene ID	Gene name or homolog	Mid-log		Transition		Stationary	
		Fold	P-value	Fold	P-value	Fold	P-value
Cell surface structures and associated proteins							
<u>Lipooligosaccharide biosynthesis</u>							
HD0454	<i>waaA</i> , 3-deoxy-D-manno-octulosonic-acid transferase					-2.1	2.84E-25
<u>Outer membrane proteins</u>							
HD0045	<i>momp</i> , major outer membrane protein	-2.1	6.38E-08			-2.6	1.94E-39
HD1155	<i>lspB</i> , large supernatant protein exporter	2.8	6.73E-13	2.8	7.90E-06		
<u>Type IVa pili/type II secretion/competence</u>							
HD0182	Prepilin peptidase dependent protein A					8.8	6.23E-167
HD0183	Prepilin peptidase dependent protein B					8.5	6.18E-163
HD0184	No known homolog					5.2	6.89E-101
HD0185	Prepilin peptidase dependent protein C					4.4	3.93E-77
HD0209	<i>comF</i> , competence protein F					2.5	3.84E-31
HD0318	Fimbrial biogenesis and twitching motility protein					3.7	1.86E-65
HD0427	<i>comA</i> , competence protein A-like protein					5.6	2.20E-105
HD0428	Tfp pilus assembly protein ComA					6.7	8.77E-109
HD0429	No known homolog					6.7	5.81E-64
HD0430	No known homolog					7.7	2.85E-87
HD0431	No known homolog					6.1	3.59E-65
HD0432	No known homolog					5.5	7.94E-92
HD0433	Pilus assembly protein PilT/ComD					5.5	4.03E-89
HD0434	<i>comE</i> , competence protein E/protein transport protein HofQ					2.8	7.05E-44
HD0650	DNA uptake protein ComEA/type II secretion protein					4.2	2.84E-82
HD0732	<i>radC</i> , DNA repair protein RadC					5.0	3.30E-61
HD0746	<i>dltA</i> , Endo-1,4-beta-xylanase A	-2.7	1.66E-12	-2.7	1.08E-05	-2.5	6.14E-38
HD1123	Prepilin peptidase dependent protein D	2.2	6.86E-07			12.3	4.89E-214
HD1124	<i>hofB</i> , protein transport protein; pili/fimbrial biogenesis protein					10.5	1.30E-199
HD1125	<i>hofC</i> , pili/fimbriae biogenesis protein					4.6	4.64E-88
HD1126	Fimbrial leader peptidase HopD					3.3	1.41E-48
HD1256	<i>rec2</i> , recombination protein 2					5.9	7.90E-121
HD1888	<i>smf</i> , DNA processing chain A					3.2	1.79E-49
HD1985	DNA transformation protein, T(foX)/Sxy	2.3	3.31E-09				
Cofactor biosynthesis							
HD1874	<i>ubiF</i> , ubiquinone biosynthesis hydroxylase					2.9	9.00E-49
Generation of precursor metabolites and energy							
HD1815	Dissimilatory sulfite reductase	-2.5	2.30E-10	-2.6	3.93E-05		
Hypothetical proteins							
HD0055	Hypothetical protein					-2.3	3.54E-18
HD0536	Hypothetical protein					5.1	1.36E-02
HD1060	Putative lipoprotein	-2.6	1.93E-11	-2.4	1.29E-04	-2.5	1.26E-38
HD1439	Hypothetical protein	2.1	2.71E-07	2.2	3.70E-04	2.1	2.56E-23
HD1471	Hypothetical protein	-2.2	2.05E-08	-2.6	3.04E-05		
HD1537	Hypothetical protein					-3.0	1.19E-08
Membrane transport/uptake							
HD0025	<i>dcuB1</i> , anaerobic C4-dicarboxylate transporter	-2.2	3.27E-08				
HD1074	<i>potD2</i> , spermidine/putrescine-binding protein	-2.2	1.63E-08				
HD1546	Putative ABC transporter					-2.8	3.96E-43
HD1814	Transporter/inner membrane protein YccA	-3.3	1.51E-17	-3.3	1.49E-07	-2.2	4.91E-27
Phage-associated proteins							
HD0535	Tail assembly protein					7.7	1.79E-03
HD1538	Putative phage-related DNA-binding protein					-2.4	1.32E-09
Translation							
HD0319	<i>rlmN</i> , Ribosomal RNA large subunit methyltransferase N					5.4	3.42E-113
HD1257	<i>queA</i> , S-adenosylmethionine:tRNA ribosyltransferase:isomerase					3.5	2.82E-63

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55 TABLE S6. Promoters containing the putative *H. ducreyi* CpxR binding logo

Gene	Motif ^a	Strand ^b	Position ^c	Score ^d	Position of additional motif(s) ^e
<i>ackA</i>	TTTACCTGATTAGC	-	129-16	4.6:2.9	
<i>bioD</i>	GTAGATAAAATGTTAA	+	431-16	3.9:3.5	213-199 (-)
<i>ccmD</i>	GCAAAATGGGGCGAA	+	305-291	4.0:2.7	376-61 (-)
<i>comA</i>	GTAAGATTTGCATA	+	290-76	4.6:2.6	364-49 (-), 283-70 (-), 72-57 (+), 353-40 (-), 324-11 (-)
<i>comF</i>	TTTGGCTTTTAAAC	-	246-33	3.1:2.1	
<i>cysK</i>	GTACATCTCGTAAT	+	439-26	3.7:3.2	194-79 (+)
<i>dsrA</i>	GCAGAATGAGTGTAA	+	225-10	3.3:3.5	152-38 (+)
<i>efp</i>	GCAAACTTGCTAA	+	396-83	4.0:2.9	105-90 (-), 379-65 (-)
<i>fumC</i>	GTAAATCGCAAGTGCA	+	138-23	4.6:2.4	279-65 (-)
<i>gcvA</i>	GTTAATAAAACCAA	+	295-82	3.5:3.1	248-33 (-), 262-49 (+), 242-28 (-), 253-38 (+), 286-73 (+), 237-24 (-)
<i>HD0003</i>	TTTACTTTTAAATTTAA	-	174-59	4.6:2.2	287-74 (-), 156-42 (+)
<i>HD0048</i>	GTAAAAGGTCGTAAA	+	140-26	4.6:4.6	286-71 (+), 80-66 (+), 403-388 (+), 344-30 (+), 157-44 (+), 54-39 (+), 339-25 (-)
<i>HD0182</i>	TTTACCTTTCTTTGG	-	416-02	4.6:3.1	303-290 (+), 204-190 (-), 426-12 (-), 171-56 (+), 208-194 (+), 359-44 (-)
<i>HD0226</i>	TTTACACGCATTGCAC	-	383-68	4.6:2.4	194-79 (-)
<i>HD0318</i>	GTAATTTGGCAA	+	76-63	4.6:4.0	179-64 (-), 386-72 (+), 341-27 (+), 204-191 (+)
<i>HD0589</i>	TTTACCTTTCTTTTAA	-	235-20	4.6:2.2	319-04 (+), 210-197 (-)
<i>HD0650</i>	TTAACTTAAATTGC	-	81-68	3.5:2.6	242-28 (-), 389-76 (-)
<i>HD0805</i>	TTTACACAACCATTAC	-	119-04	4.6:3.2	96-83 (+), 438-25 (+)
<i>HD1017</i>	GTAATAAGGGTAGA	+	364-50	4.6:3.9	344-31 (+), 354-31 (+), 245-31 (-), 200-186 (+)
<i>HD1096</i>	TTTACATTTTTTTTGC	-	75-60	4.6:4.0	64-50 (-), 140-26 (+), 93-79 (+)
<i>HD1123</i>	TTTGCTGCCCTTTC	-	210-197	4.0:4.0	201-188 (-), 322-08 (-)
<i>HD1252</i>	GTAGAATTATTTAA	+	131-18	3.9:2.2	
<i>HD1313</i>	GTAAAATACTGCAAT	+	212-198	4.6:2.6	437-23 (+), 151-37 (+)
<i>HD1432</i>	GTAATTTAAAAGTAAA	+	211-196	4.6:4.6	
<i>HD1439</i>	TTTACCGCATTAAC	-	322-09	4.6:3.5	322-09 (+)
<i>HD1495</i>	TTTACTGTTTCTGC	-	336-23	4.6:3.3	386-73 (+), 111-98 (+), 216-01 (+)
<i>HD1515</i>	TTTACATTTTTTTATGC	-	58-43	4.6:2.6	110-96 (-)
<i>HD1920</i>	GCAAATCTTGACACA	+	317-04	4.0:3.1	439-25 (-), 236-23 (+)
<i>HD1985</i>	TTTACTGTATCTTAC	-	162-49	4.6:3.9	306-292 (-), 337-24 (-), 429-14 (-)
<i>HD2037</i>	TTTACATTAATTAC	-	363-50	4.6:3.2	144-31 (-)
<i>hhdA</i>	GTAGAGTATGCAAG	+	173-60	3.9:2.4	347-33 (+)
<i>hhdB</i>	GTTAATTAGATCTAAC	+	144-29	3.5:2.3	193-80 (-)
<i>lldD</i>	TTTACAAAAAATTCAC	-	113-98	4.6:3.3	165-51 (-), 294-80 (+), 123-09 (-), 343-29 (-)
<i>lspB</i>	GTAATTAATGTATA	+	53-39	4.6:3.2	73-60 (+), 291-77 (+), 116-03 (+), 170-57 (+), 435-21 (-)
<i>moaA</i>	GCAAATTAGGTATA	+	293-80	4.0:3.2	284-70 (+)
<i>nrfA</i>	GTAATTTAAAAGTTAT	+	255-41	4.6:2.1	438-23 (-)
<i>ompA2</i>	GTAAGGTCGTAAA	+	370-56	4.6:4.6	225-12 (-), 196-81 (-), 101-88 (-)
<i>ompP1</i>	CTAAAAGATAGCTAA	+	303-288	3.7:2.9	
<i>ompP2A</i>	TTTACTTTTAAATTTAC	-	303-288	4.6:4.6	270-57 (+)
<i>ompP4</i>	TGTACTCTATATAC	-	77-64	3.7:3.2	400-386 (-)
<i>queA</i>	TTTACATCCATTAAC	-	215-01	4.6:3.5	300-286 (-), 311-296 (-), 188-74 (-)
<i>queF</i>	GTGAAAAAAAAGCAGA	+	74-59	3.3:3.3	63-50 (+)
<i>radC</i>	GTAATACCAACTAAA	+	248-34	3.2:3.7	
<i>rec2</i>	TTTACCTGATTTTAT	-	406-391	4.6:1.8	65-52(+)
<i>selD</i>	GTAAAATTTTACTAAA	+	142-27	4.6:3.7	381-66 (-), 370-55 (-), 449-34 (-), 250-37 (+), 438-23 (-)
<i>slyX</i>	TTTACTTTTTTCAGC	-	412-398	4.6:2.2	141-28 (+), 421-08 (-), 171-58 (-), 162-49 (-), 363-50 (-)
<i>smf</i>	TTACATACTTTAG	-	246-33	3.3:3.7	79-66 (-)
<i>sodC</i>	GTAAATCTTTGCATA	+	77-63	4.6:2.6	198-83 (-), 138-25 (+), 450-36 (+)
<i>torY</i>	GTAAGATTTGTTAT	+	115-01	4.6:2.1	371-57 (-), 232-19 (+), 145-32 (-)
<i>ubiF</i>	GTAATAACAGTAGC	+	72-58	4.6:2.6	321-06 (+), 105-91 (+), 211-197 (+), 273-58 (-), 341-27 (-)
<i>ulaA</i>	TTTACTTTTAAATTTAC	-	152-37	4.6:4.6	

56 ^aThe sequence corresponds to the motif with the highest match score; putative conserved residues are highlighted in bold.

57 ^bCorresponds to the motif with the highest match score.

58 ^cCorresponds to the motif with the highest match score; position of the motif in the promoter region relative to the start codon.

59 ^dCorresponds to the motif with the highest match score; match score is the sum of individual position scores from each letter in the sequence.

60 ^ePosition of additional motifs identified in the promoter regions relative to start codon.

61 +Template strand; -Complementary strand.