

**Table S3.** Differential-expression of core, phylogroup-specific, and isolate-specific genes

		Core Genes <sup>a</sup>									
Cluster ID <sup>a</sup>	Gene	Predicted Protein Function	LFC <sup>d</sup>								
			100329	401140	B171	402290	E110019	E2348/69	C581-05	401588	302053
Cluster_22333	<i>cirA</i>	colicin I receptor	7.40	4.91	3.23	6.96	4.53	4.16	5.44	2.62	4.71
Cluster_22417	<i>gfpA</i>	glycerol-3-phosphate dehydrogenase, anaerobic, A subunit	-7.80	-6.51	-7.06	-6.25	-5.52	-6.13	-7.77	-3.31	-9.21
Cluster_22418	<i>gfpB</i>	glycerol-3-phosphate dehydrogenase, anaerobic, B subunit	-6.73	-6.51	-6.83	-6.88	-5.91	-6.62	-8.18	-3.86	-7.83
Cluster_24491	<i>treC</i>	alpha,alpha-phosphotrehalase	-3.30	-5.45	-8.30	-6.95	-7.06	-7.42	-6.46	-7.03	-8.27
Cluster_24492	<i>treB</i>	PTS system trehalose-specific EIIBC component	-4.37	-5.65	-7.04	-8.28	-8.16	-8.79	-7.36	-7.09	-9.40
Cluster_25541	<i>bioD</i>	dehydrobiotin synthase	6.09	3.83	3.82	5.20	4.81	5.10	3.51	4.75	6.57
Cluster_2623	<i>gfpT</i>	glycerol-3-phosphate transporter	-6.41	-7.54	-9.27	-7.91	-7.91	-8.07	-6.53	-4.32	-9.88
Cluster_2626	<i>gfpC</i>	glycerol-3-phosphate dehydrogenase, anaerobic, C subunit	-5.44	-5.51	-5.54	-4.76	-5.64	-5.78	-6.03	-3.51	-6.06
Cluster_27245		MauM/NapG ferredoxin-type family protein	-6.11	-2.40	2.38	-2.76	3.19	-2.92	-3.12	-2.60	-6.22
Cluster_28414	<i>gfpD</i>	aerobic glycerol-3-phosphate dehydrogenase	-2.85	-4.87	-5.86	-4.60	-5.58	-5.68	-5.87	-4.41	-6.39
Cluster_30847	<i>narK</i>	nitrite extrusion protein 1	-6.92	-5.92	-2.25	-7.04	-4.52	-6.39	-6.48	-4.32	-6.16
Cluster_33251		RbsD / FucU transport family protein	-6.80	-6.87	-5.32	-7.04	-4.73	-5.62	2.31	-6.44	-4.74
Cluster_33636	<i>deoC</i>	deoxyribose-phosphate aldolase	-3.70	-3.57	-3.62	-4.05	-2.65	-3.30	-3.20	-4.17	-3.98
Cluster_34598	<i>bioC</i>	malonyl-CoA O-methyltransferase BioC	7.50	2.44	2.47	5.57	4.41	4.55	4.36	4.36	5.83
Cluster_37491	<i>dtpB</i>	dipeptide and tripeptide permease B	-3.95	-2.69	-2.37	-3.29	-3.48	-3.72	-3.29	-3.30	-5.06
Cluster_37569	<i>dtpF</i>	oligopeptide/dipeptide ABC transporter, ATP-binding, C-terminal domain protein	3.52	3.63	2.08	3.65	2.60	3.76	2.16	2.18	2.58
Cluster_23696	<i>dtpD</i>	oligopeptide/dipeptide ABC transporter, ATP-binding, C-terminal domain protein	3.69	4.14	2.38	4.42	3.12	4.95	4.18	3.32	4.24
Cluster_39493	<i>bioB</i>	biotin synthase	6.45	3.94	2.73	6.10	3.85	5.02	5.86	4.76	6.29
Cluster_39494	<i>bioF</i>	8-amino-7-oxononanoate synthase	5.65	2.05	2.81	5.84	3.93	4.83	6.02	5.36	6.10
Cluster_40107		nitrate reductase, alpha subunit	-8.34	-6.28	-3.12	-6.45	-5.18	-8.36	-9.75	-5.98	-8.71
Cluster_40648	<i>purT</i>	phosphoribosylglycinamide formyltransferase 2	3.81	2.96	4.44	3.94	4.98	2.82	3.49	3.23	2.17
		Phylogroup-Specific Genes <sup>a</sup>									
Cluster ID	Gene	Predicted Protein Function	LFC <sup>d</sup>								
<b>100329 (A)</b>											
Cluster_6463		outer membrane autotransporter barrel domain protein	2.37								
<b>401140 (A)</b>											
Cluster_6463		outer membrane autotransporter barrel domain protein	2.66								
<b>B171 (B1)</b>											
Cluster_4478		conserved hypothetical protein	2.64								
Cluster_4503		conserved hypothetical protein	2.11								
<b>402290 (B1)</b>											
Cluster_47272		conserved hypothetical protein	2.20								
<b>E110019 (B1)</b>											
None		None	None								
<b>E2348/69 (B2)</b>											
Cluster_20380		BAAT / Acyl-CoA thioester hydrolase C terminal family protein	-2.50								
Cluster_22955		PfkB carbohydrate kinase family protein	-2.65								
Cluster_23655	<i>hmuV</i>	hemin import ATP-binding protein HmuV	2.42								
Cluster_24280		His Kinase A domain protein	-2.74								
Cluster_27665		alkylhydroperoxidase AhpD family core domain protein	3.24								
Cluster_27796		PTS system, sucrose-specific IIBC component	-7.00								
Cluster_27797	<i>scrB</i>	sucrose-6-phosphate hydrolase	-5.67								
Cluster_28491		periplasmic binding family protein	5.76								
Cluster_28495		FecCD transport family protein	3.75								
Cluster_28578	<i>yiaM</i>	2,3-diketo-L-gulonate TRAP transporter small permease protein YiaM	-3.96								
Cluster_28657		PTS system, Fru family, IIB component domain protein	-2.39								
Cluster_29027		bacterial capsule synthesis PGA_cap family protein	-3.28								
Cluster_32975	<i>shuA</i>	outer membrane heme receptor ShuA	5.00								
Cluster_39344		BNR/Asp-box repeat family protein	-2.00								
Cluster_41853	<i>scrY</i>	sucrose porin	-6.62								
Cluster_42553		putative heme utilization radical SAM enzyme HutW	5.12								
Cluster_42555		NADH(P)-binding family protein	3.42								
Cluster_42637		conserved hypothetical protein	-2.28								
<b>C581-05 (B2)</b>											
Cluster_23201		ABC transporter family protein	2.49								
Cluster_23655	<i>hmuV</i>	hemin import ATP-binding protein HmuV	2.96								
Cluster_27665		alkylhydroperoxidase AhpD family core domain protein	5.13								
Cluster_27796		PTS system, sucrose-specific IIBC component	-2.11								
Cluster_28491		periplasmic binding family protein	4.63								
Cluster_28495		FecCD transport family protein	3.27								
Cluster_32975	<i>shuA</i>	outer membrane heme receptor ShuA	5.20								
Cluster_42553		putative heme utilization radical SAM enzyme HutW	4.16								
Cluster_42554		conserved hypothetical protein	2.92								
Cluster_42555		NADH(P)-binding family protein	3.19								
Cluster_43425	<i>iraD</i>	anti-adaptor protein IraD	-2.62								
<b>401588 (B2)</b>											
Cluster_23201		ABC transporter family protein	2.08								
Cluster_23655	<i>hmuV</i>	hemin import ATP-binding protein HmuV	2.31								
Cluster_25294		phage integrase family protein	-2.30								
Cluster_27665		alkylhydroperoxidase AhpD family core domain protein	3.60								
Cluster_28491		periplasmic binding family protein	2.33								
Cluster_28495		FecCD transport family protein	2.17								
Cluster_32975	<i>shuA</i>	outer membrane heme receptor ShuA	4.57								
Cluster_42098		TonB-dependent siderophore receptor family protein	3.19								
Cluster_42553		putative heme utilization radical SAM enzyme HutW	2.40								
Cluster_42554		conserved hypothetical protein	2.97								
Cluster_42555		NADH(P)-binding family protein	2.54								
<b>302053 (B2)</b>											
Cluster_19907		periplasmic binding family protein	-2.19								
Cluster_23201		ABC transporter family protein	2.43								
Cluster_23655	<i>hmuV</i>	hemin import ATP-binding protein HmuV	3.01								
Cluster_27665		alkylhydroperoxidase AhpD family core domain protein	4.06								
Cluster_28495		FecCD transport family protein	2.48								
Cluster_29027		bacterial capsule synthesis PGA_cap family protein	-2.15								
Cluster_29029		bacterial capsule synthesis PGA_cap family protein	-2.09								
Cluster_32975	<i>shuA</i>	outer membrane heme receptor ShuA	6.19								
Cluster_42098		TonB-dependent siderophore receptor family protein	3.34								
Cluster_42553		putative heme utilization radical SAM enzyme HutW	2.02								
Cluster_42554		conserved hypothetical protein	2.25								
Cluster_42555		NADH(P)-binding family protein	2.53								
Cluster_42637		conserved hypothetical protein	-2.09								
Cluster_43425	<i>iraD</i>	anti-adaptor protein IraD	-3.10								
		Isolate-Specific Genes <sup>a</sup>									
Cluster ID	Gene	Predicted Protein Function	LFC <sup>d</sup>								
<b>100329 (A)</b>											
Cluster_6731		putative dNA-Binding protein GSP	2.62								

Cluster_7611		Eag family protein	2.34
<b>401140 (A)</b>			
Cluster_34158		DDE superendonuclease family protein	-2.51
Cluster_38392		cytolethal distending toxin A/C family protein	3.82
Cluster_38393	<i>catB</i>	cytolethal distending toxin subunit B	3.80
<b>B171 (B1)</b>			
Cluster_4030		UTRA domain protein	-2.65
Cluster_4031		phosphoenolpyruvate-dependent sugar phosphotransferase system, EIIA 2 family protein	-2.72
Cluster_4032		PTS system, Lactose/Cellobiose specific IIB subunit	-2.88
Cluster_4611		conserved hypothetical protein	2.42
<b>402290 (B1)</b>			
Cluster_46067		glycosyl transferase 2 domain protein	2.37
Cluster_48546		glycosyltransferase like 2 family protein	2.08
<b>E110019 (B1)</b>			
Cluster_10956		conserved hypothetical protein	-2.69
Cluster_11127		conserved hypothetical protein	-2.06
Cluster_12490	<i>espV</i>	putative T3SS effector protein EspV	-2.43
Cluster_14838		conserved hypothetical protein	2.33
Cluster_14839		transcriptional regulatory, C terminal family protein	2.10
Cluster_14939	<i>col</i>	colicin-E2	2.05
Cluster_14941		lysis family protein	2.16
<b>E2348/69 (B2)</b>			
Cluster_17152		glycosyl transferase 11 family protein	2.43
Cluster_17153		glycosyl transferase 2 family protein	2.86
Cluster_17154		putative membrane protein	3.61
Cluster_17155		bacterial transferase hexapeptide family protein	2.77
Cluster_17156		polysaccharide biosynthesis family protein	3.49
Cluster_17212		mannitol dehydrogenase Rossmann domain protein	-3.93
Cluster_17481		putative predicted protein	3.47
Cluster_17640		putative predicted protein	2.65
Cluster_17644		putative predicted protein	2.68
Cluster_18911		putative predicted protein	-2.82
<b>C581-05 (B2)</b>			
Cluster_48767		conserved hypothetical protein	2.18
<b>401588 (B2)</b>			
Cluster_25495	<i>rtcB</i>	tRNA-splicing ligase RtcB	-2.04
Cluster_40811		Mu-like prophage FlMu gp41 family protein	3.21
Cluster_40813		phage major tail tube protein	4.20
Cluster_40830		conserved hypothetical protein	4.15
<b>302053 (B2)</b>			
None		None	None

\*Cluster IDs are listed once for each comparison group, although there may be more than one gene in a single genome that belonged to the same cluster.

<sup>b</sup>Core genes were those identified in all of the EPEC genomes with an LS-BSR  $\geq 0.8$ .

<sup>c</sup>Genes identified with significant similarity (LS-BSR  $\geq 0.8$ ) in all of the genomes of one phylogroup (phylogroup-specific) or only in one genome (isolate-specific) that were absent (LS-BSR  $< 0.4$ ) from the other EPEC isolates.

<sup>d</sup>LFC is Log<sub>2</sub> Fold-Change of the DMEM samples compared to the LB samples.