

**Table 3. *Y. pestis* genes downregulated in the bubo relative to *in vitro* growth conditions**

Gene	ORF*	Fold difference relative to:				Function of the gene product <sup>†</sup>
		21°C Exp	21°C Stat	37°C Exp	37°C Stat	
<b>Information storage and processing</b>						
<i>J. Translation, ribosomal structure and biogenesis</i>						
–	<b>YPO0628</b>	A	A	A	A	Putative translational inhibitor protein
–	YPO2018	A	A	A	A	Putative protoporphyrinogen oxidase
–	YPO3216	A	A	A	A	Putative methyltransferase
–	YPO3261	A	A	A	A	Probable amidase
<i>K. Transcription</i>						
–	YPO0758	A	A	A	A	LacI-family regulatory protein
–	YPO1938	A	A	A	A	Probable DeoR-family transcriptional regulatory protein
–	YPO2150	A	A	A	A	LysR-family transcriptional regulatory protein
–	YPO3259	A	A	A	A	Putative RpiR-family transcriptional regulatory protein
–	<b>YPO3682</b>	A	A	A	A	Putative LysR-family transcriptional regulatory protein
–	YPO3978	A	A	A	A	Putative regulatory protein
<i>betI</i>	YPO1167	A	A	A	A	TetR-family regulatory protein
<i>ilvY</i>	YPO3889	A	A	A	A	LysR-family transcriptional regulatory protein
<i>L. DNA replication, recombination and repair</i>						
–	YPO0041	A	A	A	A	Putative DNA ligase
–	YPO3736	A	A	A	A	Conserved hypothetical protein
<i>int</i>	YPO1917	A	A	A	A	Integrase
<b>Cellular processes and signaling</b>						
<i>D. Cell division and chromosome partitioning</i>						
–	YPO1062	A	A	A	A	Conserved hypothetical protein
<i>ccrB</i>	YPO2596	A	A	A	A	Putative membrane protein
<i>M. Cell envelope biogenesis, outer membrane</i>						
–	YPO1000	A	A	A	A	Putative drug efflux protein
–	YPO1364	-2.52	-2.71	-2.27	-3.10	Putative HlyD-family secretion protein
–	YPO1672	A	A	A	A	Conserved hypothetical protein

–	<b>YPO2174</b>	A	A	A	A	Putative nucleotide sugar dehydrogenase
–	YPO2494	A	A	A	A	Putative BCCT-family transporter
–	YPO3609	A	A	A	A	Conserved hypothetical protein
–	YPO4112	A	A	A	A	Putative membrane protein
<i>ddhA</i>	YPO3115	A	A	A	A	Glucose-1-phosphate cytidyltransferase
<i>mltD</i>	YPO1078	-6.56	-9.97	-6.06	-3.08	Membrane-bound lytic murein transglycosylase D precursor
<i>pla2</i>	YPO1231	A	A	A	A	Putative outer membrane-associated protease
<b><i>spr</i></b>	<b>YPO1275</b>	-2.34	-3.24	-2.24	-3.08	Putative lipoprotein
<i>yapC</i>	YPO2796	A	A	A	A	Putative autotransporter protein
<i>yapH</i>	YPO1004	A	A	A	A	Putative autotransporter protein
<i>N. Cell motility and secretion</i>						
–	YPO0271	A	A	A	A	Putative type III secretion apparatus protein
–	YPO2759	A	A	A	A	Putative mannose-resistant/Proteus-like fimbrial protein
<i>fliE</i>	YPO1831	A	A	A	A	Flagellar hook-basal body complex protein FliE
<i>hofC</i>	YPO3427	A	A	A	A	Putative type II secretion system protein
<i>tsr2</i>	YPO1229	A	A	A	A	Putative methyl-accepting chemotaxis protein
<i>O. Posttranslational modification, protein turnover, chaperones</i>						
–	YPO3916	A	A	A	A	Putative peroxiredoxin/glutaredoxin-family protein
<i>cysT</i>	YPO3014	A	A	A	A	Sulfate transport system permease protein CysT
<i>cysW</i>	YPO3013	A	A	A	A	Sulfate transport system permease protein CysW
<i>degS</i>	YPO3568	A	A	A	A	Protease
<i>P. Inorganic ion transport and metabolism</i>						
–	YPO0829	A	A	A	A	Putative sulfatase
–	YPO1527	A	A	A	A	Putative membrane protein
–	YPO2068	A	A	A	A	Putative integral membrane protein
–	YPO3047	A	A	A	A	Putative sulfatase
–	<b>YPO3049</b>	A	A	A	A	Putative binding protein-dependent transport system component
–	<b>YPO3050</b>	-11.65	-55.85	-5.76	-8.50	Putative exported protein
<i>mgtB</i>	YPO1661	A	A	A	A	Mg(2+) transport ATPase protein B
<i>nhaB</i>	YPO2142	A	A	A	A	Na <sup>+</sup> /H <sup>+</sup> antiporter
<i>ssuB</i>	YPO3627	A	A	A	A	Putative aliphatic sulfonates transport ATP-binding protein
<i>tauA</i>	YPO0182	A	A	A	A	Putative taurine-binding periplasmic protein precursor
<i>T. Signal transduction mechanisms</i>						
–	YPO2000	A	A	A	A	Putative two-component system sensor protein

–	YPO2779	A	A	A	A	Conserved hypothetical protein
<i>V. Defense mechanisms</i>						
–	YPO1001	A	A	A	A	Putative integral membrane efflux protein
<b>Metabolism</b>						
<i>C. Energy production and conversion</i>						
–	YPO1451	A	A	A	A	Putative oxidoreductase
–	YPO3637	A	A	A	A	Putative carbohydrate kinase
–	YPO3917	A	A	A	A	Putative pyridine nucleotide-disulphide oxidoreductase
<i>atpI</i>	YPO4128	-6.36	-2.23	-2.53	-2.40	ATP synthase protein I
<i>cydA</i>	YPO1117	-2.54	-2.53	-3.30	-2.04	Cytochrome D ubiquinol oxidase subunit I
<b><i>gltA</i></b>	<b>YPO1108</b>	-2.98	-2.84	-3.07	-3.30	Citrate synthase GltA
<i>nifJ</i>	YPO2334	A	A	A	A	Putative pyruvate-flavodoxin oxidoreductase
<i>ssuD</i>	YPO3625	A	A	A	A	Alkanesulfonate monooxygenase
<i>E. Amino acid transport and metabolism</i>						
–	YPO0181	A	A	A	A	Putative ABC-transport protein
–	<b>YPO0251</b>	-3.07	-5.52	-2.69	-2.81	Putative transmembrane transport protein
–	YPO1061	A	A	A	A	Conserved hypothetical protein
–	YPO1193	A	A	A	A	Putative pyridoxal-dependent decarboxylase
–	YPO1848	A	A	A	A	Putative amino-acid ABC transporter (ATP-binding protein)
–	YPO2306	A	A	A	A	Putative amino acid antiporter
–	YPO2662	A	A	A	A	Binding-protein-dependent transport protein
–	<b>YPO3048</b>	-5.74	-8.36	-2.91	-3.19	Probable ABC-transporter, ATP-binding protein
–	YPO4110	A	A	A	A	ABC transporter permease
<i>artP</i>	YPO1352	A	A	A	A	Arginine transport ATP-binding protein
<i>astA</i>	YPO1963	A	A	A	A	Arginine N-succinyltransferase
<i>dppC</i>	YPO4001	A	A	A	A	Dipeptide transport system permease protein
<i>dppD</i>	YPO4000	A	A	A	A	Dipeptide transport ATP-binding protein
<i>gltJ</i>	YPO2614	A	A	A	A	Putative glutamate/aspartate transport system permease
<i>gutB</i>	YPO2502	A	A	A	A	Putative zinc-binding dehydrogenase
<i>hutG</i>	YPO1971	A	A	A	A	Putative N-formylglutamate amidohydrolase
<i>hutH</i>	YPO4016	A	A	A	A	Histidine ammonia-lyase
<i>proV</i>	YPO2647	-16.76	-4.71	-10.17	-4.53	Glycine betaine/L-proline transport ATP-binding protein
<i>proW</i>	YPO2646	-14.28	-3.45	-9.62	-3.75	Glycine betaine/L-proline transport system permease
<i>proX</i>	YPO2645	-8.76	-2.44	-4.38	-2.43	Glycine betaine-binding periplasmic protein

<i>proY</i>	YPO3201	A	A	A	A	Probable proline-specific permease
<i>tyrP</i>	YPO1209	A	A	A	A	Tyrosine-specific transport protein
<i>F. Nucleotide transport and metabolism</i>						
–	YPO1296	A	A	A	A	Putative Mut-family protein
<i>G. Carbohydrate transport and metabolism</i>						
–	YPO0404	A	A	A	A	PTS system, IIC component
–	YPO0405	A	A	A	A	Putative phosphoenolpyruvate-protein phosphotransferase
–	YPO1221	A	A	A	A	Putative membrane protein
–	YPO1504	A	A	A	A	Putative exported protein
–	YPO1515	A	A	A	A	Putative multidrug resistance protein
–	<b>YPO1563</b>	A	A	A	A	Putative transmembrane transporter
–	<b>YPO1572</b>	A	A	A	A	Putative sugar transporter
–	<b>YPO1573</b>	A	A	A	A	Putative polysaccharide deacetylase
–	YPO1812	A	A	A	A	Putative sugar transport system permease protein
–	YPO1814	A	A	A	A	Putative sugar ABC transporter, ATP-binding protein
–	YPO1815	A	A	A	A	Putative sugar ABC transporter, permease
–	YPO1985	A	A	A	A	Putative glycosyl transferase
–	YPO2285	A	A	A	A	Putative ribose-binding periplasmic protein (partial)
–	YPO2581	A	A	A	A	Putative sugar-binding periplasmic protein
–	YPO3016	A	A	A	A	Putative sugar transporter
–	YPO3413	A	A	A	A	Putative membrane protein
–	YPO3472	A	A	A	A	Putative sugar binding protein
–	YPO3620	A	A	A	A	Putative carbohydrate transport protein
–	YPO3634	A	A	A	A	ABC transporter ATP binding protein
–	YPO3906	A	A	A	A	Putative sugar transport system permease
–	YPO3907	A	A	A	A	Putative sugar transport system ATP-binding protein
–	YPO3962	A	A	A	A	Sugar-binding transport protein
<i>agaY</i>	YPO0844	A	A	A	A	Putative aldolase
<i>agaZ</i>	YPO0832	A	A	A	A	Putative tagatose 6-phosphate kinase
<i>araF</i>	YPO2255	A	A	A	A	L-arabinose-binding periplasmic protein precursor
<i>araH</i>	YPO2257	A	A	A	A	L-arabinose transport system permease protein
<i>dhaK</i>	YPO3350	A	A	A	A	Putative dihydroxyacetone kinase
<i>mtlK</i>	YPO2480	A	A	A	A	Putative mannitol transport ATP-binding protein
<i>rosA</i>	YPO3093	A	A	A	A	Putative membrane efflux protein

<i>H. Coenzyme metabolism</i>						
–	YPO1288	A	A	A	A	Putative D-isomer specific 2-hydroxyacid dehydrogenase
<i>I. Lipid metabolism</i>						
–	<b>YPO1565</b>	A	A	A	A	Putative oxidoreductase
–	YPO2817	A	A	A	A	Putative CDP-alcohol phosphatidyltransferase
<i>acs</i>	<b>YPO0253</b>	-3.90	-7.60	-3.73	-5.56	Acetyl-coenzyme A synthetase
<i>Q. Secondary metabolites biosynthesis, transport and catabolism</i>						
–	YPO1080	A	A	A	A	Conserved hypothetical protein
–	YPO1580	A	A	A	A	Putative phosphopantetheinyl transferase
–	YPO3079	A	A	A	A	Putative ABC transporter ATP-binding protein
<i>pncA</i>	YPO2160	A	A	A	A	Putative pyrazinamidase/nicotinamidase
Poorly characterized						
<i>R. General function prediction only</i>						
–	YPO0004	A	A	A	A	Conserved hypothetical protein
–	YPO0128	A	A	A	A	Conserved hypothetical protein
–	YPO1140	A	A	A	A	Putative membrane protein
–	YPO1325	A	A	A	A	Putative membrane protein
–	YPO1496	A	A	A	A	Putative heme-binding protein
–	YPO1716	A	A	A	A	Putative transport protein
–	YPO2260	A	A	A	A	Putative membrane protein
–	YPO2467	A	A	A	A	Conserved hypothetical protein
–	YPO3051	A	A	A	A	Conserved hypothetical protein
–	YPO3961	A	A	A	A	Hypothetical protein
–	YPO4108	A	A	A	A	Putative haloacid dehalogenase-like hydrolase
<i>fadH</i>	<b>YPO0589</b>	A	A	A	A	2,4-dienoyl-CoA reductase
<i>recX</i>	YPO3306	A	A	A	A	Putative regulatory protein
<i>S. Function unknown</i>						
–	<b>YPO0252</b>	A	A	A	A	Putative membrane protein
–	YPO0505	A	A	A	A	Conserved hypothetical protein
–	YPO0513	A	A	A	A	Conserved hypothetical protein
–	YPO1158	A	A	A	A	Conserved hypothetical protein
–	YPO1754	A	A	A	A	Putative membrane protein
–	YPO1999	A	A	A	A	Putative decarboxylase

-	<b>YPO2080</b>	A	A	A	A	Conserved hypothetical protein
-	YPO3057	A	A	A	A	Putative membrane protein
-	YPO3985	-2.34	-3.65	-2.33	-2.98	Putative membrane protein
<i>mgtC</i>	YPO1660	-4.48	-10.39	-6.57	-25.50	Mg(2+) transport ATPase protein C
Unclassified in COGs						
-	YPO0142	A	A	A	A	Putative membrane protein
-	YPO0147	A	A	A	A	Putative membrane protein
-	YPO0301	A	A	A	A	Putative exported protein
-	YPO0306	A	A	A	A	Hypothetical protein
-	YPO0384	A	A	A	A	Putative lipoprotein
-	YPO0466	A	A	A	A	Hypothetical protein
-	YPO0703	A	A	A	A	Putative lipoprotein
-	YPO0757	A	A	A	A	Conserved hypothetical protein (pseudogene)
-	YPO0760	A	A	A	A	Putative membrane protein
-	YPO0769	A	A	A	A	Putative exported protein
-	YPO0822	A	A	A	A	Putative exported protein
-	YPO0870	A	A	A	A	Conserved hypothetical protein
-	YPO0886	A	A	A	A	Hypothetical protein
-	YPO1016	A	A	A	A	Putative membrane protein
-	YPO1249	A	A	A	A	Putative bacteriophage protein GP46
-	YPO1659	-2.95	-4.60	-3.14	-5.68	Hypothetical protein
-	YPO1674	A	A	A	A	Putative membrane protein (pseudogene)
-	YPO1818	A	A	A	A	Conserved hypothetical protein
-	YPO1933	A	A	A	A	Putative dicarboxylic acid hydrolase
-	YPO2079	A	A	A	A	Hypothetical protein
-	YPO2108	A	A	A	A	Hypothetical phage protein
-	YPO2113	A	A	A	A	Hypothetical phage protein
-	YPO2128	A	A	A	A	Putative phage-related lipoprotein
-	YPO2275	A	A	A	A	Putative phage protein
-	YPO2277	A	A	A	A	Putative phage protein
-	YPO2292	-3.84	-3.01	-2.87	-3.02	Putative lipoprotein
-	YPO2314	A	A	A	A	Putative invertase protein (partial)
-	YPO2644	A	A	A	A	Conserved hypothetical protein (pseudogene)
-	YPO2728	A	A	A	A	Conserved hypothetical protein
-	YPO2731	A	A	A	A	Putative membrane protein

-	<b>YPO2795</b>	-3.58	-5.82	-3.07	-4.38	Hypothetical protein
-	YPO2801	A	A	A	A	Putative membrane protein
-	YPO2802	A	A	A	A	Putative membrane protein
-	YPO3245	A	A	A	A	Hypothetical protein
-	YPO3260	A	A	A	A	Hypothetical protein
-	YPO3468	A	A	A	A	Hypothetical protein
-	YPO3473	A	A	A	A	Putative exported protein
-	YPO3486	A	A	A	A	Conserved hypothetical protein
-	YPO3611	A	A	A	A	Hypothetical protein
-	<b>YPO3681</b>	-2.53	-17.54	-2.48	-5.76	Putative insecticidal toxin
-	YPO3738	A	A	A	A	Hypothetical protein
-	YPO4020	A	A	A	A	Putative membrane protein
-	YPMT1.04c	A	A	A	A	Putative phage tail protein
-	YPMT1.45c	A	A	A	A	Hypothetical protein
-	YPMT1.68a	A	A	A	A	Unknown
-	y0065	A	A	A	A	Putative transposase
-	y0200	A	A	A	A	Hypothetical protein
-	y0930	A	A	A	A	Hypothetical protein
-	y1172	A	A	A	A	Hypothetical protein
-	y1259	A	A	A	A	Hypothetical protein
-	y1327	A	A	A	A	Hypothetical protein
-	y3533	A	A	A	A	Hypothetical protein
-	y4068	A	A	A	A	Hypothetical protein
<i>flk</i>	YPO2760	A	A	A	A	Putative flagellar assembly regulatory protein, Flk
<i>hpaG</i>	YPO1761	A	A	A	A	2-hydroxyhepta-2,4-diene-1,7-dioate isomerase (pseudogene)
<i>leuL</i>	y3643	A	A	A	A	Leu operon leader peptide
<i>ompC2</i>	YPO1967	A	A	A	A	Porin (pseudogene)
<i>yehZ</i>	YPO1195	A	A	A	A	Periplasmic choline/glycine/betaine binding protein (pseudogene)

Genes in bold type were also reported to be downregulated during pneumonic plague in mice (1). -, gene name not assigned; A, signal not detected *in vivo*.

\*YPO and y numbers refer to the *Y. pestis* CO92 and KIM genome annotations, respectively. YPO numbers are given unless the gene was annotated only in KIM

†Genes are categorized according to Clusters of Orthologous Groups (COG) database.

1. Lathem, W. W., Crosby, S. D., Miller, V. L. & Goldman, W. E. (2005) *Proc. Natl. Acad. Sci. USA* **102**, 17786-17791.