

Table 2. *Y. pestis* genes upregulated in the bubo relative to *in vitro* growth conditions

| Gene | ORF* | Fold difference relative to: | | | | Function of the gene product [†] |
|--|----------------|------------------------------|--------------|-------------|--------------|---|
| | | 21°C Exp | 21°C Stat | 37°C Exp | 37°C Stat | |
| Information storage and processing | | | | | | |
| <i>J. Translation, ribosomal structure and biogenesis</i> | | | | | | |
| <i>alcB</i> | YPO1531 | 8.54 | 4.43 | 4.98 | 2.73 | Putative siderophore biosynthetic enzyme |
| <i>ykgM</i> | YPO3134 | 44.58 | B | 33.20 | B | Putative ribosomal protein |
| – | YPO3135 | 47.21 | 25.61 | 22.74 | 35.56 | Putative ribosomal protein L36 |
| <i>K. Transcription</i> | | | | | | |
| – | YPO2458 | B | B | 2.69 | 2.08 | Putative LysR-family transcriptional regulator |
| <i>metR</i> | YPO3789 | 8.26 | B | 8.17 | B | LysR-family transcriptional regulatory protein |
| <i>rhaR</i> | YPO0333 | 3.72 | 4.29 | 2.94 | 2.00 | L-rhamnose operon transcriptional activator |
| <i>ybtA</i> | YPO1912 | 25.73 | B | 24.15 | 14.99 | Transcriptional regulator YbtA |
| Cellular processes and signaling | | | | | | |
| <i>D. Cell division and chromosome partitioning</i> | | | | | | |
| – | YPO3531 | 11.59 | 3.27 | 11.63 | 4.65 | Conserved hypothetical protein |
| <i>M. Cell envelope biogenesis, outer membrane</i> | | | | | | |
| – | YPO0284 | 10.41 | 19.13 | 6.93 | 15.31 | Conserved hypothetical protein |
| – | YPO0617 | 2.38 | 3.46 | 2.13 | 2.12 | Putative membrane protein |
| – | YPO1513 | 3.67 | 2.94 | 2.30 | 2.35 | Putative membrane protein |
| <i>tonB</i> | YPO2193 | 5.04 | 7.25 | 5.40 | 3.37 | TonB protein |
| <i>N. Cell motility and secretion</i> | | | | | | |
| <i>flaA2</i> | YPO0738 | 8.53 | 6.13 | 2.98 | 2.51 | Putative flagellin |
| <i>O. Posttranslational modification, protein turnover, chaperones</i> | | | | | | |
| – | YPO0275 | 4.26 | 2.43 | 4.03 | 2.07 | Conserved hypothetical protein |
| <i>nrdH</i> | YPO2651 | 12.32 | 41.61 | 5.40 | 6.98 | Putative glutaredoxin |
| <i>P. Inorganic ion transport and metabolism</i> | | | | | | |
| – | YPO0285 | 9.46 | 14.87 | 5.54 | 11.02 | Conserved hypothetical protein |
| – | YPO0956 | 3.19 | 6.39 | 3.31 | 4.39 | Putative hydroxamate-type ferrisiderophore receptor |

| | | | | | | |
|---|----------------|-------|-------|--------|-------|---|
| – | YPO1011 | B | B | B | B | Putative TonB-dependent outer membrane receptor |
| – | YPO1310 | 4.71 | B | 12.55 | 6.73 | Putative periplasmic substrate-binding transport protein |
| – | YPO1311 | 3.40 | 8.59 | 6.40 | 3.21 | Putative FecCD-family membrane transport protein |
| – | YPO1312 | 6.25 | B | 9.55 | 5.73 | Putative siderophore ABC transporter, ATP-binding subunit |
| – | YPO1313 | 13.73 | 11.01 | 11.94 | 4.49 | Putative outer membrane protein |
| – | YPO1753 | 6.27 | B | 7.39 | B | Ferrichrome receptor protein |
| – | YPO1854 | 2.05 | 8.19 | 5.54 | 3.27 | Putative membrane protein |
| – | YPO1855 | 2.52 | 9.99 | 5.56 | 3.77 | Putative exported protein |
| – | YPO1856 | 2.71 | 9.67 | 4.18 | 3.44 | Conserved hypothetical protein |
| – | YPO1941 | 4.54 | 6.70 | 11.78 | 4.19 | Putative membrane protein |
| – | YPO1942 | 10.72 | 5.91 | 18.64 | 4.83 | Putative exported protein |
| – | YPO3340 | 49.17 | 36.26 | 47.11 | 5.97 | Ferric siderophore receptor (pseudogene) |
| – | YPO4022 | 3.72 | 3.14 | 9.77 | 5.71 | Putative iron transport protein |
| – | YPO4023 | 2.96 | 3.79 | 6.67 | 5.80 | Putative iron transport permease |
| <i>bfd</i> | YPO0205 | 18.96 | 34.77 | 48.38 | 8.29 | Putative bacterioferritin-associated ferredoxin |
| <i>fyuA</i> | YPO1906 | 45.85 | B | 179.67 | B | Pesticin/yersiniabactin receptor protein |
| <i>hmuP</i> | y0544 | 21.65 | B | 17.68 | 8.42 | Hemin uptake system component |
| <i>hmuR</i> | YPO0283 | 19.01 | 20.44 | 10.65 | 7.24 | Hemin receptor precursor |
| <i>hmuS</i> | YPO0282 | 6.68 | 11.52 | 3.79 | 6.41 | Hemin transport protein |
| <i>hmuT</i> | YPO0281 | 7.00 | 13.04 | 3.96 | 6.75 | Hemin-binding periplasmic protein |
| <i>hmuU</i> | YPO0280 | 6.81 | 14.57 | 3.73 | 7.32 | Hemin transport system permease protein |
| <i>hmuV</i> | YPO0279 | 5.74 | 18.10 | 3.09 | 10.07 | Hemin transport system ATP-binding protein |
| <i>mntH</i> | YPO2982 | 10.75 | 3.07 | 8.52 | 2.83 | Manganese transport protein |
| <i>nirC</i> | YPO0159 | 4.93 | 4.21 | 4.34 | B | Putative nitrite transporter |
| <i>nirD</i> | YPO0160 | 5.82 | 6.10 | 3.98 | B | Nitrite reductase |
| <i>sfuA</i> | YPO2958 | 7.23 | 17.64 | 18.66 | 8.26 | Iron(III)-binding periplasmic protein |
| <i>yfeA</i> | YPO2439 | 12.30 | 8.47 | 9.61 | 5.09 | Periplasmic-binding protein |
| <i>yfeB</i> | YPO2440 | 7.27 | 6.89 | 8.30 | 4.40 | ATP-binding transport protein |
| <i>yfeC</i> | YPO2441 | 4.46 | 9.06 | 6.12 | 5.09 | Chelated iron transport system membrane protein |
| <i>yfeD</i> | YPO2442 | 5.39 | 11.35 | 6.87 | 5.53 | Chelated iron transport system membrane protein |
| <i>znuA</i> | YPO2061 | 3.75 | 2.32 | 3.15 | 2.19 | Exported high-affinity zinc uptake system protein |
| <i>U. Intracellular trafficking and secretion</i> | | | | | | |
| – | YPO0682 | 9.68 | 27.08 | 10.75 | 10.09 | MotA/TolQ/ExbB proton channel family protein |
| – | YPO0683 | 10.68 | 31.47 | 12.10 | 9.10 | ExbD/TolR-family transport protein |

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|---|----------------|--------|--------|--------|--------|--|
| <i>V. Defense mechanisms</i> | | | | | | |
| – | YPO1735 | 2.44 | 4.15 | 3.84 | 2.01 | Putative ABC transporter (ATP-binding protein) |
| – | YPO1944 | 4.82 | 3.43 | 7.09 | 2.40 | Putative membrane protein |
| – | YPO1945 | 5.60 | 3.33 | 7.06 | 2.58 | Putative membrane protein |
| – | YPO1946 | 6.22 | 3.41 | 7.54 | 2.33 | ABC transporter, ATP-binding protein |
| ybtP | YPO1913 | 86.38 | B | B | B | Lipoprotein inner membrane ABC-transporter |
| ybtQ | YPO1914 | 73.85 | B | B | B | Inner membrane ABC-transporter YbtQ |
| Metabolism | | | | | | |
| <i>C. Energy production and conversion</i> | | | | | | |
| – | YPO1948 | 4.11 | 2.91 | 4.52 | 2.10 | Putative cytochrome |
| – | YPO2492 | 7.27 | 2.94 | 6.27 | 2.51 | Putative dioxygenase beta subunit |
| <i>dmsA</i> | YPO3325 | 11.35 | 6.03 | 4.55 | 7.31 | Anaerobic dimethyl sulfoxide reductase chain A |
| <i>fdhF</i> | YPO0344 | 5.72 | 2.18 | 4.02 | 2.76 | Formate dehydrogenase H |
| <i>hcr</i> | YPO1359 | 5.42 | B | 3.60 | 2.22 | Putative oxidoreductase |
| hmp | YPO2908 | 24.36 | 16.98 | 10.10 | 19.98 | Flavohemoprotein |
| hydN | YPO0343 | 6.51 | 2.93 | 3.56 | 4.30 | 4Fe-4S ferredoxin |
| <i>nirB</i> | YPO0161 | 6.30 | 7.06 | 2.95 | B | Nitrite reductase |
| <i>ugpQ</i> | YPO3792 | 2.88 | 3.12 | 3.01 | 2.33 | Glycerophosphoryl diester phosphodiesterase |
| <i>E. Amino acid transport and metabolism</i> | | | | | | |
| – | YPO0342 | 5.87 | 2.34 | 3.36 | 3.55 | Putative oxidoreductase |
| ansB | YPO1386 | B | B | 9.54 | 3.08 | Putative L-asparaginase II precursor |
| <i>glpB</i> | YPO3825 | 5.83 | 5.33 | 2.93 | 2.91 | Anaerobic glycerol-3-phosphate dehydrogenase, subunit B |
| <i>lysC</i> | YPO3719 | 3.66 | 3.27 | 4.05 | 4.02 | Lysine-sensitive aspartokinase III |
| metA | YPO3727 | 10.44 | 19.25 | 13.65 | 25.94 | Homoserine O-succinyltransferase |
| metB | YPO0115 | 3.48 | 12.62 | 6.37 | 11.97 | Cystathionine gamma-synthase (pseudogene) |
| metE | YPO3788 | 128.78 | 183.13 | 95.50 | 194.40 | 5-methyltetrahydropteroyltriglutamate-homocysteine-methyltransferase |
| metF | YPO0117 | 30.93 | 20.44 | 42.37 | 16.88 | 5,10-methylenetetrahydrofolate reductase |
| metL | YPO0116 | 2.69 | 11.05 | 4.65 | 6.92 | Bifunctional aspartokinase/homoserine dehydrogenase II |
| <i>potH</i> | YPO1333 | 2.98 | 4.17 | 3.01 | 2.43 | Putrescine transport system permease protein |
| ybtS | YPO1916 | 149.65 | B | 222.58 | 166.40 | Putative salicylate synthetase |
| <i>F. Nucleotide transport and metabolism</i> | | | | | | |
| <i>nrdE</i> | YPO2649 | 7.74 | B | 5.38 | B | Ribonucleoside-diphosphate reductase 2 alpha chain |

| | | | | | | |
|--|----------------|--------|------|--------|--------|---|
| <i>nrdF</i> | YPO2648 | 8.42 | B | 5.47 | 6.69 | Ribonucleoside-diphosphate reductase 2 beta chain |
| <i>nrdI</i> | YPO2650 | 8.54 | 9.13 | 4.77 | 5.90 | NrdI protein reductase |
| <i>G. Carbohydrate transport and metabolism</i> | | | | | | |
| – | YPO0988 | 13.79 | B | 18.31 | 2.51 | Putative membrane protein |
| <i>bglB</i> | YPO2803 | 3.03 | 2.36 | 2.96 | 2.33 | Putative beta-glucosidase |
| <i>gpmA</i> | YPO1133 | 2.43 | 2.95 | 2.45 | 3.05 | Phosphoglycerate mutase 1 |
| <i>yegB</i> | YPO2850 | 2.39 | 3.90 | 2.84 | 2.08 | Putative membrane protein |
| <i>H. Coenzyme metabolism</i> | | | | | | |
| – | YPO0286 | 5.65 | 7.54 | 2.84 | 6.72 | Putative coproporphyrinogen III oxidase |
| – | YPO1008 | 2.94 | B | 4.40 | 2.70 | Putative integral membrane efflux protein |
| <i>bioD</i> | YPO2269 | 6.82 | 3.07 | 2.07 | 2.91 | Putative dethiobiotin synthetase |
| <i>cysG</i> | YPO0158 | 4.46 | 4.14 | 2.76 | 6.74 | Siroheme synthase |
| <i>Q. Secondary metabolites biosynthesis, transport and catabolism</i> | | | | | | |
| – | YPO0776 | 4.94 | 2.15 | 3.16 | 2.03 | Putative siderophore biosynthesis protein |
| <i>alcA</i> | YPO1530 | 10.82 | 4.02 | 4.45 | 2.27 | Putative siderophore biosynthetic enzyme |
| <i>irp1</i> | YPO1910 | 64.92 | B | B | B | Yersiniabactin biosynthetic protein |
| <i>irp2</i> | YPO1911 | 104.70 | B | 197.31 | 121.60 | Yersiniabactin biosynthetic protein |
| <i>ybtE</i> | YPO1907 | 67.81 | B | 165.76 | B | Yersiniabactin siderophore biosynthetic protein |
| <i>ybtT</i> | YPO1908 | 74.48 | B | 182.06 | B | Yersiniabactin biosynthetic protein |
| <i>ybtU</i> | YPO1909 | 69.61 | B | 178.10 | 164.70 | Yersiniabactin biosynthetic protein |
| <i>ybtX</i> | YPO1915 | 83.77 | B | 97.82 | 60.97 | Putative signal transducer |
| Poorly characterized | | | | | | |
| <i>R. General function prediction only</i> | | | | | | |
| – | YPO1528 | 11.16 | 7.91 | 11.00 | 3.67 | Putative ferric iron reductase |
| – | YPO1943 | 4.25 | 3.17 | 7.70 | 2.30 | Putative membrane protein |
| – | YPO2705 | 15.80 | 2.70 | 2.08 | 4.46 | Conserved hypothetical protein |
| <i>dcuA</i> | YPO0347 | 2.72 | 3.18 | 3.13 | B | Anaerobic C4-dicarboxylate transporter |
| <i>dmsC</i> | YPO3323 | 6.05 | 3.73 | 3.48 | 4.69 | Anaerobic dimethyl sulfoxide reductase chain C |
| <i>S. Function unknown</i> | | | | | | |
| – | YPO1307 | 4.87 | 2.35 | 4.36 | 2.48 | Putative membrane protein |
| – | YPO1516 | 2.80 | 2.11 | 2.82 | 2.29 | Hypothetical protein |
| Unclassified in COGs | | | | | | |

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|-------------|----------------|-------|-------|-------|-------|---|
| – | YPO0426 | B | B | B | B | Putative membrane protein |
| – | YPO0603 | 4.43 | 4.15 | 7.42 | 5.05 | Predicted open reading frame (pseudogene) |
| – | YPO0642 | 7.31 | 3.83 | 8.91 | 3.16 | Hypothetical protein |
| – | YPO0775 | 3.33 | 2.33 | 2.14 | 2.46 | Conserved hypothetical protein |
| – | YPO1012 | B | B | 23.11 | 11.25 | Nonribosomal peptide synthetase/polyketide synthase |
| – | YPO1532 | 6.49 | 3.65 | 5.07 | 3.39 | Putative siderophore biosynthetic enzyme |
| – | YPO2130 | 3.81 | 2.39 | 5.24 | 2.54 | Hypothetical phage protein |
| – | YPO2282 | 7.33 | 3.59 | 7.24 | 2.65 | Hypothetical protein |
| – | YPO2857 | 9.84 | 4.99 | 2.27 | 3.22 | Putative exported protein |
| – | YPO2976 | 21.68 | 19.08 | 14.54 | 18.14 | Conserved hypothetical protein |
| – | YPO4086 | 7.40 | 2.72 | 4.36 | 3.52 | Putative lipoprotein |
| – | YPMT1.16c | B | B | 5.13 | 2.51 | Hypothetical protein |
| – | y1377 | 6.07 | 2.22 | 5.82 | 2.58 | Hypothetical protein |
| – | y3874 | 2.00 | 3.37 | 2.89 | 3.31 | Hypothetical protein |
| – | y4094 | 3.85 | 2.08 | 3.82 | 2.81 | Hypothetical protein |
| <i>intA</i> | YPO1086a | 3.40 | 4.31 | 5.05 | 3.96 | Phage integrase (partial) |
| <i>iucA</i> | YPO0989 | 11.52 | B | B | B | Aerobactin-type siderophore synthetase (pseudogene) |

Genes in bold type were also reported to be upregulated during pneumonic plague in mice (1). –, gene name not assigned; B, signal detected only *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.