**Table S3.** Functional components of the biochemical network representing the central metabolism in *Pseudomonas putida* KT2440, as deduced from genomic annotations and experimental evidence*a*.

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| **Functional block** | **Code** | **BiGG ID** | **Reaction** | **Enzyme(s)** | **Name(s) and PP number(s)***b* |
| **Peripheral pathways** | 1 | GLCDpp | Glucose + Ubiquinone →  Gluconate + Ubiquinol | Glucose dehydrogenase | Gcd (PP1444) |
| 2 | GAD2ktpp | Gluconate + Ubiquinone →  2-Ketogluconate + Ubiquinol | Gluconate  2-dehydrogenase | PP3382  PP3383  PP3384  PP3623  PP4232 |
| 4 | GNK | Gluconate + ATP →  6-Phosphogluconate + ADP + H+ | Gluconate kinase | GnuK (PP3416) |
| 5 | 2DHGLCK | 2-Ketogluconate + ATP →  2-Ketogluconate-6-*P* + ADP + H+ | 2-Ketogluconate  kinase | KguK (PP3378) |
| 6 | PGLCNDH | 2-Ketogluconate-6-*P* + NADPH + H+ →  6-Phosphogluconate + NADP+ | 2-Ketogluconate-6-*P* reductase | KguD (PP3376) |
| **Pentose phosphate pathway** | 7 | G6PDH2 | Glucose-6-*P* + NADP+ →  6-Phosphoglucono-1,5-lactone  + NADPH + H+ | Glucose-6-*P*  1-dehydrogenase | Zwf-1 (PP1022) Zwf-2 (PP4042)  Zwf-3 (PP5351) |
| PGL | 6-Phosphoglucono-1,5-lactone + H2O →  6-Phosphogluconate + H+ | 6-Phospho-gluconolactonase | Pgl (PP1023) |
| 10 | GND | 6-Phosphogluconate + NADP+ →  Ribulose-5-*P* + NADPH + CO2 | 6-Phospho-gluconate dehydrogenase | Gnd (PP4043) |
| 11 | RPE | Ribulose-5-*P* ↔ Xylulose-5-*P* | Ribulose-5-*P*  3-epimerase | Rpe (PP0415) |
| 12 | RPI | Ribulose-5-*P* ↔ Ribose-5-*P* | Ribose-5-*P*  isomerase | RpiA (PP5150) |
| 13 | TKT1 | Xylulose-5-*P* + Ribose-5-*P* ↔  Sedoheptulose-7-*P* + Glyceraldehyde-3-*P* | Transketolase | TktA (PP4965) |
| 14 | TKT2 | Xylulose-5-*P* + erythrose-4-*P* ↔  Glyceraldehyde-3-*P* + Fructose-6-*P* |
| 15 | TALA | Sedoheptulose-7-*P* + Glyceraldehyde-3-*P*  ↔ Erythrose-4-*P* + Fructose-6-*P* | Transaldolase B | Tal (PP2168) |
| **Entner-Doudoroff pathway** | 8 | EDD | 6-Phosphogluconate →  2-Keto-3-deoxy-6-phosphogluconate + H2O | 6-Phospho-gluconate dehydratase | Edd (PP1010) |
| 9 | EDA | 2-Keto-3-deoxy-6-phosphogluconate →  Glyceraldehyde-3-*P* + Pyruvate | 2-Keto-3-deoxy-6-phosphogluconate aldolase | Eda (PP1024) |

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| **Embden-Meyerhof-Parnas pathway** | 3 | GLK | Glucose + ATP →  Glucose-6-*P* + ADP + H+ | Glucokinase | Glk (PP1011) |
| 16 | PGI | Glucose-6-*P* → Fructose-6-*P* | Glucose-6-*P* isomerase | Pgi-1 (PP1808)  Pgi-2 (PP4701) |
| 17 | FBP | Fructose-1,6-*P*2 + H2O + ADP →  Fructose-6-*P* + ATP | Fructose-1,6-bisphosphatase | Fbp (PP5040) |
| 18 | FBA | Dihydroxyacetone-*P* +  Glyceraldehyde-3-*P*  ↔ Fructose-1,6-*P*2 | Fructose-1,6-*P*2 aldolase | Fda (PP4960)  PP1791  PP2871  PP3224 |
| 19 | TPI | Glyceraldehyde-3-*P* ↔  Dihydroxyacetone-*P* | Triose phosphate isomerase | TpiA (PP4715) |
| 20 | GAPD | Glyceraldehyde-3-*P* + NAD+ + Pi*c* →  1,3-Bisphosphoglycerate + NADH + H+ | Glyceraldehyde-  3-*P* dehydrogenase | Gap-1 (PP1009)  Gap-2 (PP2149)  PP0665  PP3443 |
| PGK | 1,3-Bisphosphoglycerate + ADP →  Glycerate-3-*P* + ATP | Phosphoglycerate kinase | Pgk (PP4963) |
| 21 | PGM | Glycerate-3-*P* → Glycerate-2-*P* | Phosphoglycerate mutase | Pgm (PP5056)  PP2243  PP3923  PP4450 |
| ENO | Glycerate-2-*P* →  Phosphoenolpyruvate + H2O | Phosphopyruvate hydratase | Eno (PP1612) |
| 22 | PYK | Phosphoenolpyruvate + ADP + H+ →  Pyruvate + ATP | Pyruvate kinase | PykA (PP1362)  PykF (PP4301) |
| **Tricarboxylic acid cycle / Glyoxylate shunt** | 23 | PDH | Pyruvate + NAD+ + Coenzyme A →  Acetyl-Coenzyme A + NADH + CO2 | Pyruvate dehydrogenase | AcoA (PP0555)  AceF (PP0338)  AceE (PP0339)  Lpd3 (PP5366)  LdpG (PP4187)  LpdV (PP4404) |
| 24 | CS | Oxaloacetate + Acetyl-Coenzyme A + H2O  → Citrate + Coenzyme A + H+ | Citrate synthase | GltA (PP4194) |

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| **Tricarboxylic acid cycle / Glyoxylate shunt** | 25 | ACONTa/b | Citrate → D-*threo*-Isocitrate | Aconitate hydratase | AcnA (PP2112)  AcnB (PP2339)  PP2336 |
| 26 | ICDHyr | D-*threo*-Isocitrate + NADP+ →  2-Ketoglutarate + CO2 + NADPH + H+ | Isocitrate dehydrogenase | Icd (PP4011)  PP4012 |
| 27 | AKGDH | 2-Ketoglutarate + Coenzyme A + NAD+ →  Succinyl-Coenzyme A + NADH +  H+ + CO2 | 2-Ketoglutarate dehydrogenase | LpdG (PP4187)  KgdB (PP4188)  SucA (PP4189)  PP2652  PP3662 |
| SUCOAS | Succinyl-Coenzyme A + ADP + Pi*c* →  Succinate + Coenzyme A + ATP | Succinyl-coenzyme A synthetase | SucD (PP4185)  SucC (PP4186) |
| 28 | SUCDi | Succinate + Ubiquinone →  Fumarate + Ubiquinol | Succinate dehydrogenase | SdhA (PP4191)  SdhB (PP4190)  SdhC (PP4193)  SdhD (PP4192) |
| 29 | FUM | Fumarate + H2O → (*S*)-Malate | Fumarate hydratase | FumC -1  (PP0944)  FumC-2 (PP1755)  PP0897 |
| 30 | MDH | (*S*)-Malate + NAD+ →  Oxaloacetate + NADH + H+ | Malate dehydrogenase / Malate:quinone oxidoreductase | Mdh (PP0654)  PP3591  Mqo-1 (PP0751)  Mqo-2  (PP1251)  Mqo-3  (PP2925) |
| 31 | ICL | D-*threo*-Isocitrate →  Succinate + Glyoxylate | Isocitrate lyase | AceA (PP4116) |
| MALS | Glyoxylate + Acetyl-Coenzyme A  + H2O →  (*S*)-Malate + Coenzyme A + H+ | Malate synthase | GlcB (PP0356) |

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| **Anaplerosis / Gluconeogenesis** | 32 | OOADC | Pyruvate + CO2 → Oxaloacetate + H+ | Pyruvate carboxylase | OadA (PP5346) AccC-2 (PP5347) |
| 33 | PPC | Oxaloacetate + Pi*c* →  Phosphoenolpyruvate + CO2 | Phosphoenol-  pyruvate carboxylase*d* | Ppc (PP1505) |
| 34 | ME2 | (*S*)-Malate + NADP+ →  Pyruvate + CO2 + NADPH | Malic enzyme | MaeB (PP5085) |

*a* The reactions within the network were codified according to six functional blocks which are also referred to throughout the main text. The information for the network was compiled from the *Pseudomonas* Genome Database (1) and MetaCyc (2), and several studies available in the literature (3-7).

*b* In the instances in which no gene name has been assigned, the PP number is given for each open reading frame.

*c* Pi, inorganic phosphate.

*d* According to Nelson *et al*. (8), *pckA* (encoding phosphoenolpyruvate carboxykinase) contains an authentic frameshift and therefore the open reading frame is classified as a pseudogene in the *Pseudomonas* Genome Database (1).

**REFERENCES**

1. Winsor, G. L., Lam, D. K. W., Fleming, L., Lo, R., Whiteside, M. D., Yu, N. Y., Hancock, R. E. W., and Brinkman, F. S. L. (2011) *Pseudomonas* Genome Database: improved comparative analysis and population genomics capability for *Pseudomonas* genomes. *Nucleic Acids Res.* **39**, D596-D600

2. Caspi, R., Altman, T., Dreher, K., Fulcher, C. A., Subhraveti, P., Keseler, I. M., Kothari, A., Krummenacker, M., Latendresse, M., Mueller, L. A., Ong, Q., Paley, S., Pujar, A., Shearer, A. G., Travers, M., Weerasinghe, D., Zhang, P., and Karp, P. D. (2012) The MetaCyc database of metabolic pathways and enzymes and the BioCyc collection of pathway/genome databases. *Nucleic Acids Res.* **40**, D742-D753

3. Blank, L. M., Ionidis, G., Ebert, B. E., Bühler, B., and Schmid, A. (2008) Metabolic response of *Pseudomonas putida* during redox biocatalysis in the presence of a second octanol phase. *FEBS J.* **275**, 5173-5190

4. Chavarría, M., Kleijn, R. J., Sauer, U., Pflüger-Grau, K., and de Lorenzo, V. (2012) Regulatory tasks of the phosphoenolpyruvate-phosphotransferase system of *Pseudomonas putida* in central carbon metabolism. *MBio* **3**, e00028-00012

5. Chavarría, M., Nikel, P. I., Pérez-Pantoja, D., and de Lorenzo, V. (2013) The Entner-Doudoroff pathway empowers *Pseudomonas putida* KT2440 with a high tolerance to oxidative stress. *Environ. Microbiol.* **15**, 1772-1785

6. del Castillo, T., Ramos, J. L., Rodríguez-Herva, J. J., Fuhrer, T., Sauer, U., and Duque, E. (2007) Convergent peripheral pathways catalyze initial glucose catabolism in *Pseudomonas putida*: genomic and flux analysis. *J. Bacteriol.* **189**, 5142-5152

7. Sudarsan, S., Dethlefsen, S., Blank, L. M., Siemann-Herzberg, M., and Schmid, A. (2014) The functional structure of central carbon metabolism in *Pseudomonas putida* KT2440. *Appl. Environ. Microbiol.* **80**, 5292-5303

8. Nelson, K. E., Weinel, C., Paulsen, I. T., Dodson, R. J., Hilbert, H., Martins dos Santos, V. A. P., Fouts, D. E., Gill, S. R., Pop, M., Holmes, M., Brinkac, L., Beanan, M., DeBoy, R. T., Daugherty, S., Kolonay, J., Madupu, R., Nelson, W., White, O., Peterson, J., Khouri, H., Hance, I., Chris Lee, P., Holtzapple, E., Scanlan, D., Tran, K., Moazzez, A., Utterback, T., Rizzo, M., Lee, K., Kosack, D., Moestl, D., Wedler, H., Lauber, J., Stjepandic, D., Hoheisel, J., Straetz, M., Heim, S., Kiewitz, C., Eisen, J. A., Timmis, K. N., Düsterhöft, A., Tümmler, B., and Fraser, C. M. (2002) Complete genome sequence and comparative analysis of the metabolically versatile *Pseudomonas putida* KT2440. *Environ. Microbiol.* **4**, 799-808