S4 Table: List of differentially abundant pathways (identified between Cluster-1a, Cluster-1b and Cluster-2). Significantly different pathways were identified using Kruskal-Wallis rank sum test (with Benjamini-Hochberg corrected p-values < 0.001 at a False Discovery Rate of 0.0001) coupled with a bootstrap approach. Pathways with significantly different median abundances in at least 99% of iterations are shown in this table. For ease of readers, the corresponding pathway classes are also indicated. The last column titled 'Vikodak Pathway Exclusion Cut-off (PEC) threshold' indicates the PEC value thresholds at which the pathway was reported by Vikodak. Green indicates presence and red indicates absence.

| Pathway Class | Pathways that significantly differentiate | Median Pathway Abundance (at PEC 70) | | | Vikodak Pathway Exclusion Cut-off (PEC) threshold | | | | | |
|--------------------------------------|---|--|--------|--------|---|---|---|---|---|--|
| | between the three | Cluste | Cluste | Cluste | 5 | 6 | 7 | 8 | 9 | |
| 3.5 | clusters | r 1a | r 1b | r 2 | 0 | 0 | 0 | 0 | 0 | |
| Membrane transport | Phosphotransferas e system PTS | 1227 | 1147 | 742 | | | | | | |
| Carbohydrate metabolism | Glycolysis or Gluconeogenesis | 40270 | 49509 | 29060 | | | | | | |
| Nucleotide metabolism | Pyrimidine metabolism | 37800 | 46761 | 32265 | | | | | | |
| Amino acid metabolism | Alanine aspartate and glutamate | 28782 | 34174 | 18836 | | | | | | |
| Carbohydrate | Pyruvate | 20237 | 24359 | 14641 | | | | | | |
| Energy metabolism | Carbon fixation pathways in prokaryotes | 19114 | 23560 | 13591 | | | | | | |
| Carbohydrate | Butanoate | 18008 | 21509 | 11308 | | | | | | |
| Translation | Aminoacyl tRNA | 16815 | 19736 | 15286 | | | | | | |
| Energy metabolism | Carbon fixation in photosynthetic organisms | 15203 | 19199 | 10202 | | | | | | |
| Metabolism of cofactors and vitmains | Pantothenate and CoA biosynthesis | 14256 | 18111 | 11505 | | | | | | |
| Carbohydrate metabolism | Citrate cycle TCA cycle | 13957 | 17563 | 9960 | | | | | | |
| Carbohydrate metabolism | Pentose phosphate pathway | 13436 | 17101 | 9502 | | | | | | |

| Energy metabolism | Oxidative phosphorylation | 12633 | 16007 | 9807 | | | |
|--|----------------------------------|-------|-------|------|--|--|--|
| Glycan biosynthesis and metabolism | Other glycan degradation | 10308 | 14466 | 4153 | | | |
| Metabolism of cofactors and vitamins | Folate biosynthesis | 10168 | 13260 | 8159 | | | |
| Glycan biosynthesis and metabolism | Peptidoglycan biosynthesis | 10350 | 12637 | 8623 | | | |
| Metabolism of other amino acids | Selenocompound metabolism | 9603 | 12268 | 7111 | | | |
| Lipid metabolism | Fatty acid biosynthesis | 9087 | 12131 | 5429 | | | |
| Metabolism of cofactors and vitamins | One carbon pool by folate | 9492 | 11976 | 7798 | | | |
| Folding, sorting and degradation | RNA degradation | 10297 | 11228 | 9104 | | | |
| Glycan biosynthesis and | Lipopolysaccharid e biosynthesis | 8089 | 10602 | 6178 | | | |
| Replication and repair | Mismatch repair | 8610 | 10568 | 7440 | | | |
| Replication and repair | DNA replication | 7660 | 9503 | 6522 | | | |
| Cell growth and death | Cell cycle Caulobacter | 7081 | 8942 | 5820 | | | |
| Metabolism of terpenoids and polyketides | Tetracycline biosynthesis | 6453 | 8485 | 4027 | | | |
| Replication and repair | Base excision repair | 7139 | 8396 | 5891 | | | |
| Membrane transport | Bacterial secretion system | 6951 | 8067 | 4653 | | | |
| Replication and repair | Nucleotide excision repair | 6495 | 7899 | 5712 | | | |
| Metabolism of terpenoids and polyketides | Biosynthesis of ansamycins | 5919 | 7053 | 4167 | | | |

| Metabolism of cofactors and vitamins | Thiamine metabolism | 5362 | 6441 | 4988 |
|---|---|------|------|------|
| Amino acid metabolism | Valine leucine and isoleucine biosynthesis | 4419 | 5259 | 3001 |
| Translation | RNA transport | 4336 | 5108 | 3495 |
| Xenobiotics biodegradation and metabolism | Nitrotoluene degradation | 3906 | 4869 | 2538 |
| Folding, sorting and degradation | Sulfur relay system | 3452 | 4327 | 2402 |
| Metabolism of terpenoids and polyketides | Biosynthesis of type II polyketide backbone | 3063 | 4161 | 1762 |
| Cell motility | Flagellar assembly | 3299 | 3893 | 1976 |
| Membrane transport | ABC transporters | | 3516 | 1991 |
| Lipid metabolism | Synthesis and degradation of ketone bodies | 2760 | 3436 | 1936 |
| Transcription | RNA polymerase | 2715 | 3342 | 2544 |
| Folding, sorting and degradation | Protein export | 2455 | 3200 | 1769 |
| Immune diseases | Primary immunodeficiency | 2366 | 3056 | 1393 |
| Metabolism of terpenoids and polyketides | terpenoids and siderophore group | | 2646 | 1491 |
| Infectious diseases : Bacterial | Pathogenic Escherichia coli infection | 1168 | 1508 | 790 |
| Cell motility | chemotaxis | 1282 | 1473 | 632 |
| Signaling molecules and interaction | Cell adhesion molecules CAMs | 840 | 1069 | 391 |
| Signaling molecules and interaction | ECM receptor interaction | 736 | 966 | 575 |

| Biosynthesis of other secondary metabolites | beta Lactam resistance | 431 | 543 | 241 | | | |
|---|---|-----|-----|-------|--|--|--|
| Metabolism of cofactors and vitamins | Lipoic acid metabolism | 318 | 482 | 113 | | | |
| Metabolism of terpenoids and polyketides | Nonribosomal peptide structures | 194 | 199 | 161 | | | |
| Nucleotide metabolism | Purine metabolism | 0 | 0 | 35803 | | | |
| Carbohydrate metabolism | Starch and sucrose metabolism | 0 | 0 | 33378 | | | |
| Carbohydrate metabolism | Amino sugar and nucleotide sugar metabolism | 0 | 0 | 25339 | | | |
| Amino acid metabolism | Arginine and proline | 0 | 0 | 20503 | | | |
| Amino acid metabolism | Glycine serine and threonine metabolism | 0 | 0 | 16017 | | | |
| Amino acid metabolism | Cysteine and methionine | 0 | 0 | 12343 | | | |
| Carbohydrate metabolism | Propanoate metabolism | 0 | 0 | 9810 | | | |
| Metabolism of cofactors and vitamins | Porphyrin and chlorophyll metabolism | 0 | 0 | 9084 | | | |
| Xenobiotics biodegradation and metabolism | Benzoate degradation | 0 | 0 | 6971 | | | |
| Amino acid metabolism | Lysine biosynthesis | 0 | 0 | 6716 | | | |
| Metabolism of cofactors and vitamins | Riboflavin metabolism | 0 | 0 | 6063 | | | |

| Xenobiotics biodegradation and metabolism | Drug metabolism : other enzymes | 0 | 0 | 5650 | | |
|---|---|---|---|------|--|--|
| Amino acid metabolism | Valine leucine and isoleucine degradation | 0 | 0 | 4867 | | |
| Xenobiotics biodegradation and metabolism | Xylene degradation | 0 | 0 | 4771 | | |
| Metabolism of cofactors and vitamins | Biotin metabolism | 0 | 0 | 4390 | | |
| Xenobiotics biodegradation and metabolism | Dioxin degradation | 0 | 0 | 4252 | | |
| Biosynthesis of other secondary metabolites | Betalain biosynthesis | 0 | 0 | 3469 | | |
| Xenobiotics biodegradation and metabolism | Furfural degradation | 0 | 0 | 663 | | |
| Xenobiotics biodegradation and metabolism | Styrene degradation | 0 | 0 | 594 | | |
| Biosynthesis of other secondary metabolites | Puromycin biosynthesis | 0 | 0 | 549 | | |
| Metabolism of terpenoids and polyketides | Geraniol degradation | 0 | 0 | 483 | | |
| Chemical structure transformation maps | Biosynthesis of terpenoids and steroids | 3 | 2 | 176 | | |