**S8 Table. Known ligands for members of the Cache superfamily**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Cache Domain** | **Protein** | **Organism** | **Uniprot** | **Ligands** | **Reference(s)** |
| dCache\_1 | McpU | *Sinorhizobium meliloti* | F7XA01 | Proline, Histidine, Lysine | [[1](#_ENREF_1), [2](#_ENREF_2)] |
|  | CcaA (Tlp1/ Cj1506c) | *Campylobacter jejuni* | Q0P8B2 | Aspartate | [3] |
|  | CcmL  (Tlp3/Cj1564) | *Campylobacter jejuni* | Q0P864 | Attractants - Isoleucine, Purine, Malic acid, Fumaric acid; Repellants – Arginine, Lysine, Glucosamine, Succinic Acid, Thiamine | [[3](#_ENREF_3)] |
|  | McpB | *Bacillus subtilis* | P39215 | Asparagine; supports Aspartate, Glutamine, Histidine | [5] |
|  | McpC | *Bacillus subtilis* | P54576 | Direct: Cysteine, Proline, Threonine, Glycine, Serine, Valine, Alanine, Tyrosine, Phenylalanine, Leucine, Tryptophan, Isoleucine (weak); Indirect via Transporters: ArtP (Arginine, Lysine), GlnH (Glutamine), MetQ (Methionine), YckB (Tryptophan) | [6] |
|  | KinD | *Bacillus subtilis* | O31671 | Pyruvate, Propionate, Butyrate; Glycerol & Manganese | [7,8] |
|  | PctA | *Pseudomonas aeruginosa* | G3XD24 | All 20 amino acids except – Aspartate, Glutamine | [9] |
|  | PctB | *Pseudomonas aeruginosa* | Q9HW91 | Alanine, Arginine, Glutamate, Lysine, Methionine, Tyrosine, Glutamine | [9] |
|  | PctC | *Pseudomonas aeruginosa* | Q9HW93 | Histidine, Proline, GABA | [10] |
|  | PscA (Psa\_14525) | *Pseudomonas syringae pv. actinidiae* | - | D-Aspartate, L-Aspartate, Glutamate | [11] |
|  | PscB (Psa\_08785) | *Pseudomonas syringae pv. actinidiae* | - | Alanine, Asparagine, Glutamine, Methionine, Isoleucine, Leucine, Phenylalanine, Serine, Tryptophan, L-Homoserine | [11] |
|  | PscC (Psa\_18055) | *Pseudomonas syringae pv. actinidiae* | - | Isoleucine, Proline, GABA | [11] |
|  | VfcA  (VF\_0777) | *Vibrio fischeri* | Q5E6S4 | Serine, Alanine, Cysteine, Threonine | [12] |
|  | Mlp24 (Vc2161) | *Vibrio cholerae* | Q9KQ43 | Serine, Glycine, Alanine, Cysteine, Arginine, Asparagine, Histidine, Threonine, Lysine, Glutamine, Proline | [13] |
|  | Mlp37(VCA0923) | *Vibrio cholerae* | Q9KL26 | Serine | [13] |
|  | DctB | *Vibrio cholerae* | Q9KQS3 | Succinate | [22,23] |
| dCache\_2 | No information available. | | | | |
| dCache\_3 | No information available. | | | | |
| Cache\_3-Cache\_2 | No information available. | | | | |
| sCache\_2 | Adeh\_3718 | *Anaeromyxobacter dehalogenans 2CP-C* | Q2IFX2 | Acetate | [14] |
|  | TlpB | *Helicobacter pylori* | B6JPK4 | Urea; pH-Sensing | [15] |
|  | PA2652 | *Pseudomonas aeruginosa* | Q9I0I6 | Malate | [16] |
|  | VP0183 | *Vibrio parahaemolyticus* | Q87T87 | Pyruvate | PDB: 4EXO (2QHK) |
| sCache\_3\_1 | PhoR | *Escherichia coli* | P08400 | Unknown | [17] |
| sCache\_3\_2 | CitA | *Klebsiella pneumoniae* | P52687 | Citrate | [18] |
|  | DcuS | *Escherichia coli* | P0AEC8 | Fumarate, Malate, Succinate, Tartarate | [19] |
|  | MalK (YufL) | *Bacillus subtilis* | O05250 | Malate | [20] |
|  | CitS | *Bacillus subtilis* | O34427 | Citrate | [21] |
| sCache\_3\_3 | No information available. | | | | |
| CHASE | AHK4 | *Arabidopsis thaliana* | Q9C5U0 | Cytokinin Hormones | [24] |
| CHASE4 | No information available. | | | | |
| 2CSK\_N | QseC | *Escherichia coli (Enterohemorrhagic O157:H7)* | Q8X524 | Autoinducer 3, Adrenergic Hormones (Epinephrine, Norepinephrine) | [25] |
| PhoQ\_sensor | PhoQ | *Escherichia coli* | P23837 | Mg2+, Ca2+ | [26] |
| Stimulus\_sens\_1 | BvrS (ChvG/ExoS) | *Brucella abortus* | Q57AG8 | Unknown. Shown to interact with ExoR (Sel1 repeats) | [27] |
| LuxQ-periplasm | LuxQ | *Vibrio harveyi* | P54302 | Unknown. Interacts with LuxP and Autoinducer-2. | [28] |
| DUF2222 | BarA | *Escherichia coli* | P0AEC5 | Unknown | [29,30] |
| SMP\_2 | AhpA | *Pasteurella multocida* | Q9L8J3 | Unknown | [31] |
| Diacid\_rec | CdaR (SdaR/YaeG) | *Escherichia coli* | P37047 | Unknown | [32] |
| YkuI\_C | YkuI | *Bacillus subtilis* | O35014 | Unknown | [33] |

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