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ORIGINAL ARTICLES

# Comprehensive Analyses of Transport Proteins Encoded Within the Genome of "*Aromatoleum aromaticum*" Strain EbN1

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**Abstract** The denitrifying bacterium "*Aromatoleum aromaticum*" strain EbN1 is specialized for the aerobic utilization of aromatic compounds including crude oil constituents. We here report whole-genome analyses for potential transport proteins in *A. aromaticum* strain EbN1. This organism encodes very few transporters for simple sugars and most other common carbon sources. However, up to 28% of its putative transporters may act on fairly hydrophobic aromatic and aliphatic compounds. We categorize the putative transporters encoded within the genome, assign them to recognized families, and propose their preferred substrates. The bioinformatic data are correlated with available metabolic information to obtain an integrated view of the metabolic network of *A. aromaticum* strain EbN1. The results thus indicate that this organism possesses a disproportionately large percentage of transporters for the uptake and efflux of hydrophobic and amphipathic aromatic and aliphatic compounds compared with previously analyzed organisms. We predict that these findings will have important implications for our ecophysiological understanding of bioremediation.

**Keywords** Anaerobic · Aromatic compounds · Degradation · Denitrification · Transport · Genome analysis

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## Introduction

Aromatic compounds are among the most widely encountered basic chemical structures in nature. They include protein constituents in all living organism, abundant components in higher plants (e.g., the phenolic building blocks of lignin), and main constituents of crude oil (e.g., toluene). Fuel-derived alkylbenzenes and phenolic compounds are widely used in the chemical industry. Their accidental release into the environment often leads to accumulation in anoxic soils and sediments, increasingly demanding bioremediation efforts. The latter benefit from an in-depth understanding of relevant metabolic pathways and essential transport systems for their uptake and efflux at toxic concentrations.

Aerobic degraders of aromatic compounds and their metabolic pathways for initial hydroxylation and ring cleavage with $O_2$-dependent oxygenases have been known for decades (Harayama et al. 1992), but anaerobic degradation of these compounds has been discovered more recently. In fact, information concerning the involved enzyme mechanisms has been forthcoming only within the past decade (Gibson and Harwood 2002; Heider and Fuchs 1997). Since these enzymes cannot use species of reactive oxygen, their mechanisms differ fundamentally from those of the aerobic enzymes. Often they are found to involve unprecedented biochemistry (Gibson and Harwood 2002; Heider and Fuchs 1997) and provide valuable resources for

biotechnological applications (Höffken et al. 2006; Wackett and Hershberger 2001).

The degradation of aromatic compounds usually involves channeling of the various phenolic, carboxylic, and hydrocarbon substrates into the pool of central intermediates, often benzoyl-CoA (Heider and Fuchs 1997). This intermediate subsequently undergoes reductive dearomatization and hydrolytic ring cleavage (Boll et al. 2002; Harwood and Gibson 1988). The microorganisms that degrade these compounds aerobically also use unusual pathways and novel types of oxygenases for aerobic aromatic compound metabolism (Mohamed Mel et al. 2002; Zaar et al. 2001).

Most currently known anaerobic aromatic compound-degrading bacteria are denitrifiers affiliated with the $\beta$-proteobacterial *Azoarcus*/*Thauera* cluster (Spormann and Widdel 2000; Widdel and Rabus 2001). This group is distinct from plant-associated *Azoarcus* spp. (Reinhold-Hurek and Hurek 2000) and has been proposed as the new genus *Aromatoleum* (Trautwein et al. 2008; Wöhlbrand et al. 2007, 2008; Wöhlbrand and Rabus 2008; Rabus, unpublished data). Distinction of the two genera is also reflected by the low degree of genome synteny (low frequency of colocalization of genes) between strain EbN1 and strain BH72 (Krause et al. 2006). *Aromatoleum aromaticum* strain EbN1 is a well-studied and metabolically versatile representative of this group (Rabus and Widdel 1995, 1996; Rabus, unpublished data). Strain EbN1 can grow anaerobically with alkylbenzenes, constituents of crude oil, polar aromatic compounds (e.g., phenol), and a variety of small polar aliphatic compounds (e.g., acetone).

The complete genome of strain EbN1 was the first to be determined for a member of the *Aromatoleum*/*Azoarcus*/*Thauera* cluster (Rabus et al. 2005). The genome consists of a single circular chromosome (4.3 Mb) and two plasmids (0.21 and 0.22 Mb) encoding a total of 4603 predicted proteins. The genome sequence revealed the genetic blueprint for a complex degradation network including more than 10 anaerobic pathways for aromatic compounds. Their absence in the aerobic aromatic compound-degrader *Pseudomonas putida* (Nelson et al. 2002) and the aerobic alkane-degrader *Alcanivorax borkumensis* (Schneiker et al. 2006) emphasizes the metabolic distinctiveness of strain EbN1. The only other sequenced genome of a bacterium similarly capable of anaerobic aromatic compound degradation is the phototrophic *Rhodopseudomonas palustris* (Larimer et al. 2004). The presence of multiple respiratory complexes and a large number of regulatory proteins suggests that strain EbN1 can adapt well to changing nutritional conditions.

In this report, we examine the complete complement of transporters encoded within the genome of *A. aromaticum* strain EbN1 to decipher its key coordination points for solute exchange with the environment. We show that this organism encodes a larger percentage of putative transporters for the energy-driven uptake and export of aromatic/hydrophobic substances than any other previously examined organism. Potential substrates of some of these systems are identified, and the mechanisms of transport can often be deduced. The transport capabilities of this organism correlate with its previously determined degradative capacities.

## Results

### Overview of *Aromatoleum aromaticum* Strain EbN1 Transporters

Table 1 and Fig. 1 present an overview of transporters encoded within the *A. aromaticum* strain EbN1 genome. Two hundred fifty-eight transport systems were identified (see Table 3), many of them displaying multicomponent structures. These consist of 498 proteins, comprising 11% of the 4603 proteins predicted to be encoded in the genome of strain EbN1. This is comparable to the average fraction of predicted transporter proteins reported for other bacteria, although there is substantial variation (3%–17%) from organism to organism (Barabote and Saier 2005; Lorca et al. 2007; Ren and Paulsen 2007).

Forty-three of the 258 transport systems identified (17%) are simple channel proteins, either of the $\alpha$ (cytoplasmic membrane) type (11) or of the $\beta$ (outer lipopolysaccharide-containing membrane) type (32). Secondary carriers are the most numerous type of transporter found in strain EbN1 (84 systems, or 33%), with primary active transporters coming in second place (68 systems, or 26%). This is not surprising for an organism with potential for both aerobic and anaerobic lifestyles. This organism has only one group translocating sugar transporter of the phosphotransferase system (PTS) already an indication that sugar metabolism is of little importance to strain EbN1 (see Fig. 1).

Strain EbN1 has a full complement of electron carrier complexes that couple transmembrane $H^+$ or $Na^+$ transport to electron flow (11 systems). There are also many transmembrane carriers that transfer electrons across the cytoplasmic membrane, from one side of the membrane to the other, thus influencing the energetics of the cell (16 systems). Sixteen auxiliary transport proteins (TC class 8) were identified which do not actually catalyze transport but facilitate transport processes catalyzed by recognized transporters. Additionally, there are 46 homologues of poorly defined systems, 8 of TC class 9A (transporters of

**Table 1** Overview of the "*Aromatoleum aromaticum*" strain EbN1 transporter analyses

| TC class[a] | Class description | No. of transport proteins | TC subclass | Subclass description | No. of transport proteins |
|---|---|---|---|---|---|
| 1 | Channels | 43 | 1.A | α-type channels | 11 |
| | | | 1.B | β-barrel porins | 32 |
| 2 | Secondary carriers | 84 | 2.A | Porters (uniporters, symporters, antiporters) | 81 |
| | | | 2.C | Ion-gradient-driven energizers | 3 |
| 3 | Primary active transporters | 68 | 3.A | P-P-bond hydrolysis-driven transporters | 57 |
| | | | 3.D | Oxidoreduction-driven transporters | 11 |
| 4 | Group translocators | 1 | 4.A | Phosphotransfer-driven group translocators | 1 |
| 5 | Transmembrane electron carriers | 16 | 5.A | Transmembrane 2-electron transfer carriers | 12 |
| | | | | Transmembrane 1-electron transfer carrier | 4 |
| 8 | Auxillary transport protein[b] | [16] | 8.A | Auxiliary transport proteins | [16] |
| 9 | Poorly defined system | 46 | 9.A | Recognized transporters of unknown biochemical mechanism | 8 |
| | | | 9.B | Putative uncharacterized transport proteins | 38 |
| Total | | 274 | | | 274 |

[a] Transporter classes 6 and 7 have not been assigned in the TC system yet and therefore are not listed here

[b] Auxillary proteins facilitate transport via established transport systems and therefore are not counted as separate systems

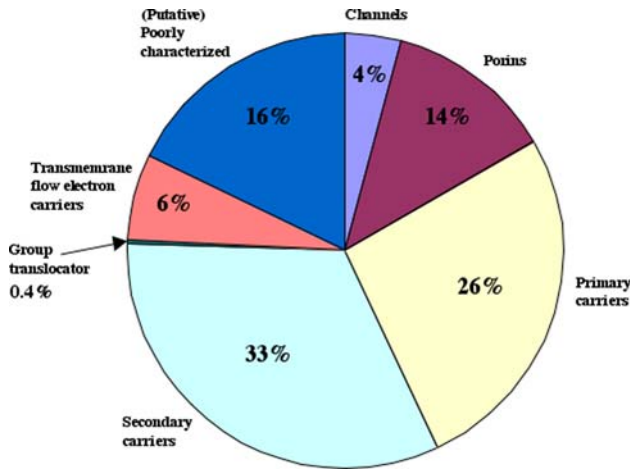


**Fig. 1** Percentages of recognized transport systems found in *A. aromaticum* (formerly *Azoarcus*) strain EbN1 according to transporter type. "Channels" are of type 1A and β-barrel porins are of type 1B in the transporter classification database (TCDB). Percentages of secondary carriers (TC class 2), primary active transporters (class 3), group translocators (class 4), transmembrane election carriers (class 5), and electron carriers that couple electron flow to $H^+$ or $Na^+$ extrusion (class 3D) are also presented. Poorly characterized transport proteins belong to TC class 9

unknown mechanisms of action) and 38 of TC class 9B (putative transporters). The latter group consists of a variety of potential transport systems, many families of which have not been characterized functionally. Finally, we have identified several distant homologues of recognized transporters with the expected topological features but unpredictable specificities (see below).

## Potential α-Type Channel-Forming Proteins

*A. aromaticum* strain EbN1 encodes a single putative member of the chloride channel (ClC) family as well as a protein showing limited sequence similarity to members of the one-TMS organellar chloride channel (O-ClC) family. The latter protein resembles in sequence full-length glutathione *S*-transferases (GSTs), eukaryotic elongation factor 1-γ, HSP26 stress-related proteins, and a stringent starvation protein in *Escherichia coli*. The last three protein types mentioned are not known to have GST activity (Williams et al. 1994). It seems unlikely that the protein in strain EbN1 showing sequence similarity to O-ClC is a chloride channel.

Strain EbN1 has four homologues similar to mammalian gp91phox, a phagocyte NADPH oxidase with a cytochrome b558 domain (Kimball and Saier 2002). The latter suggestion has recently been questioned (Ramsey et al. 2006; Sasaki et al. 2006). This enzyme and its homologues (such as ferric oxidoreductases) have only been characterized in eukaryotes. However, the presence of full-length bacterial homologues has been recognized (Kimball and Saier 2002). Their functions are unknown, but functional parallels with the eukaryotic homologues suggest that these bacterial proteins catalyze transmembrane electron flow, from the cytoplasm into the periplasm. Three of the strain EbN1 homologues appear to be full length, but the fourth is much shorter, perhaps bearing only one or two of the domains of these multidomain proteins.

Strain EbN1 has one homologue of the MscL large-conductance mechanosensitive channel (MscL) family as

well as five members of the small-conductance mechanosensitive channel (MscS) family. These channel proteins in *E. coli* have been functionally characterized in terms of their conductance properties and their high-resolution X-ray structures (Chang et al. 1998; Martinac et al. 1987, 1990; Perozo et al. 2001; Sukharev et al. 1999, 2001). One of the MscS channels in strain EbN1 has 11 putative TMSs, while the rest have 6. In *E. coli*, these proteins are known to function in osmotic stress adaptation (Pivetti et al. 2003).

A MotA bacterial flagellar motor protein homologue (Hosking et al. 2006; Zhai et al. 2003), with four putative TMSs as expected, was found encoded in the genome of strain EbN1. Mapping at a distant location, a MotB homologue with the single expected TMS, which functions together with MotA, was found. These two proteins presumably function in strain EbN1 as the flagellar motor (Berry and Armitage 1999; DeRosier 1998).

Strain EbN1 has three DnaK protein homologues. The primary function of these protein chaperone homologues is in protein folding (Winter and Jakob 2004). In eukaryotes, DnaK proteins can insert into membranes to form cation-selective channels (Arispe and De Maio 2000). There is no evidence that these chaperone proteins form channels in prokaryotes.

Finally, strain EbN1 has a single CorA homologue of the heavy metal ion transporter (MIT) family (Table 2). These homopentameric channel proteins with two TMSs per subunit allow uptake of divalent cations such as $Mg^{2+}$, $Co^{2+}$, $Ni^{2+}$, $Zn^{2+}$, and $Cd^{2+}$ (Kehres et al. 1998; Maguire 2006). The three-dimensional structure of the *E. coli* CorA has been solved (Maguire 2006).

In summary, strain EbN1 appears to have very few α-type channels in its cytoplasmic membrane. We are confident only that it has a single chloride channel of the ClC family and a single member of the MIT family of CorA proteins for uptake of divalent cations, as well as one mechanosensitive channel of the MscL family and five homologues of the MscS family. All of the Msc channels may function in hypoosmotic stress adaptation, possibly under different types of stress conditions.

## Outer Membrane Porins

Strain EbN1 has a large number of homologues of recognized outer membrane porins (both general and substrate specific porins; Tables 1 and 2) (Nikaido 2003). These include six members of the 16-TMS General Bacterial Porin (GBP) family and three members of the 8-TMS OmpA-OprF Porin (OOP) family (Table 2). They also include single members of three other porin families that may exhibit substrate specificity. Thus, the 14-TMS FadL homologue may be specific for fatty acids and other hydrophobic substances (TC 1.B.9) (van den Berg et al. 2004), and the OprB homologue may be specific for sugars such as glucose (TC 1.B.19) (Wylie and Worobec 1995). Finally, the OmpW porin homologue may be specific for alkanes, hydrophobic drugs, and dyes such as methyl viologen (TC 1.B.39) (Santiviago et al. 2002; van Beilen et al. 1992). This conclusion is supported by structural studies (Albrecht R et al. 2006).

In addition to these more "traditional" porins, strain EbN1 has eight outer membrane receptors of the OMR family. Seven of these may function in the energy-dependent active uptake of iron-siderophore complexes across the outer membrane, but the eighth probably functions in vitamin $B_{12}$ uptake (Table 2). One of the seven putative siderophore receptors is truncated due to insertion of a Tnp30 (locus tag 63243; IS5 family) transposon, present in the genome of *A. aromaticum* strain EbN1.

There are five outer membrane factors (OMFs; TC 1.B.17) that normally function in a heterotrimeric complex for the efflux of proteins, drugs, and aromatic compounds via a pathway that involves a primary cytoplasmic membrane efflux pump and a largely periplasmic "membrane fusion protein" (MFP; TC 8.A.1). These systems allow efflux from the cytoplasm, through the cytoplasmic and outer membranes, to the external milieu in a single energy-coupled step (Dinh et al. 1994).

Strain EbN1 also has two outer membrane auxiliary (OMA) family members. These proteins appear to function exclusively in complex exo- or capsular polysaccharide export together with a primary cytoplasmic membrane transporter and other auxiliary proteins. They form octameric ring-like structures in the outer membrane with an inner diameter of about 2 nm (Beis et al. 2004; Nesper et al. 2003). One such protein, Wza, may be largely α-helical, an unusual but not totally novel property of an outer membrane porin (Beis et al. 2004; Collins et al. 2007; Dong et al. 2006; Nesper et al. 2003).

Like OMA family members, secretins form oligomeric (dodecameric) ring-like structures in the outer membrane (Collins et al. 2001, 2003). They function in conjunction with types II and III protein secretion systems (Collins et al. 2005). Strain EbN1 has three secretins. One is most similar to ComE of *Haemophilus influenzae*, a protein that functions in DNA uptake; the second is most similar to XcpQ of *Pseudomonas aeruginosa*; and the third most closely resembles PulD of *Klebsiella oxytoca*. Both of the latter two homologues are components of type II protein secretion (main terminal branch) systems (Saier 2006; Sandkvist 2001). As shown below, these three secretins may function with three dissimilar macromolecular transport systems.

Strain EbN1 has all four recognized constituents of the outer membrane protein insertion porin (OmpIP) family. It has one homologue of the *E. coli* YaeT protein, most

**Table 2** Recognized transporters encoded within the genome of *Azoarcus* sp. EbN1

| TC subject protein | Family name | No. of complete sytems | EbN1ID no. | TC homologue (protein name) | EbN1 query length | TC subject length | E-value | No. of TMSs | Estimated transporter status |
|---|---|---|---|---|---|---|---|---|---|
| 1.A.11.1.1 | Ammonia Transporter Channel (Amt) | 1 | ebA3151 | AmtB | 451 | 428 | E-126 | 12 | Complete |
| 1.A.11.2.3 | Ammonia Transporter Channel (Amt) | 1 | ebA4609 | Amt1 | 401 | 391 | 6.00E-38 | 11 (TC 12) | Complete |
| 1.A.12.1.1 | Organellar Chloride Channel (O-ClC) | 1 | ebA1195 | CLIC5 orp64 | 198 | 437 | 2.00E-06 | 1 | Complete |
| 1.A.22.1.1 | Large Conductance Mechanosensitive Ion Channel (MscL) | 1 | ebA2712 | MscL | 139 | 136 | 4.00E-26 | 2 | Complete |
| 1.A.23.1.1 | Small Conductance Mechanosensitive Ion Channel (MscS) | 5 | ebA645 | KefA | 470 | 1120 | 8.00E-23 | 11 | Complete |
| 1.A.23.4.1 | Small Conductance Mechanosensitive Ion Channel (MscS) | | ebA6926 | MscMJ | 373 | 1106 | 2.00E-05 | 5 (TC 6) | Complete |
| 1.A.23.4.2 | Small Conductance Mechanosensitive Ion Channel (MscS) | | ebA4035 | MscMJLR | 385 | 350 | 1.00E-35 | 7 (TC 6) | Complete |
| 1.A.23.4.2 | Small Conductance Mechanosensitive Ion Channel (MscS) | | ebA4066 | MscMJLR | 418 | 350 | 8.00E-08 | 6 | Complete |
| 1.A.23.4.2 | Small Conductance Mechanosensitive Ion Channel (MscS) | | ebA6709 | MscMJLR | 278 | 350 | 3.00E-15 | 3 (TC 6) | Complete |
| 1.A.30.1.4 | $H^+$- or $Na^+$-translocating Bacterial Flagellar Motor (Mot) | 1 | ebA697 | MotP | 246 | 272 | 1.00E-39 | 4 | Complete |
| 1.A.30.1.4 | $H^+$- or $Na^+$-translocating Bacterial Flagellar Motor (Mot) | | ebA4407 | MotS | 190 | 261 | 2.00E-16 | 1 | |
| 1.A.35.3.1 | CorA Metal Ion Transporter (MIT) | 1 | ebA4496 | CorA | 337 | 317 | 2.00E-20 | 3 | Complete |
| 1.A total | | 11 | | | | | | | |
| 1.B.1.5.1 | General Bacterial Porin (GBP) | 1 | p2A117 | Oma1 | 397 | 326 | 2.00E-17 | 1 | Complete |
| 1.B.1.6.1 | General Bacterial Porin (GBP) | 5 | ebA1962 | Porin protein 32 | 346 | 351 | 2.00E-36 | 1 | Complete |
| 1.B.1.6.1 | General Bacterial Porin (GBP) | | ebA2143 | Porin protein 32 | 349 | 351 | 2.00E-36 | 1 | Complete |
| 1.B.1.6.1 | General Bacterial Porin (GBP) | | ebA4244 | Porin protein 32 | 359 | 351 | 2.00E-31 | 1 | Complete |
| 1.B.1.6.1 | General Bacterial Porin (GBP) | | ebA5358 | Porin protein 32 | 349 | 351 | 8.00E-32 | 1 | Complete |
| 1.B.1.6.1 | General Bacterial Porin (GBP) | | ebA5644 | Porin protein 32 | 341 | 351 | 2.00E-34 | 0 (TC 1) | Complete |
| 1.B.6.1.1 | OmpA-OmpF Porin (OOP) | 1 | ebA913 | OmpA | 238 | 346 | 6.00E-32 | 1 | Probably complete |
| 1.B.6.1.2 | OmpA-OmpF Porin (OOP) | 1 | ebA1121 | OmpF | 232 | 350 | 6.00E-24 | 3 (TC 1) | Probably complete |
| 1.B.6.1.3 | OmpA-OmpF Porin (OOP) | 1 | p1B164 | OmpATb | 202 | 326 | 5.00E-07 | 1 | Probably complete |
| 1.B.9.1.1 | FadL Outer Membrane Protein (FadL) | 1 | c1A203 | FadL | 423 | 448 | 4.00E-50 | 1 | Complete |
| 1.B.14.1.2 | Outer Membrane Receptor (OMR) | 1 | ebA3939 | FecA | 695 | 774 | 4.00E-84 | 1 | Complete |
| 1.B.14.1.4 | Outer Membrane Receptor (OMR) | 2 | ebA5333 | FhuA | 700 | 747 | 3.00E-51 | 1 | Complete |
| 1.B.14.1.4 | Outer Membrane Receptor (OMR) | | ebA3937 | FhuA | 699 | 747 | 2.00E-35 | 0 (TC 1) | Complete |
| 1.B.14.1.6 | Outer Membrane Receptor (OMR) | 1 | ebA3244 | CirA | 278 | 663 | 3.00E-14 | 1 (TC 0) | Complete |
| 1.B.14.2.3 | Outer Membrane Receptor (OMR) | 2 | ebA2117 | HemR | 686 | 687 | 9.00E-39 | 1 (TC 0) | Complete |
| 1.B.14.2.3 | Outer Membrane Receptor (OMR) | | ebA6096 | HemR | 713 | 687 | 3.00E-09 | 1 (TC 0) | Complete |
| 1.B.14.3.1 | Outer Membrane Receptor (OMR) | 1 | ebA4013 | BtuB | 646 | 614 | 1.00E-17 | 1 (TC 0) | Complete |
| 1.B.14.9.1 | Outer Membrane Receptor (OMR) | 1 | ebA6149 | RhtA | 703 | 746 | 1.00E-21 | 0 | Complete |
| 1.B.17.1.1 | Outer Membrane Factor (OMF) | 2 | ebA1642 | TolC | 453 | 495 | 3.00E-49 | 1 | Complete |
| 1.B.17.1.1 | Outer Membrane Factor (OMF) | | ebA1783 | TolC | 483 | 495 | 2.00E-20 | 0 (TC 1) | Complete |

**Table 2** continued

| TC subject protein | Family name | No. of complete sytems | EbN1ID no. | TC homologue (protein name) | EbN1 query length | TC subject length | E-value | No. of TMSs | Estimated transporter status |
|---|---|---|---|---|---|---|---|---|---|
| 1.B.17.3.2 | Outer Membrane Factor (OMF) | 1 | ebA3445 | FusA | 475 | 530 | 3.00E-46 | 0 (TC 1) | Complete |
| 1.B.17.3.3 | Outer Membrane Factor (OMF) | 1 | ebA1847 | OpcM | 501 | 512 | 2.00E-33 | 0 (TC 1) | Complete |
| 1.B.17.3.4 | Outer Membrane Factor (OMF) | 1 | ebA1679 | SilC | 477 | 461 | 4.00E-40 | 1 | Complete |
| 1.B.18.3.1 | Outer Membrane Auxiliary (OMA) Protein | 2 | ebA4247 | Wza | 211 | 379 | 3.00E-18 | 1 | Complete |
| 1.B.18.3.1 | Outer Membrane Auxiliary (OMA) Protein | | ebA6799 | Wza | 234 | 379 | 3.00E-08 | 0 (TC 1) | Complete |
| 1.B.19.1.1 | Glucose-selective OprB Porin (OprB) | | ebA1863 | OprB porin | 494 | 454 | 1.00E-04 | 1 | Complete |
| 1.B.22.1.1 | Outer Bacterial Membrane Secretin (Secretin) | | ebA3713 | PulD | 566 | 660 | 8.00E-19 | 1 | Probably complete |
| 1.B.22.1.2 | Outer Bacterial Membrane Secretin (Secretin) | | ebA1602 | XcpQ | 770 | 658 | 1.00E-31 | 1 | Complete |
| 1.B.22.4.1 | Outer Bacterial Membrane Secretin (Secretin) | | ebA1239 | ComE | 771 | 445 | 5.00E-22 | 1 | Complete |
| 1.B.33.1.2 | Outer Membrane Protein Insertion Porin (OmpIP) | | ebA1189 | D15 | 585 | 797 | 4.00E-05 | 1 | Complete |
| 1.B.33.1.3 | Outer Membrane Protein Insertion Porin (OmpIP) | | ebA773 | NlpB | 379 | 344 | 0.002 | 1 | Complete |
| 1.B.33.1.3 | Outer Membrane Protein Insertion Porin (OmpIP) | | ebA4724 | YfiO | 266 | 245 | 6.00E-37 | 1 | |
| 1.B.33.1.3 | Outer Membrane Protein Insertion Porin (OmpIP) | | ebA1258 | yfgL | 381 | 392 | 5.00E-33 | 1 | |
| 1.B.33.1.3 | Outer Membrane Protein Insertion Porin (OmpIP) | | ebA5996 | yaeT | 767 | 810 | e-147 | 0 | |
| 1.B.33.1.3 | Outer Membrane Protein Insertion Porin (OmpIP) | | ebA1141 | OstA | 787 | 784 | 2.00E-64 | 0 | |
| 1.B.39.1.1 | Bacterial Porin, OmpW (OmpW) | 1 | ebA5811 | OmpW | 225 | 212 | 8.00E-37 | 0 (TC 1) | Complete |
| 1.B total | | 32 | | | | | | | |
| 2.A.1.2.7 | Drug:$H^+$ Antiporter-1 (12 Spanner) (DHA1) | 3 | c2A195 | Bcr | 426 | 396 | 1.00E-36 | 12 | Complete |
| 2.A.1.2.7 | Drug:$H^+$ Antiporter-1 (12 Spanner) (DHA1) | | ebA3158 | Bcr | 394 | 396 | 6.00E-31 | 12 | Complete |
| 2.A.1.2.7 | Drug:$H^+$ Antiporter-1 (12 Spanner) (DHA1) | | ebA3906 | Bcr | 402 | 396 | 3.00E-13 | 12 | Complete |
| 2.A.1.2.10 | Drug:$H^+$ Antiporter-1 (12 Spanner) (DHA1) | 1 | ebA3858 | NorA | 384 | 388 | 1.00E-13 | 12 | Complete |
| 2.A.1.3.20 | Drug:$H^+$ Antiporter-1 (14 Spanner) (DHA2) | 1 | ebA3448 | FarB | 514 | 507 | e-126 | 14 | Complete |
| 2.A.1.8.2 | Nitrate/Nitrite Porter (NNP) | 1 | ebA1213 | NasA | 404 | 421 | 8.00E-61 | 12 (TC 9) | Complete |
| 2.A.1.8.11 | Nitrate/$H^+$ symporter (NNP) | 1 | ebA6289 | NarK_N | 458 | 905 | 3.00E-87 | 12 (TC 24) | Complete |
| 2.A.1.8.11 | Nitrate/Nitrite antiporter (NNP) | | ebA6288 | NarK_C | 563 | 905 | 4.00E-57 | 14 (TC 24) | |

**Table 2** continued

| TC subject protein | Family name | No. of complete sytems | EbN1ID no. | TC homologue (protein name) | EbN1 query length | TC subject length | E-value | No. of TMSs | Estimated transporter status |
|---|---|---|---|---|---|---|---|---|---|
| 2.A.1.11.1 | Oxalate:Formate Antiporter (OFA) | 1 | ebA6311 | OxlT | 419 | 418 | 0.001 | 12 | Probably complete |
| 2.A.1.15.1 | Aromatic Acid:$H^+$ Symporter (AAHS) | 2 | ebA4989 | PcaK | 467 | 448 | 7.00E-53 | 12 | Complete |
| 2.A.1.15.1 | Aromatic Acid:$H^+$ Symporter (AAHS) | | ebA5710 | PcaK | 399 | 448 | 6.00E-07 | 12 | Complete |
| 2.A.1.15.5 | Aromatic Acid:$H^+$ Symporter (AAHS) | 1 | ebA5311 | BenK | 452 | 466 | 2.00E-97 | 12 | Complete |
| 2.A.1.17.1 | Cyanate Porter (CP) | 1 | ebA3751 | CynX | 447 | 384 | 2.00E-25 | 11 | Complete |
| 2.A.1.17.1 | Cyanate Porter (CP) | 1 | ebA725 | CynX | 415 | 384 | 1.00E-10 | 12 (TC 11) | Complete |
| 2.A.1.25.2 | Peptide-Acetyl-Coenzyme A Transporter (PAT) | 1 | ebA2813 | AmpG | 431 | 491 | 9.00E-65 | 12 (TC 14) | Complete |
| 2.A.1.27.1 | Phenyl Propionate Permease (PPP) | 1 | ebA4754 | HcaT | 386 | 379 | 3.00E-26 | 12 | Complete |
| 2.A.1.30.1 | Putative Abietane Diterpenoid Transporter (ADT) | 1 | ebA5677 | DitE | 523 | 547 | 2.00E-72 | 12 | Complete |
| 2.A.1.36.1 | Acriflavin-sensitivity (YnfM) | 1 | ebA5055 | YnfM | 419 | 417 | 6.00E-56 | 12 | Complete |
| 2.A.1.42.1 | Lysophospholipid Transporter (LplT) | 2 | ebA3471 | LplT | 450 | 397 | 6.00E-63 | 12 | Complete |
| 2.A.1.42.1 | Lysophospholipid Transporter (LplT) | | ebA6485 | LplT | 416 | 397 | 1.00E-54 | 11 (TC 12) | Complete |
| 2.A.1.46.1 | Unknown Major Facilitator-5 (UMF5) | 1 | ebA2917 | Transporter | 402 | 396 | 4.00E-10 | 12 | Complete |
| 2.A.1.51.1 | Unknown Major Facilitator 7 (UMF7) | 1 | ebA1383 | Putative MFS permease | 398 | 398 | 8.00E-164 | 12 | Probably complete |
| 2.A.4.1.4 | Cation Diffusion Facilitator (CDF) | 1 | ebA4853 | ZitB | 331 | 313 | 8.00E-58 | 6 (TC 5) | Complete |
| 2.A.4.1.5 | Cation Diffusion Facilitator (CDF) | 1 | ebA4214 | YiiP | 317 | 300 | 2.00E-27 | 5 (TC 6) | Complete |
| 2.A.6.1.4 | Heavy Metal Efflux (HME) | 1 | ebA2165 | CusF | 201 | 110 | 1.00E-05 | 0 | Complete |
| 2.A.6.1.4 | Heavy Metal Efflux (HME) | | ebA2169 | CusC | 434 | 457 | | 1 (TC 2) | |
| 2.A.6.1.4 | Heavy Metal Efflux (HME) | | ebA2168 | CusB | 520 | 407 | 8.00E-38 | 0 (TC 1) | |
| 2.A.6.1.4 | Heavy Metal Efflux (HME) | | ebA2176 | CusA | 1058 | 1047 | 0 | 12 | |
| 2.A.6.2.7 | (Largely Gram-negative Bacterial) Hydrophobe/Amphiphile Efflux-1 (HAE1) | 1 | ebA3873 | AcrD | 1083 | 1037 | 2.00E-59 | 13 (TC 12) | Complete |
| 2.A.6.2.15 | (Largely Gram-negative Bacterial) Hydrophobe/Amphiphile Efflux-1 (HAE1) | 1 | ebA7101 | MexD | 1024 | 1043 | e-129 | 11 (TC 12) | Complete |
| 2.A.6.2.16 | (Largely Gram-negative Bacterial) Hydrophobe/Amphiphile Efflux-1 (HAE1) | 1 | ebA1649 | MexE | 368 | 414 | 2.00E-08 | 2 (TC 1) | Complete |
| 2.A.6.2.16 | (Largely Gram-negative Bacterial) Hydrophobe/Amphiphile Efflux-1 (HAE1) | 1 | ebA3924 | MexE | 334 | 414 | 1.00E-08 | 1 (TC 0) | Complete |
| 2.A.6.2.17 | (Largely Gram-negative Bacterial) Hydrophobe/Amphiphile Efflux-1 (HAE1) | 2 | ebA1647 | MexK | 1080 | 1025 | 0 | 12 | Complete |
| 2.A.6.2.17 | (Largely Gram-negative Bacterial) Hydrophobe/Amphiphile Efflux-1 (HAE1) | | ebA3926 | MexK | 1047 | 1025 | 3.00E-61 | 11 (TC 12) | Complete |

**Table 2** continued

| TC subject protein | Family name | No. of complete sytems | EbN1ID no. | TC homologue (protein name) | EbN1 query length | TC subject length | E-value | No. of TMSs | Estimated transporter status |
|---|---|---|---|---|---|---|---|---|---|
| 2.A.6.2.21 | (Largely Gram-negative Bacterial) Hydrophobe/Amphiphile Efflux-1 (HAE1) | 1 | ebA1973 | OprM | 475 | 485 | 3.00E-72 | 0 | Complete |
| 2.A.6.2.21 | (Largely Gram-negative Bacterial) Hydrophobe/Amphiphile Efflux-1 (HAE1) | | ebA1972 | MexY | 1054 | 1046 | 0 | 12 | |
| 2.A.6.2.21 | (Largely Gram-negative Bacterial) Hydrophobe/Amphiphile Efflux-1 (HAE1) | | ebA1971 | MexX | 404 | 389 | 7.00E-48 | 0 | |
| 2.A.6.7.1 | (Largely Archaeal Putative) Hydrophobe/Amphiphile Efflux-3 (HAE3) | 1 | ebA5169 | ORF in Afu | 787 | 750 | 2.00E-22 | 12 | Complete |
| 2.A.6.7.2 | (Largely Archaeal Putative) Hydrophobe/Amphiphile Efflux-3 (HAE3) | 6 | ebA327 | ORF in Mja | 799 | 388 | 8.00E-13 | 12 | Complete |
| 2.A.6.7.2 | (Largely Archaeal Putative) Hydrophobe/Amphiphile Efflux-3 (HAE3) | | c1A90 | ORF in Mja | 808 | 388 | 5.00E-11 | 12 (TC 6) | Probably complete |
| 2.A.6.7.2 | (Largely Archaeal Putative) Hydrophobe/Amphiphile Efflux-3 (HAE3) | | ebA1928 | ORF in Mja | 799 | 388 | 4.00E-13 | 12 (TC 6) | Probably complete |
| 2.A.6.7.2 | (Largely Archaeal Putative) Hydrophobe/Amphiphile Efflux-3 (HAE3) | | ebA4709 | ORF in Mja | 791 | 388 | 6.00E-12 | 12 (TC 6) | Probably complete |
| 2.A.6.7.2 | (Largely Archaeal Putative) Hydrophobe/Amphiphile Efflux-3 (HAE3) | | ebA5763 | ORF in Mja | 807 | 388 | 3.00E-14 | 12 (TC 6) | Probably complete |
| 2.A.6.7.2 | (Largely Archaeal Putative) Hydrophobe/Amphiphile Efflux-3 (HAE3) | | p2A399 | ORF in Mja | 791 | 388 | 4.00E-17 | 12 (TC 6) | Probably complete |
| 2.A.6.8.1 | Brominated, Aryl Polyene Pigment Exporter (ORF4) | 1 | ebA7066 | Putative inner membrane protein | 783 | 807 | 2.00E-76 | 12 | Complete |
| 2.A.7.1.3 | 4 TMS Small Multidrug Resistance (SMR) | 1 | c1A283 | EmrE | 122 | 110 | 3.00E-10 | 4 | Complete |
| 2.A.7.3.2 | TMS Drug/Metabolite Exporter (DME) | 3 | ebA2542 | YdeD | 289 | 299 | 1.00E-07 | 9 (TC 10) | Complete |
| 2.A.7.3.2 | 10 TMS Drug/Metabolite Exporter (DME) | | ebA3672 | YdeD | 294 | 299 | 2.00E-06 | 10 | Complete |
| 2.A.7.3.2 | 10 TMS Drug/Metabolite Exporter (DME) | | ebA4612 | YdeD | 306 | 299 | 6.00E-09 | 10 | Complete |
| 2.A.7.3.4 | 10 TMS Drug/Metabolite Exporter (DME) | 1 | ebA6529 | YwfM | 297 | 297 | 1.00E-06 | 10 | Complete |
| 2.A.7.3.7 | 10 TMS Drug/Metabolite Exporter (DME) | 1 | ebA4959 | Sam (RPO76) | 318 | 294 | 8.00E-18 | 10 | Complete |
| 2.A.9.3.1 | Cytochrome Oxidase Biogenesis (Oxa1) | 1 | ebA2842 | YidC | 550 | 548 | e-114 | 4 (TC 3) | Complete |
| 2.A.16.2.1 | Tellurite-resistance/Dicarboxylate Transporter (TDT) | 1 | ebA1993 | Mae1 | 358 | 438 | 4.00E-06 | 10 | Complete |
| 2.A.20.2.4 | Inorganic Phosphate Transporter (PiT) | 1 | ebA6176 | Pht2;1 | 527 | 587 | 5.00E-45 | 11 (TC 13) | Complete |
| 2.A.21.7.1 | Solute:Sodium Symporter (SSS) | 1 | ebA3695 | Phenylacetate permease Ppa | 365 | 520 | 1.00E-60 | 9 (TC 13) | Complete |
| 2.A.21.7.2 | Solute:Sodium Symporter (SSS) | 2 | ebA165 | ActP | 693 | 549 | 1.00E-23 | 14 | Complete |
| 2.A.21.7.2 | Solute:Sodium Symporter (SSS) | | ebA3537 | ActP | 572 | 549 | 0 | 14 | Complete |
| 2.A.21.8.1 | Solute:Sodium Symporter (SSS) | 1 | ebA3608 | CHT1 | 488 | 580 | 2.00E-37 | 13 | Complete |
| 2.A.21.9.2 | Solute:Sodium Symporter (SSS) | 1 | ebA169 | PrlS | 918 | 1156 | e-103 | 13 | Complete |

**Table 2** continued

| TC subject protein | Family name | No. of complete sytems | EbN1ID no. | TC homologue (protein name) | EbN1 query length | TC subject length | E-value | No. of TMSs | Estimated transporter status |
|---|---|---|---|---|---|---|---|---|---|
| 2.A.25.1.1 | Alanine or Glycine:Cation Symporter (AGCS) | 1 | ebA3983 | DagA | 475 | 542 | 1.00E-58 | 11 | Complete |
| 2.A.36.4.3 | Monovalent Cation:Proton Antiporter-1 (CPA1) | 1 | ebA6098 | Nha1 | 445 | 468 | 0.001 | 13 | Complete |
| 2.A.37.1.1 | Monovalent Cation:Proton Antiporter-2 (CPA2) | 1 | ebA1314 | KefC | 656 | 620 | 2.00E-50 | 12 | Complete |
| 2.A.37.1.1 | Monovalent Cation:Proton Antiporter-2 (CPA2) | | ebA1313 | YabF (ancillary protein) | 176 | | | 0 | |
| 2.A.38.1.1 | $K^+$ Transporter (Trk) | 1 | ebA2824 | TrkH | 485 | 483 | e-103 | 10 (TC 11) | Complete |
| 2.A.38.1.1 | $K^+$ Transporter (Trk) | | ebA2825 | TrkA | 467 | 458 | e-133 | 1 (TC 0) | |
| 2.A.38.4.3 | $K^+$ Transporter (Trk) | 2 | ebA2742 | KtrA | 231 | 222 | 6.00E-40 | 1 (TC 0) | Complete |
| 2.A.38.4.3 | $K^+$ Transporter (Trk) | | ebA2741 | KtrB | 444 | 445 | 7.00E-69 | 12 (TC 9) | |
| 2.A.38.4.3 | $K^+$ Transporter (Trk) | | ebA5556 | KtrA | 231 | 222 | 6.00E-40 | 1 (TC 0) | Complete |
| 2.A.38.4.3 | $K^+$ Transporter (Trk) | | ebA5555 | KtrB | 444 | 455 | 4.00E-53 | 12 | |
| 2.A.49.5.1 | Chloride Channel (ClC) | 1 | ebA4866 | EriC | 468 | 473 | 1.00E-18 | 10 (TC 11) | Complete |
| 2.A.51.1.2 | Chromate Ion Transporter (CHR) | 1 | ebA4644 | SrpC | 183 | 393 | 6.00E-13 | 5 (TC 12) | Probably complete |
| 2.A.51.1.2 | Chromate Ion Transporter (CHR) | | ebA4646 | SrpC | 164 | 393 | 8.00E-05 | 5 (TC 12) | |
| 2.A.53.3.1 | Sulfate Permease (SulP) | 1 | ebA4402 | Sulfate permease | 562 | 492 | 1.00E-48 | 10 (TC 13) | Complete |
| 2.A.53.4.1 | Sulfate Permease (SulP) | 1 | ebA4484 | Sulfate transporter | 570 | 566 | 1.00E-46 | 14 (TC 13) | Complete |
| 2.A.56.1.1 | Tripartite ATP-independent Periplasmic Transporter (TRAP-T) | 1 | ebA4162 | DctM | 427 | 440 | e-171 | 13 | Complete |
| 2.A.56.1.1 | Tripartite ATP-independent Periplasmic Transporter (TRAP-T) | | ebA4159 | DctQ | 238 | 227 | 2.00E-60 | 4 | |
| 2.A.56.1.1 | Tripartite ATP-independent Periplasmic Transporter (TRAP-T) | | ebA4158 | DctP | 334 | 333 | e-125 | 1 | |
| 2.A.56.1.1 | Tripartite ATP-independent Periplasmic Transporter (TRAP-T) | 1 | ebA5367 | DctM | 439 | 440 | 1.00E-28 | 12 (TC 13) | Complete |
| 2.A.56.1.1 | Tripartite ATP-independent Periplasmic Transporter (TRAP-T) | | ebA5362 | DctP | 349 | 333 | 2.00E-15 | 1 | |
| 2.A.56.1.1 | Tripartite ATP-independent Periplasmic Transporter (TRAP-T) | | ebB188 | DctQ | 227 | 173 | | 4 | |
| 2.A.56.1.1 | Tripartite ATP-independent Periplasmic Transporter (TRAP-T) | 1 | ebA729 | DctP | 344 | 333 | 7.00E-10 | 1 | Complete |
| 2.A.56.1.1 | Tripartite ATP-independent Periplasmic Transporter (TRAP-T) | | ebA732 | DctM | 443 | 440 | 7.00E-52 | 12 (TC 13) | |
| 2.A.56.1.1 | Tripartite ATP-independent Periplasmic Transporter (TRAP-T) | | ebA733 | DctQ | 214 | 227 | 2.00E-04 | 4 | |
| 2.A.56.1.2 | Tripartite ATP-independent Periplasmic Transporter (TRAP-T) | 1 | ebA4994 | YiaO (R) | 343 | 328 | 3.00E-10 | 1 | Complete |
| 2.A.56.1.2 | Tripartite ATP-independent Periplasmic Transporter (TRAP-T) | | p2A96 | 4TMS + YiaN (M) | 656 | 425 | 7.00E-13 | 18 (TC 12+4) | |

**Table 2** continued

| TC subject protein | Family name | No. of complete sytems | EbN1ID no. | TC homologue (protein name) | EbN1 query length | TC subject length | E-value | No. of TMSs | Estimated transporter status |
|---|---|---|---|---|---|---|---|---|---|
| 2.A.56.1.5 | Tripartite ATP-independent Periplasmic Transporter (TRAP-T) | C(3) | ebA1032 | RRC01191 (mannitol-binding) | 361 | 365 | 1.00E-101 | 1 | Incomplete |
| 2.A.56.1.5 | Tripartite ATP-independent Periplasmic Transporter (TRAP-T) | 1 | ebA1033 | RRC01191 (mannitol-binding) | 361 | 365 | 1.00E-105 | 1 | Complete |
| 2.A.56.1.5 | Tripartite ATP-independent Periplasmic Transporter (TRAP-T) | | ebA1036 | RRC02478 (S) | 203 | 190 | 1.00E-44 | 4 | |
| 2.A.56.1.5 | Tripartite ATP-independent Periplasmic Transporter (TRAP-T) | | ebA1037 | RRC02479 (L) | 564 | 611 | e-144 | 16 (TC 18) | |
| 2.A.59.1.2 | Arsenical Resistance-3 (ACR3) | 1 | ebA5001 | ArsB | 371 | 346 | 2.00E-46 | 10 | Complete |
| 2.A.63.1.1 | Monovalent Cation ($K^+$ or $Na^+$):Proton Antiporter-3 (CPA3) | 1 | ebA553 | PhaG | 103 | 121 | 1.00E-09 | 3 | Complete |
| 2.A.63.1.1 | Monovalent Cation ($K^+$ or $Na^+$):Proton Antiporter-3 (CPA3) | | ebA554 | PhaF | 93 | 92 | 5.00E-23 | 3 | |
| 2.A.63.1.1 | Monovalent Cation ($K^+$ or $Na^+$):Proton Antiporter-3 (CPA3) | | ebA555 | PhaE | 160 | 161 | 1.00E-27 | 3 | |
| 2.A.63.1.1 | Monovalent Cation ($K^+$ or $Na^+$):Proton Antiporter-3 (CPA3) | | ebB15 | PhaC | 115 | 115 | 6.00E-34 | 3 | |
| 2.A.63.1.1 | Monovalent Cation ($K^+$ or $Na^+$):Proton Antiporter-3 (CPA3) | | ebA558 | PhaA + PhaB | 967 | 725 | 0 | 19 | |
| 2.A.63.1.1 | Monovalent Cation ($K^+$ or $Na^+$):Proton Antiporter-3 (CPA3) | | ebA556 | PhaD | 538 | 547 | 1.00E-93 | 14 (TC 17) | |
| 2.A.64.1.1 | Twin Arginine Targeting (Tat) | 1 | ebB38 | TatE/TatA | 75 | 67 | 4.00E-08 | 1 | Complete |
| 2.A.64.1.1 | Twin Arginine Targeting (Tat) | | ebD2 | TatB | 147 | 171 | 1.00E-05 | 1 | |
| 2.A.64.1.1 | Twin Arginine Targeting (Tat) | | ebA1285 | TatC | 262 | 258 | 4.00E-56 | 6 (TC 5) | |
| 2.A.66.1.1 | Multi Antimicrobial Extrusion (MATE) | 1 | ebA6316 | NorM | 463 | 456 | 2.00E-69 | 12 | Complete |
| 2.A.66.2.7 | Polysaccharide Transport (PST) | 1 | ebA4295 | WzxC | 486 | 492 | 1.00E-20 | 14 | Complete |
| 2.A.66.4.1 | Mouse Virulence Factor (MVF) | 1 | ebA5091 | MviN | 530 | 524 | e-142 | 14 | Complete |
| 2.A.69.2.1 | Auxin Efflux Carrier (AEC) | 2 | ebA2636 | MdcF | 291 | 319 | 5.00E-08 | 10 | Complete |
| 2.A.69.2.1 | Auxin Efflux Carrier (AEC) | | ebA5059 | MdcF | 313 | 319 | 2.00E-14 | 10 | Complete |
| 2.A.71.2.1 | Folate-Biopterin Transporter (FBT) | 1 | ebA826 | Synechococcus | 541 | 453 | 8.00E-11 | 14 | Complete |
| 2.A.72.1.1 | $K^+$ Uptake Permease (KUP) | 1 | ebA3621 | KUP | 640 | 622 | e-160 | 11 (TC 13) | Complete |
| 2.A.72.1.1 | $K^+$ Uptake Permease (KUP) | | ebD71 | KUP | 82 | 622 | 4.00E-07 | 0 (TC 13) | |
| 2.A.76.1.1 | Resistance to Homoserine/Threonine (RhtB) | 1 | ebA2598 | RhtB | 211 | 206 | 2.00E-11 | 6 | Complete |
| 2.A.76.1.2 | Resistance to Homoserine/Threonine (RhtB) | 1 | ebA6561 | RhtC | 211 | 206 | 2.00E-22 | 5 (TC 6) | Complete |
| 2.A.86.1.1 | Putative Permease (PerM) | 1 | ebA7105 | PerM | 378 | 353 | 2.00E-19 | 8 (TC 7) | Complete |
| 2.A total | | 81 | | | | | | | |

**Table 2** continued

| TC subject protein | Family name | No. of complete sytems | EbN1ID no. | TC homologue (protein name) | EbN1 query length | TC subject length | E-value | No. of TMSs | Estimated transporter status |
|---|---|---|---|---|---|---|---|---|---|
| 2.C.1.1.1 | TonB-ExbB-ExbD/TolA-TolQ-TolR (TonB) of Auxiliary Proteins for Energization of Outer Membrane Receptor (OMR)-mediated Active Transport | 2 | ebA1839 | TonB | 230 | 239 | 3.00E-06 | 0 (TC 1) | Complete |
| 2.C.1.1.1 | TonB-ExbB-ExbD/TolA-TolQ-TolR (TonB) of Auxiliary Proteins for Energization of Outer Membrane Receptor (OMR)-mediated Active Transport | | ebA1841 | ExbB | 259 | 230 | 1.00E-26 | 3 | |
| 2.C.1.1.1 | TonB-ExbB-ExbD/TolA-TolQ-TolR (TonB) of Auxiliary Proteins for Energization of Outer Membrane Receptor (OMR)-mediated Active Transport | | ebA1842 | ExbD | 138 | 142 | 3/E-13 | 1 | |
| 2.C.1.1.1 | TonB-ExbB-ExbD/TolA-TolQ-TolR (TonB) of Auxiliary Proteins for Energization of Outer Membrane Receptor (OMR)-mediated Active Transport | | ebA5081 | ExbB | 202 | 244 | 2/E-10 | 3 | Complete |
| 2.C.1.1.1 | TonB-ExbB-ExbD/TolA-TolQ-TolR (TonB) of Auxiliary Proteins for Energization of Outer Membrane Receptor (OMR)-mediated Active Transport | | ebA5156 | TonB | 265 | 239 | 3.00E-04 | 0 (TC 1) | |
| 2.C.1.1.1 | TonB-ExbB-ExbD/TolA-TolQ-TolR (TonB) of Auxiliary Proteins for Energization of Outer Membrane Receptor (OMR)-mediated Active Transport | | ebB176 | ExbD | 141 | 142 | | 1 | |
| 2.C.1.2.1 | TonB-ExbB-ExbD/TolA-TolQ-TolR (TonB) of Auxiliary Proteins for Energization of Outer Membrane Receptor (OMR)-mediated Active Transport | 1 | ebA2644 | TolQ | 224 | 230 | 2/E-53 | 3 | Complete |
| 2.C.1.2.1 | TonB-ExbB-ExbD/TolA-TolQ-TolR (TonB) of Auxiliary Proteins for Energization of Outer Membrane Receptor (OMR)-mediated Active Transport | | ebA2650 | TolB | 426 | 430 | 2.00E-74 | 1 | |
| 2.C.1.2.1 | TonB-ExbB-ExbD/TolA-TolQ-TolR (TonB) of Auxiliary Proteins for Energization of Outer Membrane Receptor (OMR)-mediated Active Transport | | ebA2645 | TolR | 137 | 141 | 2.00E-11 | 1 | |

**Table 2** continued

| TC subject protein | Family name | No. of complete sytems | EbN1ID no. | TC homologue (protein name) | EbN1 query length | TC subject length | E-value | No. of TMSs | Estimated transporter status |
|---|---|---|---|---|---|---|---|---|---|
| 2.C.1.2.1 | TonB-ExbB-ExbD/TolA-TolQ-TolR (TonB) of Auxiliary Proteins for Energization of Outer Membrane Receptor (OMR)-mediated Active Transport | | ebA2648 | TolA/TonB | | | 5.00E-11 | 1 | |
| 2.C.1.2.1 | TonB-ExbB-ExbD/TolA-TolQ-TolR (TonB) of Auxiliary Proteins for Energization of Outer Membrane Receptor (OMR)-mediated Active Transport | | ebA2652 | Pal | 175 | 173 | 2.00E-19 | 0 (TC 1) | |
| 2.C.1.2.1 | TonB-ExbB-ExbD/TolA-TolQ-TolR (TonB) of Auxiliary Proteins for Energization of Outer Membrane Receptor (OMR)-mediated Active Transport | | ebA2654 | YbgF | 246 | 263 | 3.00E-18 | 0 (TC 1) | |
| 2.C total | | 3 | | | | | | | |
| 3.A.1.3.4 | Polar Amino Acid Uptake Transporter (PAAT) | 1 | ebA4561 | GltI (R) | 298 | 302 | 8.00E-78 | 1 | Complete |
| 3.A.1.3.4 | Polar Amino Acid Uptake Transporter (PAAT) | | ebA4562 | GltK (M) | 226 | 224 | 3.00E-57 | 5 | |
| 3.A.1.3.4 | Polar Amino Acid Uptake Transporter (PAAT) | | ebA4564 | GltJ (M) | 247 | 246 | 1.00E-50 | 5 | |
| 3.A.1.3.4 | Polar Amino Acid Uptake Transporter (PAAT) | | ebA4567 | GltL (C) | 242 | 241 | 5.00E-99 | 0 | |
| 3.A.1.4.1 | Hydrophobic Amino Acid Uptake Transporter (HAAT) | 1 | ebA3394 | LivG (C) | 241 | 255 | 1.00E-27 | 0 | Complete |
| 3.A.1.4.1 | Hydrophobic Amino Acid Uptake Transporter (HAAT) | | | LivF (C) | | | | | |
| 3.A.1.4.1 | Hydrophobic Amino Acid Uptake Transporter (HAAT) | | ebA2070 | LivJ (R) | 382 | 454 | 3.00E-15 | 1 | |
| 3.A.1.4.1 | Hydrophobic Amino Acid Uptake Transporter (HAAT) | | ebA2700 | LivK (R) | 386 | 369 | 1.00E-16 | 1 | |
| 3.A.1.4.1 | Hydrophobic Amino Acid Uptake Transporter (HAAT) | | ebA2706 | LivM (M) | 321 | 425 | 1.00E-15 | 11 (TC 10) | |
| 3.A.1.4.1 | Hydrophobic Amino Acid Uptake Transporter (HAAT) | | ebA2710 | LivH (M) | 292 | 308 | 1.00E-16 | 8 (TC 9) | |
| 3.A.1.4.1 | Hydrophobic Amino Acid Uptake Transporter (HAAT) | 1 | ebA3167 | LivF | 250 | 237 | 6.00E-55 | 0 | Complete |
| 3.A.1.4.1 | Hydrophobic Amino Acid Uptake Transporter (HAAT) | | ebA3169 | LivG | 258 | 255 | 5.00E-55 | 0 | |
| 3.A.1.4.1 | Hydrophobic Amino Acid Uptake Transporter (HAAT) | | ebA3170 | LivM | 366 | 425 | 4.00E-58 | 8 (TC 10) | |
| 3.A.1.4.1 | Hydrophobic Amino Acid Uptake Transporter (HAAT) | | ebA3172 | LivH | 310 | 308 | 2.00E-43 | 9 | |

**Table 2** continued

| TC subject protein | Family name | No. of complete sytems | EbN1ID no. | TC homologue (protein name) | EbN1 query length | TC subject length | E-value | No. of TMSs | Estimated transporter status |
|---|---|---|---|---|---|---|---|---|---|
| 3.A.1.4.1 | Hydrophobic Amino Acid Uptake Transporter (HAAT) | | ebA3173 | LivK | 372 | 369 | 5.00E-41 | 0 (TC 1) | |
| 3.A.1.4.1 | Hydrophobic Amino Acid Uptake Transporter (HAAT) | | ebA3175 | BraC | 370 | 381 | 5.00E-50 | 1 | |
| 3.A.1.4.1 | Hydrophobic Amino Acid Uptake Transporter (HAAT) | 1 | ebA3556 | LivK | 382 | 454 | 7.00E-16 | 1 | Complete |
| 3.A.1.4.1 | Hydrophobic Amino Acid Uptake Transporter (HAAT) | | ebA3558 | LivH | 345 | 308 | 1.00E-12 | 9 | |
| 3.A.1.4.1 | Hydrophobic Amino Acid Uptake Transporter (HAAT) | | ebA3559 | LivG + LivM | 600 | 255 | 1.00E-43 | 7 (TC 0) | |
| 3.A.1.4.1 | Hydrophobic Amino Acid Uptake Transporter (HAAT) | | ebA3560 | LivF | 259 | 233 | 9/E-54 | 0 | |
| 3.A.1.4.1 | Hydrophobic Amino Acid Uptake Transporter (HAAT) | | ebA5316 | LivJ | 380 | 367 | 8.00E-09 | 0 (TC 1) | |
| 3.A.1.4.2 | Hydrophobic Amino Acid Uptake Transporter (HAAT) | 1 | ebA3425 | NatC | 309 | 331 | 2.00E-14 | 8 (TC 9) | Complete |
| 3.A.1.4.2 | Hydrophobic Amino Acid Uptake Transporter (HAAT) | | ebA3426 | NatD | 304 | 290 | 5.00E-19 | 7 | |
| 3.A.1.4.2 | Hydrophobic Amino Acid Uptake Transporter (HAAT) | | ebA3428 | NatB | 405 | 434 | 8.00E-08 | 0 (TC 1) | |
| 3.A.1.4.2 | Hydrophobic Amino Acid Uptake Transporter (HAAT) | | ebA3429 | NatE | 243 | 237 | 2.00E-40 | 0 | |
| 3.A.1.4.2 | Hydrophobic Amino Acid Uptake Transporter (HAAT) | | ebA3430 | NatA | 251 | 267 | 2.00E-44 | 0 (TC 1) | |
| 3.A.1.4.4 | Hydrophobic Amino Acid Uptake Transporter (HAAT) | 1 | ebA5303 | UrtA | 395 | 434 | 2.00E-11 | 2 (TC 1) | Complete |
| 3.A.1.4.4 | Hydrophobic Amino Acid Uptake Transporter (HAAT) | | ebA5304 | UrtB | 288 | 294 | 7.00E-26 | 7 (TC 8) | |
| 3.A.1.4.4 | Hydrophobic Amino Acid Uptake Transporter (HAAT) | | ebA5306 | UrtC | 324 | 359 | 5/E-23 | 8 (TC 9) | |
| 3.A.1.4.4 | Hydrophobic Amino Acid Uptake Transporter (HAAT) | | ebA5307 | UrtD | 253 | 242 | 9/E-42 | 0 | |
| 3.A.1.4.4 | Hydrophobic Amino Acid Uptake Transporter (HAAT) | | ebA5309 | UrtE | 238 | 237 | 7.00E-41 | 0 | |
| 3.A.1.5.2 | Peptide/Opine/Nickel Uptake Transporter (PepT) | 1 | ebA6466 | DppD (C) | 660 | 335 | 4.00E-74 | 0 | Probably complete |
| 3.A.1.5.2 | Peptide/Opine/Nickel Uptake Transporter (PepT) | | ebA6658 | DppC (M) | 476 | 320 | 2.00E-29 | 9 (TC 6) | |
| 3.A.1.5.2 | Peptide/Opine/Nickel Uptake Transporter (PepT) | | ebA6661 | DppB (M) | 325 | 308 | 3.00E-29 | 6 | |
| 3.A.1.5.2 | Peptide/Opine/Nickel Uptake Transporter (PepT) | | ebA6662 | MppA (R) | 723 | 543 | 7.00E-11 | 1 | |
| 3.A.1.5.2 | Peptide/Opine/Nickel Uptake Transporter (PepT) | | | DppA (C) | | 274 | | | |

**Table 2** continued

| TC subject protein | Family name | No. of complete sytems | EbN1ID no. | TC homologue (protein name) | EbN1 query length | TC subject length | E-value | No. of TMSs | Estimated transporter status |
|---|---|---|---|---|---|---|---|---|---|
| 3.A.1.5.11 | Peptide/Opine/Nickel Uptake Transporter (PepT) | 1 | ebA5654 | YliA | 703 | 629 | 5/E-93 | 0 | Complete |
| 3.A.1.5.11 | Peptide/Opine/Nickel Uptake Transporter (PepT) | | ebA5655 | YliC (M) | 317 | 306 | 1.00E-40 | 6 | |
| 3.A.1.5.11 | Peptide/Opine/Nickel Uptake Transporter (PepT) | | ebA5658 | YliD | 304 | 303 | 9.00E-35 | 7 (TC 5) | |
| 3.A.1.5.11 | Peptide/Opine/Nickel Uptake Transporter (PepT) | | ebA5660 | YliB (precursor) | 527 | 512 | 1.00E-15 | 1 (TC 0) | |
| 3.A.1.6.1 | Sulfate/Tungstate Uptake Transporter (SulT) | 1 | ebA6204 | SUBI (R) | 333 | 329 | e-102 | 0 | Probably complete |
| 3.A.1.6.1 | Sulfate/Tungstate Uptake Transporter (SulT) | | ebA6206 | CysT (M) | 299 | 277 | 4.00E-64 | 6 | |
| 3.A.1.6.1 | Sulfate/Tungstate Uptake Transporter (SulT) | | ebA6207 | CysW (M) | 299 | 291 | 8.00E-75 | 6 | |
| 3.A.1.6.1 | Sulfate/Tungstate Uptake Transporter (SulT) | | ebA6208 | CysA (C) | 354 | 365 | 9.00E-87 | 0 (TC 1) | |
| 3.A.1.6.1 | Could be ebB221 (67 aa) but does not hit a TC sequence? | | | CysP (R) | | 338 | | | |
| 3.A.1.6.2 | Sulfate/Tungstate Uptake Transporter (SulT) | 1 | ebA3597 | TupA | 273 | 286 | 2.00E-62 | 1 | Complete |
| 3.A.1.6.2 | Sulfate/Tungstate Uptake Transporter (SulT) | | ebA5014 | TupC | 237 | 214 | 7.00E-34 | 0 | |
| 3.A.1.6.2 | Sulfate/Tungstate Uptake Transporter (SulT) | | ebA5015 | TupB | 246 | 228 | 3.00E-30 | 6 (TC 5) | |
| 3.A.1.7.1 | Phosphate Uptake Transporter (PhoT) | 1 | ebA4826 | PstS | 330 | 346 | 3.00E-06 | 0 (TC 1) | Complete |
| 3.A.1.7.1 | Phosphate Uptake Transporter (PhoT) | | ebA4828 | PstC | 319 | 319 | 7.00E-24 | 6 | |
| 3.A.1.7.1 | Phosphate Uptake Transporter (PhoT) | | ebA4829 | PstA | 307 | 296 | 8.00E-23 | 6 | |
| 3.A.1.7.1 | Phosphate Uptake Transporter (PhoT) | | ebA4830 | PstB | 289 | 257 | 3.00E-81 | 0 | |
| 3.A.1.8.1 | Molybdate Uptake Transporter (MolT) | 1 | ebA2719 | ModC (C) | 377 | 352 | 2.00E-65 | 0 (TC 1) | Complete |
| 3.A.1.8.1 | Molybdate Uptake Transporter (MolT) | | ebA2720 | ModB (M) | 224 | 229 | 5.00E-18 | 5 | |
| 3.A.1.8.1 | Molybdate Uptake Transporter (MolT) | | ebA2721 | ModA (R) | 255 | 257 | 2.00E-13 | 1 | |
| 3.A.1.10.1 | Ferric Iron Uptake Transporter (FeT) | 1 | ebA6521 | SfuA | 374 | 338 | | 1 | Probably complete |
| 3.A.1.10.1 | Ferric Iron Uptake Transporter (FeT) | | ebA6523 | SfuC | | 345 | | 0 (TC 1) | |
| 3.A.1.10.1 | Ferric Iron Uptake Transporter (FeT) | | ebA6524 | SfuB | | 527 | | 7 (TC 12) | |
| 3.A.1.10.2 | Ferric Iron Uptake Transporter (FeT) | 1 | ebA4893 | FutB | 560 | 557 | e-123 | 12 | Complete |
| 3.A.1.10.2 | Ferric Iron Uptake Transporter (FeT) | | ebA4918 | FutA1/FutA2 | 339 | 346 | 1.00E-82 | 0 (TC 1) | |
| 3.A.1.10.2 | Ferric Iron Uptake Transporter (FeT) | | ebA4892 | FutC | 372 | 368 | 2.00E-63 | 1 (TC 0) | |
| 3.A.1.10.2 | Ferric Iron Uptake Transporter (FeT) | C(4) | ebA2111 | FutC | 360 | 368 | 2.00E-60 | | Incomplete |
| 3.A.1.13.1 | Vitamin B12 Uptake Transporter (B12T) (similar to 3.A.1.14) | 1 | ebA3688 | BtuF | 297 | 266 | 1.00E-26 | 0 (TC 1) | Complete |
| 3.A.1.13.1 | Vitamin B12 Uptake Transporter (B12T) (similar to 3.A.1.14) | | ebA4019 | BtuC | 326 | 326 | 4.00E-15 | 10 (TC 9) | |

**Table 2** continued

| TC subject protein | Family name | No. of complete sytems | EbN1ID no. | TC homologue (protein name) | EbN1 query length | TC subject length | E-value | No. of TMSs | Estimated transporter status |
|---|---|---|---|---|---|---|---|---|---|
| 3.A.1.13.1 | Vitamin B12 Uptake Transporter (B12T) (similar to 3.A.1.14) | | ebA4020 | BtuD | 259 | 249 | 8.00E-34 | 0 | |
| 3.A.1.14.3 | Iron Chelate Uptake Transporter (FeCT) | C(3) | ebA3857 | FhuC | 957 | 265 | 7.00E-10 | 0 | CDD-PRK00349, uvrA, excinuclease ABC subunit A |
| 3.A.1.15.2 | Manganese/Zinc/Iron Chelate Uptake Transporter (MZT) (similar to 3.A.1.12 & 3.A.1.16) | 1 | ebA1813 | ScaB | 289 | 278 | 1.00E-26 | 7 | Complete |
| 3.A.1.15.2 | Manganese/Zinc/Iron Chelate Uptake Transporter (MZT) (similar to 3.A.1.12 & 3.A.1.16) | | ebA1814 | ScaA | 303 | 305 | 2.00E-48 | 1 | |
| 3.A.1.15.2 | Manganese/Zinc/Iron Chelate Uptake Transporter (MZT) (similar to 3.A.1.12 & 3.A.1.16) | | ebA1812 | ScaC | 255 | 266 | 6.00E-37 | 0 | |
| 3.A.1.17.1 | Taurine Uptake Transporter (TauT) (similar to 3.A.1.12 & 3.A.1.16) | 2 | ebA2113 | TauB (C) | 285 | 255 | 2.00E-34 | 0 (TC 1) | Complete |
| 3.A.1.17.1 | Taurine Uptake Transporter (TauT) (similar to 3.A.1.12 & 3.A.1.16) | | ebA2114 | TauC (M) | 265 | 275 | 1.00E-10 | 6 | |
| 3.A.1.17.1 | Taurine Uptake Transporter (TauT) (similar to 3.A.1.12 & 3.A.1.16) | | ebA2115 | TauA (R) | 338 | 320 | 0.002 | 0 | |
| 3.A.1.17.1 | Taurine Uptake Transporter (TauT) (similar to 3.A.1.12 & 3.A.1.16) | | p2A122 | TauC (M) | 269 | 275 | 2.00E-35 | 6 | Complete |
| 3.A.1.17.1 | Taurine Uptake Transporter (TauT) (similar to 3.A.1.12 &3.A.1.16) | | p2A128 | TauA (R) | 348 | 320 | 5.00E-07 | 1 (TC 0) | |
| 3.A.1.17.1 | Taurine Uptake Transporter (TauT) (similar to 3.A.1.12 & 3.A.1.16) | | p2A125 | TauB (C) | 285 | 255 | 7.00E-32 | 0 (TC 1) | |
| 3.A.1.102.1 | Lipooligosaccharide Exporter (LOSE) | 4 | ebA3579 | NodJ (M) | 263 | 262 | 3.00E-54 | 6 | Complete |
| 3.A.1.102.1 | Lipooligosaccharide Exporter (LOSE) | | ebA3580 | NodI (C) | 325 | 347 | 8.00E-85 | 0 | |
| 3.A.1.102.1 | Lipooligosaccharide Exporter (LOSE) | | ebA6231 | NodJ (M) | 253 | 262 | 2.00E-13 | 6 | Complete |
| 3.A.1.102.1 | Lipooligosaccharide Exporter (LOSE) | | ebA6230 | NodI (C) | 311 | 325 | 1.00E-39 | 1 (TC 0) | |
| 3.A.1.102.1 | Lipooligosaccharide Exporter (LOSE) | | ebA6744 | NodI + NodJ (CM) | 972 | 347 | 3.00E-39 | 6 (TC 0) | Complete |
| 3.A.1.103.1 | Lipopolysaccharide Exporter (LPSE) | | ebA1592 | RfbA (M) | 273 | 259 | 6.00E-13 | 6 | Complete |
| 3.A.1.103.1 | Lipopolysaccharide Exporter (LPSE) | | ebA1593 | RfbB (C) | 483 | 246 | 9.00E-53 | 0 | |
| 3.A.1.105.2 | Drug Exporter-1 (DrugE1) | 2 | ebA6267 | OleC4 (C) | 317 | 325 | 1.00E-36 | 0 | Complete |
| 3.A.1.105.2 | Drug Exporter-1 (DrugE1) | | ebA6745 | OleC5 (M) | 393 | 273 | 2.00E-08 | 7 (TC 6) | |
| 3.A.1.105.2 | Drug Exporter-1 (DrugE1) | | ebA1306 | OleC4 (C) | 298 | 325 | 4.00E-39 | 0 | Complete |
| 3.A.1.105.2 | Drug Exporter-1 (DrugE1) | | ebA1304 | OleC5 (M) | 256 | 262 | 1.00E-07 | 6 | |
| 3.A.1.106.1 | Lipid Exporter (LipidE) | 1 | ebA3992 | MsbA | 601 | 582 | e-122 | 6 (TC 5) | Complete |
| 3.A.1.107.1 | Putative Heme Exporter (HemeE) | 1 | ebA3514 | CycV (C) | 214 | 200 | 8.00E-26 | 0 | Complete |
| 3.A.1.107.1 | Putative Heme Exporter (HemeE) | | ebA3516 | CycW (M) | 225 | 222 | 1.00E-04 | 6 | |

**Table 2** continued

| TC subject protein | Family name | No. of complete sytems | EbN1ID no. | TC homologue (protein name) | EbN1 query length | TC subject length | E-value | No. of TMSs | Estimated transporter status |
|---|---|---|---|---|---|---|---|---|---|
| 3.A.1.107.1 | Putative Heme Exporter (HemeE) | | ebA3518 | CycZ (M) | 257 | 263 | 1.00E-43 | 6 | |
| 3.A.1.109.1 | Protein-1 Exporter (Prot1E) | 1 | ebA1666 | HlyB | 1021 | 707 | e-124 | 6 (TC 8) | Complete |
| 3.A.1.109.3 | Protein-1 Exporter (Prot1E) | 1 | ebA1807 | LapB | 742 | 718 | e-156 | 6 | Complete |
| 3.A.1.110.9 | Protein-2 Exporter (Prot2E) | 1 | ebA7181 | HasD (M-C) | 574 | 580 | e-108 | 6 | Complete |
| 3.A.1.114.1 | Probable Glycolipid Exporter (DevE) | 1 | ebA6251 | DevC (M) | 401 | 385 | 2.00E-05 | 4 (TC 6) | Complete |
| 3.A.1.114.1 | Probable Glycolipid Exporter (DevE) | | ebA6253 | DevA (C) | 237 | 244 | 1.00E-36 | 0 | |
| 3.A.1.120.1 | (Putative) Drug Resistance ATPase-1 (Drug RA1) | 1 | ebA2533 | SrmB | 655 | 550 | 1.00E-51 | 0 | Complete |
| 3.A.1.120.1 | (Putative) Drug Resistance ATPase-1 (Drug RA1) | 1 | ebA7225 | SrmB | 640 | 550 | 1.00E-56 | 0 | Complete |
| 3.A.1.120.3 | (Putative) Drug Resistance ATPase-1 (Drug RA1) | 1 | ebA2876 | OleB | 612 | 569 | 2.00E-42 | 0 | Complete |
| 3.A.1.120.4 | (Putative) Drug Resistance ATPase-1 (Drug RA1) | 1 | ebA6102 | CarA | 554 | 551 | 1.00E-47 | 0 | Complete |
| 3.A.1.121.2 | (Putative) Drug Resistance ATPase-2 (Drug RA2) | 1 | ebA2792 | VgaB | 545 | 552 | 1.00E-52 | 0 | Complete |
| 3.A.1.122.1 | Macrolide Exporter (MacB) | 2 | ebA1848 | MacB | 662 | 648 | e-142 | 4 | Complete |
| 3.A.1.122.1 | Macrolide Exporter (MacB) | | ebA1846 | MacA | 448 | 371 | 1.00E-52 | 1 | |
| 3.A.1.122.1 | Macrolide Exporter (MacB) | | ebA4059 | MacB | 402 | 648 | 1.00E-35 | 4 | Probably complete |
| 3.A.1.122.1 | Macrolide Exporter (MacB) | | ebA4061 | SalX domain | 232 | 648 | 1.00E-45 | 0 (TC 4) | |
| 3.A.1.122.1 | Macrolide Exporter (MacB) | C(2) | ebA2970 | MacB? | 1888 | 648 | 3.00E-08 | 0 (TC 4) | COG0178, UvrA, excinuclease ATPase subunit |
| 3.A.1.123.1 | Peptide-4 Exporter (Pep4E) | 1 | ebA2229 | PepT | 575 | 571 | 3.00E-49 | 6 (TC 5) | Complete |
| 3.A.1.125.1 | Lipoprotein Translocase (LPT) | 1 | ebA5819 | LolE (M) | 417 | 413 | 3.00E-63 | 4 | Complete |
| 3.A.1.125.1 | Lipoprotein Translocase (LPT) | | ebA5820 | LolD (C) | 228 | 233 | 2.00E-66 | 0 (TC 1) | |
| 3.A.1.125.1 | Lipoprotein Translocase (LPT) | | ebA4058 | LolC (M) | 400 | 233 | 1.00E-33 | 4 | |
| 3.A.1.125.1 | Lipoprotein Translocase (LPT) | 1 | ebA6805 | LolE (M) | 849 | 413 | 3.00E-07 | 11 (TC 4) | LolC missing (reverse blast result—LolE) |
| 3.A.1.125.1 | Lipoprotein Translocase (LPT) | | ebA6806 | LolD (C) | 239 | 233 | 8.00E-39 | 0 | |
| 3.A.1.125.1 | Lipoprotein Translocase (LPT) | | ebA6813 | LolD (C) | 231 | 233 | 2.00E-41 | 1 (TC 0) | ? |
| 3.A.1.201.2 | Multidrug Resistance Exporter (MDR) (ABCB) | 1 | ebA5186 | BSEP | 572 | 1321 | 7.00E-31 | 6 (TC 12) | Probably complete |
| 3.A.1.210.3 | Heavy Metal Transporter (HMT) (ABCB) | 2 | ebA2601 | ABC transporter homologue | 604 | 609 | e-154 | 6 (TC 8) | Complete |
| 3.A.1.210.3 | Heavy Metal Transporter (HMT) (ABCB) | | ebA6882 | ABC transporter homologue | 906 | 609 | e-130 | 6 (TC 8) | Complete |
| 3.A.1.212.1 | Mitochondrial Peptide Exporter (MPE) (ABCB) | 1 | ebA6704 | Mdl1p | 600 | 695 | 4.00E-69 | 6 (TC 8) | Complete |

**Table 2** continued

| TC subject protein | Family name | No. of complete sytems | EbN1ID no. | TC homologue (protein name) | EbN1 query length | TC subject length | E-value | No. of TMSs | Estimated transporter status |
|---|---|---|---|---|---|---|---|---|---|
| 3.A.2.1.1 | $H^+$- or $Na^+$-translocating F-type, V-type, & A-type ATPase (F-ATPase) superfamily | 1 | ebA2999 | ATP6 | 276 | 271 | 6.00E-61 | 6 | Complete |
| 3.A.2.1.1 | $H^+$- or $Na^+$-translocating F-type, V-type, & A-type ATPase (F-ATPase) superfamily | | ebA3000 | ATPL | 82 | 79 | 6.00E-08 | 2 | |
| 3.A.2.1.1 | $H^+$- or $Na^+$-translocating F-type, V-type, & A-type ATPase (F-ATPase) superfamily | | ebA3002 | ATPF | 157 | 156 | 5.00E-17 | 1 | |
| 3.A.2.1.1 | $H^+$- or $Na^+$-translocating F-type, V-type, & A-type ATPase (F-ATPase) superfamily | | ebA3003 | ATPD | 178 | 177 | 7.00E-24 | 0 | |
| 3.A.2.1.1 | $H^+$- or $Na^+$-translocating F-type, V-type, & A-type ATPase (F-ATPase) superfamily | | ebA3004 | ATPA | 512 | 513 | 0 | 0 | |
| 3.A.2.1.1 | $H^+$- or $Na^+$-translocating F-type, V-type, & A-type ATPase (F-ATPase) superfamily | | ebA3006 | ATPG | 289 | 287 | 1.00E-88 | 0 | |
| 3.A.2.1.1 | $H^+$- or $Na^+$-translocating F-type, V-type, & A-type ATPase (F-ATPase) superfamily | | ebA3007 | ATPB | 466 | 459 | 0 | 1 | |
| 3.A.2.1.1 | $H^+$- or $Na^+$-translocating F-type, V-type, & A-type ATPase (F-ATPase) superfamily | | ebA3008 | ATPE | 141 | 138 | 7.00E-36 | 0 | |
| 3.A.3.2.4 | P-type ATPase (P-ATPase) superfamily | 2 | ebA224 | Putative Ca2 + -ATPase | 911 | 905 | 0 | 10 | Complete |
| 3.A.3.2.4 | P-type ATPase (P-ATPase) superfamily | | ebA4146 | Putative Ca2 + -ATPase | 897 | 905 | e-143 | 10 | Complete |
| 3.A.3.5.1 | P-type ATPase (P-ATPase) superfamily | 2 | ebA5128 | CopA | 817 | 727 | 1.00E-97 | 9 (TC 8) | Complete |
| 3.A.3.5.1 | P-type ATPase (P-ATPase) superfamily | | ebA5154 | CopA | 803 | 727 | e-141 | 8 | Complete |
| 3.A.3.5.4 | P-type ATPase (P-ATPase) superfamily | 1 | ebA2180 | Ag + -ATPase, SilP | 785 | 824 | 0 | 8 (TC 9) | Complete |
| 3.A.3.6.1 | P-type ATPase (P-ATPase) superfamily | 1 | ebA609 | CadA | 694 | 727 | 1.00E-68 | 9 | Complete |
| 3.A.5.1.1 | General Secretory Pathway (Sec) | 1 | ebA1390 | FtsE | 220 | 222 | 3.00E-61 | 0 (TC 1) | Complete |
| 3.A.5.1.1 | General Secretory Pathway (Sec) | | ebA1393 | FtsY | 386 | 497 | 4.00E-88 | 0 | |
| 3.A.5.1.1 | General Secretory Pathway (Sec) | | ebA1433 | SecA | 907 | 901 | 0 | 0 (TC 1) | |
| 3.A.5.1.1 | General Secretory Pathway (Sec) | | ebA1417 | SecD | 635 | 615 | | 5 (TC 6) | |
| 3.A.5.1.1 | General Secretory Pathway (Sec) | | ebA1418 | SecF | 310 | 323 | | 6 | |
| 3.A.5.1.1 | General Secretory Pathway (Sec) | | ebB40 | YajC | 108 | 110 | 1.00E-14 | 1 | |
| 3.A.5.1.1 | General Secretory Pathway (Sec) | | ebB90 | RNPA | 119 | 119 | 1.00E-06 | | |
| 3.A.5.1.1 | General Secretory Pathway (Sec) | | ebC15 | SecG | 119 | 110 | 5.00E-04 | 3 | |
| 3.A.5.1.1 | General Secretory Pathway (Sec) | | ebA3810 | SecE | 115 | 127 | 3.00E-07 | 3 | |
| 3.A.5.1.1 | General Secretory Pathway (Sec) | | ebA3846 | SecY | 441 | 443 | e-164 | 10 | |

**Table 2** continued

| TC subject protein | Family name | No. of complete sytems | EbN1ID no. | TC homologue (protein name) | EbN1 query length | TC subject length | E-value | No. of TMSs | Estimated transporter status |
|---|---|---|---|---|---|---|---|---|---|
| 3.A.5.1.1 | General Secretory Pathway (Sec) | | ebA4351 | Ffh | 452 | 453 | e-151 | 0 | |
| 3.A.7.4.1 | Type IV (Conjugal DNA-Protein Transfer or VirB) Secretory Pathway (IVSP) | 1 | p2B10 | TrbK | 76 | 75 | 2.00E-09 | 0 | Complete |
| 3.A.7.4.1 | Type IV (Conjugal DNA-Protein Transfer or VirB) Secretory Pathway (IVSP) | | p2B2 | TrbB | 319 | 320 | e-152 | 1 | |
| 3.A.7.4.1 | Type IV (Conjugal DNA-Protein Transfer or VirB) Secretory Pathway (IVSP) | | p2B3 | TrbC | 141 | 154 | 8.00E-35 | 3 | |
| 3.A.7.4.1 | Type IV (Conjugal DNA-Protein Transfer or VirB) Secretory Pathway (IVSP) | | p2B4 | TrbE | 845 | 852 | 0 | 2 | |
| 3.A.7.4.1 | Type IV (Conjugal DNA-Protein Transfer or VirB) Secretory Pathway (IVSP) | | p2B5 | TrbF | 261 | 260 | 4.00E-99 | 1 | |
| 3.A.7.4.1 | Type IV (Conjugal DNA-Protein Transfer or VirB) Secretory Pathway (IVSP) | | p2B6 | TrbG | 298 | 306 | e-136 | 1 | |
| 3.A.7.4.1 | Type IV (Conjugal DNA-Protein Transfer or VirB) Secretory Pathway (IVSP) | | p2B8 | TrbI | 462 | 473 | e-178 | 2 | |
| 3.A.7.4.1 | Type IV (Conjugal DNA-Protein Transfer or VirB) Secretory Pathway (IVSP) | | p2B9 | TrbJ | 252 | 254 | 9.00E-74 | 1 | |
| 3.A.7.4.1 | Type IV (Conjugal DNA-Protein Transfer or VirB) Secretory Pathway (IVSP) | | p2D1 | TrbD | 103 | 103 | 1.00E-50 | 2 | |
| 3.A.7.4.1 | Type IV (Conjugal DNA-Protein Transfer or VirB) Secretory Pathway (IVSP) | | p2B11 | TrbL | 548 | 572 | e-113 | 9 (TC 8) | |
| 3.A.11.1.1 | Bacterial Competence-related DNA Transformation Transporter (DNA-T) | 1 | ebA5822 | ComEC | 782 | 776 | 2.00E-24 | 11 (TC 12) | Complete |
| 3.A.11.1.1 | Bacterial Competence-related DNA Transformation Transporter (DNA-T) | | ebA3678 | ComEA | 155 | 205 | 1.00E-12 | 0 (TC 1) | |
| 3.A.11.1.1 | Bacterial Competence-related DNA Transformation Transporter (DNA-T) | | ebA6555 | ComFA | 1157 | 463 | 1.00E-05 | 0 | |
| 3.A.12.1.1 | Septal DNA Translocator (S-DNA-T) | 1 | ebA7041 | SpoIIIE | 767 | 787 | e-121 | 4 | Complete |
| 3.A.15.1.1 | Outer Membrane Protein Secreting Main Terminal Branch (MTB) | 1 | ebA4900 | PulL | 405 | 398 | 2.00E-08 | 0 | Probably complete |
| 3.A.15.1.1 | Outer Membrane Protein Secreting Main Terminal Branch (MTB) | | ebA4904 | PulK | 307 | 326 | 2.00E-16 | 1 | |
| 3.A.15.1.1 | Outer Membrane Protein Secreting Main Terminal Branch (MTB) | | ebA4906 | PulJ | 184 | 198 | 2.00E-07 | 1 | |
| 3.A.15.1.1 | Outer Membrane Protein Secreting Main Terminal Branch (MTB) | | ebA4908 | PulI | 122 | 121 | 2.00E-12 | 1 | |
| 3.A.15.1.1 | Outer Membrane Protein Secreting Main Terminal Branch (MTB) | | ebA4910 | ? | 176 | 140 | 0.41 | 1 | |
| 3.A.15.1.1 | Outer Membrane Protein Secreting Main Terminal Branch (MTB) | | ebA4913 | PulF | 400 | 381 | 2.00E-49 | 3 | |
| 3.A.15.1.1 | Outer Membrane Protein Secreting Main Terminal Branch (MTB) | | ebB170 | PulG | 147 | 140 | 3.00E-25 | 1 | |
| 3.A.15.1.1 | Outer Membrane Protein Secreting Main Terminal Branch (MTB) | | ebA4914 | PulE | 489 | 497 | e-140 | 0 | |

**Table 2** continued

| TC subject protein | Family name | No. of complete sytems | EbN1ID no. | TC homologue (protein name) | EbN1 query length | TC subject length | E-value | No. of TMSs | Estimated transporter status |
|---|---|---|---|---|---|---|---|---|---|
| 3.A.15.1.1 | Outer Bacterial Membrane Secretin (Secretin) | | ebA4915 | PulD | 719 | 660 | 1.00E-72 | 1 | |
| 3.A.15.2.1 | Outer Membrane Protein Secreting Main Terminal Branch (MTB) | 1 | ebA1770 | PilT | 347 | 344 | e-148 | 0 | Complete |
| 3.A.15.2.1 | Outer Membrane Protein Secreting Main Terminal Branch (MTB) | | ebA1772 | PilU | 377 | 382 | e-130 | 1 | |
| 3.A.15.2.1 | Outer Membrane Protein Secreting Main Terminal Branch (MTB) | | ebA1997 | PilA | 138 | 149 | 9.00E-06 | 2 (TC 1) | |
| 3.A.15.2.1 | Outer Membrane Protein Secreting Main Terminal Branch (MTB) | | ebA4343 | PilD | 283 | 290 | 2.00E-75 | 8 (TC 6) | |
| 3.A.15.2.1 | Outer Membrane Protein Secreting Main Terminal Branch (MTB) | | ebA4345 | PilC | 411 | 374 | 2.00E-95 | 4 | |
| 3.A.15.2.1 | Outer Membrane Protein Secreting Main Terminal Branch (MTB) | | ebA4346 | PilB | 571 | 566 | e-173 | 1 | |
| 3.A.15.2.1 | Outer Membrane Protein Secreting Main Terminal Branch (MTB) | | ebA5112 | FimT | 173 | 168 | 6.00E-04 | 2 (TC 1) | |
| 3.A.15.2.1 | Outer Membrane Protein Secreting Main Terminal Branch (MTB) | | ebD88 | PilE | 137 | 141 | 2.00E-07 | 2 (TC 1) | |
| 3.A.15.2.1 | Outer Membrane Protein Secreting Main Terminal Branch (MTB) | | ebA2259 | PilQ | 721 | 714 | e-130 | 1 | |
| 3.A.15.2.1 | Outer Membrane Protein Secreting Main Terminal Branch (MTB) | | ebA5118 | FimU | 184 | 168 | 7.00E-06 | 1 (TC 1) | |
| 3.A total | | 57 | | | | | | | |
| 3.D.1.2.1 | Proton or Sodium Ion-translocating NADH Dehydrogenase (NDH) | 1 | ebB168 | NQOB | 101 | 101 | 3.00E-36 | 3 | Complete |
| 3.D.1.2.1 | Proton or Sodium Ion-translocating NADH Dehydrogenase (NDH) | | ebD11 | NQO7 | 124 | 121 | 2.00E-34 | 3 | |
| 3.D.1.2.1 | Proton or Sodium Ion-translocating NADH Dehydrogenase (NDH) | | ebA4835 | Nqo6 | 158 | 173 | 6.00E-53 | 1 (TC 0) | |
| 3.D.1.2.1 | Proton or Sodium Ion-translocating NADH Dehydrogenase (NDH) | | ebA4836 | NQO5 | 201 | 206 | 7.00E-37 | 1 | |
| 3.D.1.2.1 | Proton or Sodium Ion-translocating NADH Dehydrogenase (NDH) | | ebA4837 | NQO4 | 417 | 412 | e-148 | 0 | |
| 3.D.1.2.1 | Proton or Sodium Ion-translocating NADH Dehydrogenase (NDH) | | ebA4838 | NQO2 | 159 | 239 | 2.00E-21 | 1 | |
| 3.D.1.2.1 | Proton or Sodium Ion-translocating NADH Dehydrogenase (NDH) | | ebA4840 | NQO1 | 437 | 431 | e-109 | 0 (TC 1) | |
| 3.D.1.2.1 | Proton or Sodium Ion-translocating NADH Dehydrogenase (NDH) | | ebA4841 | NQO3 | 779 | 672 | 5.00E-95 | 1 | |
| 3.D.1.2.1 | Proton or Sodium Ion-translocating NADH Dehydrogenase (NDH) | | ebA4842 | NQO8 | 349 | 345 | 3.00E-91 | 8 | |
| 3.D.1.2.1 | Proton or Sodium Ion-translocating NADH Dehydrogenase (NDH) | | ebA4843 | NQO9 | 161 | 163 | 1.00E-54 | 0 (TC 1) | |

**Table 2** continued

| TC subject protein | Family name | No. of complete sytems | EbN1ID no. | TC homologue (protein name) | EbN1 query length | TC subject length | E-value | No. of TMSs | Estimated transporter status |
|---|---|---|---|---|---|---|---|---|---|
| 3.D.1.2.1 | Proton or Sodium Ion-translocating NADH Dehydrogenase (NDH) | | ebA4844 | NQOA | 200 | 200 | 2.00E-22 | 5 | |
| 3.D.1.2.1 | Proton or Sodium Ion-translocating NADH Dehydrogenase (NDH) | | ebA4846 | NQOC | 673 | 703 | e-133 | 16 | |
| 3.D.1.2.1 | Proton or Sodium Ion-translocating NADH Dehydrogenase (NDH) | | ebA4847 | NQOD | 493 | 513 | e-131 | 14 | |
| 3.D.1.2.1 | Proton or Sodium Ion-translocating NADH Dehydrogenase (NDH) | | ebA4848 | NQOE | 489 | 499 | 1.00E-59 | 14 (TC 15) | |
| 3.D.2.2.1 | Proton-translocating Transhydrogenase (PTH) | 1 | ebA4497 | PNTAA | 374 | 384 | 3.00E-75 | 0 | Complete |
| 3.D.2.2.1 | Proton-translocating Transhydrogenase (PTH) | | ebA4498 | PNTAB | 100 | 139 | 1.00E-10 | 3 | |
| 3.D.2.2.1 | Proton-translocating Transhydrogenase (PTH) | | ebA4500 | PNTB | 457 | 464 | 8.00E-99 | 10 | |
| 3.D.3.1.1 | Proton-translocating Quinol:Cytochrome *c* Reductase (QCR) superfamily | 1 | ebA1197 | CYB | 440 | 444 | 5.00E-96 | 11 (TC 10) | Complete |
| 3.D.3.1.1 | Proton-translocating Quinol:Cytochrome *c* Reductase (QCR) superfamily | | ebA1196 | CY1 | 252 | 309 | 4.00E-14 | 2 | |
| 3.D.3.1.1 | Proton-translocating Quinol:Cytochrome *c* Reductase (QCR) superfamily | | ebA1198 | UCRI | 198 | 190 | 1.00E-23 | 1 | |
| 3.D.4.3.1 | Proton-translocating Cytochrome Oxidase (COX) superfamily | 1 | ebA5131 | Cox1 | 474 | 593 | 5.00E-10 | 12 | Complete |
| 3.D.4.3.1 | Proton-translocating Cytochrome Oxidase (COX) superfamily | | ebA4638 | Cox2 | 336 | 331 | 3E-24 | 8 (TC 9) | |
| 3.D.4.4.2 | Proton-translocating Cytochrome Oxidase (COX) superfamily | C(4) | ebA182 | CtaE | 199 | 205 | 4.00E-13 | 5 | Incomplete |
| 3.D.4.4.1 | Proton-translocating Cytochrome Oxidase (COX) superfamily | C(6) | ebA2294 | COXX | 295 | 305 | 5.00E-09 | 9 | Incomplete |
| 3.D.4.4.1 | ebD10 membrane protein, putative accessory subunit of cytochrome c oxidase | 1 | ebD10 | COXX | 100 | | | | Complete |
| 3.D.4.4.1 | Proton-translocating Cytochrome Oxidase (COX) superfamily | | ebA4544 | COX1 | 607 | 622 | e-112 | 10 (TC 14) | |
| 3.D.4.4.1 | Proton-translocating Cytochrome Oxidase (COX) superfamily | | ebA4547 | COX2 | 310 | 356 | 5.00E-16 | 2 (TC 3) | |
| 3.D.4.4.1 | Proton-translocating Cytochrome Oxidase (COX) superfamily | | ebA4542 | COX3 | | | | | |
| 3.D.4.4.1 | Proton-translocating Cytochrome Oxidase (COX) superfamily | | ebA4540 | COX4 | 120 | 356 | 6.00E-05 | 0 (TC 3) | |
| 3.D.4.4.2 | Proton-translocating Cytochrome Oxidase (COX) superfamily | C(4) | ebA6329 | CtaE | 198 | | 2E-13 | 5 | Incomplete |
| 3.D.4.5.1 | Proton-translocating Cytochrome Oxidase (COX) superfamily | C(5) | ebA4237 | CyoE | 305 | 296 | 2.00E-30 | 9 | Incomplete |

**Table 2** continued

| TC subject protein | Family name | No. of complete sytems | EbN1ID no. | TC homologue (protein name) | EbN1 query length | TC subject length | E-value | No. of TMSs | Estimated transporter status |
|---|---|---|---|---|---|---|---|---|---|
| 3.D.4.6.1 | Proton-translocating Cytochrome Oxidase (COX) superfamily | 1 | ebA3665 | CycA | 177 | 155 | | 2 (TC 3) | Probably complete |
| 3.D.4.6.1 | Proton-translocating Cytochrome Oxidase (COX) superfamily | | ebA3666 | CX1B | 495 | 558 | 1.00E-15 | 12 | |
| 3.D.4.7.1 | Proton-translocating Cytochrome Oxidase (COX) superfamily | 1 | ebA156 | COX1 + COX3 | 836 | 622 | e-136 | 18 (TC 13) | Complete |
| 3.D.4.7.1 | Proton-translocating Cytochrome Oxidase (COX) superfamily | | ebA158 | COX2 | 280 | 356 | 5.00E-16 | 2 (TC 3) | |
| 3.D.4.8.1 | Proton-translocating Cytochrome Oxidase (COX) superfamily | 1 | ebA4231 | Cox3p | | | | | Probably complete |
| 3.D.4.8.1 | Proton-translocating Cytochrome Oxidase (COX) superfamily | | ebA4227 | Cox2p | 301 | 227 | 7.00E-34 | 3 (TC 2) | |
| 3.D.4.8.1 | Proton-translocating Cytochrome Oxidase (COX) superfamily | | ebA4228 | Cox1p | 526 | 514 | e-149 | 12 (TC 13) | |
| 3.D.4.8.1 | Proton-translocating Cytochrome Oxidase (COX) superfamily | | ebA4229 | Cox11p | | | | | |
| 3.D.4.8.1 | Proton-translocating Cytochrome Oxidase (COX) superfamily | | ebA4233 | Shy1p | | | | | |
| 3.D.4.10.1 | Proton-translocating Cytochrome Oxidase (COX) superfamily | 1 | ebB6 | NorC | 198 | 261 | 1.00E-34 | 0 (TC 1) | Complete |
| 3.D.4.10.1 | Proton-translocating Cytochrome Oxidase (COX) superfamily | | ebA179 | NorB | 460 | 593 | 1.00E-154 | 12 | |
| 3.D.6.1.1 | Putative Ion ($H^+$ or $Na^+$)-translocating NADH:Ferredoxin Oxidoreductase (NFO) | 2 | ebA2575 | RnfA | 193 | 193 | 3.00E-59 | 6 | Complete |
| 3.D.6.1.1 | Putative Ion ($H^+$ or $Na^+$)-translocating NADH:Ferredoxin Oxidoreductase (NFO) | | ebA2576 | RnfB | 176 | 187 | 7.00E-29 | 1 | |
| 3.D.6.1.1 | Putative Ion ($H^+$ or $Na^+$)-translocating NADH:Ferredoxin Oxidoreductase (NFO) | | ebA2578 | RnfD | 362 | 358 | 1.00E-48 | 6 (TC 7) | |
| 3.D.6.1.1 | Putative Ion ($H^+$ or $Na^+$)-translocating NADH:Ferredoxin Oxidoreductase (NFO) | | ebA2579 | RnfC | 508 | 519 | e-117 | 0 (TC 2) | |
| 3.D.6.1.1 | Putative Ion ($H^+$ or $Na^+$)-translocating NADH:Ferredoxin Oxidoreductase (NFO) | | ebA2581 | RnfG | 211 | 217 | 2.00E-44 | 1 | |
| 3.D.6.1.1 | Putative Ion ($H^+$ or $Na^+$)-translocating NADH:Ferredoxin Oxidoreductase (NFO) | | ebA2585 | RnfE | 225 | 441 | 1.00E-63 | 5 (TC 6) | |
| 3.D.6.1.1 | Putative Ion ($H^+$ or $Na^+$)-translocating NADH:Ferredoxin Oxidoreductase (NFO) | | ebA2586 | RnfH | 101 | 85 | 3.00E-22 | 0 | |

**Table 2** continued

| TC subject protein | Family name | No. of complete sytems | EbN1ID no. | TC homologue (protein name) | EbN1 query length | TC subject length | E-value | No. of TMSs | Estimated transporter status |
|---|---|---|---|---|---|---|---|---|---|
| 3.D.6.1.1 | Putative Ion ($H^+$ or $Na^+$)-translocating NADH:Ferredoxin Oxidoreductase (NFO) | | ebA4878 | RnfG | 232 | 441 | 2.00E-48 | 5 (TC 6) | Complete |
| 3.D.6.1.1 | Putative Ion ($H^+$ or $Na^+$)-translocating NADH:Ferredoxin Oxidoreductase (NFO) | | ebA4881 | RnfG | 220 | 217 | 3.00E-25 | 1 | |
| 3.D.6.1.1 | Putative Ion ($H^+$ or $Na^+$)-translocating NADH:Ferredoxin Oxidoreductase (NFO) | | ebA4882 | RnfD | 335 | 358 | 2.00E-42 | 10 (TC 7) | |
| 3.D.6.1.1 | Putative Ion ($H^+$ or $Na^+$)-translocating NADH:Ferredoxin Oxidoreductase (NFO) | | ebA4883 | RnfC | 547 | 519 | 7.00E-87 | 2 | |
| 3.D.6.1.1 | Putative Ion ($H^+$ or $Na^+$)-translocating NADH:Ferredoxin Oxidoreductase (NFO) | | ebA4884 | RnfB | 183 | 187 | 2.00E-37 | 2 (TC 1) | |
| 3.D.6.1.1 | Putative Ion ($H^+$ or $Na^+$)-translocating NADH:Ferredoxin Oxidoreductase (NFO) | | ebA4887 | RnfA | 194 | 193 | 1.00E-46 | 6 | |
| 3.D.6.1.1 | Putative Ion ($H^+$ or $Na^+$)-translocating NADH:Ferredoxin Oxidoreductase (NFO) | | ebA6652 | RnfH | 107 | 85 | 7.00E-11 | 0 | |
| 3.D total | | 11 | | | | | | | |
| 4.A.2.1.1 | PTS Fructose-Mannitol (Fru) | 1 | ebA3391 | PTFA (IIA) | 162 | 376 | 3.00E-06 | 0 | Complete |
| 4.A.2.1.1 | PTS Fructose-Mannitol (Fru) | | ebA1726 | PTFB (IIB) | 274 | 563 | 4.00E-04 | 8 | |
| 4.A.6.1.1 | PTS Mannose-Fructose-Sorbose (Man) | | ebA2794 | MANX (IIA) | 128 | 322 | 6.00E-10 | 0 | Incomplete |
| | 4.A total : | 1 | | | | | | | |
| 5.A.2.1.1 | Disulfide Bond Oxidoreductase-B (DsbB) | 1 | ebA3876 | DsbB | 166 | 176 | 1.00E-11 | 5 (TC4) | Complete |
| 5.A.3.1.1 | Prokaryotic Molybdopterin-containing Oxidoreductase (PMO) | 1 | ebA6282 | NarI | 232 | 225 | 4.00E-53 | 5 | Complete |
| 5.A.3.1.1 | Prokaryotic Molybdopterin-containing Oxidoreductase (PMO) | | ebA6286 | NarG | 1251 | 1246 | 0 | 0 | |
| 5.A.3.1.1 | Prokaryotic Molybdopterin-containing Oxidoreductase (PMO) | | ebA6285 | NarH | 516 | 514 | 0 | 0 | |
| 5.A.3.2.1 | Disulfide Bond Oxidoreductase D (DsbD) | 1 | ebA2749 | FdnG | 951 | 1015 | 1.00E-35 | 2 | Probably complete |
| 5.A.3.2.1 | Disulfide Bond Oxidoreductase D (DsbD) | | ebA2750 | FdnH + FdnI | 585 | 294 | | 4 | |
| 5.A.3.2.1 | Prokaryotic Molybdopterin-containing Oxidoreductase (PMO) | 1 | ebA2935 | FdnH | 201 | 192 | 1.00E-26 | 0 | Complete |
| 5.A.3.2.1 | Prokaryotic Molybdopterin-containing Oxidoreductase (PMO) | | ebA2933 | FdnI | 375 | 217 | 2.00E-17 | 6 (TC 4) | |
| 5.A.3.2.1 | Prokaryotic Molybdopterin-containing Oxidoreductase (PMO) | | ebA2936 | FdnG | 969 | 1015 | 2.00E-60 | 2 | |

**Table 2** continued

| TC subject protein | Family name | No. of complete sytems | EbN1ID no. | TC homologue (protein name) | EbN1 query length | TC subject length | E-value | No. of TMSs | Estimated transporter status |
|---|---|---|---|---|---|---|---|---|---|
| 5.A.3.3.2 | Prokaryotic Molybdopterin-containing Oxidoreductase (PMO) | 1 | ebA3328 | Anaerobic dimethyl sulfoxide reductase chain A precursor a.k.a. DMSO reductase (DmsA) | 694 | 814 | 6.00E-62 | 1 | Complete |
| 5.A.3.3.2 | Prokaryotic Molybdopterin-containing Oxidoreductase (PMO) | | ebA5004 | Sulfoxide reductase chain B a.k.a. DMSO reductase iron-sulfur subunit (DmsB) | 158 | 204 | 4.00E-17 | 0 | |
| 5.A.3.3.2 | Prokaryotic Molybdopterin-containing Oxidoreductase (PMO) | | ebA5396 | Anaerobic dimethyl sulfoxide reductase chain C a.k.a. DMSO reductase anchor subunit (DmsC) | 303 | 287 | 0.001 | 8 | |
| 5.A.3.4.1 | Prokaryotic Molybdopterin-containing Oxidoreductase (PMO) | 1 | ebA1211 | Trimethylamine oxidase 1 | 939 | 848 | 4.00E-16 | 1 (TC 0) | Complete |
| 5.A.3.4.1 | Prokaryotic Molybdopterin-containing Oxidoreductase (PMO) | | ebA1009 | Cytochrome *c*-type protein torC | 203 | 390 | 2.00E-09 | 2 (TC 1) | |
| 5.A.3.4.1 | Prokaryotic Molybdopterin-containing Oxidoreductase (PMO) | | ebA5795 | Chaperone protein torD | 219 | 199 | 5.00E-04 | 0 | |
| 5.A.3.5.2 | Prokaryotic Molybdopterin-containing Oxidoreductase (PMO) | 1 | ebA1012 | Reductase chain B a.k.a. sulfur reductase chain B | 256 | 191 | 4.00E-38 | 1 (TC 0) | Complete |
| 5.A.3.5.2 | Prokaryotic Molybdopterin-containing Oxidoreductase (PMO) | | ebA1013 | Reductase chain C a.k.a. sulfur reductase chain C | 312 | 317 | 5.00E-16 | 8 | |
| 5.A.3.5.2 | Prokaryotic Molybdopterin-containing Oxidoreductase (PMO) | | ebA1017 | Reductase chain A precursor | 841 | 763 | 1.00E-45 | 0 | |
| 5.A.3.5.2 | Prokaryotic Molybdopterin-containing Oxidoreductase (PMO) | 1 | ebA6426 | Reductase chain A precursor a.k.a. sulfur reductase chain A | 877 | 763 | 3.00E-63 | 0 | Complete |
| 5.A.3.5.2 | Prokaryotic Molybdopterin-containing Oxidoreductase (PMO) | | ebA6432 | Reductase chain C a.k.a. sulfur reductase chain C | 283 | 317 | 8.00E-08 | 8 | |
| 5.A.3.5.2 | Prokaryotic Molybdopterin-containing Oxidoreductase (PMO) | | ebA6435 | Reductase chain B a.k.a. sulfur reductase chain B | 236 | 257 | 2.00E-50 | 0 | |
| 5.A.3.9.1 | Prokaryotic Molybdopterin-containing Oxidoreductase (PMO) | 2 | c1A62 | Anaerobic ethylbenzene dehydrogenase subunit C | 214 | 214 | e-122 | 0 | Complete |

**Table 2** continued

| TC subject protein | Family name | No. of complete sytems | EbN1ID no. | TC homologue (protein name) | EbN1 query length | TC subject length | E-value | No. of TMSs | Estimated transporter status |
|---|---|---|---|---|---|---|---|---|---|
| 5.A.3.9.1 | Prokaryotic Molybdopterin-containing Oxidoreductase (PMO) | | c1A63 | Anaerobic ethylbenzene dehydrogenase subunit B | 352 | 352 | 0 | 0 | |
| 5.A.3.9.1 | Prokaryotic Molybdopterin-containing Oxidoreductase (PMO) | | c1A65 | Ethylbenzene dehydrogenase subunit A | 976 | 974 | 0 | 1 | |
| 5.A.3.9.1 | Prokaryotic Molybdopterin-containing Oxidoreductase (PMO) | | ebA5790 | Ethylbenzene dehydrogenase subunit A | 978 | 974 | 0 | 1 | Complete |
| 5.A.3.9.1 | Prokaryotic Molybdopterin-containing Oxidoreductase (PMO) | | ebA5791 | Anaerobic ethylbenzene dehydrogenase subunit B | 352 | 352 | 0 | 0 | |
| 5.A.3.9.1 | Prokaryotic Molybdopterin-containing Oxidoreductase (PMO) | | ebA5793 | Anaerobic ethylbenzene dehydrogenase subunit C | 214 | 214 | 8.00E-71 | 0 | |
| 5.A.3.10.1 | Prokaryotic Molybdopterin-containing Oxidoreductase (PMO) | 2 | ebA5622 | Tetrathionate reductase subunit A | 868 | 1053 | 2.00E-28 | 3 (TC 0) | Complete |
| 5.A.3.10.1 | Prokaryotic Molybdopterin-containing Oxidoreductase (PMO) | | ebA5630 | Tetrathionate reductase subunit B | 200 | 257 | 7.00E-42 | 0 | |
| 5.A.3.10.1 | Prokaryotic Molybdopterin-containing Oxidoreductase (PMO) | | ebA5631 | Tetrathionate reductase subunit C | 308 | 344 | 6.00E-07 | 8 (TC 9) | |
| 5.A.3.10.1 | Prokaryotic Molybdopterin-containing Oxidoreductase (PMO) | | ebA3055 | Tetrathionate reductase subunit B | 247 | 257 | 8.00E-69 | 1 (TC 0) | |
| 5.A.3.10.1 | Prokaryotic Molybdopterin-containing Oxidoreductase (PMO) | | ebA3056 | Tetrathionate reductase subunit C | 362 | 344 | 7.00E-45 | 9 | Complete |
| 5.A.3.10.1 | Prokaryotic Molybdopterin-containing Oxidoreductase (PMO) | | ebD4 | Tetrathionate reductase subunit A | 1027 | 1053 | 0 | 1 (TC 0) | |
| 5.A total | | 12 | | | | | | | |
| 5.B.1.6.1 | gp91phox Phagocyte NADPH Oxidase-associated Cytochrome b558 (CytB) $H^+$-channel | 4 | ebA3186 | Putative oxido-reductase | 439 | 450 | 5.00E-58 | 7 | Complete |
| 5.B.1.6.1 | gp91phox Phagocyte NADPH Oxidase-associated Cytochrome b558 (CytB) $H^+$-channel | | ebA4977 | Putative oxido-reductase | 442 | 450 | 3.00E-80 | 7 | Complete |
| 5.B.1.6.1 | gp91phox Phagocyte NADPH Oxidase-associated Cytochrome b558 (CytB) $H^+$-channel | | ebA7152 | Putative oxido-reductase | 439 | 450 | 9.00E-63 | 6 (TC 7) | Complete |

**Table 2** continued

| TC subject protein | Family name | No. of complete sytems | EbN1ID no. | TC homologue (protein name) | EbN1 query length | TC subject length | E-value | No. of TMSs | Estimated transporter status |
|---|---|---|---|---|---|---|---|---|---|
| 5.B.1.6.1 | gp91phox Phagocyte NADPH Oxidase-associated Cytochrome b558 (CytB) $H^+$-channel | | ebA2594 | Putative oxido-reductase | 159 | 450 | 5.00E-12 | 3 (TC 7) | Complete |
| 5.B total | | 4 | | | | | | | |
| 8.A.1.1.1 | Membrane Fusion Protein (MFP) | 1 | ebA3446 | EmrA | 433 | 390 | 1.00E-78 | 2 (TC 1) | Complete |
| 8.A.1.2.1 | Membrane Fusion Protein (MFP) | 1 | ebA6248 | CzcB | 383 | 395 | 7.00E-10 | 1 | Complete |
| 8.A.1.3.1 | Membrane Fusion Protein (MFP) | 3 | ebA1673 | HlyD | 457 | 478 | 1.00E-13 | 1 | Complete |
| 8.A.1.3.1 | Membrane Fusion Protein (MFP) | | ebA1805 | HlyD | 473 | 478 | 6.00E-34 | 1 | Complete |
| 8.A.1.3.1 | Membrane Fusion Protein (MFP) | | ebA7180 | HlyD | 434 | 478 | 4.00E-12 | 1 | Complete |
| 8.A.1.6.1 | Membrane Fusion Protein (MFP) | 3 | ebA3872 | AcrA | 349 | 397 | 1.00E-10 | 1 | Complete |
| 8.A.1.6.1 | Membrane Fusion Protein (MFP) | | ebA4062 | AcrA | 390 | 397 | 1.00E-04 | 1 | Complete |
| 8.A.1.6.1 | Membrane Fusion Protein (MFP) | | ebA7103 | AcrA | 386 | 397 | 9.00E-22 | 1 | Complete |
| 8.A.3.1.1 | Cytoplasmic Membrane-Periplasmic Auxiliary-1 (MPA1) Protein with Cytoplasmic (C) Domain (MPA1-C or MPA1 + C) | 1 | ebA6797 | ExoP | 760 | 786 | 5.00E-45 | 2 (TC 3) | Complete |
| 8.A.5.1.3 | $K^+$ Transport/Nucleotide-binding Regulatory Domain/Protein (KTN) | 1 | p2A379 | $\beta$1a | 336 | 401 | 2.00E-19 | 0 | Complete |
| 8.A.7.1.1 | Phosphotransferase System Enzyme I (EI) | 1 | ebA2795 | Enzyme I | 576 | 575 | 5.00E-91 | 2 (TC 0) | Complete |
| 8.A.7.1.1 | Phosphotransferase System Enzyme I (EI) | | ebA5781 | PEP synthetase | 592 | 575 | 6.00E-06 | 0 | Probably complete |
| 8.A.7.1.1 | Phosphotransferase System Enzyme I (EI) | 1 | ebA5830 | Phenyl-phosphate synthetase | 788 | 575 | 1.00E-21 | 0 | Complete |
| 8.A.8.1.1 | Phosphotransferase System HPr (HPr) | 1 | ebD68 | HPr | 89 | 85 | 1.00E-05 | 0 | Complete |
| 8.A.9.1.1 | rBAT Transport Accessory Protein (rBAT) | 3 | ebA583 | rBAT | 562 | 677 | 8.00E-65 | 1 | Complete |
| 8.A.9.1.1 | rBAT Transport Accessory Protein (rBAT) | | ebA6923 | rBAT | 767 | 677 | 1.00E-04 | 0 (TC 1) | Complete |
| 8.A.9.1.1 | rBAT Transport Accessory Protein (rBAT) | | ebA7001 | rBAT | 1114 | 677 | 9.00E-57 | 1 | Complete |
| 8.A total | | 16 | | | | | | | |
| 9.A.8.1.1 | Ferrous Iron Uptake (FeoB) | 2 | ebA503 | FeoB (GTPase) | 467 | 773 | 8.00E-04 | 1 (TC 11) | Probably complete |
| 9.A.8.1.1 | Ferrous Iron Uptake (FeoB) | | ebA5540 | FeoB (GTPase) | 305 | 773 | 9.00E-08 | 0 (TC 11) | Probably complete |
| 9.A.8.1.3 | Ferrous Iron Uptake (FeoB) | 2 | ebA1256 | FeoB | 442 | 614 | 8.00E-09 | 1 (TC 12) | Probably complete |
| 9.A.8.1.3 | Ferrous Iron Uptake (FeoB) | | ebA4139 | FeoB | 363 | 614 | 1.00E-06 | 1 (TC 12) | Probably complete |
| 9.A.19.1.1 | $Mg2^+$ Transporter-E (MgtE) | 1 | ebA1741 | MgtE | 522 | 312 | 3.00E-36 | 5 | Complete |
| 9.A.40.1.2 | HlyC/CorC (HCC) of Putative Transporters | 1 | ebA1335 | CorC | 282 | 292 | 3.00E-59 | 0 (TC 1) | Complete |
| 9.A.40.2.1 | HlyC/CorC (HCC) of Putative Transporters | 2 | ebA4147 | YrkA | 444 | 434 | 2.00E-27 | 3 (TC 4) | Complete |

**Table 2** continued

| TC subject protein | Family name | No. of complete sytems | EbN1ID no. | TC homologue (protein name) | EbN1 query length | TC subject length | E-value | No. of TMSs | Estimated transporter status |
|---|---|---|---|---|---|---|---|---|---|
| 9.A.40.2.1 | HlyC/CorC (HCC) of Putative Transporters | | ebA6189 | YrkA | 432 | 434 | 1.00E-33 | 4 | Complete |
| 9.A total | | 8 | | | | | | | |
| 9.B.3.1.1 | Putative Bacterial Murein Precursor Exporter (MPE) | 1 | ebA1445 | FtsW | 410 | 414 | 2.00E-67 | 10 | Complete |
| 9.B.3.1.2 | Putative Bacterial Murein Precursor Exporter (MPE) | 1 | ebA3041 | RodA | 380 | 370 | 3.00E-73 | 10 (TC 9) | Complete |
| 9.B.11.1.1 | Putative ER-chloroplast Lipid Translocase (ECLT) | 1 | ebA1312 | Tgd1 protein | 264 | 350 | 3.00E-23 | 6 (TC 5) | Complete |
| 9.B.14.1.1 | Putative Heme Exporter Protein (HEP) | 2 | ebA2222 | CcmF (Ccl1) | 713 | 653 | 1.00E-05 | 15 | Complete |
| 9.B.14.1.1 | Putative Heme Exporter Protein (HEP) | | ebA3521 | CcmF (Ccl1) | 657 | 653 | e-168 | 15 | Complete |
| 9.B.17.1.4 | Putative Fatty Acid Transporter (FAT) | 15 | ebA1206 | FadD | 563 | 561 | 2.00E-30 | 1 (TC 2) | Complete |
| 9.B.17.1.4 | Putative Fatty Acid Transporter (FAT) | | ebA1960 | FadD | 549 | 561 | 3.00E-39 | 1 (TC 2) | Complete |
| 9.B.17.1.4 | Putative Fatty Acid Transporter (FAT) | | ebA2757 | FadD | 534 | 561 | 7.00E-41 | 2 | Complete |
| 9.B.17.1.4 | Putative Fatty Acid Transporter (FAT) | | ebA321 | FadD | 664 | 561 | 2.00E-05 | 2 | Complete |
| 9.B.17.1.4 | Putative Fatty Acid Transporter (FAT) | | ebA4297 | FadD | 546 | 561 | 3.00E-43 | 1 (TC 2) | Complete |
| 9.B.17.1.4 | Putative Fatty Acid Transporter (FAT) | | ebA4326 | FadD | 522 | 561 | 2.00E-20 | 1 (TC 2) | Complete |
| 9.B.17.1.4 | Putative Fatty Acid Transporter (FAT) | | ebA4661 | FadD | 562 | 561 | 2.00E-67 | 0 (TC 2) | Complete |
| 9.B.17.1.4 | Putative Fatty Acid Transporter (FAT) | | ebA4749 | FadD | 555 | 561 | 0 | 3 (TC 2) | Complete |
| 9.B.17.1.4 | Putative Fatty Acid Transporter (FAT) | | ebA5317 | FadD | 624 | 561 | 2.00E-12 | 0 (TC 2) | Complete |
| 9.B.17.1.4 | Putative Fatty Acid Transporter (FAT) | | ebA5705 | FadD | 831 | 561 | 4.00E-27 | 4 (TC 2) | Complete |
| 9.B.17.1.4 | Putative Fatty Acid Transporter (FAT) | | ebA6518 | FadD | 550 | 561 | 4.00E-37 | 0 (TC 2) | Complete |
| 9.B.17.1.4 | Putative Fatty Acid Transporter (FAT) | | ebA727 | FadD | 523 | 561 | 1.00E-46 | 2 | Complete |
| 9.B.17.1.4 | Putative Fatty Acid Transporter (FAT) | | ebA5301 | FadD | 533 | 561 | 3.00E-48 | 1 (TC 2) | Complete |
| 9.B.17.1.4 | Putative Fatty Acid Transporter (FAT) | | ebA5368 | FadD | 493 | 561 | 2.00E-24 | 2 | Complete |
| 9.B.17.1.4 | Putative Fatty Acid Transporter (FAT) | | ebA172 | FadD | 662 | 561 | 4.00E-26 | 2 | Complete |
| 9.B.17.1.6 | Putative Fatty Acid Transporter (FAT) | 6 | ebA2050 | CaiC | 510 | 522 | 1.00E-46 | 1 (TC 0) | Complete |
| 9.B.17.1.6 | Putative Fatty Acid Transporter (FAT) | | ebA3433 | CaiC | 546 | 522 | 4.00E-38 | 0 | Complete |
| 9.B.17.1.6 | Putative Fatty Acid Transporter (FAT) | | ebA7220 | CaiC | 630 | 522 | 6.00E-12 | 3 (TC 0) | Complete |
| 9.B.17.1.6 | Putative Fatty Acid Transporter (FAT) | | p2A386 | CaiC | 558 | 522 | 8.00E-64 | 3 | Complete |
| 9.B.17.1.6 | Putative Fatty Acid Transporter (FAT) | | ebA4666 | CaiC | 662 | 522 | 5.00E-08 | 1 (TC 0) | Complete |
| 9.B.17.1.6 | Putative Fatty Acid Transporter (FAT) | | ebA4717 | CaiC | 663 | 522 | 1.00E-25 | 0 | Complete |
| 9.B.20.2.1 | Putative $Mg2^{+}$ Transporter-C (MgtC) | 1 | ebB238 | SrpB | 159 | 182 | 9.00E-27 | 5 | Complete |
| 9.B.24.2.1 | Testis-Enhanced Gene Transfer (TEGT) | 2 | ebA4143 | YccA | 221 | 219 | 4.00E-58 | 7 | Complete |
| 9.B.24.2.1 | Testis-Enhanced Gene Transfer (TEGT) | | p1B299 | YccA | 220 | 219 | 2.00E-55 | 7 | Complete |
| 9.B.26.1.1 | PF27 (PF27) | 1 | ebA1709 | Y615 | 192 | 206 | 9.00E-07 | 5 (TC 6) | Complete |
| 9.B.27.1.1 | YdjX-Z (YdjX-Z) | 1 | ebA6946 | YdjX | 743 | 236 | 3.00E-07 | 7 (TC 6) | Complete |
| 9.B.31.1.1 | YqiH (YqiH) | 1 | ebA4373 | YgiH | 197 | 205 | 1.00E-28 | 5 | Complete |
| 9.B.32.1.2 | Putative Vectorial Glycosyl Polymerization (VGP) | 1 | ebA6116 | IcaA | 905 | 412 | 2.00E-07 | 9 (TC 4) | Complete |

**Table 2** continued

| TC subject protein | Family name | No. of complete sytems | EbN1ID no. | TC homologue (protein name) | EbN1 query length | TC subject length | E-value | No. of TMSs | Estimated transporter status |
|---|---|---|---|---|---|---|---|---|---|
| 9.B.32.1.3 | Putative Vectorial Glycosyl Polymerization (VGP) | 3 | ebA1112 | YcdQ | 234 | 441 | 5.00E-04 | 0 | Probably complete |
| 9.B.32.1.3 | Putative Vectorial Glycosyl Polymerization (VGP) | | ebA600 | YcdQ | 247 | 441 | 8.00E-09 | 5 | Complete |
| 9.B.32.1.3 | Putative Vectorial Glycosyl Polymerization (VGP) | | ebA7076 | YcdQ | 287 | 441 | 1.00E-07 | 2 (TC 5) | Complete |
| 9.B.42.1.1 | ExeAB Secretin Assembly/Export Complex | | ebA4256 | ExeA | 360 | 547 | 2.00E-50 | 1 (TC 2) | Incomplete |
| 9.B.60.2.1 | YfcA | 1 | ebA3571 | DsbD | 628 | 601 | 2.00E-86 | 10 (TC 9) | Complete |
| 9.B.67.1.1 | Putative Inorganic Carbon ($HCO_3^-$) Transporter/O-antigen Polymerase (ICT/OAP) | 1 | ebA4277 | IctB | 444 | 467 | 6.00E-04 | 10 | Complete |
| 9.B total | | 38 | | | | | | | |

closely related to the Neisserial Omp85 homologue (Wu et al. 2005). It also has a single YfiO homologue, a single NlpB homologue, and a single YfgL homologue. OmpIP complexes function to insert $\beta$-structured proteins into the outer membrane.

Finally, strain EbN1 has one homologue of the OstA protein, proposed to function in lipopolysaccharide export across the outer membrane (TC 1.B.42) (Bos et al. 2004; Hu and Saier 2006). It also has an RlpB homologue that in *E. coli* functions in conjunction with OstA (Wu et al. 2006).

## Secondary Carriers

The largest superfamily of secondary carriers found in nature is the major facilitator superfamily (MFS) (Chang et al. 2004). Strain EbN1 has 22 (8.5% of the total transporters) recognized members of this superfamily, but surprisingly it contains no MFS sugar transporters. In fact, this organism has no primary or secondary transporters that take up sugars. A single fructose-type PTS permease (see below) is the only system that serves as a good candidate for sugar uptake. The deficiency in sugar uptake systems agrees well with the apparent inability of strain EbN1 to utilize sugars as growth substrates (Rabus and Widdel 1995).

Recognized MFS permeases in strain EbN1 include five putative drug (MDR):proton antiporters (four in family 2.A.1.2 and one in family 2.A.1.3). It also has two probable nitrate/nitrite antiporters and one nitrate:$H^+$ symporter, all of family 2.A.1.8. There is a distant member of the oxalate/formate antiporter family (2.A.1.11) and seven systems for the potential uptake of aromatic compounds. These include four potential systems of TC family 2.A.1.15 (aromatic acid:$H^+$ symporter), one of the phenyl propionate permease (PPP) family (2.A.1.27), one of the putative abietane deterpenoid transporter (ADT) family (TC 2.A.1.30), and one of the acriflavine sensitivity (YnfM) family (2.A.1.36.1; unpublished preliminary observations). Another MFS aromatic uptake permease may transport compounds resembling folate/biopterin (a member of TC family 2.A.71). Strain EbN1 may have a single cyanate uptake permease. It also has a single putative peptide uptake system of the PAT family (TC 2.A.1.25) and two homologues of the lysophospholipid uptake (LplT) family. LplT family proteins are required for periplasmic lipoprotein acylation as has been demonstrated in *E. coli* (Harvat et al. 2005). We also identified two MFS permeases of unknown function (see Table 2).

Strain EbN1 has two members of the CDF family of divalent cation diffusion facilitators. These systems are usually responsible for the active export of heavy metals such as $Co^{2+}$, $Cd^{2+}$, $Zn^{2+}$, $Ni^{2+}$, $Hg^{2+}$, and $Fe^{2+}$. Both of

the CDF systems in strain EbN1 are likely to be of broad specificity. Strain EbN1 also has a single heavy metal efflux pump of the RND superfamily (Table 2). This unusual system probably functions with auxiliary proteins to directly export heavy metals from the cytoplasm to the external milieu. Similarly to the CusABCF system of *E. coli* (TC 2.A.6.1.4), it requires a periplasmic binding receptor. There are no other secondary carrier candidates for heavy metal efflux; only a single $Fe^{3+}$ primary active uptake system of the ABC superfamily was identified. It appears that strain EbN1 takes of metals primarily via a CorA channel and expels them via CDF- and RND-type systems.

Within the RND superfamily (TC 2.A.6), we found 13 putative MDR efflux pumps of two different families (HAE1 [2.A.6.2] and HAE3 [2.A.6.7]), a single SecDF pair of auxiliary proteins TC 2.A.6.4.1 of the general secretory (Sec; TC 3.A.5.1.1) pathway, and a single member of the brominated aryl polyene pigment exporter family (2.A.6.8).

The drug/metabolite transporter (DMT) superfamily (Jack et al. 2001) is represented by one member of the four-TMS small multidrug resistance (SMR) family of cationic drug exporters and five members of the 10-TMS metabolite exporters of the DME family. Most of these proteins exhibit low BLAST scores ($e^{-6}$–$e^{-10}$), but our analyses clearly suggest that they are true members of the DME family within the DMT superfamily. Their substrate specificities cannot be reliably ascertained.

Another important superfamily for the export of macromolecules and drugs is the multidrug/oligosaccharidyl-lipid/polysaccharide (MOP) superfamily (TC 2.A.66) (Hvorup et al. 2003). Three of the twelve families within the MOP superfamily are represented in strain EbN1. One of these is likely to be specific for drugs; one undoubtedly exports polysaccharides; and one (within the mouse virulence factor [MVF] family) is of unknown specificity, as no member of this family has been functionally characterized.

Bacterial Oxa1 family members (YidC homologues; family 2.A.9) can function together with the general secretory (Sec) pathway to insert proteins into the cytoplasmic membrane. These proteins may also be able to insert some integral membrane proteins without the aid of the Sec system (Chen et al. 2002, 2003; Luirink et al. 2001; Yen et al. 2001). These YidC homologues form a complex with the SecDF proteins of the RND superfamily (Nouwen and Driessen 2002).

Strain EbN1 has 17 secondary carriers that are probably specific for various organic and inorganic anions in addition to those in the MFS. These fall into nine TC families: (1) one is in the tellurite/dicarboxylate transporter (TDT) family (TC 2.A.16); (2) one is in the phosphate transporter (PiT) family (TC 2.A.20); (3) two putative acetate/glyoxylate uptake systems and a phenyl acetate uptake permease are in the SSS family (TC 2.A.21); (4) one putative sulfate transporter of the CHR family (TC 2.A.51) consists of two half-sized proteins as occurs in *B. subtilis* (Nies et al. 1998); (5) two possible sulfate transporters belong to the SulP family (2.A.53); (6) five complete systems are in the tripartite TRAP-T family, each with three components as expected (TC 2.A.56) (Kelly and Thomas 2001; Mulligan et al. 2007; Rabus et al. 1999), all of which may take up organic anions (see TCDB); (7) one member belongs to the arsenical resistance (Acr3) family (TC 2.A.59) of the BART superfamily (Mansour et al. 2007); (8) two possible malate/malonate transporters are in the AEC family (TC 2.A.69); and (9) a single member of the putative $HCO_3^-$ transporter is in the ICT family (TC 9.B.69). There is some confusion in the literature concerning the ICT family. Members of this family may actually be o-antigen polymerases involved in lipopolysaccharide synthesis (see description in TC 9.B.69).

Strain EbN1 also has four recognizable primary active uptake transporters of the ABC superfamily specific for inorganic anions. These are probably specific for (1) sulfate (taken up by a member of the SulT family; TC 3.A.1.6) [the thiosulfate receptor that in *E. coli* can function with this transporter was not found]; (2) tungstate, taken up by a homologue of the TupABC system of *Eubacterium acidaminophilum*, also of the SulT family; (3) phosphate, taken up by a homologue of the *E. coli* high-affinity Pst porter of the PhoT family (3.A.1.7); and (4) molybdate, taken up by a homologue of the MolT family system of *E. coli*.

Amino acids, organic cations, and peptides are transported in strain EbN1 by at least six secondary porters and eight ABC-type active transporters, and these fall into six (super)families as follows: (1) peptides can probably be taken up via a member of the PAT family (TC 2.A.1.25) within the MFS as mentioned previously; (2) short semipolar amino acids such as alanine and glycine can be taken up via a member of the AGCS family (TC 2.A.25); (3) choline may be taken up via a member of the SSS family (TC 2.A.21.8), and interestingly, a member of the same family may be a sensor for amino acids, part of a sensor kinase (Nishijyo et al. 2001); (4) a single member of the TRAP-T family of tripartite systems may take up ectoine (a zwitterionic compound) and its derivatives (Grammann et al. 2002); and (5) finally, six ATP-hydrolysis-driven transport systems of the ABC superfamily are likely to take up amino acids. Interestingly, five of these are in the HAAT family (TC 3.A.1.4), and four of them probably transport hydrophobic (and sometimes semipolar) amino acids, while the fifth shows greatest similarity to a urea uptake porter of cyanobacteria (TC 3.A.1.4.4). There is only one member of the PAAT family (TC 3.A.1.3) which

undoubtedly takes up polar amino acids as is characteristic of the members of this family. This porter may take up acidic amino acids based on its best fit in TCDB (see Table 2). There are also two possible peptide uptake permeases of the PepT family (TC 3.A.1.5) in the ABC superfamily; one of these may have specificity for glutathione (Suzuki et al. 2005), which is important as a cytoplasmic reducing agent.

Monovalent inorganic cation transporters are numerous in strain EbN1, and these fall into five (super)families. (1) Two monovalent cation:proton antiporters are present. One belongs to the CPA1 family; it could be a $Na^+/H^+$ antiporter. The other belongs to the CPA2 family. Both of these families are within the CPA superfamily. The CPA2 family member could be a glutathione-regulated $K^+$ efflux porter. (2) Three members of the Trk family of heterodimeric $K^+$ uptake systems are present. (3) We found two members of the Amt family of probable $NH_3$ or $NH_4^+$ channel proteins (Fong et al. 2007; Ishikita and Knapp 2007; Javelle et al. 2005; Khademi et al. 2004). (4) One complete member of the multicomponent CPA3 family is present, with two of the seven constituents (the PhaA and PhaB equivalents) fused in a single large polypeptide chain. These complex permeases may be energized by NAD oxidoreduction. (5) Finally, there are two members of the KUP family of $K^+$ uptake permeases. Primary active monovalent cation transporters are described below.

## Outer Membrane Transport Energizers

The TonB heteromeric complexes span the cytoplasmic membrane and the periplasm and interact with outer membrane receptors in Gram-negative bacteria. Homologues have been found only in Gram-negative bacteria. *E. coli* has two types of homologous outer membrane transport energizers, the TonB-ExbB-ExbD system and the TolA-TolQ-TolR system, both using the proton motive force and both in the TonB family (TC 2.C.1). These energizers act together with OMR-type outer membrane receptors. They have overlapping but distinct functions.

The TonB system of *E. coli* energize transport (uptake) via OMR-type porins (TC 1.B.14) specific for vitamin $B^{12}$, iron siderophores, group B colicins, and the DNA of filamentous bacteriophage such as $\phi$80 and T1. They may also be involved in the extrusion of drugs and organic solvents. The TolA system transports group A colicins and the DNA of other filamentous phages. Colicin import requires close proximity of the inner and outer membranes. Loss of one of the TolA-TolQ-TolR proteins results in loss of periplasmic enzymes and increased sensitivity to drugs and bile salts. Surface localization of O-antigen lipopolysaccharide in *E. coli* depends on the TolA protein, possibly explaining the leakiness of TolA mutants. The *E. coli* TolA/Pal system has also been reported to be necessary for the uptake of certain solutes (sugars, polyols, amino acids) (Bouveret et al. 2002; Cao and Klebba 2002; Llamas et al. 2003; Lloubes et al. 2001).

Different bacteria have different numbers and sets of these proteins. Strain EbN1 has two TonB-ExbBD systems, one TolAB-TolRQ-YbgF system, and eight OMR-type outer membrane receptors. Although we were able to identify all other constituents of this last system, a TolA-like protein, similar throughout its length to the *E. coli* TolA, could not be found. However, EbA2648 has a distant homologue of TonB, and this protein may serve the function of TolA. TonB and TolA of *E. coli* are distant homologues of each other.

## Primary Active Transporters

### *The ABC Superfamily*

Table 2 reports the ABC systems of strain EbN1 that resemble those in TCDB. In addition to the six amino acid uptake systems, the four inorganic anion uptake systems, and the two taurine uptake systems noted above, strain EbN1 has a single $Fe^{3+}$ uptake transporter of the FeT family (TC 3.A.1.10), a $Mn^{2+}/Zn^{2+}/Fe^{2+}$ chelate uptake transporter of the MZT family (3.A.1.15.2), and a vitamin $B_{12}$ uptake system (3.A.1.13). Surprisingly, strain EbN1 has no additional recognizable complete ABC uptake systems. It does, however, have many ABC-type multidrug efflux systems belonging to five different ABC families known to be involved in their extrusion. Most of these (11 systems including MsbA which can transport both lipids and drugs) (Reuter et al. 2003) may export hydrophobic and amphipathic substances including toxic metabolites, thereby protecting the organism. We also found a single putative heme exporter (TC 3.A.1.10.7), two probable heavy metal exporters similar to those in eukaryotes (TC 3.A.1.210), and two sequence dissimilar putative peptide exporters (TC 3.A.1.123 and 3.A.1.212), one resembling prokaryotic systems and one more similar to eukaryotic mitochondrial systems.

Ten macromolecular ABC-type efflux systems, three complete systems specific for lipooligosaccharides (3.A.1.102), one for lipopolysaccharides or their precursors (3.A.1.103), one specific for lipids (MsbA-type; 3.A.1.106), one specific for lipoproteins (LPT family; 3.A.1.125, as well as one incomplete system of this type), and three specific for proteins (TCs 3.A.1.109 and 3.A.1.110). All such systems use ATP hydrolysis to drive macromolecular export, and they are often coupled to membrane fusion proteins (MFP; 8.A.1) and outer membrane channel forming factors (OMF; 1.B.17) to pump solutes across both membranes and the periplasm of the Gram-negative bacterial envelope.

### Other ATP-Driven Transporters

Strain EbN1 has a single F-type ATPase (3.A.2) for the interconversion of chemiosmotic (pmf) and chemical (ATP) energy. All eight expected constituents were identified ($\alpha$, $\beta$, $\gamma$, $\delta$, $\varepsilon$, a, b, c). It also has six full-length P-type ATPases, all probably specific for monovalent or divalent cations (one for $Ag^{+}$, two for $Cu^{+}$, one for $Cd^{2+}$ and other heavy metals, and two for $Ca^{2+}$). No other pyrophosphate hydrolysis-driven ion pumps were identified.

### Protein Secretion Systems

Strain EbN1 has an ATP/GTP/pmf-driven general secretory (Sec) pathway, undoubtedly the most important system for protein secretion from the cytoplasm to the periplasm (Cao and Saier 2003). All of the components of the Sec system found in *E. coli* are also present in strain EbN1. Strain EbN1 has a three-component pmf-driven Tat system (TC 2.A.64), as do many bacteria (Yen et al. 2002b). The system in strain EbN1 has TatA, -C, and -E but seems to lack TatB. TatA, -B, and -E are homologous to each other, and only one of these homologues is absolutely required (Yen et al. 2002b). While the TatA, -B, and -E proteins form an expandable pore that accommodates fully folded and assembled substrate protein complexes, the TatC protein recognizes the substrate complex and nucleates pore formation (Holzapfel et al. 2007).

Three ABC-type I protein secretion systems were identified as discussed above. These systems transport their protein substrates across both membranes of the Gram-negative bacterial envelope in a single energy-coupled step. This process depends on a membrane fusion protein (MFP; TC 8.A.1) and an outer membrane factor (OMF; TC 1.B.17). Strain EbN1 has nine recognizable MFP homologues and six identifiable OMF homologues. An OMF-like TolC of *E. coli* can function with multiple transporter-MFP pairs (Yen et al. 2002a). The three ABC type I exporters most resemble characterized systems specific for (1) a hemolysin (HlyB), (2) hydrolytic enzymes such as proteases and lipase (LapB), and (3) an adhesin (HasD). It should be noted that MFPs and OMFs are very sequence divergent, so the possibility of additional homologues cannot be excluded.

Strain EbN1 has a single type IV (conjugal) DNA-protein secretory system (Cao and Saier 2001). The system most resembles the 10-component Trb system of plasmid IncP from *Enterobacter aerogenes*. All 10 proteins were identified, encoded on a strain EbN1 plasmid (Table 2). This *A. aromaticum* strain also has a three-component bacterial competence-related DNA transformation transporter (DNA-T) (Dubnau 1999; Kidane and Graumann 2005). This system resembles the *B. subtilis* DNA-T system. A septal DNA translocator (S-DNA-T), resembling SpoIIIE, a well-characterized system in *B. subtilis*, is also present. Homologues of this protein are found in most, if not all, bacteria, where they function to translocate DNA across newly formed septa.

The *B. subtilis* DNA-T competence system has three components, Cme1 (ComEA), Cme3 (ComEC), and Cmf1 (ComEF). The Cmf1 homologue in strain EbN1 is nearly three times longer than its *B. subtilis* homologue. These two proteins show an overlap of about 300 residues, and this overlapping region includes two domains, the DEXH box helicases domain, including a Walker B motif for ATP binding, and the HELICc domain, also characteristic of helicases. The extra N-terminal 600 residues, lacking in the *B. subtilis* Cmf1 protein, includes a UvrB domain, a helicase subunit of the DNA excision repair complex involved in DNA replication, recombination and repair, and a CarD-TrcF domain, involved in binding to stalled RNA polymerase. At the C-terminus of this protein is a TrcF domain of unknown function. It seems likely that this large protein in strain EbN1 is multifunctional, possibly coordinating DNA uptake with recombination of the single DNA strand into the bacterial chromosome.

Strain EbN1 has many proteins showing homology to the Pul (pullulanase secretion system) and Pil (pilus secretion system), main terminal branch (MTB) protein secretion type II systems. Interestingly, 8 chromosomally encoded proteins most resemble Pul proteins (TC 3.A.15.1.1) of *Klebsiella pneumoniae*, and 10 chromosomally encoded proteins most resemble the homologous Pil proteins (TC 3.A.15.2.1) of *Pseudomonas aeruginosa*. Type II secretion systems do not all have the same numbers of constituents (Peabody et al. 2003; Sandkvist 2001). Thus, while the Pil-like system of strain EbN1 has all of the constituents recognized for the *P. aeruginosa* Pil system, the Pul-like system is not complete by the same criterion. We postulate that strain EbN1 has a chromosomally encoded MTB-type protein secretion system, a chromosomally encoded Pil-type pilus subunit secretion system, and a plasmid-encoded Trb system for protein/DNA export during conjugation.

### Electron Flow-Driven $H^{+}$/$Na^{+}$ Pumps

Bacteria have a variety of energy-coupled electron flow-carrier complexes. Strain EbN1 has 15 components of a single $Na^{+}$-translocating NADH dehydrogenase (NDH) complex and three constituents of a single complete proton-translocating transhydrogenase (PTH). Three components of a single proton-translocating quinol:cytochrome *c* reductase (QCR) are also present. Multiple subunits of as many as five distinct cytochrome oxidase (COX) systems were identified, but it is not certain that all of these are

complete. Several of these subunits most resemble subunits of the mammalian COX system (Table 2; see TCDB—www.tcdb.org). Interestingly, *E. coli* has three cytochrome oxidase systems. One of these has a high affinity for $O_2$ and functions under microaerophilic conditions, while the second has low affinity for $O_2$ and functions under strongly aerobic conditions (Calhoun et al. 1994). The third system (AppBC) is poorly characterized but may function as an oxygen scavenger (Dassa et al. 1991). Finally, strain EbN1 has two complete multicomponent (six or seven components each) $H^+$- or $Na^+$-translocating NADH:ferridoxin oxidoreductases (NFO; TC 3.D.6).

### The Phosphoenolpyruvate:Sugar-Transporting Phosphotransferase System (PTS)

Strain EbN1 has a complete phosphotransferase system, but only one PTS permease. Based on homology results, this system is likely to be specific for fructose. It probably is a high-affinity system that phosphorylates the sugar at the 1-position, yielding cytoplasmic fructose-1-phosphate (Barabote and Saier 2005). It is the only recognizable sugar transporter encoded within the strain EbN1 genome. We were not able to find the IIB constituent of the fructose permease, but these small proteins are easy to miss. No nitrogen regulatory PTS phosphoryl transfer chain is present in strain EbN1 (Rabus et al. 1999).

### Transmembrane Electron Flow Systems

Transmembrane oxidoreductases that transfer electrons from one side of the cytoplasmic membrane to the other without coupling proton movement to the process alter the energetics of the cell (Kimball and Saier 2002). Those which transfer electrons from in to out diminish the electrochemical potential, while those that transfer electrons from out to in increase the electrochemical potential. Strain EbN1 has several such systems. These include both a disulfide bond oxidoreductase B (electrons transferred from out to in) and a disulfide bond oxidoreductase D (electrons transferred from in to out) (see Table 2). These electron carriers are believed to function primarily in the reversible formation of disulfide bonds in extracytoplasmic (e.g., periplasmic) proteins (Nakamoto and Bardwell 2004).

Strain EbN1 has multiple prokaryotic molybdopterin-containing oxidoreductases of the PMO family (TC 5.A.3) (Rothery et al. 2008). These include (1) a nitrate reductase (Nar), (2) two potential tetrathionate reductases (Ttr), (3) a dimethylsulfoxide (DMSO) reductase (Dms), (4) a formate dehydrogenase (Fdn), (5) two polysulfide reductases (Psr), and (6) two homologues of the anaerobic ethylbenzene dehydrogenase, Ebd, one of which is already in TCDB. The three subunits of these two enzyme complexes exhibit 74% (A), 80% (B), and 57% (C) identity, respectively, suggesting similar function. Ethylbenzene dehydrogenase is a soluble periplasmic enzyme assumed to transfer electrons, derived from anaerobic dehydrogenation of ethylbenzene, to a periplasmic *c*-type cytochrome (Kloer et al. 2006). Thus, it does not catalyze transmembrane electron flow as is true for several members of this family.

### Auxiliary Proteins

Strain EbN1 has several auxiliary proteins that play essential roles for the normal functioning of various transporters. It has at least nine "membrane fusion proteins" that connect primary cytoplasmic active efflux pumps to outer membrane pore-forming factors (TC 1.B.17), allowing export of substrates from the cytoplasm to the extracellular medium in a single energy-coupled step (Hu and Saier 2006; Paulsen et al. 1997). Strain EbN1 also has a single system of the MPA1 family for facilitating export of polysaccharides.

As noted above, *A. aromaticum* has a single system for the transport and phosphorylation of fructose via the PTS (TC 4.A.2). To be functional, it must also possess the energy-coupling phosphoryl transfer proteins of the PTS, enzyme I and HPr. These, as well as a mannose-type IIA protein (see Table 2), were found. The three enzyme I homologues proved to resemble (1) PEP synthetases, (2) a phenylphosphate synthetase (Schleissner et al. 1994), and (3) enzyme I of the PTS. Thus, strain EbN1 has just one enzyme I. Other auxiliary proteins identified are listed in Table 2.

### Incompletely Characterized Systems

Proteins in the 9 category of the TC system are either known transporters of poorly defined mechanism (9.A) or putative transporters where proof of transport function is incomplete (9.B). Only two types of transporters in the 9.A category were identified, and these are specific for divalent metal cations. PbrT homologues transport lead ($Pb^{2+}$), while MgtE homologues transport magnesium ($Mg^{2+}$). In neither of these cases is the mechanism of transport well defined.

We identified four FeoB ($Fe^{2+}$ transporting) homologues (9.A.8) in strain EbN1, but all four of these give low scores with the homologues in TCDB. Moreover, characterized FeoB proteins have 8–12 C-terminal TMSs as well as an N-terminal ATP/GTP hydrolyzing domain, but the four putative FeoB homologues encoded within the genome of strain EbN1 have 0 or 1 putative TMS. Consequently they are probably G-proteins unrelated in function to $Fe^{2+}$ transporters.

In TC category 9.B, several homologues encoded within the genome of strain EbN1 are likely to be transporters. Strain EbN1 has two putative bacterial murine precursor exporters (9.B.3), proteins that are found in virtually all bacteria. They also have two putative lipid translocases (9.B.11). All four of these homologues give good scores with TCDB entries. Two putative heme exporters (9.B.14) were identified, one with a very good score and one with a poor score. This second system may be specific for something other than heme.

Strain EbN1 encodes 21 fatty acyl CoA synthetases (FAT family; TC 9.B.17), some of which may catalyze fatty acid uptake (Zou et al. 2002). Several other putative transporters are listed in Table 2, but the transport functions of these TC entries are even less well defined than those discussed above.

## Topologies of Putative Transport Proteins

Figure 2 presents the predicted topologies of the putative transport proteins encoded within the genome of strain EbN1. Many of these, including energy-coupling ATPases and phosphoryl transfer proteins, have no TMSs, while others, periplasmic solute binding receptors, targeted for secretion via the general secretory (Sec) pathway or the twin arginine translocating (TAT) system, have just one TMS. There are significantly more 6-TMS proteins than 5- or 7-TMS proteins, and more 12-TMS proteins than 11- or 13-TMS proteins; 10-TMS proteins are also more numerous than 9- or 11-TMS proteins. Although proteins with even numbers of TMSs predominate over those with odd numbers of TMSs in all organisms, the pattern shown here is quantitatively different from those observed for certain other proteobacteria such as *Bdellovibrio bacteriovorans* and other prokaryotic microorganisms (Barabote et al. 2007; Heider and Fuchs 1997; Paulsen et al. 2000). The patterns observed must reflect the types of transport proteins that predominate. The distribution of topological types with more even-numbered TMS proteins than odd-numbered TMS proteins is not entirely surprising, as it reflects the evolutionary process (Saier 2003).

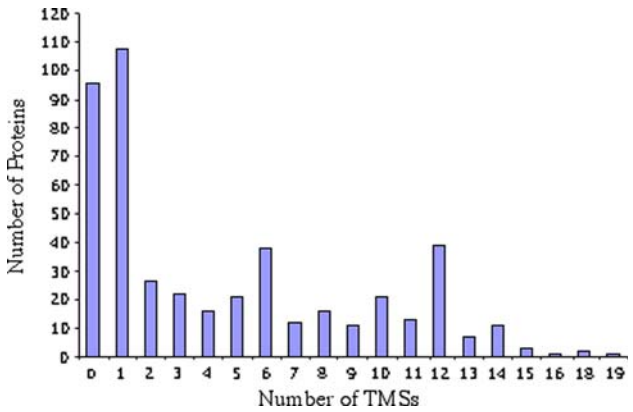


**Fig. 2** Distribution of predicted topological types of proteins among the identified transporters in *A. aromaticum* strain EbN1. The numbers of proteins exhibiting a specific topological type (i.e., of a putative number of TMSs) (on the *x*-axis) is plotted versus the putative numbers of TMSs per polypeptide (on the *y*-axis)

## Subdivision of Strain EbN1 Transporters According to Probable Substrate Specificity

Table 3 summarizes the results presented in Table 2, subdividing the systems identified in terms of both transporter type and probable substrate specificity. Of the α-type channels, six are nonselective, six are specific for cations, and two transport anions. Of the outer membrane porins, 11 are nonspecific, although 2 prefer anionic substrates and 5 prefer cationic substrates. There are many porins that exhibit specificity for a type of substrate. One possibly recognizes sugars, while another recognizes monocarboxylates. While one takes up vitamin $B_{12}$ across the outer membrane, seven take up iron siderophore complexes, again in agreement with an organism that relies on electron transfer as a primary means of energy production. Four systems allow facilitation of small hydrophobic substrates such as drugs across the outer membrane, while seven function in macromolecular export (two for carbohydrates, four for proteins, and one for lipids).

Examining the primary and secondary carriers, we see some interesting parallels and differences. There are more than twofold more cation-specific carriers of both types than anion-specific carriers. In addition to the single PTS permease, there is only one potential secondary sugar transporter and no primary active transporter for sugars. However, the presence of eight monocarboxylate transporters and eight di- and tricarboxylate transporters clearly implies the importance of these exogenous metabolites as sources of energy. Amino acids and their derivatives are of moderate importance to strain EbN1, with nine primary active transporters and five secondary carriers exhibiting these specificities. Cytoplasmic membrane transporters for vitamins and cofactors are also present as expected. Macromolecular transporters, mostly exporters, are prevalent, with at least 8 for proteins, as many as 10 for carbohydrates, 6 for lipids and related compounds, and at least 2 for nucleic acids.

## Transporters Specific for Hydrophobic and Aromatic Compounds

Including all types of transporters classified in TCDB, a total of 72 systems are predicted to act on hydrophobic and aromatic compounds. This corresponds to 28% of all the transporters in strain EbN1 (Table 4). This value

**Table 3** Distribution of transporters based on substrate specificity

| Substrate | No. of families of indicated type using substrate | | | | | | | Total no. of systems |
|---|---|---|---|---|---|---|---|---|
| | Channels | Porins | Primary carriers | Secondary carriers | Group translocator | Transmembrane electron flow carriers | (Putative) Poorly characterized | |
| I. Inorganic molecules | | | | | | | | |
| A. Nonselective | 6 | 10 | | | | | | 16 |
| B. Cations | 2 | | 21 | 17 | | | 6 | 46 |
| C. Anions | 1 | | 6 | 6 | | | | 13 |
| D. Electrons | | | | | | 16 | | 16 |
| II. Carbon sources | | | | | | | | |
| A. Sugars & polyols | | 1 | | | 1 | | | 2 |
| B. Monocarboxylates | | | | 2 | | | 21 | 23 |
| C. Di- & tricarboxylates | | | | 8 | | | | 8 |
| D. Organoanions (noncarboxylic) | | | 2 | | | | | 2 |
| E. Aromatic compounds | | | | 10 | | | | 10 |
| III. Amino acids & their derivatives | | | | | | | | |
| A. Amino acids & conjugates | | | 3 | 4 | | | | 7 |
| B. Amines, amides, polyamines, & organocations | 2 | | | 1 | | | | 3 |
| C. Peptides | | | 4 | 1 | | | 2 | 7 |
| IV. Vitamins, cofactors, & cofactor precursors | | | | | | | | |
| A. Vitamins & vitamin or cofactor precursors | | | 1 | | | | | 1 |
| B. Enzyme & redox cofactors | | | 1 | | | | 2 | 3 |
| C. Siderophores; siderophore-Fe complexes | | 8 | | | | | | 8 |
| V. Drugs, dyes, sterols, & toxics | | | | | | | | |
| A. Multiple drugs | | 5 | | 16 | | | | 21 |
| B. Specific drugs | | | 9 | | | | | 9 |
| C. Pigments | | | | | | | | |
| D. Other hydrophobic substances | | | 4 | 9 | | | | 13 |
| VI. Macromolecules | | | | | | | | |
| A. Carbohydrates | | 2 | 4 | 1 | | | 4 | 11 |
| B. Proteins | | 5 | 9 | 3 | | | | 17 |
| C. Nucleic acids | | | 2 | | | | | 2 |
| D. Lipids | | 1 | 2 | 2 | | | 1 | 6 |
| VII. Unknown | | | | 4 | | | 10 | 14 |
| Total | 11 | 32 | 68 | 84 | 1 | 16 | 46 | 258 |

corresponds to the largest percentage yet recorded for a living organism, to the best of our knowledge (see Fig. 3). Among these, 10% to 13% are predicted to be specific for aromatic compounds. Again, this is a higher percentage than observed for most bacteria. These values are consistent with expectation for an organism that makes its living eating hydrophobic and aromatic substances.

## Discussion

*A. aromatoleum* strain EbN1 is best known for its ability to degrade hydrophobic and aromatic substances. We examined the genome of strain EbN1 for transporters likely to be specific for these types of compounds (Table 4) and found 9 uptake transporters (3%) for small aromatic compounds,

**Table 4** Transporters specific for hydrophobic and aromatic compounds

| Compound | TC no. | TC homologue | Number | Total |
|---|---|---|---|---|
| Hydrophobic/amphipathic compounds | 2.A.1.2 | DHA1 | 4 | 32 |
| | 2.A.1.3 | DHA2 | 1 | |
| | 2.A.6.2 | HAE1 | 9 | |
| | 2.A.6.7 | HAE3 | 7 | |
| | 2.A.6.8 | ORF4 | 1 | |
| | 2.A.7.1 | SMR | 1 | |
| | 2.A.66.1.1 | MATE | 1 | |
| | 3.A.1.105 | DrugE1 | 2 | |
| | 3.A.1.120 | DrugRA1 | 4 | |
| | 3.A.1.121 | DrugRA2 | 1 | |
| | 3.A.1.122 | MacB | 2 | |
| | 3.A.1.201 | MDR | 1 | |
| Hydrophobic amino acids | 3.A.1.4.1 | ABC HAAT | 3 | 3 |
| Fatty acids/lipids | 1.B.9.1.1 | FndL | 1 | 27 |
| | 2.A.1.42.1 | LplT | 2 | |
| | 3.A.1.106 | LipidE | 1 | |
| | 3.A.1.114 | DevE | 1 | |
| | 9.B.11.1.1 | Tgd1 | 1 | |
| | 9.B.17.1.4 | FadD | 15 | |
| | 9.B.17.1.6 | CaiC | 6 | |
| Aromatic compounds | 2.A.1.15 | AAHS | 3 | 10 |
| | 2.A.1.27 | PPP | 1 | |
| | 2.A.1.30 | ADT | 1 | |
| | 2.A.1.36 | YnfM | 1 | |
| | 2.A.21.7.1 | Ppa | 1 | |
| | 2.A.71.2.1 | FBT | 1 | |
| | 5.A.3.9 | PMO | 2 | |
| Total no. of transporters for hydrophobic & aromatic compounds | | | | 72 |

30 efflux transporters (11%) for hydrophobic/amphiphilic drug-like substances, and 5 ($\sim$2%) specific for the uptake of hydrophobic amino acid-like compounds. It should be recalled that these systems might show broad specificities. In particular, the putative drug exporters are likely to be able to act on a variety of aromatic and hydrophobic compounds encountered by strain EbN1 in the natural environment, particularly at contaminated sites.

The uptake systems for aromatic compounds could be of broad specificity, transporting a variety of aromatic toxins. The five ABC hydrophobic amino acid uptake systems probably transport aromatic amino acids and other hydrophobic/aromatic substances. The high percentage of transporters for aromatic and hydrophobic substances correlates with the very low percentage of transporters for sugars (at most two systems, which may not be complete) and hydrophilic or semipolar amino acids (five systems: three uptake and two efflux systems).

Although ABC uptake systems are sparse in strain EbN1 compared to many other bacteria, ABC efflux systems are more numerous. In addition to protecting cells against toxic substances, ABC efflux pumps export periplasmic, surface, and extracellular macromolecules: carbohydrates, lipids, and proteins. Surprisingly, four of the ABC efflux systems in strain EbN1 more closely resemble characterized eukaryotic systems than known prokaryotic systems. All of these are half-sized pumps which presumably function as dimers. One of the two heavy metal efflux pumps (3.A.1.210) is 50% larger than its nearest eukaryotic homologue. The system that resembles a mitochondrial peptide exporter (3.A.1.212) may have shared a common ancestry with it, both having diverged from each other during vertical descent.

An ABC transporter with an extra C-terminal 300 hydrophilic residues (EbA6882) proved to have an unusual domain structure as revealed by screening the conserved domain database (CDD). The extra 300 residues contained two adjacent domains, a histidine kinase-like ATPase (HATPase-c) domain and a signal receiver (REC) domain, common to all response regulators. The latter are

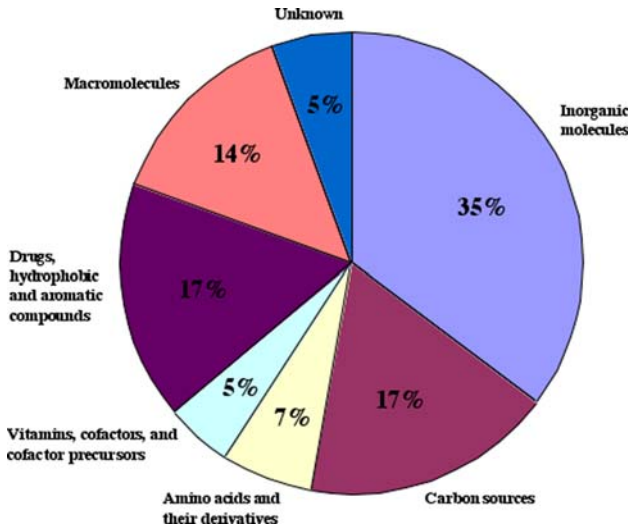


**Fig. 3** Estimates of the percentages of recognized transport systems found in *A. aromaticum* sp. EbN1 according to substrate type. Inorganic molecules are primarily ionic species and small, hydrophilic, neutral molecules such as $H_2O$, $NH_3$, and $CO_2$. Macromolecules include proteins, complex cell surface carbohydrates, and lipids. Other categories are self-explanatory

phosphorylated by histidine kinases. Three possibilities therefore can be considered concerning their mode of regulation: (1) phosphorylation of this domain may regulate the ABC transport activity, (2) the transporter could provide a signal for control of regulatory phosphoryl transfer via the C-terminal domains, and (3) the transport and regulatory components may function independently. A BLAST search revealed that this fusion arrangement, with an ABC transporter fused to HATPase and REC domains, is only found in a few $\beta$-proteobacteria closely related to strain EbN1 (species of *Ralstonia* and *Burkholderia*). These fusion proteins have not previously been investigated. They may provide a novel regulatory mechanism.

Strain EbN1 has a huge variety of macromolecular transport systems. It has a full complement of proteins for assembly of (1) the general secretory (Sec) pathway; (2) the Oxa system, which can insert proteins into the cytoplasmic membrane dependently and independently of the Sec system; (3) the twin arginine targeting and translocating (Tat) system; (4) the outer membrane protein insertion porin (OmpIP) complex; (5) three type I ABC protein secretion systems; (6) two type IIb (MTB)-type outer membrane protein secretion systems, one of the Pul type for general protein secretion and one of the Pil type for pilus subunit secretion; (7) a type IV conjugation-type (Conj) secretion system for export of DNA-protein complexes involved in conjugation; and (8) a septal DNA translocator (S-DNA-T). It also has numerous transporters for lipids, fatty acids, lipoproteins, and complex carbohydrates.

The results described here provide a comprehensive overview of the transport capability of *A. aromaticum* strain EbN1. They should serve as guides for future research concerning the ecophysiological role of this organism in its natural habitat and assessment of bioremediation prospects. Strain EbN1 can be regarded as an aquatic degradation specialist feeding on low molecular weight compounds ranging from plant exudates (e.g., dicarboxylic acids) to naturally as well as anthropogenically released toxic aromatic compounds (e.g., toluene and phenol). The present study reveals that the transporter complement of strain EbN1 matches its degradative capacities, whereby a well-integrated system is established for uptake and complete oxidation (to $CO_2$) of organic growth substrates. Notably, strain EbN1 contains paralogous transport systems in several cases, agreeing with the high genome plasticity of strain EbN1. One may speculate that these systems possess different ranges of substrate specificity and/or affinity, allowing strain EbN1 to adapt its transporter equipment to changing substrate concentrations in the natural environment. Considering the high degree of substrate-dependent regulation of catabolic pathways in this organism (Kühner et al. 2005; Wöhlbrand et al. 2007, 2008), similar regulatory control mechanisms can be envisioned for some of the transporters defined in the present in silico analysis.

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