**Table 1.** Essential and non-essential amino acids and derivates present in the *BAp* network and determination of the putative importers and exporters required for their biosynthesis

| Amino acids | Biosynthesis in *BAp* | Required transporter |
|---|---|---|
| ***Non essential amino acids*** | | |
| glutamate / glutamine | Both absent from α-ketoglutarate, present for Glu from Gln (irreversible reaction), needs at least direct import of Gln | Glu [I], Gln [I] |
| proline | Absent from α-ketoglutarate, needs direct import | Pro [I] |
| serine / glycine | Both absent from 3-phosphoglycerate, reversible interconversion is possible, needs direct import of at least one of the two | Ser [I], Gly [I] |
| cysteine | Absent from 3-phosphoglycerate, present from Ser, needs sulphate import and ATP | Ser [I], sulphate [I] |
| aspartate / asparagine | Absent from oxaloacetate, needs direct import | Asp [I], Asn [I] |
| alanine | Absent from aspartate and pyruvate, present from Cys (alternative pathway), needs direct import or ser import for Cys biosynthesis | Ala [I], Ser [I] |
| tyrosine | Absent in *Buchnera*, produced from Phe in the bacteriocyte, needs Phe or penylpyruvate export and direct import | Phe [E], Tyr [I] |
| ***Essential amino acids*** | | |
| methionine | Absent from Asp, present from homocystéine and THF | Cys [I], homocysteine [I], THF [I] |
| threonine | Complete from Asp | Asp [I] |
| lysine | Complete from Asp and Glu | Asp [I], Glu [I] |
| valine | Incomplete from glucose (pyruvate), needs export of 2-ketoisovalerate for final transamination in the bacteriocyte and direct import. | glucose [I], 2-ketoisovalerate [E], Val [I] |
| leucine | Incomplete from glucose (pyruvate), needs export of 2-ketoisocaproate for final transamination in the bacteriocyte and direct import. | glucose [I], 2-ketoisocaproate [E], Leu [I] |
| isoleucine | Incomplete from Asp (Thr), needs export of Thr, import of 2-oxobutanoate, export of 2-keto-3-methyl-valerate for final transamination in the bacteriocyte and direct import. | Asp [I], Thr [E], 2-oxobutanoate [I], 2-keto-3-methyl-valerate [E], ile [I] |
| tryptophan / phenylalanine | Complete from glucose (chorismate), needs Ser and Gln (for Trp), phenylpyruvate (for Phe) is probably exported for final transamination in the bacteriocyte | glucose [I], Ser [I], Gln [I], phenylpyruvate [E] |
| histidine | Complete from glucose (ribose 5-P), needs Gln | glucose [I], Gln [I] |
| arginine | Complete from Glu and Asp, needs Glu and Asp | Glu [I], Asp [I] |
| ***Derivates*** | | |
| homocysteine | Incomplete from sulfite, needs direct import | Cys [E], homocysteine [I] |
| ornithine | Complete in the Arg pathway, might be imported however (Poliakov et al. 2011) | Ornithine [I] |

**Table 2.** List of cofactors and vitamins present in the *BAp* network and determination of the putative importers and exporters required for their biosynthesis

| Cofactors / vitamins | Biosynthesis pathway | Required transporters |
|---|---|---|
| AMP , ADP, ATP, UDP, UTP, GDP, GTP, CMP, CDP, CTP, dADP, dATP | Incomplete, needs to import guanosine, inosine and putrescine, putative export of adenine | guanosine [I], inosine [I], putrescine [I], adenine [E] |
| biotin (vitamin B7) | Incomplete, needs malonyl-CoA (if the pathway is complete) or 7-keto-8-aminopelargonate (although not produced by the aphid), putative export for the host | malonyl-CoA [I], 7-keto-8-aminopelargonate [I], biotin [E] |
| CO-A, pantothenate (vitamin B5) | Incomplete, from panthoténate (vitamin B5) needs direct import or import of pantetheine phosphate | CoA [I], pantetheine 4'-P [I] |
| cobalamin (vitamin B12) | Absent, used as cofactor by cysG only (HAMAP), needs direct import | cobalamin [I] |
| Cyt-C (cytochrome C) | Incomplete, needs direct import or import of uroporphyrinogen III and protohaem | Cyt C [I], uroporphyrinogen III [I], protohaem [I] |
| DHF, THF (dihydro- and terahydro-folate, vitamin B9) | Incomplete from GTP and chorismate, needs direct import or import of dihydropteroate | DHF [I], 7-8,dihydropteroate [I], formaldehyde [I] |
| FAD, FADH2, FMN, FMNH2 (vitamin B2) | Almost Complete from GTP and ribulose 5-P, putative export for the host | riboflavin [E], |
| gluthatione | Present from Glu and Cys (Cys is produced from Ser and Sulphate), needs Gly, probably exported (Poliakov et al. 2011) | Glu [I], Ser [I], sulphate [I], Gly [I], glutathione [E] |
| niacine, NAD, NADH, NADPH (vitamin B3) | Incomplete, needs import of nicotinate (vitamin B3) | nicotinate [I] |
| pyridoxine (vitamin B6) | Absent, pyridoxal used by > 5 enzymes (HAMAP), needs direct import | pyridoxine [I] |
| SAM, SAH | Complete from methionine, needs import of homocysteine and export of cysteine | homocysteine [I], Cys [E] |
| thiamine (vitamin B1) | Absent, used by >5 enzymes (HAMAP), needs direct import | thiamine [I] |
| ubiquinol, ubiquinone | Absent, needs direct import | ubiquinol [I], ubiquinone [I] |

**Table 3.** List of the input compounds (precursors) from the metabolic network of *Bap,* found with MetExplore.

| Input compound | Main biosynthesis pathways | TI [1] |
|---|---|---|
| amino acids (see Table 3) | | |
| Vitamins and cofactors (see Table 3) | | |
| 2-oxobutanoate | Ile | [a] |
| 7,8-dihydropteroate | THF | |
| α-D-glucose 6-phosphate | Central metabolism | |
| formaldehyde | Methyl donor (especially useful if THF is imported rather than 5,10-methylene THF | |
| inosine | Pyrimidine biosynthesis | |
| L-1-phosphatidyl-glycerol | Cardiolipin biosynthesis | |
| 7-keto-8-aminopelargonate | Biotin biosynthesis (not produced by *A. pisum*). Malonyl-CoA might be the true precursor | |
| Mannitol-1P | Central metabolism | |
| pantetheine 4'-P | Biosynthesis of CoA | |
| putrescine | Biosynthesis of purines and pyrimidines | |
| uroporphyrinogen and protoheme | Biosynthesis of CytC | |

[1] Topological Information: [a] Source, the metabolite is not produced by any reaction and is consumed by one reaction; (from MetExplore, http://metexplore.toulouse.inra.fr).

**Table 4.** List of the output compounds from the metabolic network of *Bap,* found with MetExplore.

| Output compound | Main reaction | TI[1] |
|---|---|---|
| Amino acids (see Table 4) | | |
| Vitamins and cofactors (see Table 4) | | |
| 2-keto-3-methyl-valerate | Ile biosynthesis, the transamination is occurring in the bacteriocyte |  a |
| 2-ketoisocaproate | Leu biosynthesis, the transamination is occurring in the bacteriocyte |  |
| 2-ketoisovalerate | Val biosynthesis, the transamination is occurring in the bacteriocyte |  |
| ADP-D-glycero-D-manno-heptose | Compound used for the LPS biosynthesis (the last step with the racemase is lacking) and the biosynthesis of the lipid part is not known |  |
| biotin | biotin biosynthesis |  |
| FAD (flavin adenine dinucleotide) | flavin and derivates biosynthesis |  |
| FMNH2 (reduced flavin mononucleotide) | flavin and derivates biosynthesis |  b |
| fumarate | Arg biosynthesis, as the TCA cycle is non functional fumarate might accumulate and might be exported |  |
| glutathione | might need export as the salvage pathway is absent |  |
| glycerol | Produced in the cardiolopine biosynthesis pathway |  |
| phenylpyruvate | Phe biosynthesis, the transamination is occurring in the bacteriocyte |  |
| spermidine | Purine and pyrimidine pathway, might accumulate with no possibility of salvage |  |
| succinate | linked with fumarate, as the TCA cycle is non functional it might accumulate |  |

[1] Topological information: [a] Dead End Choke Point, the metabolite is uniquely produced by a specific reaction and not consumed by any reaction; [b] Dead End, the metabolite is not consumed by any reaction and is produced by several reactions (from MetExplore, http://metexplore.toulouse.inra.fr).

**Table 5.** False positives (manually removed) from the list of the input compounds found with MetExplore.

| Input compound | Comment about manual removing | TI[1] |
|---|---|---|
| (2S)-2-amino-3-oxo-4-phosphonooxybutanoate | Not relevant as the corresponding pathway is incomplete (correspond to a putative spontaneous reaction) | a |
| 2-oxo-3-hydroxy-4-phosphobutanoate | Pyridoxal 5-P biosynthesis, the reaction pointed for SerC is probably not relevant here. | |
| 3-phospho-hydroxypyruvate | Ser biosynthesis, probably not used as serine is imported in the cell | |
| β-alanine | Probably not used as CoA is directly imported | |
| cadaverine | Probably not used, as metabolism is oriented towards spermidine rather than aminopropyl-cadaverine | |
| coproporphyrinogen III | Probably not imported as uroporphyrinogen-III is imported | |
| CPD-689, cob(II)yrinate a,c-diamide | Probably not used in the network as cobalamine is imported | |
| CPD-9451, isopropylmaleate | Probably not used as the flux is oriented toward leucine production | b |
| CPD-1302, 5-methyltetrahydropteroyltri-L-glutamate | Another methyl donor is probably used | |
| CPD-5727, 5,10-methenyl-tetrahydropteroyl-[γ-Glu](n) | Not used in the network, the enzyme FolD is also the methylene-THF desydrogenase | |
| D-alanyl-D-alanine | Peptidoglycan biosynthesis - the ddlB might be functional in *BAp* (Poliakov et al. 2011) | |
| D-myo-inositol (3)-monophosphate | Probably not used (myo-inositol pathway), the phosphatase *suhB* is probably active for other processes | |
| glutamate-1-semialdehyde | The reaction pointed for ArgD is probably not relevant here (tetrapyrrole biosynthesis) | |
| L-pantoate | Probably not used as panthotenate (or coA) is directly imported | |
| N2acetyl-α-aminoadipyl-δ-phosphate | The role of ArgC in the biosynthesis pathway of the Lys is not relevant | |
| porphobilinogen | Probably not imported as uroporphyrinogen-III is imported | |
| propionyl-CoA | The enzymes Pta and AckA are probably not used in this incomplete patway (thr degradation) | |
| 5-amino-6-(5-phospho-ribitylamino)-uracil | One step (hydrolase/phosphorilase) lacking in the riboflavine biosynthesis. The shuttle may not be possible for such a reaction that is probably occurring with another enzyme in *Buchnera*. | |
| SAICAR, 5'-phosphoribosyl-4-(N-succinocarboxamide)-5-aminoimidazole | Probably not used as import of inosine and adenine should initiate the pathways | |
| S-lactoyl-glutathione | The enzyme Glob is probably not relevant for this reaction as lactate is not involved in the network of *B. aphidicola* | |
| xanthine | The reaction pointed for Gpt is probably not relevant as salvage and biosynthesis of purine are altered | |

[1] Topological Information: [a] Source, the metabolite is not produced by any reaction and is consumed by several reactions; [b] Source or Dead End Choke Point, the metabolite is uniquely consumed or produced by the same reversible reaction (from MetExplore, http://metexplore.toulouse.inra.fr).

**Table 6.** False positives (manually removed) from the list of the output compounds found with MetExplore.

| Output compound | Comment about manual removing | TI[1] |
|---|---|---|
| 1-amino-propan-2-one-3-phosphate | Not produced (artefact linked to a spontaneous reaction in the pyridoxal 5-P biosynthesis pathway) | a |
| 2-dehydropantoate | Probably not produced in the network as coA is imported | |
| 3-phospho-serine | Probably not produced in the network as Ser is imported | |
| 4-(phosphonooxy)-threonine | Probably not produced (the transaminase SerC is not active on this process) | |
| 5-amino-levulinate | The enzyme ArgD is not relevant for this degenerated pathway (tetrapyrrole biosynthesis) | |
| cardiolipin | Probably not accumulated (salvage through reversible reaction) | |
| CPD-694 (cob(I)yrinate a,c-diamide) | Probably not produced in the network as cobalamine is imported | |
| CPD-1086 (5-amino-6-(5'-phosphoribitylamino)uracil) | The compound is probably not accumulated nor exported, the dephosphorylation is probably occurring in the cell by an unknown phosphatase | |
| CPD-1301, tetrahydropteroyltri-L-glu | Probably not produced as folate, is imported in the cell | |
| deoxyribose-5-phosphate | Probably not accumulated (reversible reaction) | |
| CPD0-1065, aminopropylcadaverine | Probably not produced in the network as the flux is oriented towards spermidine | |
| D-lactate | Probably not accumulated as the transformation lactate to pyruvate is feasible | |
| erythronate-4-phosphate | Probably not produced by GapA in this degenerated pathway (pyridoxal biosynthesis) | |
| hydroxymethylbilane | Probably not produced as protohaem is imported in the cell | |
| myo-inositol | Probably not used, the phosphatase *suhB* is probably active for other processes | |
| N2-acetyl-α-aminoadipate semialdehyde | The role of ArgC in the biosynthesis pathway of the Lys is not relevant | |
| PAPS, phosphoadenosine-5'-phosphosulfate | Probably not produced in the network as coA is imported | |
| protoporphyrinogen IX | Involved in the Met/SAM cycle (probably not accumulated) | |
| S-adenosyl-4-methylthio-2-oxobutanoate | biotin and methionine biosynthesis, might not accumulate with possibility of salvage (SAM + 2-oxobutanoate) | |
| S-methyl-5'-thioadenosine | Probably not produced in the network as coA is imported | |
| sirohaem | Probably not accumulated (however the salvage is not described in BioCyc and KEGG) | |
| thiamin diphosphate | The reaction is not occurring as thiamin is imported | |
| UDP-N-acetylmuramoyl-tripeptide | Probably not exported, D-ala should be imported and the 6.3.2.10 reaction may happen although the corresponding enzyme is not known | |
| xanthosine-5-phosphate | Probably not produced as the purine salvage is degraded | |

[1] Topological Information: [a] Source, the metabolite is not produced by any reaction and is consumed by several reactions (from MetExplore, http://metexplore.toulouse.inra.fr).