

Text S1: Variant pathways and enzymes in GapMind

Besides pathways from MetaCyc, GapMind also describes:

- Proline synthesis via ornithine cyclodeaminase (Graupner and White 2001)
- Arginine synthesis via succinylated intermediates (see the Results)
- Cysteine synthesis via O-succinylserine (Bastard et al. 2017)

Also, GapMind includes tyrosine biosynthesis from phenylalanine (see the Results), even though MetaCyc describes it as occurring only in Metazoa.

GapMind also describes some variant enzymes that might not be expected from MetaCyc's pathway descriptions or from the other curated databases. These variants are from the literature (as opposed to being from our genetic data):

- The methionine synthase from methanogens, which probably uses corrinoid proteins as the methyl donor instead of tetrahydrofolate (Schröder and Thauer 1999).
- The three-part methionine synthase from *Phaeobacter inhibens* (Price et al. 2018).
- The reactivation of vitamin B12 (the reduction of co(II)balamin to co(I)balamin) is described as a separate step that is required for the activity of vitamin B12-dependent methionine synthase. GapMind associates two families with the reactivation of vitamin B12: PF02965, which is part of MetH in *E. coli* and many other bacteria, and the RamA-like domain PF14574 (Ferguson et al. 2009; Price et al. 2018).
- Although MetaCyc includes the reductive sulfuration of aspartate semialdehyde as part of the pathway "L-methionine biosynthesis IV", it links this activity to just one gene. Based on genetic evidence from both *Methanosarcina acetivorans* and *Desulfovibrio vulgaris*, we believe that two other genes are also required (Rauch et al. 2014; Rauch and Perona 2016; Price et al. 2018).
- The histidinol-phosphate phosphatase HisJ from *Bacillus subtilis* (Ghodge et al. 2013). (This protein is annotated in Swiss-Prot, but does not have an experimental evidence code for its catalytic activity, so it was not included in PaperBLAST's database.)
- MetI from *Bacillus subtilis* is O-acetylhomoserine sulfhydrylase and cystathionine γ -synthase (Auger et al. 2002).
- 2-oxobutanoate:ferredoxin oxidoreductase provides an alternate route to 2-oxobutanoate (which is a precursor to isoleucine). MetaCyc describes this reaction but links it to one subunit instead of to both subunits (Fukuda and Wakagi 2002).

References

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