SUBSYSTEM : UDP-N-acetylmuramate from Fructose-6-phosphate Biosynthesis

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Introduction

UDP-N-acetylmuramate pathway in bacteria provides a major building block for the biosynthesis of peptidoglycan. UDP-N-acetylglucosamine, a nucleotide-activated form of N-acetylglucosamine and a key intermediate of this pathway, plays a very important role in the biochemistry of all living organisms. In addition to peptidoglycan biosynthesis, it is required for other essential components of a bacterial cell envelope, such as lipopolysaccharides. teichoic acids and enterobacterial common antigen. In eukaryotes, UDP-N-acetylglucosamine is involved in the synthesis of sialic acid, N/O-glycan conjugates and protein O-glycosylation.

Almost all enzymes of this pathway are essential and conserved in most bacteria (with a well-known exception of Mycoplasma ssp). An interesting variant (a branching pathway) of this subsystem is present in eukaryotes, where a similar sequence of reactions (with a different order of two steps, epimerization and acetylation) stops at the formation of UDP-GlcNAc. A comparative analysis of >200 bacterial genomes has revealed only one locally missing gene. All sequenced genomes of Chlamydiales (nine integrated in SEED) contain only a truncated (single-domain) variant of a universally conserved bi-functional (two-domain) Glucosamine-1-phosphate N-acetyltransferase (EC 2.3.1.157)/ N-acetylglucosamine-1-phosphate uridyltransferase (EC 2.7.7.23) (GA1PAT/AG1PUT, glmU gene in E.coli). A missing bacterial form of domain AG1PUT appears to be replaced by a nonorthologous eukaryotic variant of this enzyme, for example, in Chlamydia trachomatis:
- CT629 is a homolog of the GA1PAT domain of bacterial fusion protein, while
- CT715 is a homolog of an alternative (nonorthologous) AG1PUTe characteristic of eukaryotes.

No other bacteria contain detectable homologs of eukaryotic AG1PUT (human gene UAP1L1), with a notable exception of all sequenced Staphylococci (in addition to a conventional glmU homolog). This observation suggests an interesting evolutionary scenario, and it may be important for the exploration of pathogenesis of these species.

References:

1. Mengin-Lecreulx D, van Heijenoort J. Copurification of glucosamine-1-phosphate acetyltransferase and N-acetylglucosamine-1-phosphate uridyltransferase activities of Escherichia coli: characterization of the glmU gene product as a bifunctional enzyme catalyzing two subsequent steps in the pathway for UDP-N-acetylglucosamine synthesis. J Bacteriol. 1994 Sep;176(18):5788-95.

2. Pompeo F, Bourne Y, van Heijenoort J, Fassy F, Mengin-Lecreulx D. Dissection of the bifunctional Escherichia coli N-acetylglucosamine-1-phosphate uridyltransferase enzyme into autonomously functional domains and evidence that trimerization is absolutely required for glucosamine-1-phosphate acetyltransferase activity and cell growth. J Biol Chem. 2001 Feb 9;276(6):3833-9.

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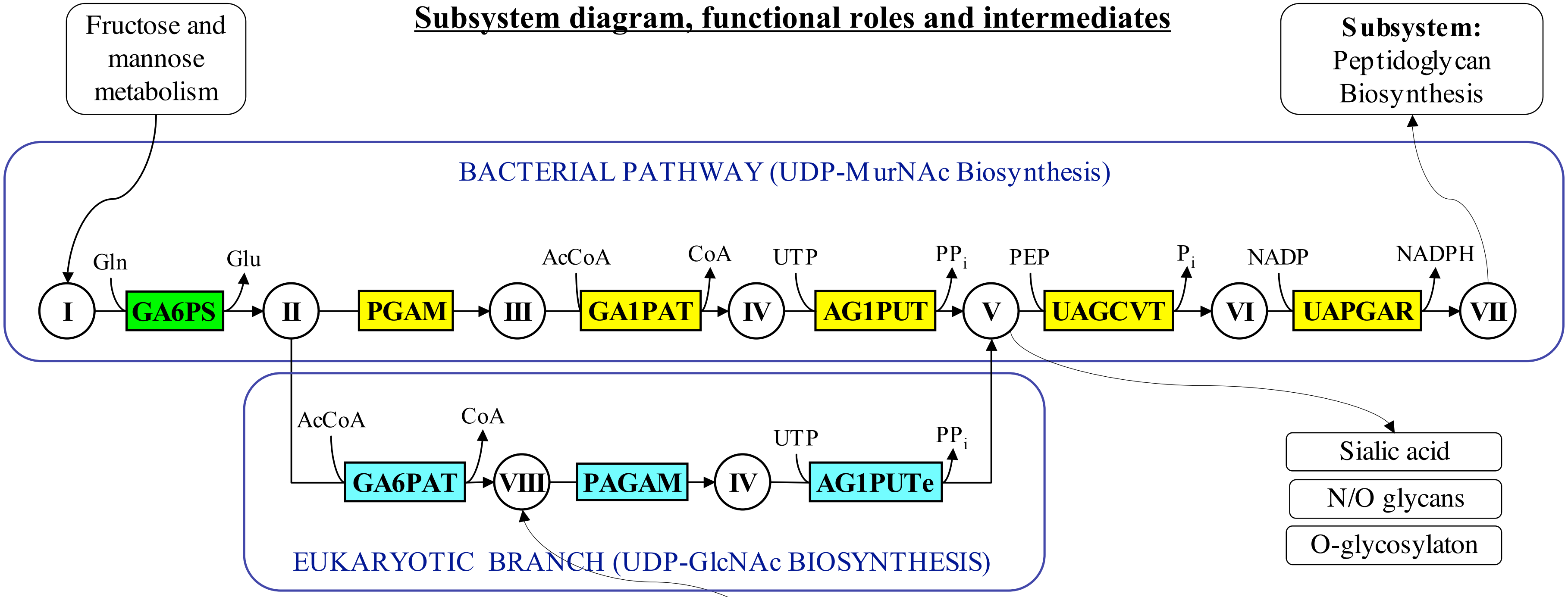
Subsystem diagram, functional roles and intermediates



Abbrev	Committed intermediates
I	D-fructose 6-phosphate
II	D-glucosamine 6-phosphate
III	D-Glucosamine 1-phosphate
IV	N-acetyl-alpha-D-glucosamine 1-phosphate
V	UDP-N-acetyl-D-glucosamine
VI	UDP-N-acetyl-3-O-(1-carboxyvinyl)-D-glucosamine
VII	UDP-N-acetylmuramate [CPD:C01050]
VIII	N-acetyl-alpha-D-glucosamine 1-phosphate
	Other intermediates
Gln	L-glutamine
Glu	L-glutamate
AcCoA	acetyl-CoA
CoA	CoA
UTP	UTP
PPi	diphosphate
PEP	phosphoenolpyruvate
Pi	phosphate

Subsystem:
N-Acetyl-D-Glucosamine Utilization

🟨 **in bacteria**

🟦 **in eukaryotes**

🟩 **in both**

	Abbrev	Functional Role
1	**GA6PS**	Glucosamine--fructose-6-phosphate aminotransferase [isomerizing] (EC 2.6.1.16
2	**PGAM**	Phosphoglucosamine mutase (EC 5.4.2.10)
3	**GA1PAT**	Glucosamine-1-phosphate N-acetyltransferase (EC 2.3.1.157)
4	**AG1PUT**	N-acetylglucosamine-1-phosphate uridyltransferase (EC 2.7.7.23)
5	**UAGCVT**	UDP-N-acetylglucosamine 1-carboxyvinyltransferase (EC 2.5.1.7)
6	**UAPGAR**	UDP-N-acetylenolpyruvoylglucosamine reductase (EC 1.1.1.158)
7	**GA6PAT**	Glucosamine 6-phosphate N-acetyltransferase (EC 2.3.1.4)
8	**PAGAM**	Phosphoacetylglucosamine mutase (EC 5.4.2.3)

UDP-N-acetylmuramate from Fructose-6-phosphate Biosynthesis. Subsystem spreadsheet (fragment)

	Bacterial Pathway						Eukaryotic branch		
GENOMES	**GA6PS**	**PGAM**	**GA1PAT**	**AG1PUT**	**UAGCYT**	**UAPGAR**	**GAR6PA**	**PAGAM**	**AG1PUTe**
Escherichia coli K12	+	+	+	+	+	+	-	-	-
Escherichia coli 042	+	+	+	+	+	+	-	-	-
Synechocystis sp. PCC 6803	+	+	+	+	+	+	-	-	-
Campylobacter jejuni RM1221	+	+	+	+	+	+	-	-	-
Thermotoga maritima MSB8	+	+	+	+	+	+	-	-	-
Bacillus cereus ATCC 10987	+	+	+	+	+	+	-	-	-
Staphylococcus aureus N315	+	+	+	+	+	+	-	-	+
Staphylococcus aureus MW2	+	+	+	+	+	+	-	-	+
Staphylococcus aureus Mu50	+	+	+	+	+	+	-	-	+
Staphylococcus epidermidis	+	+	+	+	+	+	-	-	+
Chlamydophila abortus	+	+	+	-	+	+	-	-	+
Chlamydophila caviae GPIC	+	+	+	-	+	+	-	-	+
Chlamydophila pneumoniae AR39	+	+	+	-	+	+	-	-	+
Chlamydophila pneumoniae CWL029	+	+	+	-	+	+	-	-	+
Chlamydophila pneumoniae J138	+	+	+	-	+	+	-	-	+
Chlamydophila pneumoniae TW-183	+	+	+	-	+	+	-	-	+
Anopheles gambiae str. PEST	+	-	-	-	-	--	+	+	+
Arabidopsis thaliana	+	-	-	-	-	-	+	+	+
Caenorhabditis elegans	+	-	-	-	-	-	+	+	+
Drosophila melanogaster	+	-	-	-	-	-	+	+	+
Homo sapiens	+	-	-	-	-	-	+	+	+
Mus musculus	+	-	-	-	-	-	+	+	+
Saccharomyces cerevisiae	+	-	-	-	-	-	+	+	+
Schizosaccharomyces pombe	+	-	-	-	-	-	+	+	+
Mycoplasma gallisepticum R	-	-	-	-	-	-	-	-	-
Mycoplasma genitalium G-37	-	-	-	-	-	-	-	-	-
Mycoplasma penetrans HF-2	-	-	-	-	-	-	-	-	-
Mycoplasma pneumoniae M129	-	-	-	-	-	-	-	-	-
Mycoplasma pulmonis UAB CTIP	-	-	-	-	-	-	-	-	-

⬛ -- Classic bacterial pathway
🟦 -- Staphyloccocci appear to have both forms of AG1PUT: bacterial and eukaryotic
🟩 -- In all Chlamydia sp bacterial AG1PUT is replaced by the eukaryotic form AG1PUTe
🟧 --Eukaryotic branch:UDP-GlcNAc BIOSYNTHESIS
⬜ --Mycroplasmas (as well as archaea) do not have this pathway
🟨 --Enzymes involved in Prokaryotic pathway