Subsystem: Peptidoglycan Biosynthesis

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Introduction

The wall of a typical Gram-negative cell consists of a single sac-like molecule of murein (peptidoglycan), one or a few layers thick. The wall of Gram-positive bacteria is made up of many layers of murein plus teichoic acid. The assembly of peptidoglycan components begins with the synthesis of precursors in the cytoplasm, their transport across the cell membrane and final polymerization. A battery of enzymes catalazes covalent reactions that result in the extension,crosslinking between glycan strands,morphogenesis, and eventual septation of murein sacculus. These proteins have also a unique ability to bind penicillin and other beta-lactam antibiotics and are known as penicillin binding proteins, or PBPs. The number of PBPa varies among species.

Open questions, comments, conjectures

- Gene encoding MurH has not been identified, even though a number of early papers point to MurH presence in *E. coli* [1]
- Although function of PBP7 is not entirely clear, it has been included in this subsystem . Carboxypeptidase PBP4 hydrolyzing cross-links in peptidoglycan during cell elongation has been included as well.

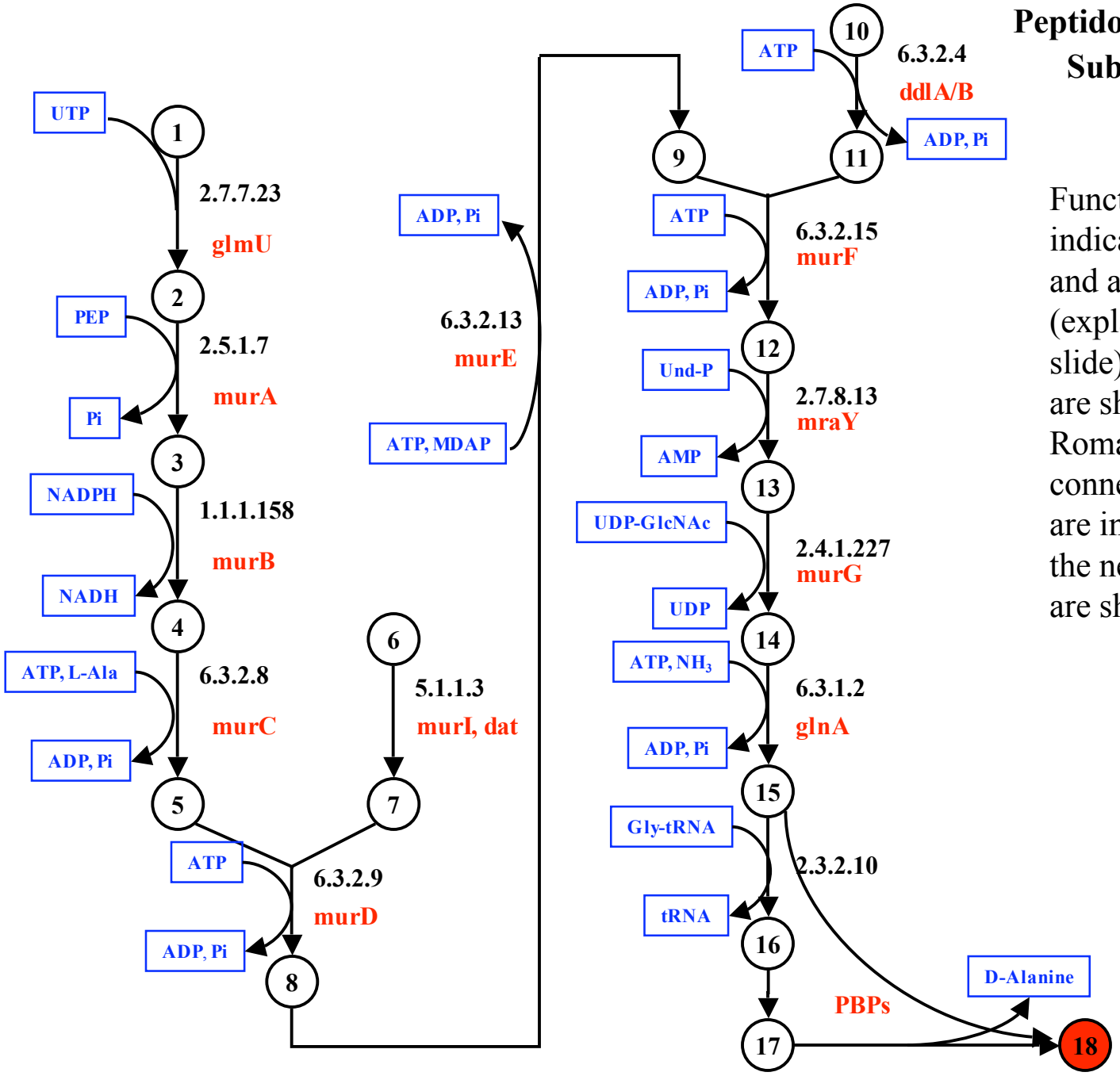
Subsystem spreadsheet (a fragment)

Organism	Variant Code	glmU	murA	murB	murC	murI	murD	murE	*dll	murF	mraY	murG	glnA	pbp7	*CP	*PBP1	FtsI
Escherichia coli O157:H7 [B]	1	4643	4042	4874	183	4873	180	177	508-8, 184-10	178	179	182	4766	4675	4035-20	241-17, 3384-17, 4212-17, 4212-18	176, 749
Escherichia coli O157:H7 EDL933 [B]	1	4677	4071	4915	95	4914	92	89	427-8, 96-10	90	91	94	4803	4709	4064-20	153-17, 4243-17, 4243-18	669, 88
Bacillus anthracis str. A2012 [B]	1	945	691, 743	482, 2490, 4826	5665	1737, 5459	4829, 4830	3408, 4832	1120-8	1122, 2988	4831	4827, 5232	4610	2244, 2660	2874-20, 3328-20, 5489-20, 5830-20	1929-17, 2399-17, 3149-17, 786-17, 1423-18	3051, 3474, 4833, 4834, 5252
Klebsiella pneumoniae MGH78578 [B]	1	4045, 4046	3929, 3930, 3931	4051	2307	5638, 5639	413, 414	1183, 1184, 1185, 1187	2303-8, 2304-8, 6243-8, 6244-8, 6245-8	1188	1190, 1191	2309	5918, 5919, 5929	6476	5986-20, 5987-20, 7650-20, 7884-20, 3915-21, 3916-21	1168-17, 1169-17, 357-17, 355-18, 4883-18	2496, 853
Lactobacillus plantarum WCFS1 [B]	1	391	424, 1962	690	1207	1888	1827	821	1949-8	432	1828	1826	1311	1983	845-20	1168-17, 1457-17	1300, 1829

Peptidoglycan Biosynthesis: List of functional roles

Abbrev	Functional Roles	EC number
GlmU	N-acetylglucosamine-1-phosphate Uridyltransferase	2.7.7.23
MurA	UDP-N-acetylglucosamine-1-Carboxyvinyltransferase	2.5.1.7
MurB	UDP-N-acetylenolpyruvoylglucosamine Reductase	1.1.1.158
MurC	UDP-N-acetylmuramate--Alanine Ligase	6.3.2.8
MurI	Glutamate Racemase	5.1.1.3
MurD	UDP-N-acetylmuramoylalanine--D-Glutamate Ligase	6.3.2.9
DdlA / B	D-alanine--D-alanine Ligase subunits A and B	6.3.2.4
MurE	UDP-N-acetylmuramoylalanyl-D-glutamate--2,6-diaminopimelate Ligase	6.3.2.13
MurF	UDP-N-acetylmuramoylalanyl-D-glutamyl-2,6-diaminopimelate--D-alanyl-D-alanyl Ligase	6.3.2.15
MraY	Phospho-N-acetylmuramoyl-pentapeptide-Transferase	2.7.8.13
MurG	UDP-N-Acetylglucosamine--N-Acetylmuramyl-(pentapeptide) pyrophosphoryl-undecaprenol N-acetylglucosamine Transferase	2.4.1.227
GlnA	Glutamine Synthetase	6.3.1.2
MurH*	UDP-N-Acetylmuramoylpentapeptide-Lysine N6-Alanyltransferase	2.3.2.10
MtgA, MrcA, pbp	Transpeptidases,Transglycosylases (PBP1A, PBP1B, PBP2, PBP3)	2.4.1.129 2.4.2.- 3.4.-.-

Peptidoglycan Biosynthesis: Subsystem diagram



Functional roles are indicated by EC numbers and abbreviations (explained in the previous slide). Key intermediates are shown in circles with Roman numerals, non-connecting intermediates are in boxes (explained in the next slide). Reactions are shown by arrows.

Peptidoglycan Biosynthesis: Subsystem diagram
(continued)

Abbrev	Committed intermediates
1	N-Acetyl-D-Glucosamine-1-Phosphate
2	UDP-N-acetyl-D-glucosamine (UDP-GlcNAc)
3	UDP-GlcNAc-pyruvate enol ether
4	UDP-N-Acetylmumarate (UDP-MurNAc)
5	UDP-MurNAc-L-Ala
6	L-Glutamate
7	D-Glutamate
8	UDP-MurNAc-L-Ala-D-Glu
9	UDP-MurNAc-L-Ala-D-Glu-meso-2,6-diaminoheptanedioate
10	D-Alanine
11	D-Alanyl-D-Alanine (D-Ala-D-Ala)
12	UDP-MurNAc-L-Ala-D-Glu-meso-2,6-diaminopimeloyl-D-Ala-D-Ala
13	Und-PP-MurNAc-L-Ala-D-Glu-meso-2,6-diaminopimeloyl-D-Ala-D-Ala
14	Und-PP-MurNAc-(GlcNAc)L-Ala-D-Glu-meso-2,6-diaminopimeloyl-D-Ala-D-Ala
15	Und-PP-MurNAc-(GlcNAc)L-Ala-D-Gln-meso-2,6-diaminopimeloyl-D-Ala-D-Ala
16	Und-PP-MurNAc-(GlcNAc)L-Ala-D-Gln-meso-2,6-diaminopimeloyl-(Gly)5-D-Ala-D-Ala
17	Peptidoglycan
18	Crosslinked peptidoglycan
Abbrev	**Other intemediates**
PEP	Phosphoenolpyruvate
L-Ala	L-Alanine
MDAP	Meso-Diaminopimelate
Und-P	Undecaprenyl Phosphate

References:

1. D.Dai, E.E. Ishiguro. 1988. MurH, a New Genetic Locus in *Escherichia coli* Involved in Cell Wall Peptidoglycan Biosynthesis. J Bacteriol. 170(5):2197-201.

2. Chopra I, Storey C, Falla TJ, Pearce JH. 1998. Antibiotics, peptidoglycan synthesis and genomics: the chlamydial anomaly revisited. Microbiology 144, 2673-8. Review