Part 1

Metabolic Pathways

Roche Biochemical Pathways

4th Edition, Part 1 – Editor: Gerhard Michal

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General Remarks for Part 1 and 2

1) Enzymes are shown in blue. The "Recommended Names" in the "Enzyme Nomenclature 1984" (Academic Press, Orlando etc.) and its supplements (Eur.J. Biochem. 157,1 (1986) and 179, 489 (1989) are used. Enzymes not listed there are printed in parentheses.
2) Coenzymes are shown in red, other reaction participants in black.
3) Color of the arrows shows type of organism in which the reaction was obseved or is likely to occur:
   → general biochemical pathways, → animals,
   → higher plants, → unicellular organisms + fungi
   Dashed arrows are used for catabolic pathways, continuous lines for anabolic and bidirectional (amphibolic) pathways. Points on both ends of arrows indicate reversibility. An orange arrow alongsite of it shows the preferred direction.
4) Regulatory effects are shown in orange. Metal ions and similar activators are located next to the reaction arrow, Effectors with a "fast" regulation of the flow (e. g. by allosteric mechanisms) have a contiuos orange arrow coming from thr side,those with a "slow" regulation (e.g. induction or repression of the enzyme synthesis) a dashed orange arrow. ⊕ = increase, ⊖ = decrease of enzymatic activity. Roman numerals indicate, that that only one of multiple enzyems is regulated this way.Regulators shown in parentheses are effective in only one group or species of organisms.
5) Compounds enclosed in black lined, sharp edged boxes occur in several places in the chart. Coenzymes or compounds with very simple structures are not in boxes.
6) Boxes with rounded corners are sometimes used in part 2 to indicate enzymes (inactiv in black, active in blue). Protein sequences are abbreviated by ~~
7) Compound names in orange boxes indicate excretory or end- products of metabolism.
8) For ionized compounds, the name of the salt is used to correspond with enzyme names. Structural formulas, however, show the free acid or base, since frequently at physiclogical pH different grades of ionization occur simultaneously. Therefore, participation of H^+ or OH^- is not shown (except in $NADH+H^+$ and $NADPH+H^+$).
9) Organic phosphate is abbreviated to -P, inorganic phosphate to Pi, pyrophosphate to PPi.
10) All amino acids can be attached to their respective tRNAs by the appropriate ligases. Some of this reactions are shown here as examples.
11) Cellular surface membranes, membranes of the endplasmic reticulum, of the Golgi apparatus etc. have approximately the same thickness. For graphical raesons, however, they have been drawn in part 2 with different widths.
12) While notations for genes are written with small letters (e.g. raf.), the respective gene products (proteins) are written with captalized first letters (e.g. Raf.). Another way of designating them is p 74 $^{c\text{-}raf}$, indicating the molecular weight (in kD) and the origin (c = cellular, v = virus).

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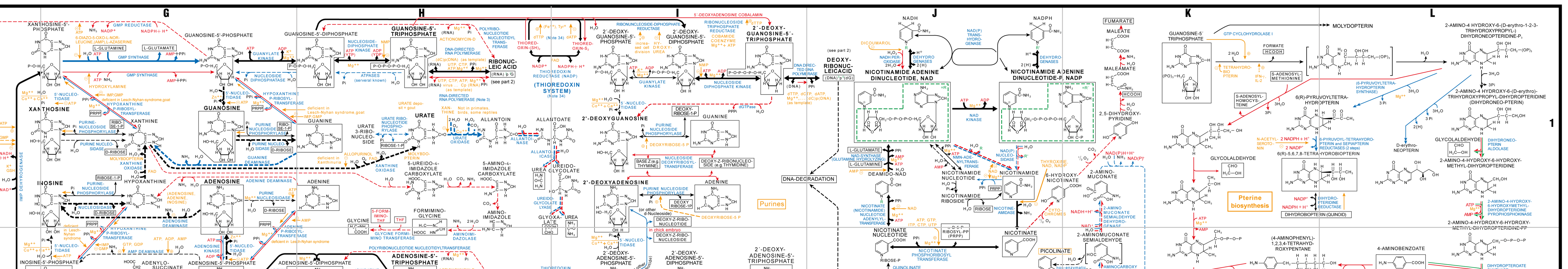
Abbreviations for Part 1

Acc	acceptor (in redox reactions)
ACP	acyl carrier protein
ACTH	adrenocorticotropic hormone
A-3,5-MP	(cyclic)adenosine-3′,5′-monophosphate (cAMP)
ATP, ADP, AMP, A	adenosine nucleotites,adenosine
CoASH,CoA-S-	coenzymeA
CTP,CDP,CMP,C	cytidine nucleotides,cytidine
CYT	cytochrome
dATPetc.	deoxynucleotides
DNA	deoxyribonucleic acid
E	enzyme
ETF	electron transferring flavoprotein (transfers electrons to ubiquinone)
F430	a corrinoid coenzyme (Ni)
$FAD,FADH_2$	flavin-adenine dinucleotide
Fd	ferredoxin
$FMN,FMNH_2$	flavin-adenine mononucleotide
Fp	flavoprotein
FSH	follicle-stimulating hormone
G6P	glucose 6-phosphate
GSH,GSSG	gluatathione,oxidized glutathione
GTP,GDP,GMP,G	guanosine nucleotides,guanosine
HCG	chorionic gonadotropin
HTP	mercaptoheptanoyl-threonine-P
IFN-γ	interferon γ
ITP,IDP,IMP,I	inosine nucleotides,inosine
LH	luteinizing hormone
Lip<SH SH, Lip<S S	α-lipoate
MFR	methanofuran
N	any nucleotide,nucleoside,nucleobase
$NAD^+,NADH+H^+$	nicotinamide-adenine dinucloetide
$NADP^+, NADPH+H^+$	nicotinamide-adenine dinucloetide phosphate
OSCP	oligomycin sensitive conferring protein
PAP	adenosine-3′,5′-diphosphate
PAPS	3′-phospho-adenylylsulfate
PEP	phosphoenolpyruvate
PQQ	pyrroloquinoline quinone
PRRP	α-D-5-phosphoribosyl-pyrophosphate
Pyr P	pyridoxal 5-phosphate
RNA	ribonucleic acid
mRNA,rRNA,tRNA	messenger,riposomal,transfer RNA
R-S-S-R	disulfide of amino acids or pepdides
THF	5,6,7,8-tetrahydrofolate
THMPT	5,6,7,8-tetrahydromethanopterin
ThPP	thiamine pyrophosphate (cocarboxylase)
TTP,TDP,TMP,T	deoxythymidine nucleotides, deoxythymidine
UDPG	Uridine diphosphate glucose
UTP,UDP,UMP,U	uridine nucleotides,uridine

Notes for Part 1

1) 5-Dehydro-4-deoxy-D-glucarate is also split by this enzyme.
2) Intermediates are likely L-galactonate and L-galactonolactone. The latter compound, in turn,is oxidized by galactonolactone dehydrogenase or L-galactonolactone oxidase.
3) RNA-directed RNA polymease (replicase) is active in RNA-virus infected cells.
4) Choline oxidase also oxidizes betaine aldehyde to betaine,forming H_2O(*in vitro* H_2O_2).
5) In some conditions, chlorophyllide a can be esterified by geranylgeranyl pyrophosphate,followed by its reduction to phytol.
6) In most bacteriochlorophylls,ring B is also reduced (besides ring D,common to all chlorophylls).
7) In animals, the fatty acid is removed from ACP by oleyl-[ACP] hydrolase and is subsequently converted to acyl-CoA.
8) This conversion proceeds by kinase and uridilyltransferase reactions.
9) Intermediates in the glucoronate conversion by induced enzymes in *E.coli* are D-fructuronate and D-mannonate,in the galacturonate conversion D-tagaturonate and D-altronate.
10) In some microorganisms,cystathionine synthesis takes place via O-acetyl-L-homoserine.
11) The enzyme funktions for formation and degration of fructose-2,6-bisphosphate are located on the same peptide chain.Their relative activities are regulated by phosphorylation and dephosphorylation.In muscle,the phophorylated enzyme increases biphosphate formation. In liver, it is the dephosphorylated enzyme which shows this effect.
12) While in microorganisms the existence of 2 enzymes has been established,in Mammals probably only 1 bifunctional enzyme exists.
13) The equilibrium of the reaction is shifted homocysteine through removal of adenosine via adenosine deaminase reaction.
14) Glutamate dehydrogenase is activated by phosphorylation,catalyzed by protein kinase A or possibly by calmodulin-dependent protein kinase and activator protein. It is deactivated by dephosphorylation,which is catalyzed by a phosphatase.
15) The identity of the enzymes catalyzing both reactions has not been proven completely.
16) In *Pseudomonas*, the reaction proceeds via 5-aminovaleramide,5-aminovalerate and glutarate semialdehyde.
17) In yeast, the reaction proceeds via 2-hydroxy-6-aminocapronate and further intermediates or via 5-acetamidovalerate and further steps similar to *Pseudomonas*.
18) Only peptide-bound lysine and proline are hydroxylated.
19) The malonate semialdehyde pathway is mostly used by algae (e.g.*Prototheca zopfii*), a malonate semialdehyde-CoA pathway by *Clostridium kluyveri*.
20) (S-adenosyl-5′)-3-methylthiopropylamine is formed from S-adenosylmethionine by S-adenosylmethionine decarboxylase.It is involved in spermidine and spermine biosynthesis.
21) 4 enzymes of this function are known (crotonyl-, 3-hydroxyoctanoyl-, 3-hydroxydecanoyl- and 3-hydrxypalmitoyl-ACP dehydratases).
22) The *E.coli* sequence is shown. In animals, 4-hydroxybenzoate is formed from phenylpyruvate or 4-hydrxyphenylpyruvate. The further steps proceed via coenzyme A derivatives and in a different order.
23) Other Enzymes catalyzing conversions of lactate to pyruvate are D-2-hydroxyacid dehydrogenase and glycolate oxidase.
23) NAD is used by the liver enzyme, NADP or both coenzymes by microbial enzymes.
25) NAD s used by the maize and by a yeast enzyme, NADP by another yeast enzyme, both coenzymes by animal enzymes.
26) Presqualene diphosphate or prephytoene diphosphate are intermedites of these reactions.
27) The conversion proceeds in 3 steps,catalyzed by the enzymes aquacobalamin reductase (to cob(II)alamin),cob(II)alamin reductase (to cob(I)alamin) and cob(I)alamin adenosyltransferase.
28) Siderochromes have also been demonstratet in mammalian liver.
29) Degradation proceeds similarly to lecithin degradation.
30) Other enzymes (glycerol dehydrogenase and glycerol 2-dehygrogenase) convert glycerol to dihydroxyacetone (=glycerone).
31) Mitochondrial chain elongation of palmitoyl-CoA occorus by reversal of ß-oxitation.Only enoyl-CoA reductase is different.The microsomal system employs malonyl-CoA instead of acetyl -CoA.
32) The yeast system is shown here.The central SH group is written at the bottom,the marginal SH group at the top. In animals and in *E.coli*, the enzyme, $E(SH)_2$,is replaced by acyl carrier protein, ACP.
33) Examples are GSH-homosystine transhydrogenase and protein disulfide reductase.
34) Reduction of nucleoside diphosphates was observed in *E.coli* and in eukaryotes. Reduction of nucleoside triphosphates takes place in *Lactobacillus leichmannii.* In *E.coli*, thioredoxin and thioredoxin reductase may be replaced by glutaredoxin,glutathione reductase and by glutathione.
35) The enzymes are induced in T-even-phage-infected E.coli.
36) Pancreas DNase I split this way.The *Streptococcus* enzyme splits preferably between pyrimidine and purine groups, forming 5′-nucleotides. Other splitting types are also known.
37) In many species,the biosynthesis of purines, pyramidines,amino acides,fatty acides etc. is performed by multienzyme complexes or even multifunctional proteins.
38) NADP is used by animal and yeast enzymes,NAD by the bacterial enzyme.
39) Intermediates are phytofluene and ζ-carotene. An isomerization *cis* *trans* takes place.
40) Formation of α- and ß-carotene occurs via γ-carotene.α-carotene may also be formed via δ-carotene. Pathways starting with a cyclization of neurosporene have been discussed.
41) The regulation of cholesterol 7 α-monooxygenase is correlated to the regulation of hydroxymetheylglutaryl-CoA reductase.
42) This reaction may also occur with the 26-hydoxylated compound.
43) These steps are analogous to the reactions of cholate precursors.
44) These reactions appear to be similar to fatty acid activation and ß-oxydation of fatty acids.
45) From deoxycholate, several other compounds are also formed.
46) Intermediates of this multistep reaction in *Psydomonas* have been described.
47) A ß-oxidation type reaction takes place.
48) In plants,epoxysqualene cyclization leads to cycloartenol.
49) Many C_1 transfer reactionstake place with polyglutamyl derivatives of tertahydrofolate. Glutamate addition to the tetrahyrofolate moiety is catalyzed by folylpolyglutamate synthase(EC 6.3.2.17).