AROMATIC AMINO ACID DEGRADATION AND ASSOCIATED INBORN ERRORS OF METABOLISM

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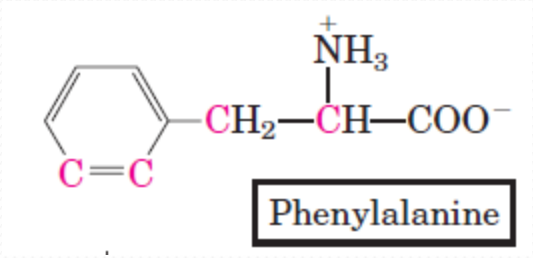
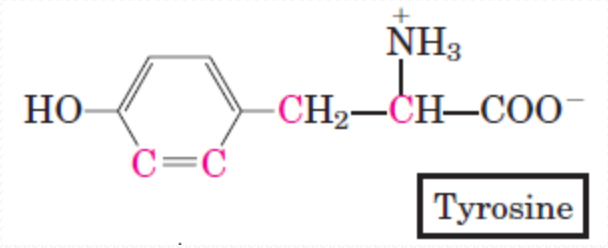
AROMATIC AMINO ACID DEGRADATION

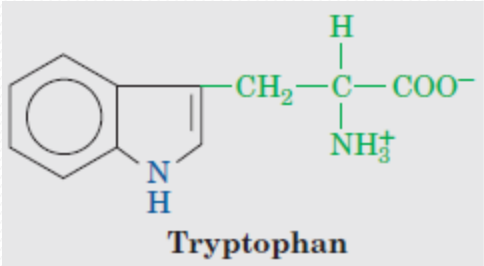
- The aromatic amino acids are those containing aromatic or benzene ring in their side chains
- Examples include phenylalanine, tyrosine and tryptophan
- The degradation of aromatic amino acids require molecular oxygen to break down the aromatic rings



Phenylalanine

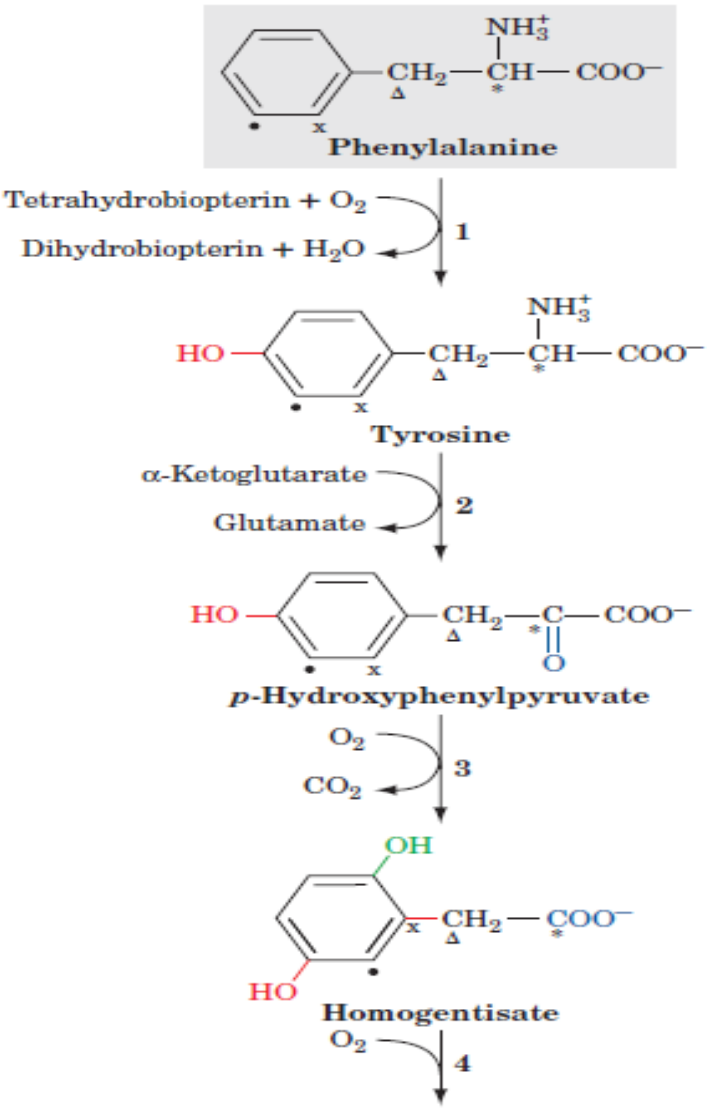


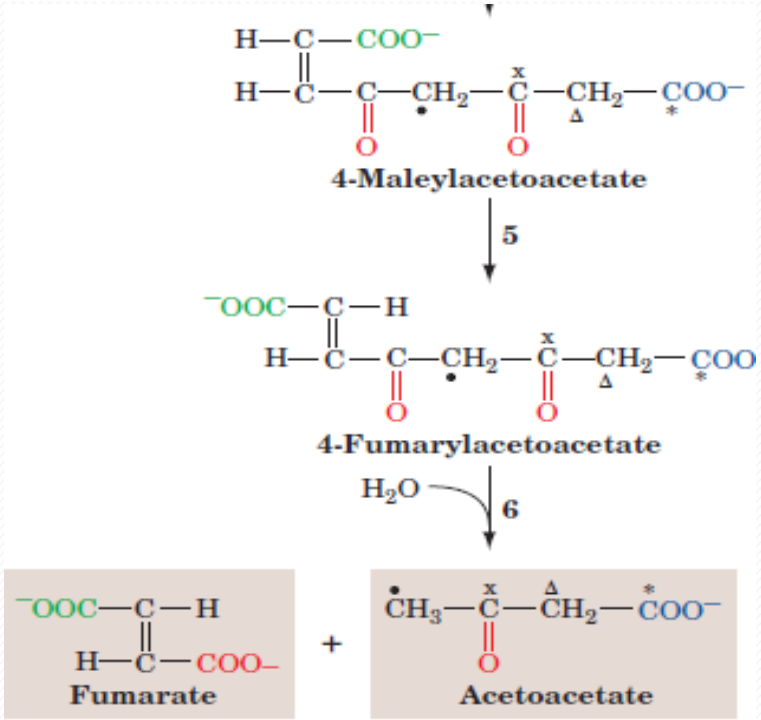
Tyrosine



Tryptophan

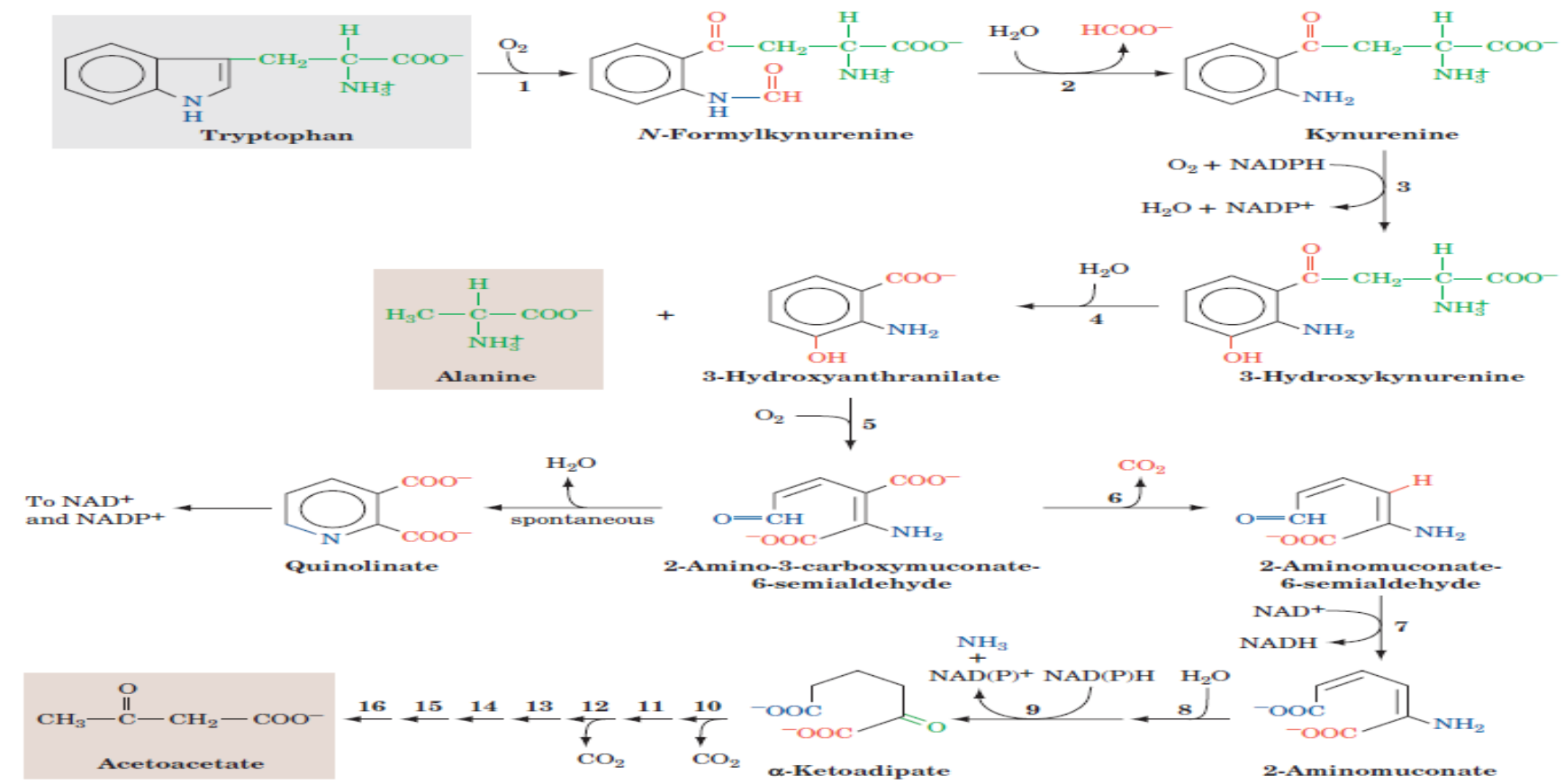
DEGRADATION OF PHENYLALANINE





enzymes involved are (1) phenylalanine hydroxylase, (2) aminotransferase, (3) *p*-hydroxyphenylpyruvate dioxygenase, (4) homogentisate dioxygenase, (5) maleylacetoacetate isomerase, and (6) fumarylacetoacetase.

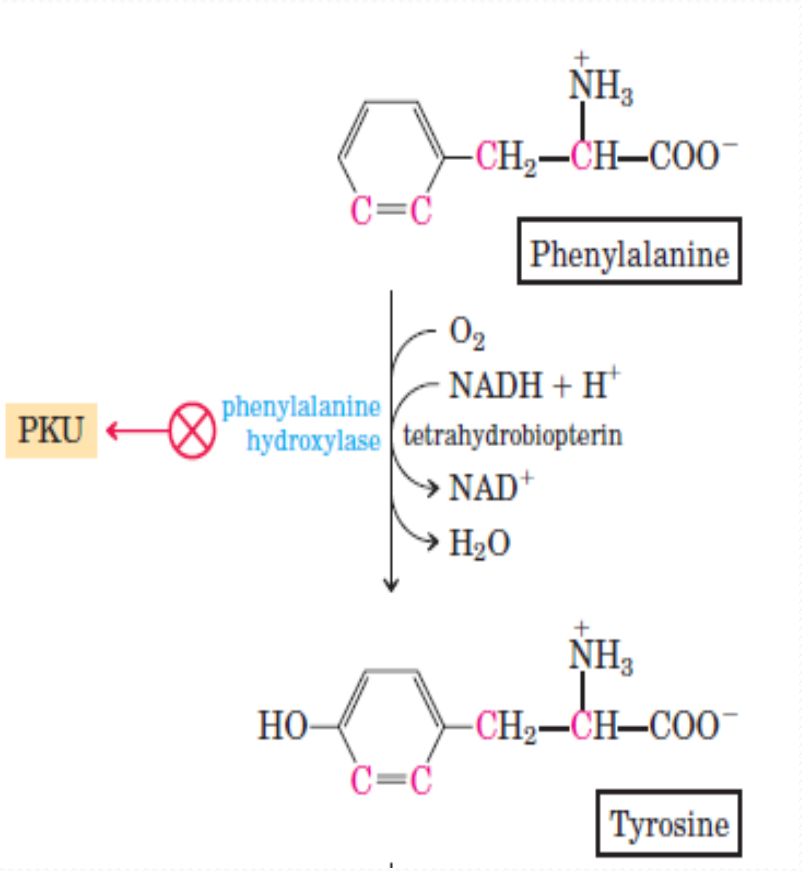
DEGRADATION OF TRYPTOPHAN



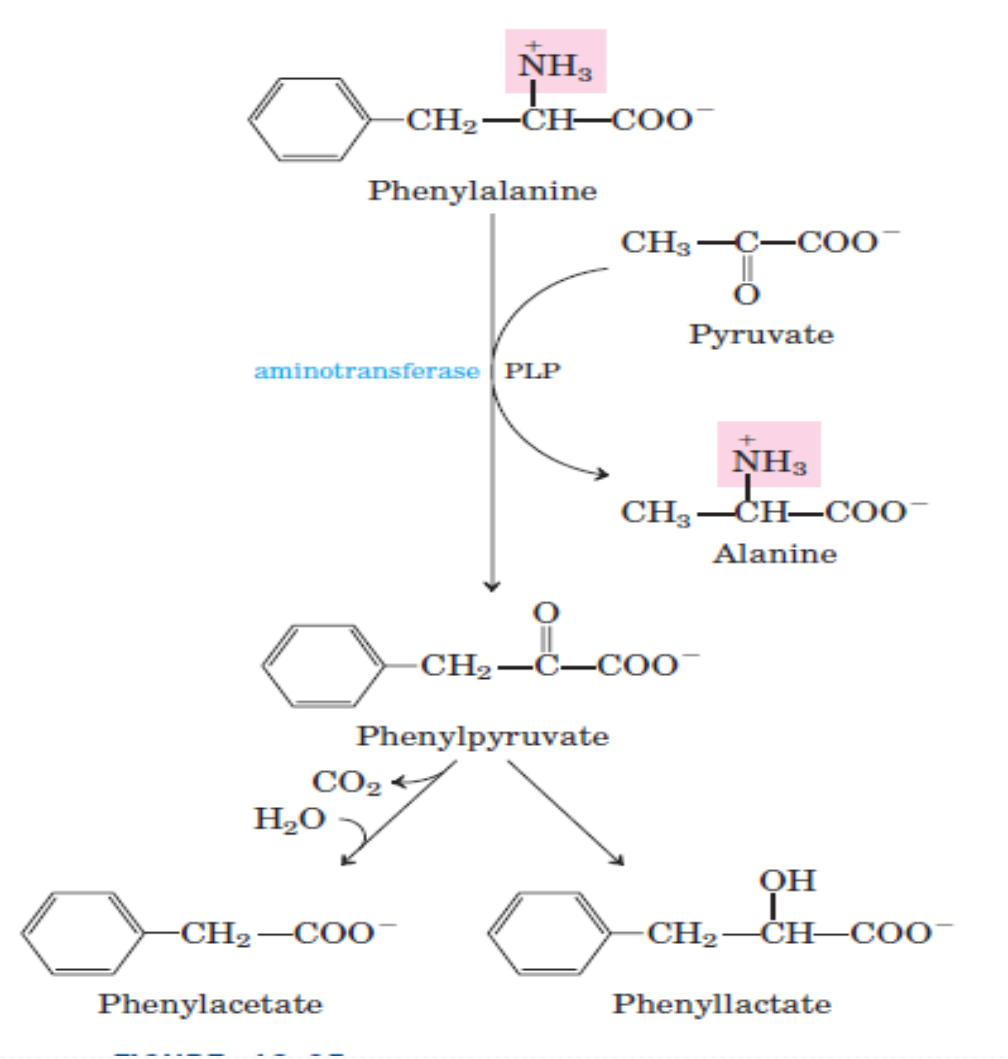
The pathway of tryptophan degradation. The enzymes involved are **(1)** tryptophan-2,3-dioxygenase, **(2)** formamidase, **(3)** kynurenine-3-monooxygenase, **(4)** kynureninase (PLP dependent), **(5)** 3-hydroxyanthranilate-3,4-dioxygenase, **(6)** amino carboxymuconate semialdehyde decarboxylase, **(7)** aminomuconate semialdehyde dehydrogenase, **(8)** hydratase, **(9)** dehydrogenase, and **(10–16)** enzymes of Reactions 5 through 11 in lysine degradation (Fig. 26-23). 2-Amino-3-carboxymuconate-6-semialdehyde, in addition to undergoing Reaction 6, spontaneously forms **quinolinate,** an NAD^+ and $NADP^+$ precursor

INBORN ERRORS OF METABOLISM: PHENYLKETONURIA

- Many genetic defects of phenylalanine catabolism in humans have been identified
- A deficiency in phenylalanine hydroxylase is responsible for the disease phenylketonuria (PKU)
- Individuals with a deficiency in phenylalanine hydroxylase rely on a secondary catabolic pathway which in normal individuals is not used

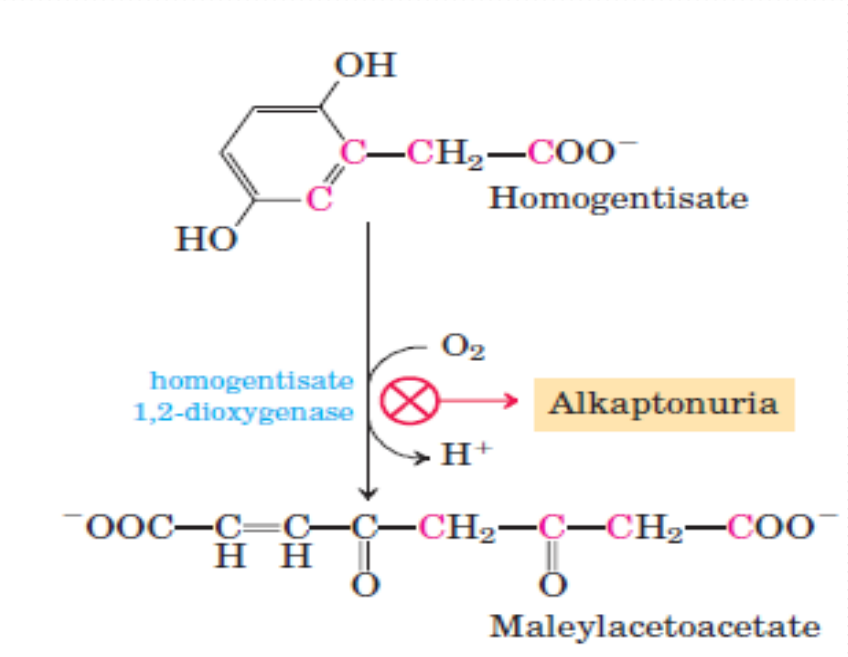


INBORN ERRORS OF METABOLISM: PHENYLKETONURIA CONT'D

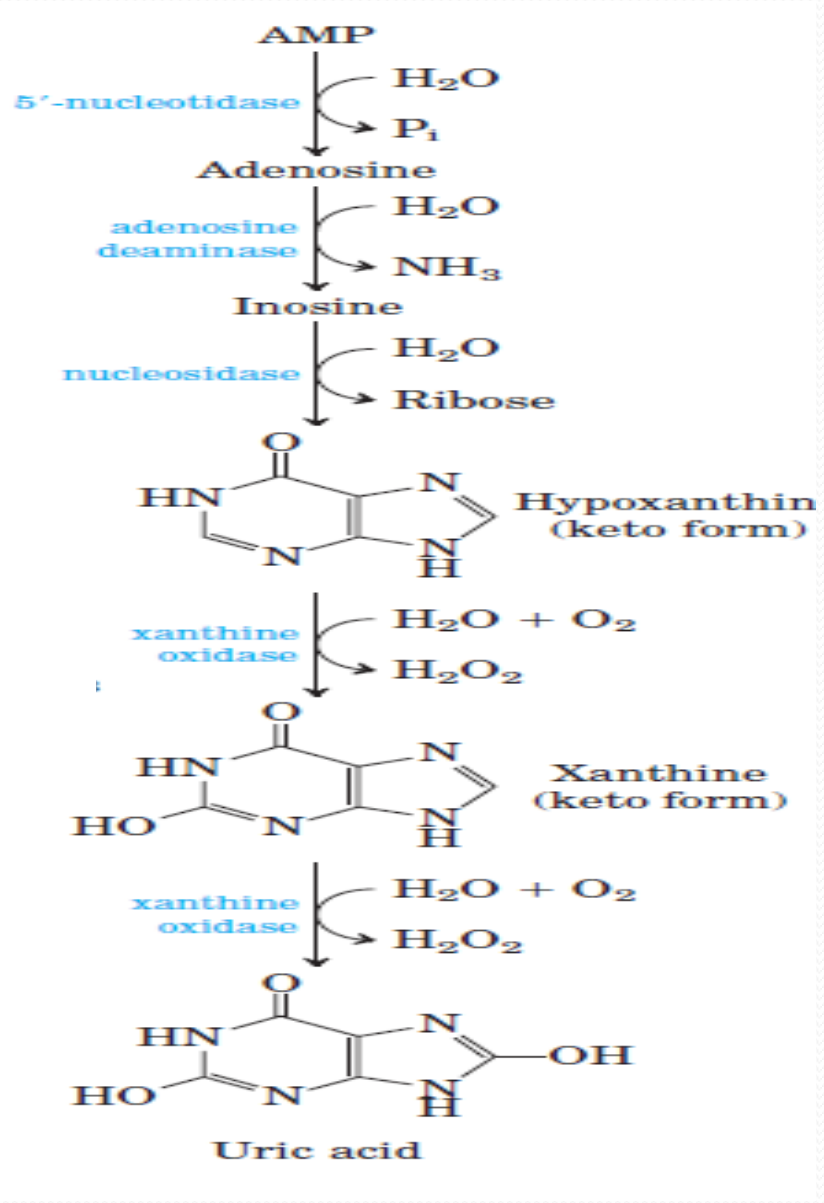


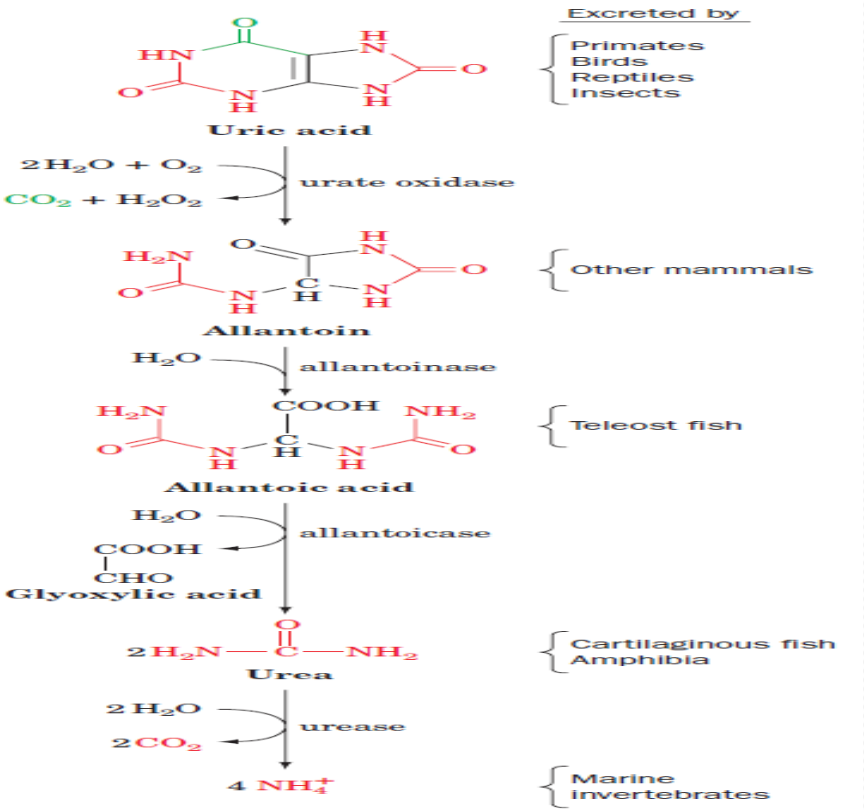
INBORN ERRORS OF METABOLISM:ALKAPTONURIA

- Another inheritable disease of phenylalanine catabolism is alkaptonuria in which the defective enzyme is homogentisate dioxygenase
- It less serious than PKU



METABOLIC OF URIC ACID





INTERGRATION AND COMPARTMENTATION IN INTERMEDIARY METABOLISM

- Metabolism is the sum of all the chemical transformations taking place in a cell or organism
- It occurs through a series of enzyme-catalyzed reactions that constitute metabolic pathways
- Metabolism is broadly divided into anabolism and catabolism
- Precursors are converted into products through a series of metabolic intermediates called metabolites
- The term intermediary metabolism is often applied to the combined activities of all metabolic pathways that interconverts precursors, metabolites and products of low molecular weights

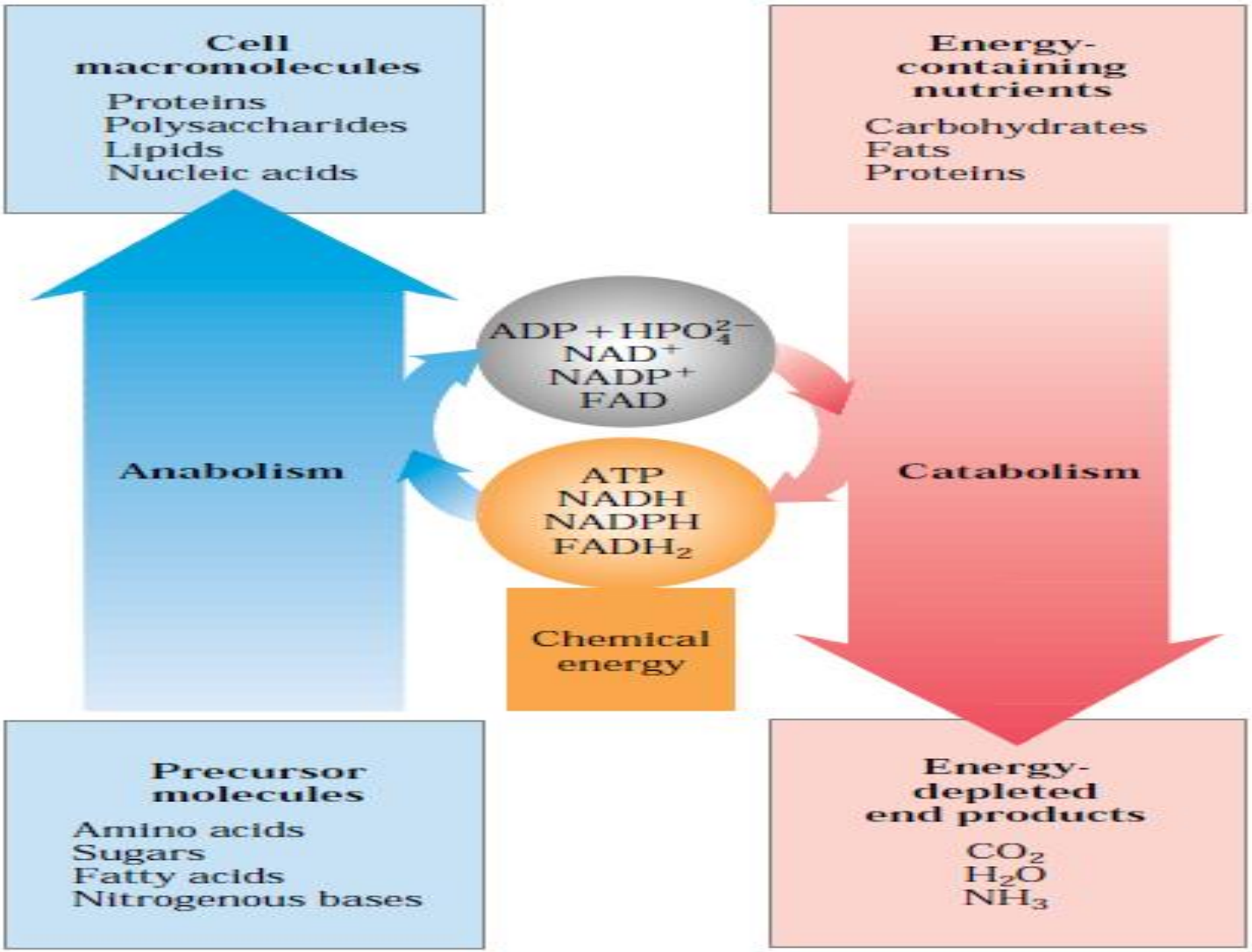
INTERGRATION AND COMPARTMENTATION IN INTERMEDIARY METABOLISM CONT'D

- Catabolism is the degradative phase of metabolism in which organic nutrient molecules (carbohydrates, fats and proteins) are converted into smaller, simpler end products (such as lactic acid, Co2 and NH_3
- Catabolic pathways release energy , some of which is conserved in the formation of ATP and reduced electron carriers (NADH,NADPH and $FADH_2$); the rest as heat
- In Anabolism, also called biosynthesis, small simple precursors are built into larger and more complex molecules including lipids, polysaccharides, proteins and nucleic acids
- Anabolic reactions require an input of energy, generally in the form of the phosphoryl group transfer potential of ATP and the reducing power of NADH,NADPH and $FADH_2$

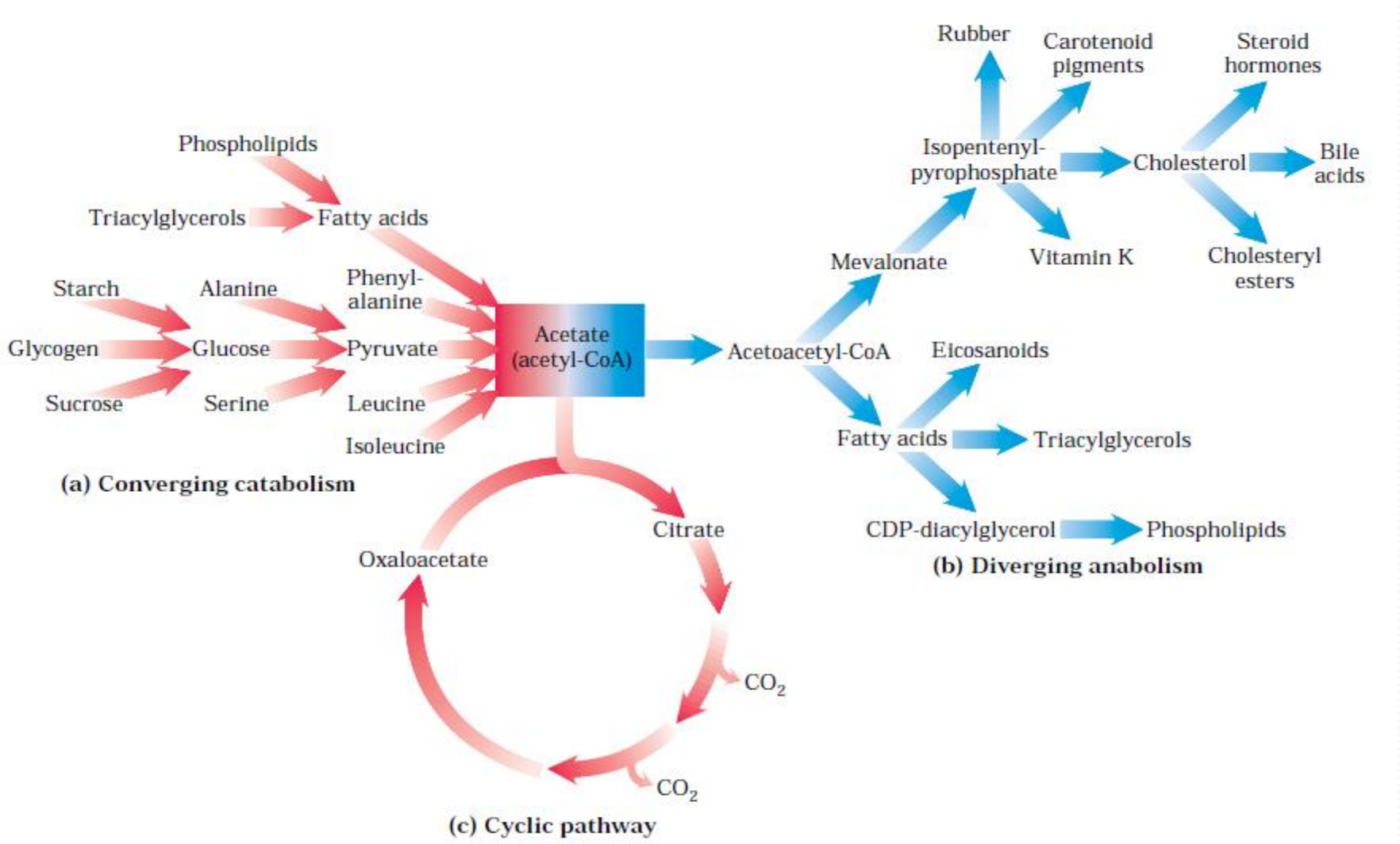
INTERGRATION AND COMPARTMENTATION IN INTERMEDIARY METABOLISM CONT'D

- Some metabolic pathways are linear, and some are branched, yielding multiple useful end products from a single products
- In general, catabolic pathways are convergent and
- Anabolic pathways divergent
- Some pathways are cyclic: one starting point of the pathway is regenerated in a series of reactions that converts another starting component into a product
- Anabolic and catabolic reactions are reciprocally regulated, when one is active, the other is supressed
- Paired catabolic and anabolic reactions/pathways commonly take place in different cellular compartments- as a further contribution to regulation

INTERGRATION AND COMPARTMENTATION IN INTERMEDIARY METABOLISM CONT'D



INTERGRATION AND COMPARTMENTATION IN INTERMEDIARY METABOLISM CONT'D



INTEGRATION OF METABOLISM

- The co-ordination between three metabolites (carbohydrates, lipids and protein) is called integration of metabolism
- Integration of metabolism ensures a supply of suitable fuel for all tissues, at all times
- The major pathways*glycolysis*gluconeogenesis*T.C.A cycle, pentose phosphate pathways*glycogen and fat metabolism* are all coordinately regulated and integrated to meet the needs of the cell
- Integration of metabolism must be studied at two levels (a) cellular (b) tissue and organ level

INTEGRATION OF METABOLISM, CONT'D

(a) integration of metabolism at cellular level

- It includes the flow of key metabolites (glucose, fatty acids, glycerol and amino acids) between different metabolic pathways at cellular levels

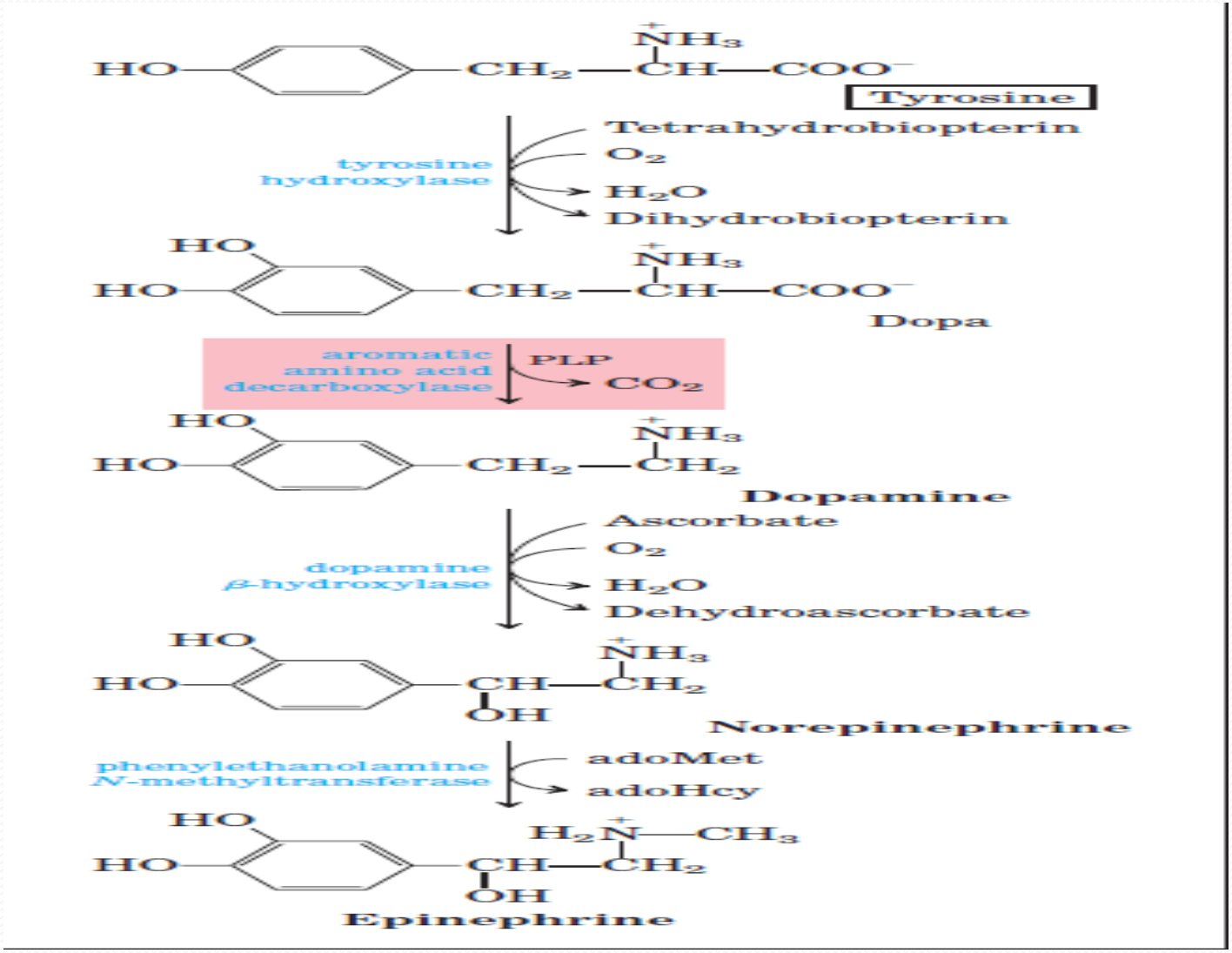
(b) Integration of metabolism at tissue or organ level

This includes the inter-relationship of different tissues and organs to meet metabolic demands for the whole body

BIOSYNTHESIS OF HORMONES DERIVED FROM AMINO ACIDS

- Amino acids are the building blocks of peptides and proteins.
- They also serve as precursors of specialized biomolecules, such as hormones, coenzymes, nucleotides e.t.c
- The amino acid –derived hormones include epinephrine and norepinephrine, which are synthesized in the medulla of the adrenal glands and thyroxine, which is produced by the thyroid gland

BIOSYNTHESIS OF EPINEPHRINE AND NOREPHRINE



BIOSYNTHESIS OF THYROID HORMONES

- The thyroid gland produces two related hormones, triiodothyronine (T3) and thyroxine (T4)