Synthesis of melanin

Melanin (Greek : melan—black) is the pigment of skin, hair and eye. The synthesis of melanin occurs in melanosomes present in melanocytes, the pigment-producing cells. Tyrosine is the precursor for melanin and only one enzyme, namely **tyrosinase** (a copper-containing oxygenase), is involved in its formation. Tyrosinase hydroxylates tyrosine to form 3,4-dihydroxyphenylalanine (DOPA) (**Figure 1**). DOPA can act as a cofactor for tyrosinase. The next reaction is also catalysed by tyrosinase in which DOPA is converted to dopaquinone. It is believed that the subsequent couple of reactions occur spontaneously, forming leucodopachrome followed by 5,6-dihydroxyindole. The oxidation of 5, 6-dihydroxyindole to indole 5, 6-quinone is catalysed by tyrosinase, and DOPA serves as a cofactor. This reaction, inhibited by tyrosine regulates the synthesis of melanin. **Melanochromes** are formed from indole quinone, which on **polymerization** are converted **to black** melanin.

Another pathway from dopaquinone is also identified. Cysteine condenses with dopaquinone and in the next series of reactions results the synthesis of red melanins. The structure of melanin pigments is not clearly known.

Melanin—the colour pigment :

The skin colour of the individual is determined by the relative concentrations of black and red melanins. This, in turn, is dependent on many factors, both genetic and environmental. These include the activity of tyrosinase, the density of melanocytes, availability of tyrosine etc. The presence of **moles** on the body represents a localized severe **hyperpigmentation** due to hyperactivity of melanocytes. On the other hand, localized absence or degeneration of melanocytes results in **white patches** on the skin commonly known as **leucoderma**. **Greying of hair** is due to lack of melanocytes at hair roots. **Albinism** is an **inborn error** with generalized lack of melanin synthesis.

Biosynthesis of catecholamines

The name catechol refers to the **dihydroxylated phenyl ring**. The amine derivatives of catechol are called catecholamines. Tyrosine is the precursor for the synthesis of catecholamines, namely **dopamine**, **norepinephrine** (noradrenaline) and **epinephrine** (adrenaline).

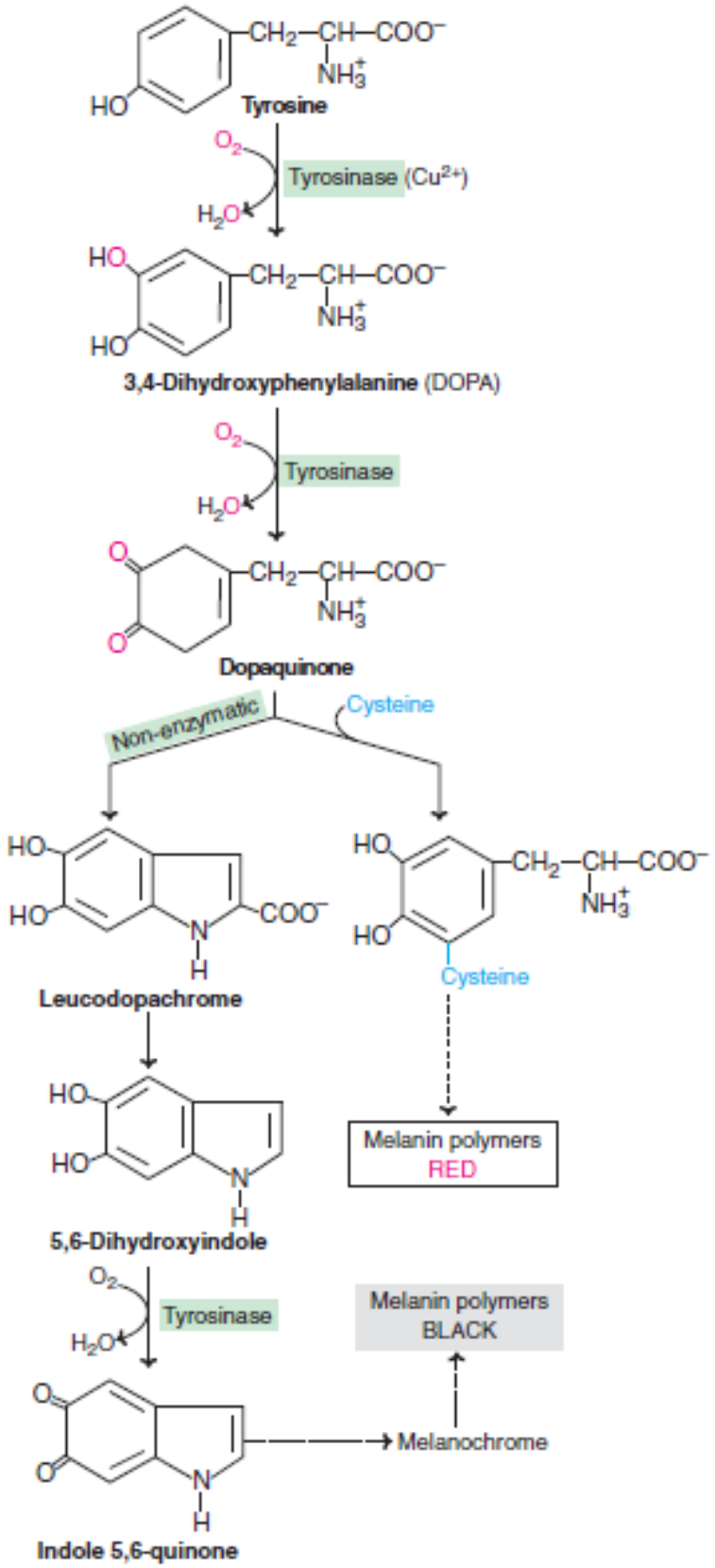

Figure 1: Metabolism of tyrosine—biosynthesis of melanin

The conversion of tyrosine to catecholamines occurs in adrenal medulla and central nervous system involving the following reactions (**Figure 2**). Tyrosine is hydroxylated to 3,4-dihydroxyphenylalanine (DOPA) by **tyrosine hydroxylase**. This enzyme catalyses the **rate limiting** reaction and requires tetrahydrobiopterin as coenzyme (like phenylalanine hydroxylase). In contrast to this enzyme, tyrosinase present in melanocytes converts tyrosine to DOPA. Hence, two different enzyme systems exist to convert tyrosine to DOPA. DOPA undergoes PLP-dependent decarboxylation to give dopamine which, in turn, is hydroxylated to produce norepinephrine. Methylation of norepinephrine by S-adenosylmethionine gives epinephrine. The difference between epinephrine and norepinephrine is only a methyl group (remember that **nor**epinephrine has **no** methyl group). There exists tissue specificity in the formation of catecholamines. In adrenal medulla, synthesis of the hormones, norepinephrine and epinephrine is prominent. Norepinephrine is produced in certain areas of the brain while dopamine is predominantly synthesized in substantia nigra.

Functions of catecholamines : Norepinephrine and epinephrine regulate carbohydrate and lipid metabolisms. They stimulate the degradation of triacylglycerol and glycogen. They cause an increase in the blood pressure. Dopamine and norepinephrine serve as neurotransmitters in the brain and autonomous nervous system.

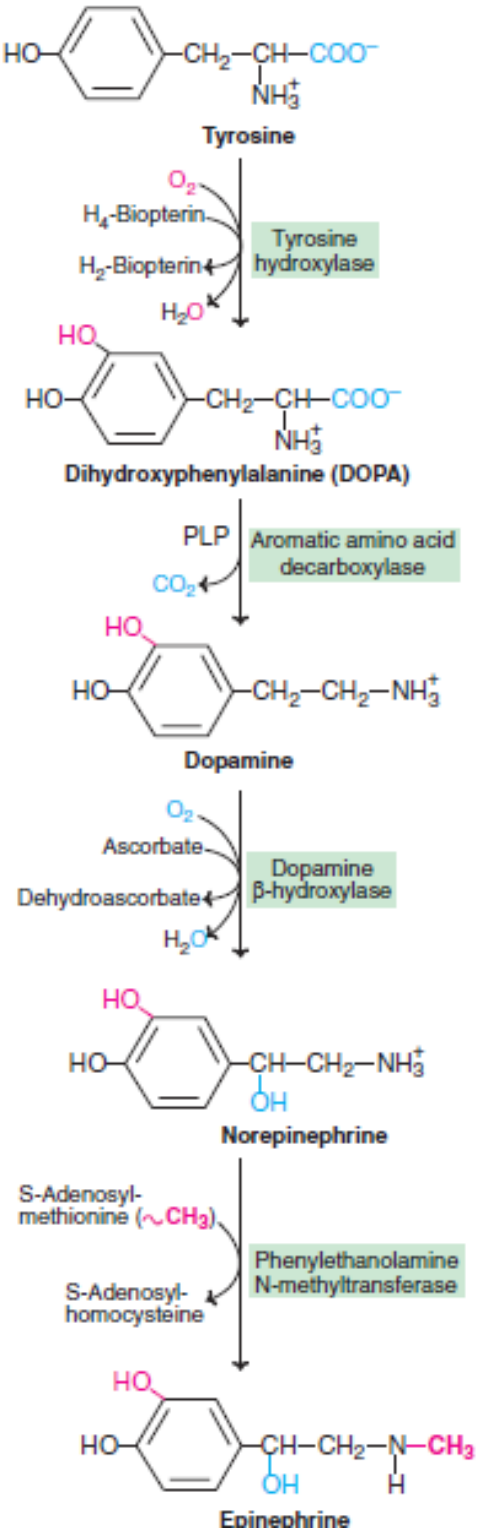

Figure 2: Metabolism of tyrosine-synthesis of catecholamines (dopamine, norepinephrine, epinephrine; PLP–pyridoxal phosphate).