DISORDERS OF PIGMENTATION

TYBSC PAPER II

SKIN PIGMENTATION

- Normal human skin color ranges from white to brown to black

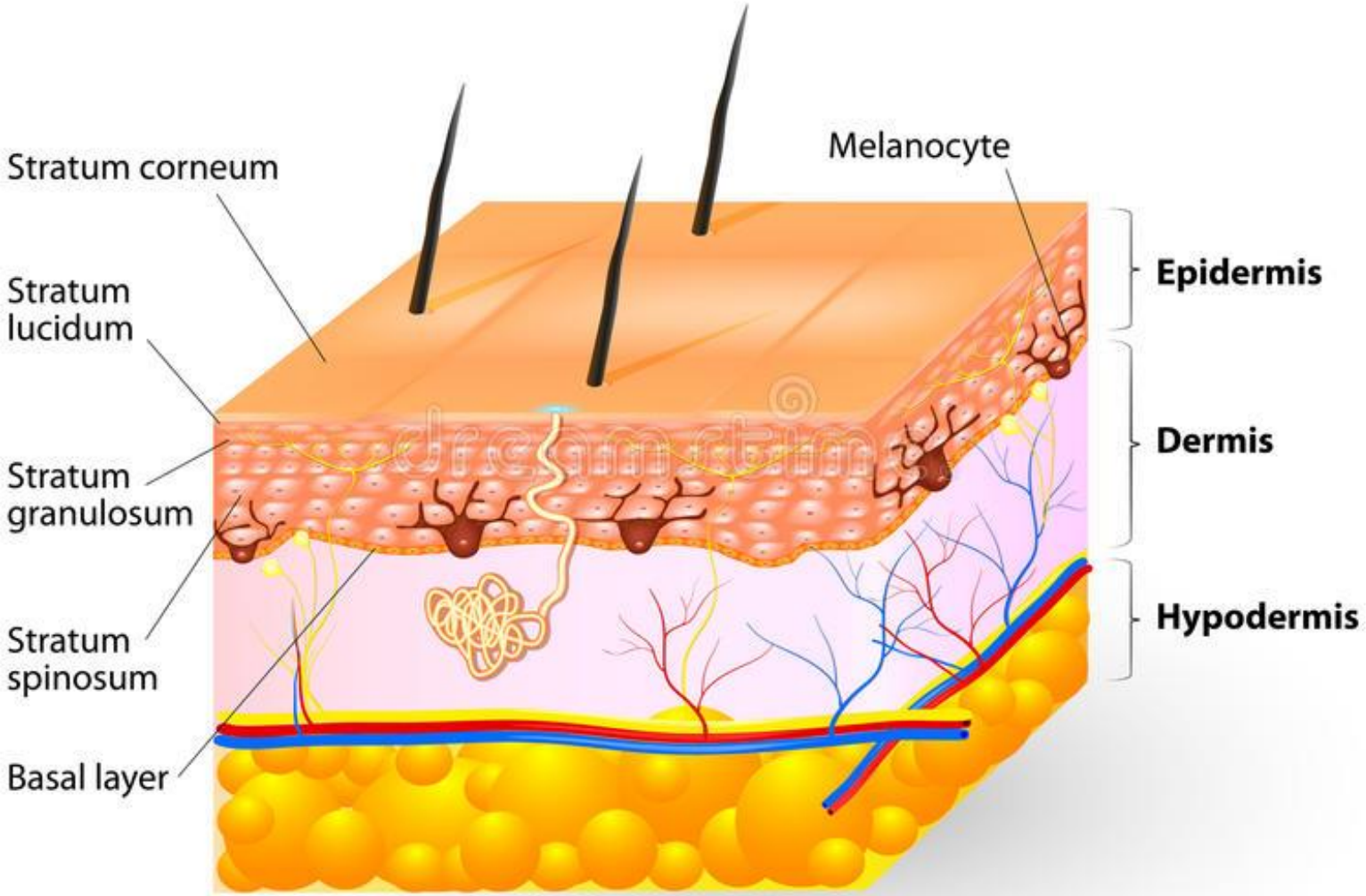
Results from the mixed contribution of 3 pigments:

- **Oxygenated hemoglobin (red)** in the capillaries
- **Reduced hemoglobin (blue)** in the venules of the dermis
- Endogenously produced **melanin (brown).**

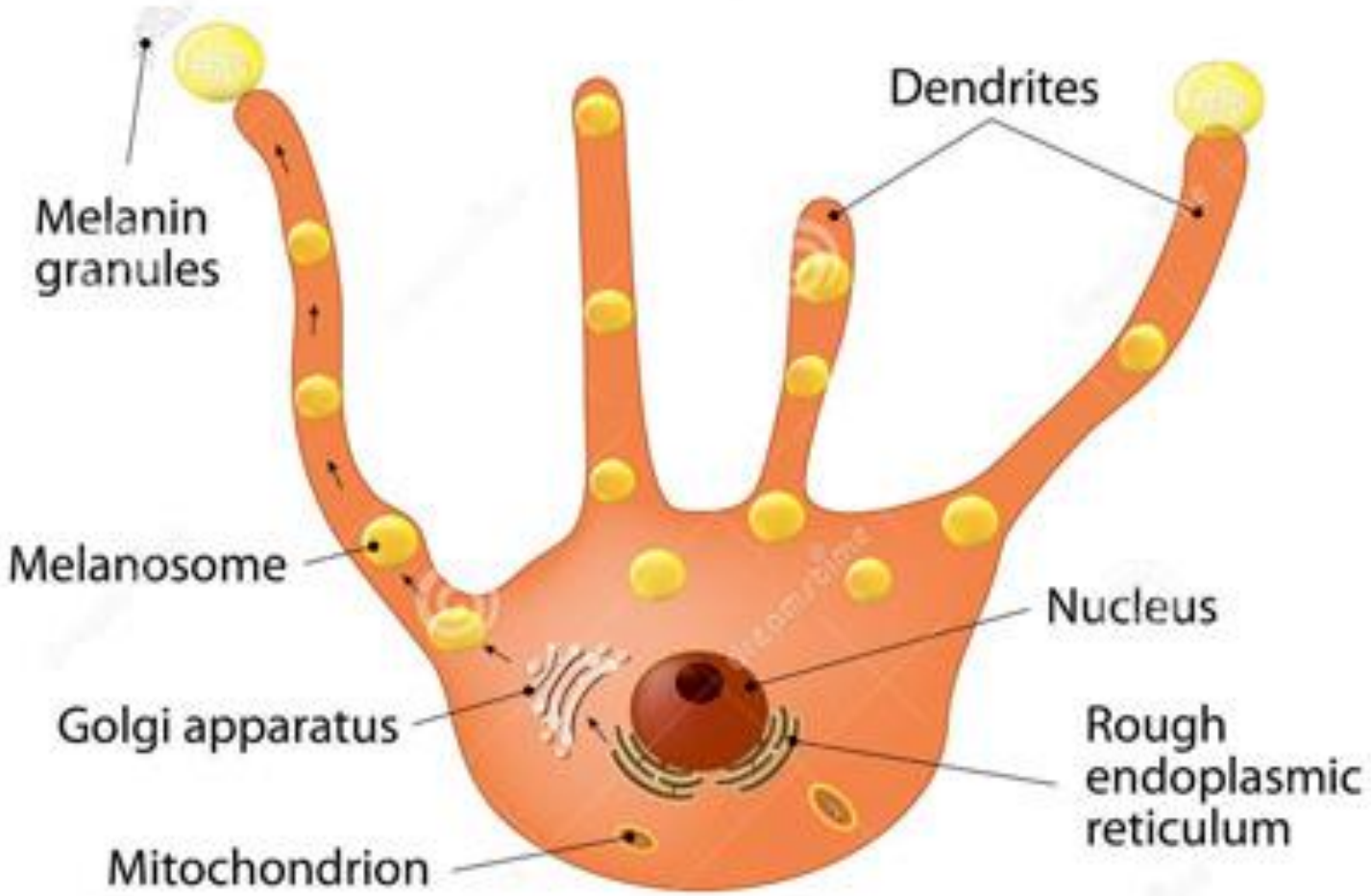
SKIN PIGMENTATION

- Amount and type of **Melanin** pigment produced
- **Melanosomes**
- By Cutaneous and Follicular **Melanocytes**
- Largely determine the differences in skin and hair color between individuals.

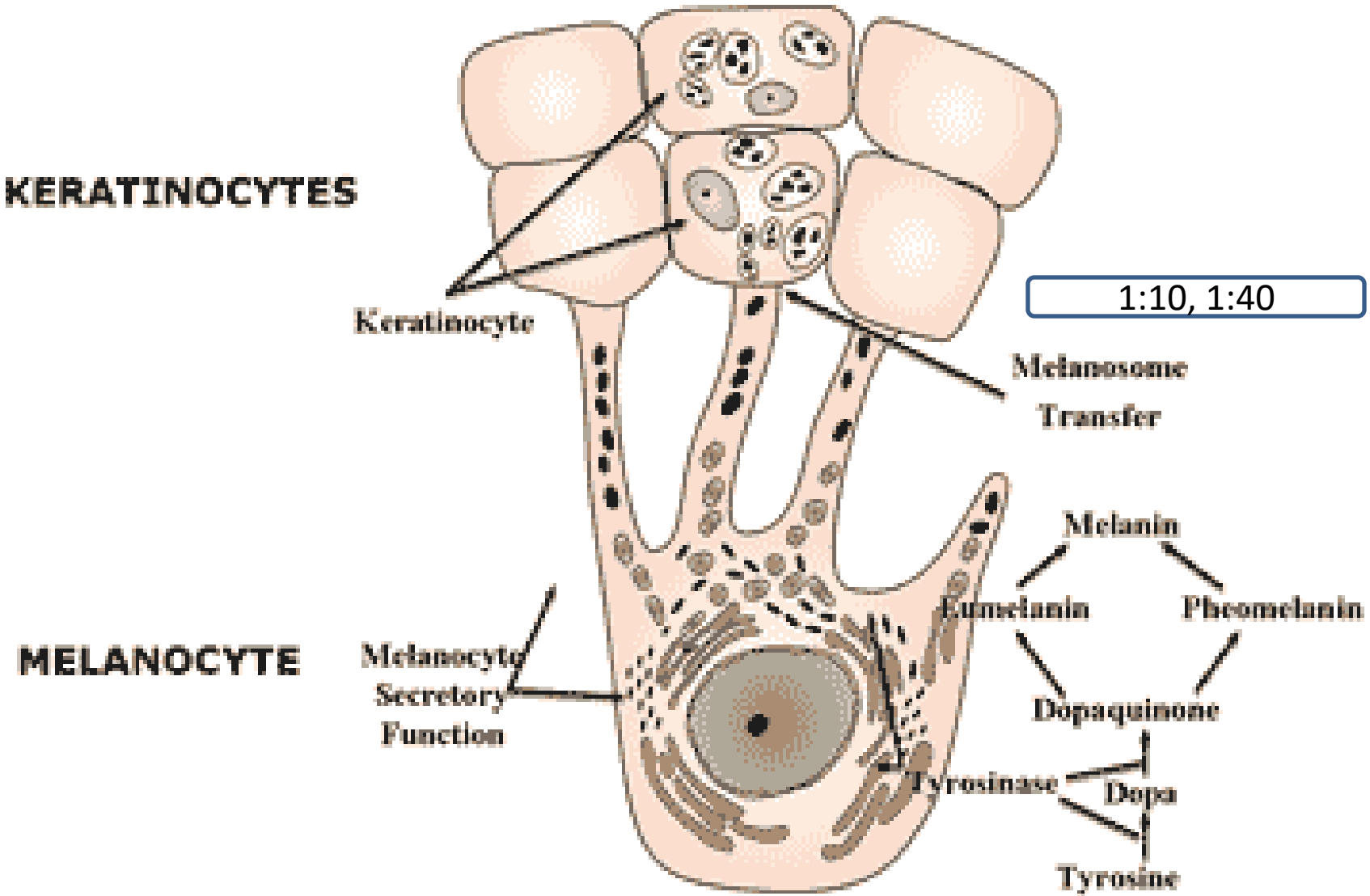
THE LAYERS OF HUMAN SKIN



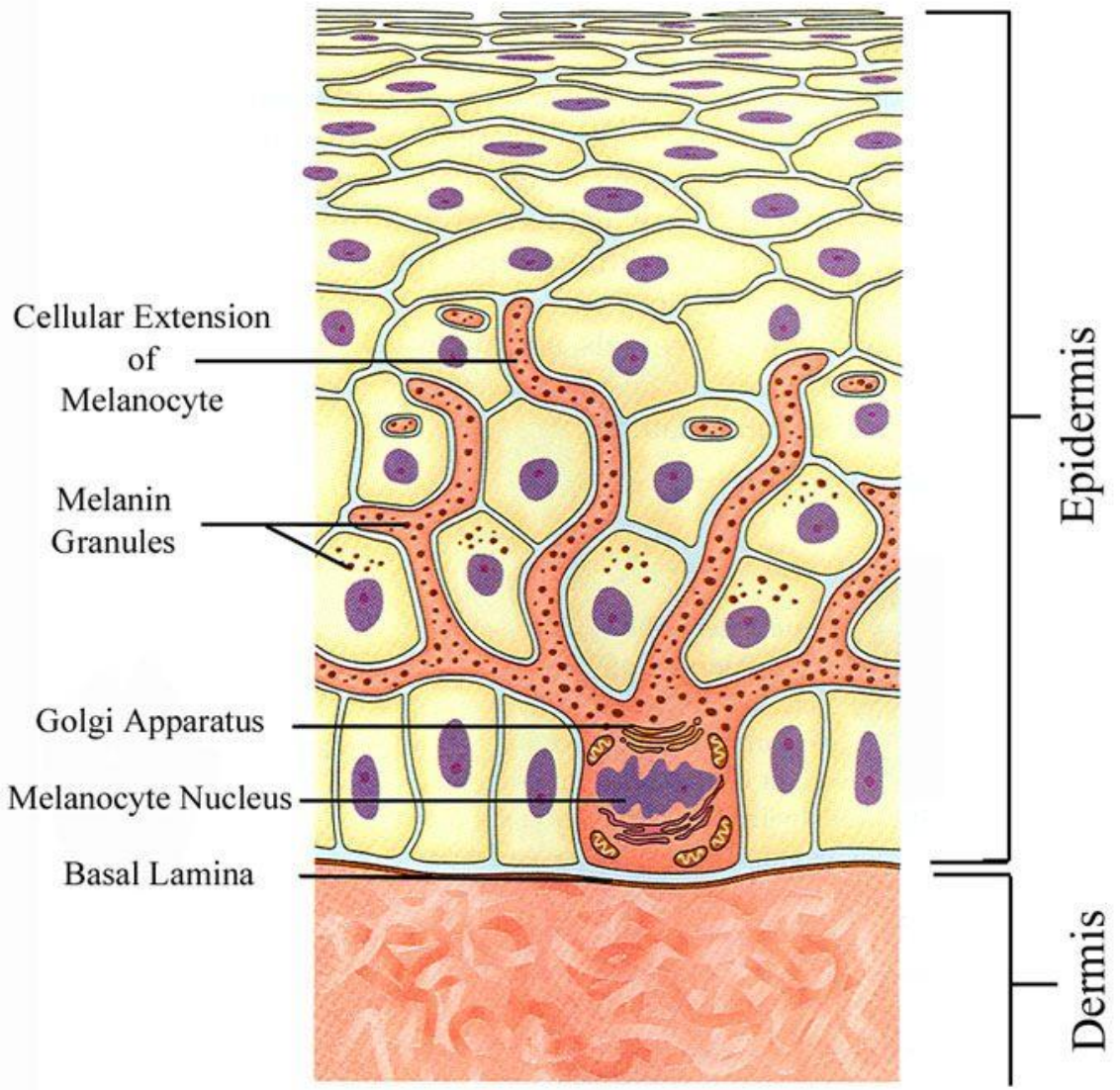
MELANOCYTE


Dendrites
Melanin granules
Melanosome
Nucleus
Golgi apparatus
Rough endoplasmic reticulum
Mitochondrion

EPIDERMAL MELANIN UNIT



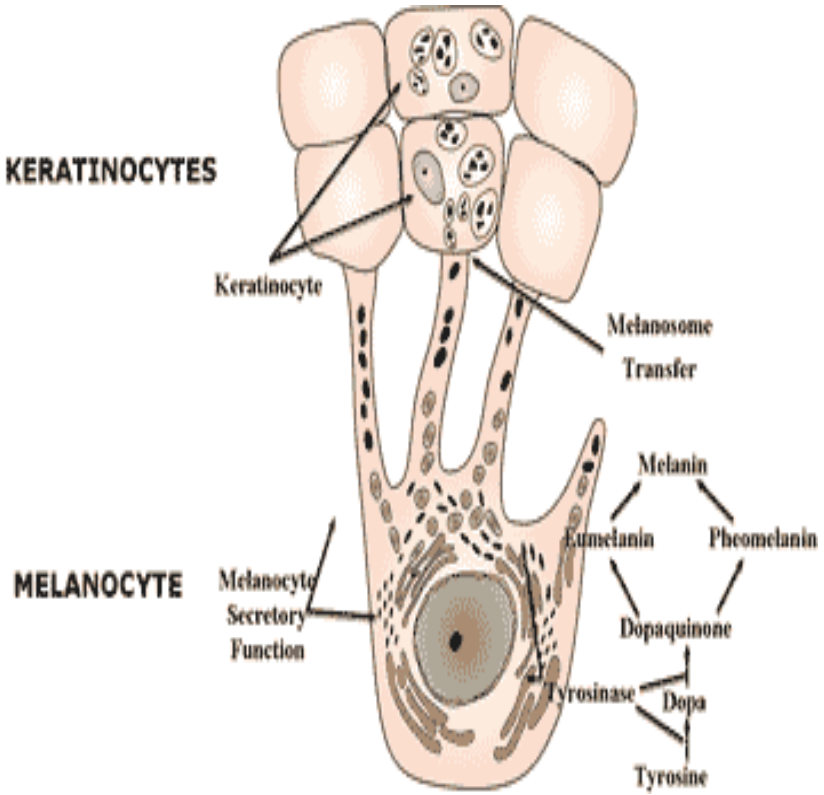
FORMATION OF MELANIN CAP



SKIN PIGMENTATION

- Epidermal melanocytes are regularly dispersed, at an approximate ratio of 1:10, among basal keratinocytes and distribute the melanin they produce to around 40 overlying suprabasal keratinocytes

- The anatomical relationship between keratinocytes and melanocytes is known as “**the epidermal melanin unit”.**



SKIN PIGMENTATION

- Normal skin pigmentation is a **complex process**
- **Epidermis** and **Hair follicles**

Begins with the **synthesis of melanin** within melanosomes in the melanocytes

Followed by **melanosome transfer** to neighboring basal and suprabasal keratinocytes.

In basal cells, **melanin granules are translocated** to the upper pole of the nucleus, forming a **melanin cap** that protect DNA from UV rays.

Melanin granules are **eventually degraded** as the keratinocyte undergoes terminal differentiation.

SKIN PIGMENTATION

- The epidermal melanocyte activity is **continuous activity**.
- Melanocyte proliferation occurs in non stimulated, unexposed human skin and is increased after UV irradiation.
- Melanocytes of the hair follicle follow its **rhytmical activity**
- They are active during the **anagen phase of growth** and have no detectable tyrosinase activity during the **resting (telogen)** phase.
- In hair follicle, melanocyte proliferation and melanin synthesis are both synchronized with hair growth.

MELANOSOMES

- PHEOMELANOSOMES
- EUMELANOSOMES

MELANINS

- Black-brown---------- **Eumelanin**
- Yellow-reddish---------- **Pheomelanin**
- Eumelanin is a highly heterogeneous polymer consisting of DHI (DiHydroxyIndole) and DHICA ((DiHydroxyIndole Carboxylic Acid) units in reduced or oxidized states.
- Pheomelanin consists mainly of sulfur-containing benzothiazine derivatives.

ENZYMES OF PIGMENTATION

- Tyrosinase
- Tyrosinase-related protein 1 (Tyrp1)
- Tyrosinase-related protein 2 (Tyrp2/Dct)

SYNTHESIS OF EUMELANIN

- Melanins are synthesized from tyrosine exogenously supplied by blood

↓

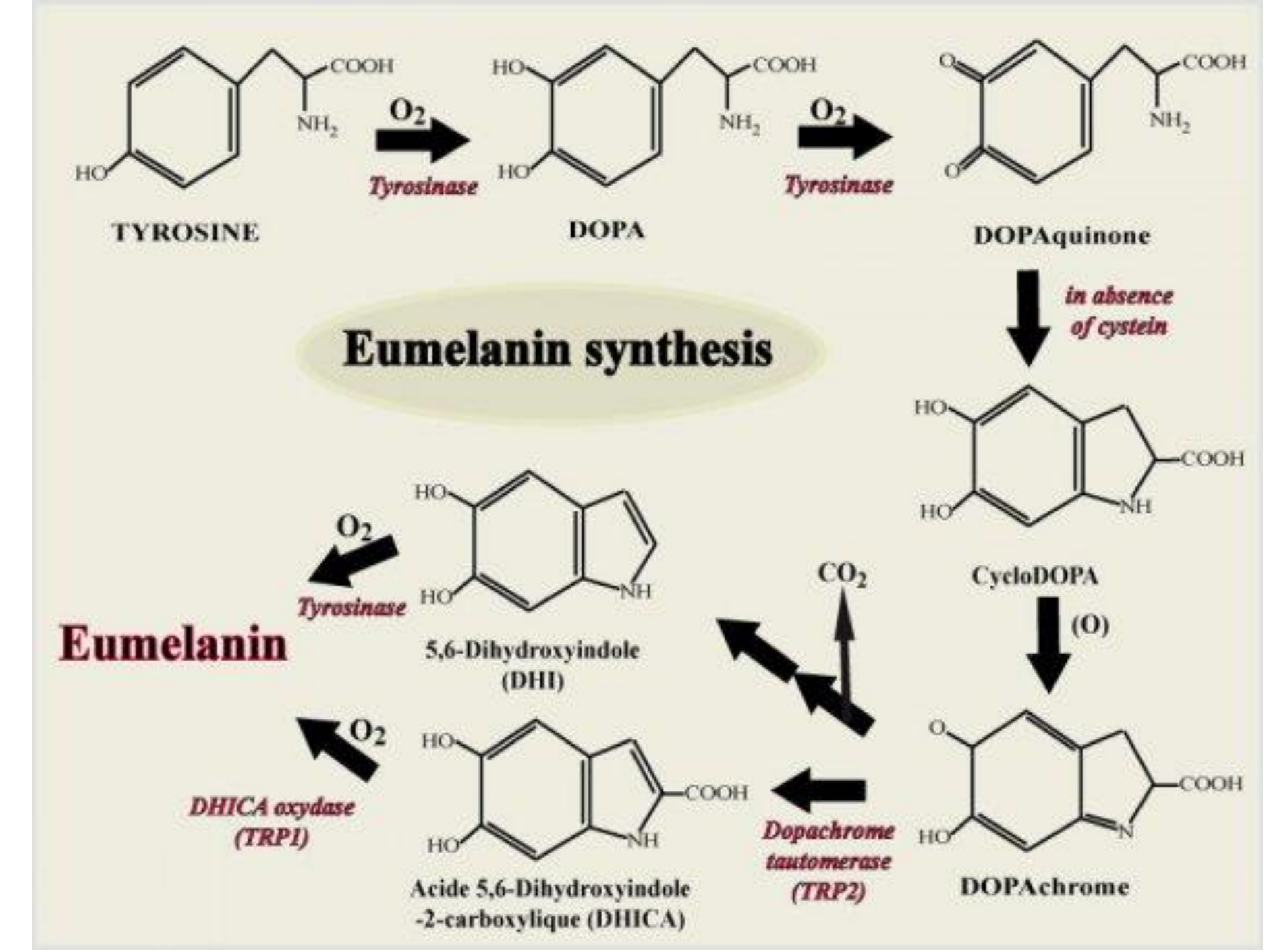
- Tyrosines are oxidized by tyrosinase and metabolised into DOPAs (DIHYDROXY PHENYLALANINE)

↓

- DOPA gets converted into DOPAquinones which are automatically oxidized into indole compounds

↓

- Indole compounds connect to each other to produce eumelanins.


TYROSINE
O_2
Tyrosinase
DOPA
O_2
Tyrosinase
DOPAquinone
in absence of cystein
Eumelanin synthesis
CycloDOPA
(O)
DOPAchrome
Dopachrome tautomerase (TRP2)
CO_2
Acide 5,6-Dihydroxyindole -2-carboxylique (DHICA)
DHICA oxydase (TRP1)
O_2
5,6-Dihydroxyindole (DHI)
O_2
Tyrosinase
Eumelanin

SYNTHESIS OF PHEOMELANIN

- The pheomelanin synthesis pathway involves sulfur compounds, the amino acid cystein **OR** glutathion that liberates cysteins through the action of a glutamyl-transpeptidase.

In presence of cysteins

↓

DOPAquinones connect with cysteins

↓

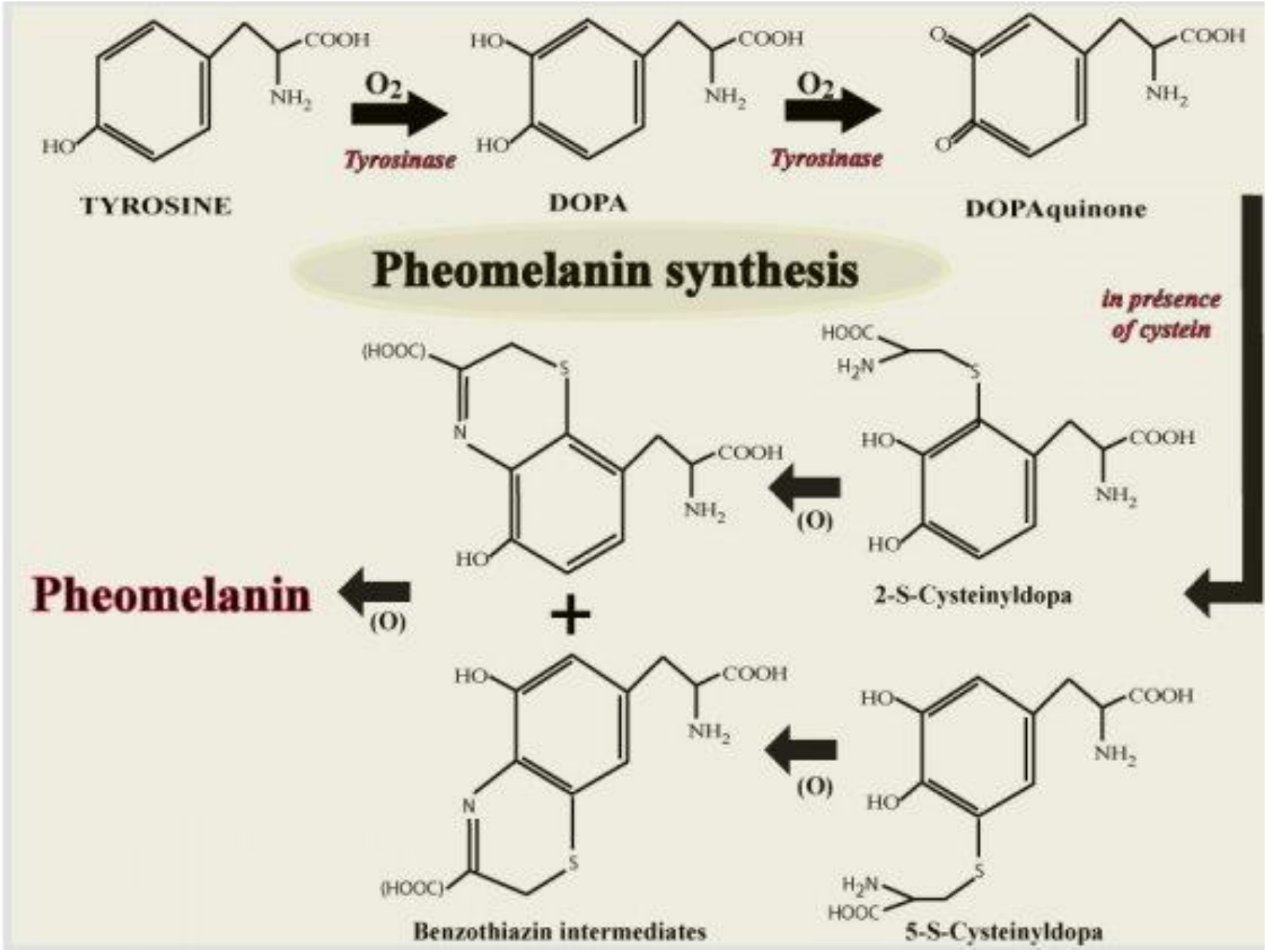
5-S-cysteinyl DOPA and 2-S-cysteinylDOPA

↓

Benzothiazin intermediates

↓

Polymerise to produce pheomelanins.


TYROSINE
O2
Tyrosinase
DOPA
O2
Tyrosinase
DOPAquinone
Pheomelanin synthesis
in présence of cystein
2-S-Cysteinyldopa
(O)
Benzothiazin intermediates
+
Pheomelanin
(O)
5-S-Cysteinyldopa
(O)

FUNCTIONS OF MELANIN

- Protect skin from the harmful effects of UV rays
- Prevent skin cancer
- Both eumelanin and pheomelanin play an important protective role within melanocytes and keratinocytes due to their ability to bind cations, anions, drugs, and chemicals.

TYPES OF PIGMENTATION

- **Constitutive pigmentation**
- **Facultative pigmentation**

TYPES OF PIGMENTATION

- **Constitutive skin pigmentation** corresponds to a genetically determined level of cutaneous melanin, in the absence of acquired exogenous or endogenous influences.

- **Facultative pigmentation** designates an induced level of increased epidermal melanin content as a result of solar radiation, hormones or other environmental factors.

FACTORS AFFECTING SKIN PIGMENTATION

- INTRINSIC FACTORS
- EXTRINSIC FACTORS

FACTORS AFFECTING SKIN PIGMENTATION

- Body distribution
- Ethnicity
- Gender differences
- Genetic defects, Age
- Variable hormone-responsiveness
- Hair cycle-dependent changes
- Climate/season
- UV-radiation
- Toxin
- Pollutants
- Chemical exposure

DISORDERS IN PIGMENTATION

- Melanosis

Hyperpigmentation

- Jaundice

Yellow

Old /Defective RBCs→Liver→Broken down-→ Heamoglobin→ Heme oxygenase→Biliverdin-→ B Reductase -→Bilirubin→Conjugated bilirubin-→ Bile duct→ Intestine-→ Urobilinogen (Stercobilinogen)-→ Stercobilin-→ Yellow colour stool

Jaundice

Yellow pigmentation of skin, eyes, mucous membrane of mouth

Hemolytic Jaundice Hepatocellular Jaundice

Liver-→ Bile-→ Gall Baldder -→ Stone GallObstructive Jaundice--→ Neonatal Jaundice-→

Melanosis→ Hyperpigmentation-→ Increased Melanin Synthesis

Oral Melanosis

Occular Melanosis

Facial Melanosis

Oral Melanonsis--→ Hyperpigmentation in Buccal cavity and the surrounding regions

Smokers Melanosis: Content in Tobacco -→ Stimulating the production

Diffuse pigmentation in oral cavity-→ Palate region, Labial Gingiva, Lips, Inner buccal mucosa

Spread-→Diffuse Focal-→ at one point

Intensity Pigmentation: Dose and Duration

Diagnosis-→

Mangement: Cessation of tobacco,

Drug Induced Malanosis: Antimalarial drug-→ Hydrroxyquinone, Clofazamine→ Leprosy

MELANOSIS

- **Melanosis** is a form of hyperpigmentation associated with increased melanin

TYPES:

- Ocular Melanosis
- Oral Melanosis
- Facial Melanosis

OCULAR MELANOSIS

Ocular melanocytosis
Melanosis oculi

Congenital disease of the eye
1 in every 5000 people
Risk factor for **Uveal melanoma**

Increase of melanocytes in the iris, choroid, and surrounding structures

↓

Overproduction of pigment by these cells can block the trabecular meshwork through which fluid drains from the eye

Increased fluid in the eye leads to increased pressure, which can lead to **glaucoma**

Pigment dispersion syndrome.

SMOKER'S MELANOSIS

- Brown to black pigmentation of the oral tissue i.e. the gums, cheeks or palate as well as in larynx.
- It is most often seen in the lower labial gingiva of tobacco users.
- The brown to black colour is melanin.
- In skin, melanin prevents harmful UV-light from reaching deeper, sensible parts of the tissue. If UV-light penetrates deep, some of the toxic substances due to the UV-light damage to the cells, are bound to melanin in the epithelial cells and travel with the ageing cells to the skin surface, where they are expelled from the tissue surface. In this way the melanocytes and kerationocytes together protect the tissue with melanin serving as a toxic defence- and cleaning agent.

ORAL MELANOSIS

- In the oral mucosa, where the ageing epithelial cells move faster to the surface compared to skin, a similar defence-mechanism seems to be present, but here acting to clean the mucosa from different toxic chemicals entering the mouth.
- Besides chemicals in tobacco also antimalaria-drugs cause an oral pigmentation.

SMOKING ASSOCIATED MELANOSIS

*Clinical features_*

- Diffuse macular melanosis
- Seen on the buccal mucosa, lateral tongue, palate and floor of the mouth.
- Lesions are brown, flat and irregular.

ORAL MELANOSIS

- **Oral melanosis** is pigmentation of the oral cavity
- 

RIEHL MELANOSIS

- **Contact dermatitis**
- **Pruritus**
- **Erythema**
- **Pigmentation** that gradually spreads which, after reaching a certain extent, becomes stationary.

RIEHL MELANOSIS

- **Contact dermatitis** is a type of **inflammation** of the skin.

- Allergic contact dermatitis
- Irritant contact dermatitis
- Phototoxic dermatitis

- Diagnosis of allergic contact dermatitis can often be supported by patch testing.

JAUNDICE

- Jaundice is characterized by a **yellowish pigmentation of the skin, eyes and mucous membranes in the mouth.**

- **Excessive amounts of bilirubin** in the blood stream.
- Bilirubin is a brownish yellow substance produced when the liver **breaks down old/defective red blood cells** as part of the red blood cells natural life-cycle.
- Bilirubin is typically removed from the body through stool and is what gives feces its brownish color.
- Jaundice is most common among newborn babies and typically lasts a few days to one week.
- Jaundice in adults can be indicative of deeper underlying health issues, the causes of which should be investigated swiftly.

JAUNDICE

- **Body's inability to process bilirubin**, the causes of which can stem from :

  Excessive red blood cell destruction
  Dysfunctional bilirubin metabolism
  Obstruction
  Immature liver (Neonatal jaundice)