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Melanogenesis — an update

Human skin and hair colour are due to a pigment, melanin, which is produced at the dermal epidermal level by specialized cells, the melanocytes, in a process named melanogenesis.

The melanocytes are derived from their precursors, melanoblasts, with migrate to their definitive locations in the course of the final steps of embryogenesis. The melanocytes produce melanosomes, small organelles where melanin synthesis will take place. There are four stages of development of melanosomes, and only from the third stage onward melanosomes can synthesize melanin. Then, the transfer of melanin from the melanocytes to the keratinocytes can take place. According to the individuals, there is a phenotypic diversity of pigmentation, which is described in Fitzpatrick classification, and due to the ratio eumelanin (dark melanin) and phaeomelanin (reddish melanin) produced by the melanocytes. Melanogenesis is quite a complex series of chemical reactions, along which three enzymes, tyrosinase (TYR), tyrosinase-related protein 1 (TRP1) and DOPAchrome tautomerase (DCT) are absolutely required. Other enzymes also play a role in this process.

Melanocortin-1 receptor (MC1R) and Microphthalmia-associated transcription factor (MITF) also play a pivotal role in the stimulation (or not) of the melanocytes. Skin pigmentation is regulated by a series of intrinsic factors such as peptides, cytokines, prostaglandins, NO, but also oestrogens. On the other hand, UV radiation (UVR) is a potent extrinsic regulator of melanogenesis. In this paper, it was emphasized on the importance of the paracrine regulation of skin pigmentation. The major role of keratinocytes is well known, but other skin cells like fibroblast, immune cells or endothelial cells are of major importance in this cell-to-cell communication with the melanocytes and will regulate melanogenesis.

Finally, a brief glossary was proposed about various existing melanins.

Key words

Melanocyte, melanin, melanogenesis, pigmentation, UV-radiation, keratinocytes.

INTRODUCTION

Human skin colour stems from the deep epidermis, where the pigment-producing cells melanocytes are located [1]. The epidermal melanin unit (EMU) was described, composed by one melanocyte surrounded by keratinocytes in a ratio of 1 : 30—40. These epidermal units are responsible for melanin production and distribution in a process called melanogenesis [2]. Melanin produced along this process will be the primary determinant of skin, hair, and eye colour [2]. On the other hand, melanin also possesses a critical role in the natural photoprotection of the skin due to its ability to absorb ultraviolet radiation [3]. Melanogenesis is under the influence of intrinsic and extrinsic factors modulating constitutive pigmentation. This is a complex mechanism which may be disturbed and lead to disorders classified as hypopigmentation or hyperpigmentation.

MELANOCYTES

Melanoblasts, the precursors of melanocytes, derive from the neural crest from the second month of human embryonic life and migrate throughout the mesenchyme of the developing embryo [4]. They reach specific target sites, mainly the dermis, epidermis, and hair follicles, the uveal tract of the eye, the stria vasculare, the vestibular organ and the endolymphatic sac of the ear, and leptomeninges of the brain [4]. After reaching their final destinations, melanoblasts differentiate into melanocytes and at 6 month of foetal life they establish themselves in the basal layer of the epidermis [5].

STAGES OF MELANOGENESIS

Once established, melanocytes start producing melanosomes, featuring elliptic organelles in which melanin synthesis takes place [4]. There are four maturation stages of melanosomes (I—IV) depending on their structure and the quantity, quality, and arrangement of the melanin produced [6]. Stage I melanosomes are spherical vacuoles lacking tyrosinase (TYR) activity and with no internal structural components.

At some point takes place the transformation of stage I melanosomes to elongated, fibrillar organelles known as stage II melanosomes [6]. At this stage, they already contain tyrosinase. After this,

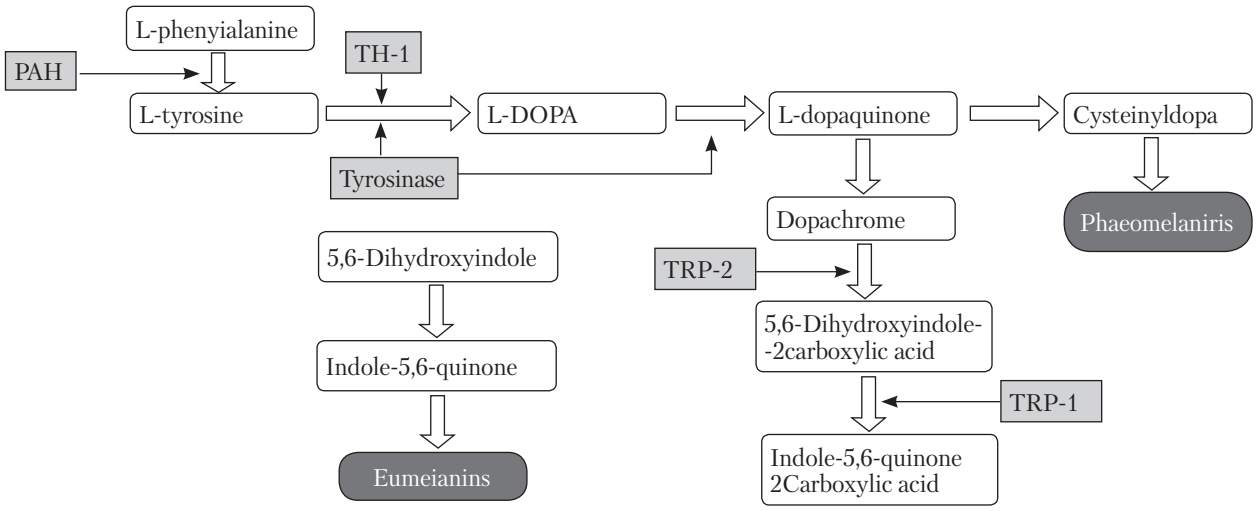

Figure. **Enzymes intervening in the process of melanogenesis**

melanin synthesis starts. the pigment being uniformly deposited on the internal fibrils: this is stage III. Their last developmental stage (IV) is only detected in highly pigmented melanocytes; these melanosomes are either elliptical or ellipsoidal, electron-opaque due to complete melanization, and have minimal TYR activity [4]. There is a consistent difference between eu-melanosomes (containing black-brown pigments) and pheomelanosomes (containing yellow-reddish melanin): the latter remain round and are not fibrillar during maturation [4].

For full maturation of melanosomes, there is a need for an increase in intramelanosomal pH from 5 to 6.8 [7]. As it was mentioned, in the epidermis, each melanocyte interacts through dendrites with 30 to 40 keratinocytes. The role of keratinocytes in melanogenesis is important, and not limited to the passive reception of melanin from the melanocytes. There is a permanent crosstalk between keratinocytes and melanocytes in the epidermal melanin unit via exosomal miRNAs, which regulates pigmentation [8]. The transfer of melanin from the melanocytes to the keratinocytes is not fully understood, and different mechanisms such as exocytosis, cytophagocytosis, fusion of plasma membranes, and transfer by membrane vesicles were suggested [9].

PHENOTYPIC DIVERSITY OF PIGMENTATION AND TYPES OF MELANIN

The number of melanocytes is relatively constant in different ethnic groups. However, the size and number of melanosomes, the amount and type of melanin, and melanin transfer and distribution in keratinocytes vary according to ethnic groups and are responsible for the phenotypic diversity of pigmentation among humans [3]. From birth, the melanosomes of dark-skinned individuals are larger, more numerous, and elongated. This results in delayed degradation in keratinocytes and consequently in increased visible pigmentation [4]. These differences in melanosomes are not influenced by extrinsic factors such as UVR [4].

There are two types of melanin: eumelanin — brown-black or dark insoluble polymer- and pheomelanin — red-yellow soluble polymer formed by the conjugation of cysteine or glutathione [10]. Eumelanin is the major type in individuals with dark skin and hair and is more efficient in photoprotection. Pheomelanin is predominantly found in individuals with red hair and skin phototypes I and II, in whom skin tumours are more common [11].

ENZYMES OF MELANOGENESIS

Figure describes with details the role of enzymes in melanogenesis. Within melanosomes, at least three enzymes are absolutely required to synthesize different types of melanin: **tyrosinase (TYR), tyrosinase-related protein 1 (TRP1) and DOPAchrome tautomerase (DCT)**. TYR is responsible for the critical steps of melanogenesis and the latter two are further involved in modifying the melanin into different types [4]. TYR is a copper-dependent enzyme catalyzing the conversion of L-tyrosine into L-DOPA, the rate-limiting stage in melanin synthesis [2]. Tyrosinase related protein-1 (TRP-1) and **tyrosinase-related protein-2 (TRP-2)**, are also present in the membrane of melanosomes and catalyzing the hydroxylation of tyrosine to -3,4-dihydroxyphenylalanine (DOPA) (which is the initial rate limiting step in melanogenesis) and the subsequent oxidation of DOPA to DOPAquinone.

Further, it is possible that TRP-1 has a role in the activation and stabilization of tyrosinase, mela-

nosome synthesis, increased eumelanin/pheomelanin ratio and a role against oxidative stress due to its peroxidase effect [9]. 5,6-dihydroxyindole (DHI) melanins are generated from DOPAquinone after several steps of decarboxylation, oxidation, and polymerization. However, in the presence of DCT, the carboxylic acid group of 5,6-dihydroxyindole-2-carboxylic acid (DHICA) is retained when derived from DOPAchrome, and therefore the so-called DHICA melanins are produced. The synthesis of pheomelanin involves the production of cysteinyldopa conjugates from DOPAquinone after the production of DOPA from tyrosine [4].

Protease-activated receptor 2 (PAR2) also mediates crucial steps in skin pigmentation. The transfer of melanosomes from melanocytes to keratinocytes is believed to occur via PAR2-induced dendrite extension and phagocytosis of these organelles [12]. J.Y. Kim et al. showed that inhibition of PAR2 signalling in keratinocytes resulted in loss of SCF mRNA and protein upregulation [13]. This direct induction of SCF expression via PAR2 activation adds a leading role of this versatile receptor in melanogenesis. SCF is a key player in the production of melanin, and its paracrine regulation by keratinocytes is a novel and important discovery on the course to unravelling the complex network of pathways involved in skin pigmentation [14].

MELANOCORTIN-1 RECEPTOR (MC1R)

Epidemiological studies revealed that the human MC1R is highly polymorphic, with around 200 coding region allelic variants with protein sequence alterations expressed in different human populations [15]. For instance, the association of specific MC1R polymorphisms was shown to be associated with the red hair colour (RHC) phenotype which also includes fair and freckled skin, impaired or absent tanning response to UVR and propensity to sunburn [16]. MC1R variants are also associated with increased melanoma and non-melanoma skin cancer risk [17], MC1R has also effects extending beyond pigmentation, and involves activation of the DNA damage response, including DNA repair pathways in human melanocytes [18].

Upon stimulation by its endogenous agonists (principally ACTH, α-MSH and agouti -signalling protein [ASIP]), MC1R initiates a complex series of events, mainly mediated by the cAMP-signalling cascade. This mechanism ultimately leads to an increase in tyrosinase activity, increased protein levels of tyrosinase, tyrosinase-related protein (TRP)-1 and -2, and, subsequently, activation of biosynthesis of eumelanin pigments [19]. Binding of ASIP to the MC1R prevents the stimulation of eumelanin synthesis in response to α-MSH. This shifts dramatically the ratio of melanins synthesized toward phaeomelanins, which accounts for the banding pattern in hair, characteristic of the agouti phenotype, and yellow coat colour in agouti mutant mice [20]. In addition to its role in the regulation of constitutive human melanin pigmentation, MC1R is a major determinant of the facultative pigmentation induced by UVR, as UVR-induced tanning is largely dependent on the production and release of α-MSH and ACTH by irradiated keratinocytes [21]. UVR activates MC1R transcription in human epidermis and a paracrine and autocrine activation of MC1R occur, thus leading to increased cAMP signalling, activation of MITF and induction of MC1R transcription [22].

MICROPHTALMIA-ASSOCIATED TRANSCRIPTION FACTOR (MITF)

Microphthalmia-associated transcription factor (MITF) is the master regulator of melanocyte, controlling the production of melanin. Mutations in the human MITF locus are associated with increased risk for familial melanoma, Waardenburg syndrome, and Tietz syndrome [23]. While published studies suggest that MITF-M is the main isoform expressed in melanocytes, it was demonstrated that the human MITF-A isoform is also expressed in melanocytes and its expression is regulated by retinoids [24]. Further, the pigmentation response to UVR is driven by MITF [25].

INTRINSIC REGULATION OF SKIN PIGMENTATION

Melanocytes produce proopiomelanocortin (POMC) peptides, cytokines, NO, prostaglandins, and leukotrienes, which act via an autocrine or paracrine way on keratinocytes and are involved in immune and inflammatory responses [2].

Keratinocytes also produce several factors in response to UVR exposure, with paracrine action on melanocytes, which may stimulate or inhibit melanogenesis [26]. Table is describing these interactions. UVR also activates endocannabinoid production by keratinocytes and a paracrine cannabinoid receptor type 1-mediated endocannabinoid signalling negatively regulates melanin synthesis [27].

POMC/MC1-R/cAMP is the main pathway but there are other melanocyte receptors associated with adenyl cyclase and cAMP production, such as muscarinic receptors and α and β oestrogen receptors [2]. The increase in oestrogen levels during pregnancy can cause hyperpigmentation (melasma, areolar hyperpigmentation and line nigricans) [28]. Catecholamines may be produced by keratinocytes from L-DOPA and can bind to α_1 and β_2 adrenergic

Table. **Effects of factors secreted by keratinocytes after exposure to UVR**

	Melanin proliferation	Dendricity	Melanin synthesis	Melanosome transfer	Cytoprotection
ACTH	+		+		+
α-MSH	+	+	+		+
βFGF	+				
ET-1	+	+	+		
GM-CSF	+		+		
NO			+		
NGF		+			+
PGE2		+	+	+	
IL-1	+	+	+		
TNF-α			+		

receptors in melanocytes, stimulating melanogenesis via the cAMP pathway and PKC-β [7]. This redundancy of cAMP production reveals the importance of this second messenger in melanogenesis.

PARACRINE REGULATION OF SKIN PIGMENTATION

Paracrine signalling is a form of cell signalling or cell-to-cell communication in which a cell produces a signal to induce changes in nearby cells, altering the behaviour of those cells.

In addition to keratinocytes, there are other types of cells in the skin, such as fibroblasts and immune cells that are also actively involved in the regulation of melanocyte behaviour through the production of paracrine factors.

Regulation of melanocytes by keratinocytes

The main pathways of melanocyte activation and melanogenesis in which keratinocytes are involved were previously described.

However, in response to UV exposure, human epidermal keratinocytes also produce another important POMC-derived peptide **β-endorphin**, which has been reported to upregulate melanocyte dendricity, proliferation, and pigmentation by binding with the μ-opiate receptor [29, 30]. Studies have revealed that each of these POMC peptides (α-MSH, ACTH, and β-endorphin) are secreted not only by human epidermal keratinocytes but also by human hair follicle keratinocytes in vitro and suggest a potent role in the upregulation of hair follicular melanogenesis mediated by paracrine effect during hair cycle [31, 32].

TGF-β (transforming growth factor-β), is an important keratinocyte-derived cytokine that regulates melanocyte differentiation. In the absence of UV irradiation, TGF-β secreted from human keratinocytes inhibits melanocyte differentiation by suppressing paired box 3 (PAX3) via induction of Smad signalling [33]. However, UV irradiation activates the Jun N-terminal kinase (JNK)/activating protein-1 (AP1) pathway to repress TGF-β production in keratinocytes, leading to the stimulation of melanogenesis in cultured normal human melanocytes [33]. After UVB irradiation, **Stem Cell Factor (SCF)** and m-KIT levels are both increased in human epidermal keratinocytes and melanocytes, respectively and the expression of s-KIT in melanocytes and the combined melanogenic effect of these different forms of KIT results in enhanced melanogenesis, which may contribute to UV-induced hyperpigmentation [34].

Endothelins (ETs) are mainly secreted from keratinocytes and bind to EDN receptors on melanocytes to regulate melanogenesis [35]. In response to UV, expression of ETs is highly elevated to enhance the signalling cascades, among which the ET-1/ET receptor type B (ETRB) pathway is considered to play significant role in UVB-induced pigmentation by modulating MITF phosphorylation in normal human melanocytes [36, 37].

Nitric oxide (NO) production can be significantly increased after exposure to UV irradiation, leading to the activation of soluble guanylate cyclase followed by activation of cyclic guanosine 3′,5′-monophosphate (cGMP)-dependent protein kinase (PKG) through a strong and rapid increase in intracellular cGMP, resulting in upregulation of MITF and tyrosinase to stimulate melanogenesis [38, 39].

PGE2 and PGF2α, the main keratinocyte-derived prostaglandins, rapidly increase after UV irradiation and promote melanocytes dendricity

and tyrosinase expression in human melanocytes to enhance pigmentation [40—42].

Nerve growth factor (NGF), a neurotropic polypeptide mainly secreted from keratinocytes is suggested as an efficient inducer of melanogenesis in normal human melanocytes by enhancing melanin synthesis, melanosome maturation, and melanocyte dendricity [43].

Other important keratinocyte-derived factors positively regulate melanogenesis such as **basic fibroblast growth factor (bFGF), hepatocyte growth factor (HGF), granulocyte-macrophage colony-stimulating factor (GM-CSF) and leukaemia inhibitory factor (LIF)** [44].

Several inflammatory cytokines secreted from keratinocytes with antimelanogenic effects are closely related to post-inflammatory hypopigmentation [44]. **Interferon-γ (IFN-γ)**, produced by keratinocytes mainly in inflammatory skin conditions, can inhibit basal and α-MSH induced melanogenesis in normal human melanocytes by sequestrating CBP (CREB binding protein) via its association with STAT1, thereby suppressing MITF, suggesting that IFN-γ may contribute to inflammation associated hypopigmentation [45]. In addition to IFN-γ, several keratinocyte-derived cytokines are known to inhibit skin pigmentation, such as **tumour necrosis factor-α (TNF-α), interleukin-6 (IL-6), and IL-1α/β** [46, 47].

Regulation of melanocytes by fibroblasts

Dermal fibroblasts are traditionally recognized as synthesizing, remodeling and depositing collagen and non-collagen extracellular matrix (ECM), the structural framework for tissues, helping to bring thickness and firmness to the skin [48]. Studies increasingly elucidated the significant role of fibroblast in pigmentation. Various findings confirm an important cross-talking between fibroblasts and melanocytes in pigmentation. Specifically, there are fibroblast-derived secreted factors which are involved in the fibroblast interactions with melanocytes.

There are four crucial signalling pathways of fibroblast-derived factors in melanocytes [48].

MAPK/ERK (mitogen-activated protein kinases/ extracellular signal-regulated kinases) signalling is essential to the proliferation and differentiation of melanocytes.

Wnt/β-catenin signalling is another important pathway in pigmentation process and melanocytes differentiation, but also for melanocyte stem cell. cAMP/PKA (cyclic adenosine monophosphate/ protein kinase A) signalling can also contribute to MITF expression.

PI3K/Akt (phosphatidylinositol 3′-kinase/Akt) signalling pathway plays a critical role in melanocyte proliferation and apoptosis through the cell cycle regulation with GSK3 and protein cyclin D1 [49].

Numerous **mediators secreted from fibroblasts** play significant roles in the process of skin pigmentation through different signalling pathways, them being involved in down-regulation, modulation and induction of pigmentation, or proliferation and survival of melanocytes [48].

DKK1 secretes proteins that antagonize Wnt signalling. DKK1 is produced by fibroblasts and has an inhibitory effect on MITF expression which results mainly from the decreased activity of GSK-3β and β-catenin [50]. In addition, DKK1 upregulates the expression of myoactive tetradeca peptide (MATP) which reduce TYR activity [51]. Therefore, DKK1 acts on melanocytes by suppressing proliferation and melanin production. These combined effects explain the lower pigmentation observed on the palms and soles [48].

sFRP (Secreted frizzle-related protein) are part of these mediators secreted by fibroblasts. It was suggested that sFRP2 functions as a melanogenic stimulator through Wnt/β-catenin signalling, but the precise mechanism needs to be clarified [52].

KGF (keratinocyte growth factor) derived from fibroblasts participates in melanogenesis process by inducing melanosome transfer [48]. Interleukin-1 α (IL-1α), produced by keratinocytes after UVB exposure, stimulates fibroblasts to generate KGF. In synergy with cAMP, transferrin, ET-1 and bFGF, KGF increases differentiation, cell body expansion, dendrites extension and melanosome transfer [53]. In addition, KGF alone or in synergy with IL-1α and bFGF, induces melanin deposition and elongated rete ridges [54].

Neuregulin-1 (NRG-1) visibly increases skin pigmentation [55]. In addition, the amount and size of melanocytes, as well as thickness of dendrites are increased [56].

Stem cell factor (SCF), secreted by fibroblasts, binds to the c-kit receptor of melanocytes and activates the MAPK/ERK signalling pathway [48]. SCF increases proliferation and differentiation of melanocytes with or without factors produced by keratinocytes, as cAMP, ET-1 and bFGF [57].

Transforming growth factor-β (TGFβ) regulates a multitude of cellular processes, including cell survival, proliferation and apoptosis [58]. TGFβ signalling has been shown to exhibit a repressive effect on both melanocyte differentiation and melanogenesis via downregulation of MITF and PAX3 [59].

Hepatocyte growth factor, highly expressed by fibroblasts, binds to melanocyte receptor c-MET and triggers the MAPK and the PI3K-Akt signal-

ling pathways, modulating melanocyte proliferation, migration, and melanogenesis [60, 61].

Regulation of melanocytes by immune cells

Inflammatory cytokines produced from immune cells not only function by direct effect but also by indirect or combinational effect on melanogenesis [62]. Histamine stimulates melanogenesis through histamine receptor 2 (HR2) via complex signalling pathways, including PKA phosphorylation in normal human melanocytes [63].

It was shown that the Th2 cytokine, IL4, can directly inhibit melanogenesis in normal human melanocytes through the JAK2-STAT6 (signal transducers and activators of transcription 6) signalling pathway [62].

In addition, IL-17 secreted by Th17 cells also has direct suppressive effect on melanogenesis. The combination of IL-17 and TNF secreted by T cells and dendritic cells, can synergistically enhance the reduction of melanin synthesis in normal human melanocytes [64, 65].

More recently, it was reported that the microenvironment in the epidermis and innate immune stimuli, such as microbiome and ultraviolet represented here by TLR2 and TLR3 agonists, could affect the melanogenesis in human melanocytes, and that Toll-like receptors 2 and 3 enhance melanogenesis and melanosome transport in human melanocytes [66].

Regulation of melanocytes by endothelial cells

Recently, it was found that HDMEC-derived clusterin inhibit melanogenesis through MITF/tyrosinase downregulation [67]. These findings suggest that HDMECs secrete copious amounts of clusterin and that the clusterin is a factor contributing to the inhibitory effect of endothelial cells on melanogenesis via paracrine crosstalk between endothelial cells and melanocytes [67].

EXTRINSIC REGULATION OF MELANOGENESIS: THE ROLE OF UV-RAYS

UVR is the most important extrinsic factor in the regulation of melanogenesis. It is the main stimulus for induced or acquired pigmentation, known as «tanning» [28]. There are two types of induced pigmentation: immediate and delayed pigmentation.

Immediate pigmentation appears 5—10 minutes after exposure to UVR, disappears minutes or days later, is largely due to UVA, and is not dependent on increased melanin synthesis, but on the oxidation of pre-existing melanin and redistribution of melanosomes to the epidermal upper layers [2].

Delayed pigmentation occurs 3—4 days after exposure to UVR, disappears within weeks and is due to UVA and mainly UVB radiation, resulting from an increased level of epidermal melanin, particularly eumelanin, providing photoprotection [4].

UVR increases proliferation and/or recruitment of melanocytes, the number of dendrites, and the transfer of melanosomes to a supranuclear location on the keratinocytes for DNA photoprotection, whilst the expression of POMC peptides, MC1-R, and melanogenic enzymes increases in keratinocytes and melanocytes respectively [10]. An elderly individual, depending on constitutive pigmentation and cumulative UVR dose, may have hyperpigmented lesions (solar lentigines) that indicate photoaging. This can be explained by the fact that aged melanocytes possess an enhanced functional activity after years of cumulative UVR exposure [2].

MELANINS

Unlike the vast majority of natural pigments, the melanins cannot be described in terms of a single well-defined structure and, as a result, there still remains today a lack of general consensus what actually melanin is [68].

Nicolaus (1969) suggested a classification of melanins into three main groups, Eumelanins, Pheomelanins and Allomelanins, the former two groups comprising animal pigments and the latter encompassing the broad variety of dark nonnitrogenous pigments of plant, fungal and bacterial origin [69]. To limit confusion, Prota proposed a more restrictive usage of the term melanin «to include only those pigments which are formed intracellularly byoxidation of tyrosine and related metabolites» [70].

The following classification seems to be currently the most accurate [68]:

Melanins: Pigments of diverse structure and origin derived by the oxidation and polymerization of tyrosine in animals or phenolic compounds in lower organisms.

Eumelanins: Black-to-brown insoluble subgroup of melanin pigments derived at least in part from the oxidative polymerization of L-dopa via 5,6-dihydroxyindole intermediates.

Examples: Sepia melanin, black hair melanin.

Pheomelanins: Yellow-to-reddish brown, alkali-soluble, sulfur-containing subgroup of melanin pigments derived from the oxidation of cysteinyldopa precursors via benzothiazine and benzothiazole intermediates.

Examples: red hair melanin, hen feather melanin (it should be noticed however that the red hair pigment is rarely pure pheomelanin).

Neuromelanins: Dark pigments produced within neurons by oxidation of dopamine and other catecholamine precursors.

Example: Substantia nigra melanin.

Pyomelanins. Dark pigments produced by microorganisms mainly, but not exclusively, from homogenisate.

CONCLUSIONS

Human skin colour is due to the melanin pigments, produced deep in the epidermis by the melanocytes through a process named melanogenesis. Melanogenesis is a complex chemical mechanism which is now well known. As the melanocytes are responsible of the pigment production, we must remind that the same are under multiple influences of intrinsic and extrinsic (especially UVR) factors. Paracrine factors are of utmost importance, as the human skin is constituted by various cell types which are not only juxtaposed, but more likely living harmoniously with lots of interferences between each other. Melanocytes are not an exception, and signalling paracrine factors emitted by all cell types in the epidermis and dermis are influencing them, and consequently the melanogenesis process. All these cellular cross talks will have strong implications in the occurrence of pigmentary skin diseases, but also in the elaboration of treatments.

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Меланогенез — нова інформація

Колір шкіри і волосся людини зумовлені пігментом, меланіном, який виробляється на рівні дерми і епідермісу спеціалізованими клітинами, меланоцитами, в процесі, який називається меланогенез.

Меланоцити утворюються зі своїх попередників, меланобластів, і мігрують до своїх остаточних місць під час кінцевих етапів ембріогенезу. Меланоцити виробляють меланосоми, маленькі органели, в яких відбуватиметься синтез меланіну. Є чотири стадії розвитку меланосом, і тільки починаючи з третьої стадії і далі меланосоми можуть синтезувати меланін. Потім може відбуватися перенесення меланіну з меланоцитів у кератиноцити. Існує фенотипічна різноманітність пігментації, яка описана в класифікації Фітцпатріка й зумовлена співвідношенням еумеланіну (темного меланіну) і феомеланіну (червонуватого меланіну), що продукуються меланоцитами. Меланогенез є досить складною серією хімічних реакцій, в яких обов'язково необхідні три ферменти: тирозиназа (TYR), тирозиназаспоріднений білок 1 (TRP1) і ДОФАхромтаутомераза (DCT). Інші ферменти також відіграють роль у цьому процесі.

Рецептор меланокортину-1 (MC1R) і фактор транскрипції, пов'язаний з мікрофтальмією (MITF), також відіграють ключову роль у стимуляції (чи ні) меланоцитів. Пігментація шкіри регулюється низкою внутрішніх чинників, таких як пептиди, цитокіни, простагландини, NO, а також естрогени. З іншого боку, УФ-випромінювання є потужним зовнішнім регулятором меланогенезу. У цій статті наголошувалося на важливості паракринної регуляції пігментації шкіри.

Основна роль кератиноцитів добре відома, але інші клітини шкіри, такі як фібробласти, імунні клітини або ендотеліальні клітини, мають велике значення в міжклітинній комунікації з меланоцитами і регулюють меланогенез.

Нарешті, був запропонований короткий словник різних існуючих меланінів.

Ключові слова: меланоцит, меланін, меланогенез, пігментація, УФ-випромінювання, кератиноцити.

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Меланогенез — новые данные

Цвет кожи и волос человека обусловлен пигментом, меланином, который вырабатывается на уровне дермы и эпидермиса специализированными клетками, меланоцитами, в процессе, который называется меланогенезом.

Меланоциты происходят от своих прекурсоров, меланобластов, и мигрируют в свои окончательные локации в ходе заключительных этапов эмбриогенеза. Меланоциты производят меланосомы, маленькие органеллы, в которых будет происходить синтез меланина. Есть четыре стадии развития меланосом, и только начиная с третьей стадии и далее меланосомы могут синтезировать меланин. Затем может происходить перенос меланина из меланоцитов в кератиноциты. Существует фенотипическое разнообразие пигментации, которое описано в классификации Фитцпатрика и обусловлено соотношением эумеланина (темного меланина) и феомеланина (красноватого меланина), продуцируемых меланоцитами. Меланогенез представляет собой довольно сложную серию химических реакций, в которых обязательно необходимы три фермента: тирозиназа (TYR), тирозиназародственный белок 1 (TRP1) и ДОФАхромтаутомераза (DCT). Другие ферменты также играют роль в этом процессе.

Рецептор меланокортина-1 (MC1R) и фактор транскрипции, связанный с микрофтальмией (MITF), также играют ключевую роль в стимуляции (или нет) меланоцитов. Пигментация кожи регулируется рядом внутренних факторов, таких как пептиды, цитокины, простагландины, NO, а также эстрогены. С другой стороны, УФ-излучение является мощным внешним регулятором меланогенеза. В этой статье подчеркивалась важность паракринной регуляции пигментации кожи.

Основная роль кератиноцитов хорошо известна, но другие клетки кожи, такие как фибробласты, иммунные клетки или эндотелиальные клетки, имеют большое значение в межклеточной коммуникации с меланоцитами и регулируют меланогенез.

Наконец, был предложен краткий словарь различных существующих меланинов.

Ключевые слова: меланоцит, меланин, меланогенез, пигментация, УФ-излучение, кератиноциты.

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