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內文：

1. Under physiological conditions the number of melanocytes in the oral epithelium is the same regardless of racial/ethnic origin

一般來說， oral epithelium 的 melanocyte 數目在不同人種間差別不大

2. Oral mucosa 的顏色通常由以下因素決定：

a. Basal cell layer 中 melanocyte 的數目和 melangenic activity

b. Melanosome 的數目，大小，分佈

c. Melanins 種類(eumelanin: black-brown/pheomelanin:yellow-red)

d. 角質化上皮的遮蔽效果

3. Oral mucosa pigmentation 易發生於膚色較深的人(98% of black persons has it)，有 patchy 或 uniform 兩種類型，最常影響 gingiva

4. Melanocyte 在 membrane-bound 或 ganelles termed melanosome 中製造出 melanin，melanosome 所含的蛋白質與酵素足以供給 melanin biosynthesis，維持 melanosome 的結構，並讓 immature pre-melanosome 成熟

melanosome 成熟後，會經由 microtibuli 運送到 elongated dendrites of the melanocytes 的表面，最後再被傳送到 keratinocyte melanin unit 中的 keratinocyte 中，然後在 nuclei 內形成 supranuclear caps 來防護 UV 的傷

5. Non-physiological alterations in melanin pigmentation of the oral mucosa 與以下因素相關：

基因，新陳代謝，內分泌，化學/物理因子，感染原，發炎，neoplastic (genetic, metabolic, endocrine, chemical or physical factors, to infective agents and to inflammatory or neoplastic processe)

30%的 case 中 melanoma 發生在 hyperpigmentation 的部位

6. Melanocytes 發源於 neural crest，發育過程中 melanocytes stem cell 會遷移到 skin 和 mucous membranes

Active melanocytes 分布：

stria vascularis of the cochlea/leptomeninges/substantia nigra and locus coerulus of the brain/heart

Melanocyte stem cells 分布：bulge region of hair follicles (epidermal，口腔中未知)

7. Epidermal melanocyte stem cells -> transient- amplifying melanocyte precursors -> mature melanin producing melanocytes

a. (胎兒)epidermal melanocyte development during embryogenesisz:

Stem cell factor (SCF) and its tyrosine kinase receptor C-kit signalling pathways

b. (成人)maintenance of adult melanocyte stem cells, and thus for melanocyte homeostasis : notch signalling pathways

c. Differentiation of melanocyte precursors : ndothelin 1

d. Melanogenesis : micropthalmia-associated transcription factor (MITF) with its cAMP response element

8. Precursor melanocyte migrates from skin to basal cell layer 受 c-kit/SCF, endothelin 1&3, HGF, bFGF 調控
跨過 basement membrane 後會釋放出 E-cadherin 幫助與 basal cell layer 中相鄰 keratinocytes 的 intercellular communication
這些 precursor 如果滯留在 lamina propria/dermis 的話就會形成痣
9. fibroblasts 會影響 melanocyte 的 functional activity
10.keratinocytes 能夠控制 dendritic melanosome transfer 是因為 capacity of keratinocytes to phagocytose the melanosomes 由 keratinocytes 表面 protease-activated receptor 2 (PAR-2)控制
11. a. Melanocyte 可調控 keratinocyte 的 functional activity
b. keratinicyte 可藉由 paracrine 的方式調控 melanocyte melanogenesis，而這些介質包括 α-MSH, ACTH, β- endorphin, bFGF, endothelins, HGF 和 SCF 然而我們對於這些調控機制的瞭解仍是粗略
12. Melanocyte 的功能包括決定眼睛頭髮的顏色，降低環境中 UV radiation, reactive oxygen species (ROS) 和 free radicals 的傷害，sequester metal ions ,bind certain drugs and organic molecules
13. Intermediates of melanogenesis
a. Toxic or mutagenic: Quinones and semiquinones
b. Down regulating immune and inflammatory responses: L-dopa(inhibit the production of proinflammatory cytokines by T lymphocytes and monocytes)
c. Neutralize ROS generated: Melanins produced by melanocytes residing in the basal cell layer of the gingival epithelium
(dentogingival plaque-in- duced inflammation in the periodontal microenvironment)
14. Melanin 可以 inhibit proliferation of bacterial and fungal microorganisms
an integral part of the innate immune system with a role in neutralising the products of superficial bacterial and fungal infective agents melanogenesin
a. Melanocortin system through the cAMP/MITF pathway can stimulate proliferation of undifferentiated melanocytes
b. α-MSH can stimulates melanogenesis, and also downregulates inflam- matory responses
c. Epidermal adrenergic signalling pathway increase melanin biosynthesis and the number and complexity of melanocytic dendrites
d. Adrenalin/ β2-adrenoceptor/cAMP/MITF pathway
e. Mediators of inflammation such as histamine and ara- chidonic acid metabolites trigger melanogenesis
17. 病理性的 oral pigmentations：
Addison’s disease, neurofibromatosis, oral melanotic maculae, oral mucosal melanoma, drug-induced oral mucosal pigmentation, Kaposi sarcoma, vascular malformations, haemangioma
18. Physiological melanin pigmentation
男女比例差不多，無症狀的，solitary or multiple brown maculae with well-defined borders

Figure 2 Physiological oral pigmentation on the gingiva presenting as bilateral, symmetrical, dark brown discolouration of the labial gingiva, including the marginal and papillary gingiva but not transgressing the mucogingival junction.

Figure 3 Diffuse, light brown physiological oral pigmentation on the hard palate.

Figure 5 Physiological oral pigmentation in a black male: a well demarcated brown band on the attached gingiva, not transgressing the mucogingival junction and not affecting the marginal/interdental papillary gingiva. (The foreign body at the upper left is a post-biopsy suture).

a. 最常發生在 gingiva，多為 bilaterally symmetrical 並且不會超過 mucogingival junction，有些時候亦不會影響 free gingiva
b.會在二十歲之前逐漸顯現，並且隨著年齡增長而擴大，加深顏色
c. More extensive in the anterior than in the posterior portion of the mouth
d. Buccal/labial surfaces are more intensely pigmented than the lingual/palatal surfaces

題號	題目
1	Which following disease do not cause melanin pigmentation ? (A) Peutz-Jeghers syndrome (B) Addison disease (C) Chronic pulmonary disease (D) Ranula
答案(D)	出處：oral and maxillofacial pathology 3edition P.316~318, 456~457
題號	題目
2	Which of the following is the ideal way to distinguish physiological melanin pigmentation from smoker's melanosis ?
	(A) Medical history (B) Common in anterior gingiva (C) Diffuse pigmentation (D) Increased melanin pigmentation in basal cell layer
答案(A)	出處： oral and maxillofacial pathology 3edition P.106~114