Acta Derm Venereol (Stockh) 1991; 71: 283–286

Melanosome Complexes and Melanin Macroglobules in Normal Human Skin

JACEK BARTOSIK

Department of Medical Cell Research, University of Lund, Lund, Sweden

The presence of melanin macroglobules, and sometimes that of melanosome complexes also, in epidermal melanocytes has been considered a feature of various skin diseases. Opinions differ as to whether these structures can occur in normal skin.

We have studied these melanin inclusions in normal Caucasian skin in the entire soma of 116 melanocytes and the occurrence of melanosomes in phagosomes of 77 Langerhans' cells obtained in different seasons. During winter the melanocytes contained few melanosomes but many melanosome complexes and melanin macroglobules. These melanosome inclusions were in 86%, localized in the most basal part of the melanocytes, particularly in the dermal protrusions. It is suggested that these structures can be transferred from epidermal melanocytes to dermal cells and that melanin macroglobules derive from melanosome complexes.

Irrespective of the season, most of the Langerhans' cells contained melanosomes in their phagosomes, which suggests a phagocytic capacity of these cells and a role in the elimination of the melanin. ***Key words: Ultrastructure; Melanocytes; Langerhans' cells.***

(Accepted January 16, 1991.)

Acta Derm Venereol (Stockh) 1991; 71: 283–286.

J. Bartosik, Department of Medical Cell Research, University of Lund, Biskopsg 5, S-223 62 Lund, Sweden.

It is a generally held view that the melanosome complex (MCo) represents heterolysosomes within keratinocytes and macrophages, and autolysosomes within melanocytes (1–4). In cells which do not produce melanin but take up melanosomes, the MCo may arise de novo by fusion of individual melanosomes (1). Autophagocytosis of melanosomes is seen only rarely in normal melanocytes and has been interpreted as an indication of excessive melanosome production in normal (5) or pathological conditions (2) and/or as disturbance of melanosome transfer (3). This autophagocytosis has been recognized as a sign of pathological alteration in the cell (6, 7). The MCo are only occasionally found in normal skin (3, 8). Melanosome complexes were also reported to exist in Langerhans' cells in normal human skin (9) and vitiligo (10) and their presence was considered as evidence for phagocytic activity of the Langerhans' cell.

Another melanin inclusion, melanin macroglobule (MMG), also called macromelanosome or giant melanosome, has been described in different skin diseases in melanocytes (11–13). It is rarely found in normal skin (14).

The MMG are described as similar to degraded MCo (2, 3, 15) and thus are considered to be related to them (2, 15–17). There is a contradicting view that MMG are not related to the MCo. According to this latter view, MMG are morphologically different, e.g. a homogeneous and amorphous structure of larger ∅ than MCo, with smooth contour and vesiculoglobular bodies in the periphery (18) and thus

Table I. *Distribution of MCo in 116 melanocytes*

INDIVIDUAL	A	B	C	D	E	F	G
Hair colour*	b**	d	b	r	d	b	d
Skin type	II	III	II	I	III	II	III
Age	58	37	37	31	31	24	25
SUMMER:							
No. of melanocytes	7	7	7	6	11	10	12
No. of melanocytes with MCo	3	4	4	0	5	3	1
No. of SMCo	2	8	2	0	2	4	1
No. of LMCo	2	1	3	0	7	0	0
							Total: 32 MCo
WINTER:							
No. of melanocytes	7	7	6	6	12	11	7
No. of melanocytes with MCo	1	4	6	0	7	3	6
No. of SMCo	0	5	5	0	11	4	4
No. of LMCo	1	21	21	0	9	3	5
							Total: 89 MCo

* b = blond, d = dark, r = red

** blond hair and red beard

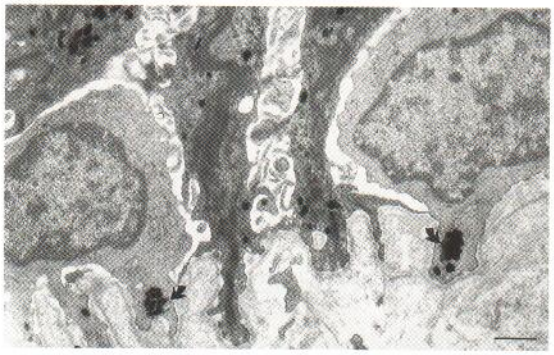

Fig. 1. Melanocytes often contain MCo in their protrusion towards the dermis (arrows). Bar = 1μ.

represent a result of abnormal melanogenesis (11, 13, 18, 19).

In order to elucidate the nature of these melanin inclusions, we examined the occurrence of these structures in normal human skin in melanocytes and Langerhans' cells.

MATERIAL AND METHODS

Two punch biopsies (3 mm) were obtained from 7 healthy volunteers (see Table I, individuals D and G were females) without any pretreatment. The biopsies were taken from the radial projection of volar forearm skin lacking ephelides, during winter (Jan.–Feb.) and summer (July–Aug.), and were processed for EM according to Falck et al. (20). The fixation time was doubled due to the size of the tissue pieces.

Three hundred serial sections (each about 200 μm long and 50 nm thick) from each specimen were distributed on 15 slot grids. Only those melanocytes which had their entire cell body within the section series were examined. In some cases 2 section series were taken to obtain a minimum of 6 fully sectioned melanocytes from each biopsy.

Every section was viewed in the electron microscope and all MCo in the soma of the cells were mapped. Two groups of MCo were distinguished, small MCo (SMCo) with $\varnothing < 0.5$ μm and large MCo (LMCo) with $\varnothing > 0.5$ μm.

For the analysis of phagocyted melanin in Langerhans' cells, twenty-three forearm skin biopsies from 7 healthy volunteers (including 3 of the volunteers above) were taken during winter, summer and autumn (Nov.). Series of two hundred sections were obtained from each specimen. The number of lysosomes containing melanin was estimated within the entire cell body of 77 Langerhans' cells.

The experiment was performed as a single-blind study.

RESULTS

All MCo were mapped in the entire soma of a total of 116 melanocytes in an average of 180 consecutive sections per cell. There were found 5 inactive melanocytes, i.e. with few cell organelles, small Golgi fields, no prominent dendrites and extremely few melanosomes. These cells were seen in biopsies taken during the winter (individuals A, B, D, F). Melanocytes from summer skin generally contained more melanosomes than those from winter specimens.

The majority of melanocytes possessed one cilium. The cilia were of various lengths and could point in any direction but approximately half were found in the basal part of the cell.

No melanocytes from the red-haired individual D contained MCo but the greater part of the melanin in the keratinocytes was aggregated. Of all the 116 melanocytes, 33% of those from summer and 48% of those from winter specimens possessed one or more MCo (Table I). Moreover, winter skin contained a far greater total number of MCo than did summer skin. This difference was statistically significant (Wilcoxon's rank sum test) in individuals C ($p = 0{,}04$) and G ($p = 0{,}001$).

Of all MCo in the melanocytes, 86% occupied the most basal part of the cytoplasm and were very often localized in small protrusions towards the dermis (Fig. 1). Only 2 out of all 49 LMCo and 8 out of 26 SMCo occupied the position above the nucleus. Extensive accumulations of separated melanosomes, were often observed in the protrusions towards the dermis (Fig. 2).

A limiting membrane was always observed around the MCo, but was not clearly visible in all sections. Extensive tilting of the grid in the electron microscope was sometimes necessary to visualize the membrane. Groups of tightly packed melanosomes in different stages of degradation were often seen within these organelles. In some MCo most of the

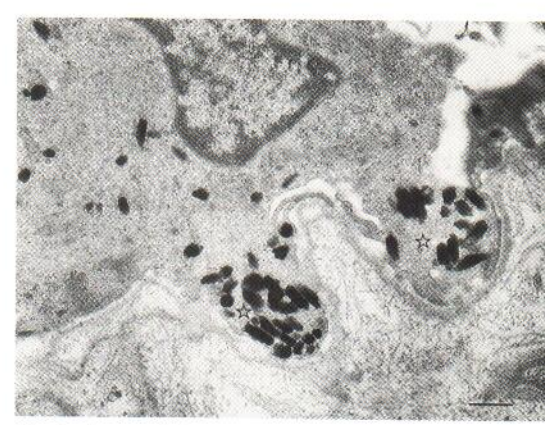

Fig. 2. Accumulation of melanosomes in melanocyte's protrusions towards the dermis (stars). Bar = 0.5 μ.

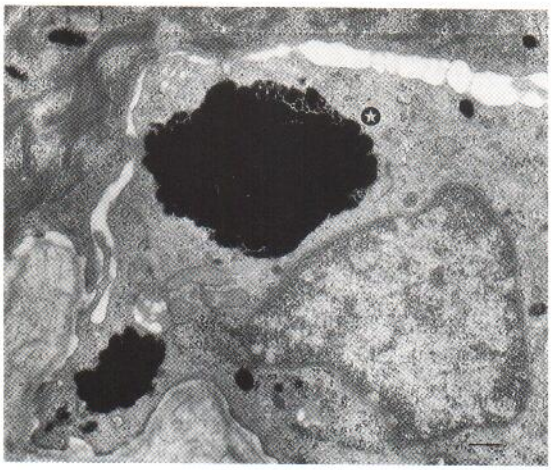

Fig. 3. MMG (star) with central homogenous mass and melanosomes in the periphery. Bar = 0.25 μ.

degraded melanosomes formed a central homogenous mass surrounded by an outer zone consisting of separated melanosomes and sometimes of microvesicles with ∅ about 40–50 nm (Fig. 3). Such MCo varied widely in shape. They had either little central mass and several separated melanosomes in the periphery or resembled a typical MMG by having a huge central homogenous part and only very few melanosomes in the outer zone. These structures, however, did not always have a smooth contour. Few of them were found only in individuals B, C and G.

The largest MCo which did not contain degraded melanosomes could consist of hundreds of separate melanosomes (Fig. 4).

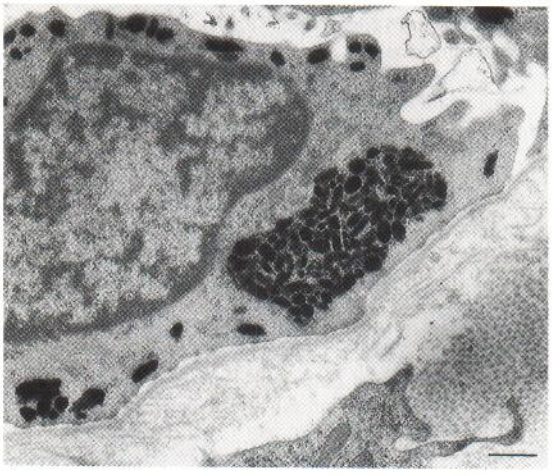

Fig. 4. LMCo with abundance of aggregated melanosomes. Bar = 0.5 μ.

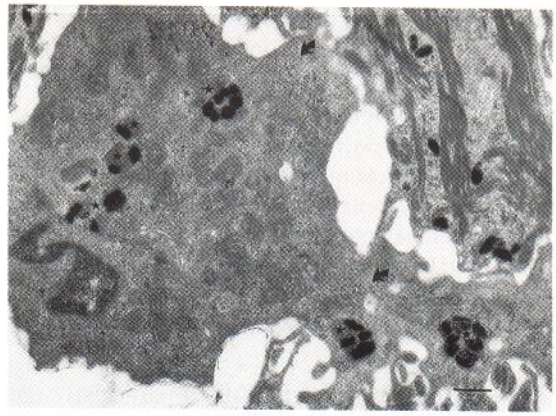

Fig. 5. Phagosomes filled with melanosomes in a Langerhans' cell (stars). Some Birbeck's granules are indicated by arrows. Bar = 0.5 μ.

In the keratinocytes, melanin was often localized within SMCo. The LMCo within keratinocytes were never observed in this material.

Subjects B, C, E, F and G had few dermal fibroblasts, macrophages or endothelial cells containing LMCo.

All phagosomes which contained melanosomes were mapped in the 77 Langerhans' cells. About 30% of the Langerhans' cells contained no melanosomes. The rest contained at least one lysosome filled with melanosomes (Figs 5, 6). There were no significant differences either between individuals or between seasons.

DISCUSSION

There is still much disagreement concerning the origin of the MMG and MCo in melanocytes and whether they can occur in normal skin.

Our observations show that MCo can occur in relatively high numbers in normal human epidermis. Moreover, the fact that MCo frequently occur in less

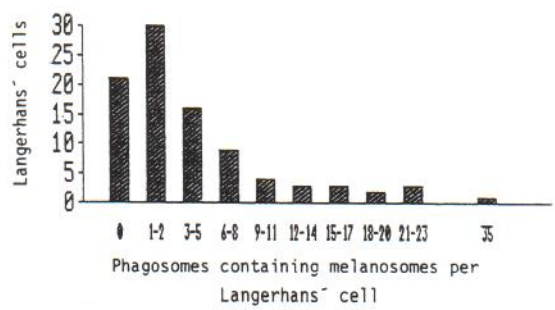

Fig. 6. Distribution of phagosomes containing melanosomes in 77 Langerhans' cells.

melanosome-rich melanocytes (winter skin), contradicts the commonly held opinion that these structures appear only in melanocytes with excessive melanin production (2, 5). The occurrence of MCo in normal epidermis may be a consequence of the withdrawal of melanosomes from melanocytes under conditions of lessened melanin demand paralleled by cessation of melanin production. It is known that, in unexposed keratinocytes, there is a predominance of aggregated melanosomes while exposure to solar radiation leads to a predominance of dispersed melanosomes (21).

The vast majority of the MCo, particularly the largest ones, occupied the most basal part of the melanocytes, very often in the cell protrusions towards the dermis. This observation with the fact that dermal cells (particularly melanophages) can contain LMCo, supports the view that melanocytes can discharge melanosomes directly, through their protrusions into the dermis (22, 23).

Some of MCo contained a central amorphous homogeneous mass of varying size, which may represent degraded melanosomes within an MCo. MCo with a very large central, amorphous part and narrow outer zone containing separated melanosomes, were identical with MMG described earlier (2, 3, 15). However they did not have a perfectly rounded and smooth contour over their entire circumference as was claimed by others (18). This observation concerning the ultrastructure thus nevertheless supports the view that MMG are an end-product of MCo (2, 3, 15).

The presence of phagosomes which contain melanosomes in the Langerhans' cells, shows that these cells also can play a role in the elimination of melanin and demonstrates the phagocytic capacity of these cells.

REFERENCES

1. Wolff K, Höningsmann H. Are melanosome complexes lysosomes? J Invest Dermatol 1972; 59: 170–176.
2. Hirone T, Eryu Y. Ultrastructure of giant pigment granules in lentigo simplex. Acta Derm Venereol (Stockh) 1978; 58: 223–229.
3. Nakagawa H, Rhodes AR, Momtaz K, Fitzpatrick TB. Morphologic alteration of epidermal melanocytes and melanosomes in PUVA lentigines: A comparative ultrastructural investigation of lentigines induced by PUVA and sunlight. J Invest Dermatol 1984; 82: 101–107.
4. Nakagawa H, Rhodes AR, Fitzpatrick TB, Hori Y. Acid phosphatase in melanosome formation: A cytochemical study in normal human melanocytes. J Invest Dermatol 1984; 83: 140–144.
5. Hedin AC, Larsson A. Large melanosome complex in human gingival epithelium. J Peridont Res 1987; 22: 108–113.
6. Drzewiecki KT. The epidermal melanocytes in patients with cutaneous malign melanoma. A transmission electron microscopic investigation. Scan J Plast Reconstr Surg 1979; 13: 393–400.
7. Kanerva L, Lauharanta J, Niemi K-M, Juvakoski T, Lassus A. Persistent ashen-gray maculae and freckles induced by long-term PUVA treatment. Dermatologica 1983; 166: 281–286.
8. Drzewiecki KT, Pitz-Drzewiecka J. The epidermal melanocyte system in individuals of scandinavian origin, determined by DOPA-staining and TEM. Scand J Reconstr Surg 1979; 13: 381–391.
9. Elofsson R. Evidence for endocytotic mechanism in the epidermal Langerhans cells. Acta Derm Venereol (Stockh) Suppl 1981; 99: 29–39.
10. Breathnach AS, Wyllie LMA. Melanin in Langerhans cells. J Invest Dermatol 1965; 45: 401–403.
11. Konrad K, Wolff K, Höningsmann H. The giant melanosome: A model of deranged melanosome-morphogenesis. J Ultrastruct Res 1974; 48: 102–123.
12. Hu F. Aging of melanocytes. J Invest Dermatol 1979; 73: 70–79.
13. Rennie IG, Bleehen SS. Melanosis oculi: An ultrastructural study of an affected iris. Arch Ophthamol 1983; 101: 1912–1916.
14. Konrad K, Höningsmann H. Riesenmelanosomen in Nävuszellnävi und in normaler menschlicher Epidermis. Wiener Klin Wochenschrift 1975; 87: 7 März.
15. Nakagawa H, Hori Y, Sato S, Fitzpatrick TB, Martuza RL. The nature and origin of the melanin macroglobule. J Invest Dermatol 1984; 83: 134–139.
16. Perrot H, Ortonne JP. Xeroderma pigmentosum: ultrastructural study with special reference to abnormalities of the melanin pigmentary system. Arch Dermatol Res 1980; 268: 43–51.
17. Adam BA. Macromelanosomes in dermal macrophages. J Cutan Pathol 1981; 8: 263–266.
18. Horikoshi Y, Jimbow K, Sugiyama S. Comparison of macromelanosomes and autophagic giant melanosome complexes in nevocellular nevi, lentigo simplex and malignant melanoma. J Cutan Pathol 1982; 9: 329–339.
19. Jimbow K, Horikoshi T. The nature and significance of macromelanosomes in pigmented skin lesions: Their morphological characteristics, specificity for their occurrence, and possible mechanisms for their formation. Am J Dermatopathol 1982; 4: 413–420.
20. Falck B, Andersson A, Elofsson R, Sjöborg S. New views on epidermis and its Langerhans cells in the normal state and in contact dermatitis. Acta Derm Venereol (Stockh) Suppl. 1981; 99: 3–27.
21. Toda K, Pathak MA, Parrish JA, Fitzpatrick TB. Alteration of racial differences in melanosome distribution in human epidermis after exposure to ultraviolet light. Nature (New Biology) 1972; 236: 143–145.
22. Mishima Y. Lysosomes in melanin phagocytosis and synthesis. Nature 1967; 216: 67.
23. Wong CK, Guerrier CJ, Macmillian DC, Vickers HR. An electron microscopical study of Bloch-Sulzberger syndrome (incontinentia pigmenti). Acta Derm Venereol (Stockh) 1971; 51: 161–168.