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Presence of melanin in normal human Schwann cells

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Summary. The presence of melanin granules in Schwann cells of unmyelinated nerve fibres in the normal skin of a black woman is demonstrated by electron microscopy. Pathological conditions associated with the differentiation ability of Schwann cells for melanogenic are reviewed. This capacity may be due to the common origin of Schwann cells and melanocytes in the neural crest.

Key words: Schwann cell, Melanin, Dermis, Unmyelinated fibre

Introduction

The presence of melanin in Schwann cells has been described in both human (Enzinger and Weiss, 1983; El-Labban, 1988) and experimental pathology (Nakai and Rappaport, 1963; Kanno et al., 1986). However, the existence of melanin in this glial cell type of the peripheral nervous system has been described only exceptionally in normal human tissues. In a review of the literature, a single paper has been found describing the presence of melanosomes in dermal Schwann cells in the normal forearm skin of a 35-year-old darkly pigmented male from the Solomon Islands (Melanesia) (García and Szabo, 1979). In this same report, the presence of melanin in the pigmented scrotal skin of an adult black Long-Evans rat was noted as well.

In the present ultrastructural study we report a new description of melanin in normal human Schwann cells in undamaged dermis.

Materials and methods

The specimen was a fragment of abdominal skin from a 40-year-old black woman. The patient presented neither neoplastic nor dermatological diseases. The sample was fixed by immersion in 0.1 M phosphate-buffered 3% glutaraldehyde, pH 7.4. After washing in the same buffer, the specimen was postfixed in phosphate-buffered 1% osmium tetroxide and embedded in Vestopal. Ultrathin sections were cut on an LKB ultramicrotome, double stained with uranyl acetate and lead citrate and examined in a Philips EM 201 electron microscope.

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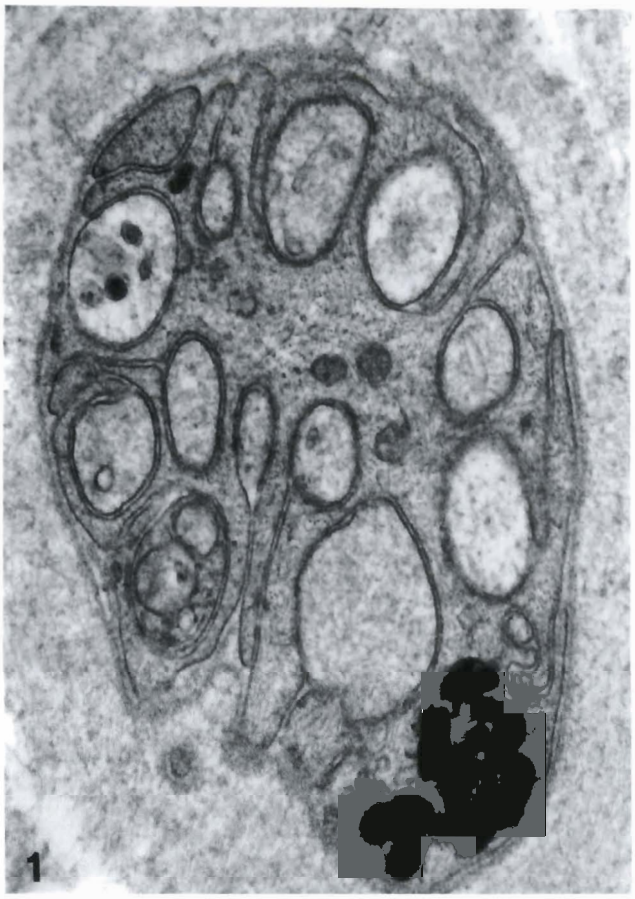
Results

Typical unmyelinated nerve fibres were noted in the dermal connective tissue. These structures were composed of Schwann cells containing several axons (Fig. 1). Mesoaxons and the basal lamina surrounding Schwann cells were easily identified. Occasionally, unmyelinated nerve fibres were close to the epidermis (Fig. 2). Scattered Schwann cells with abundant organelles, including short rough endoplasmic reticulum profiles, free ribosomes, well-developed Golgi complex and vesicles, centriole and sparse mitochondria, were observed (Fig. 3). Clusters of ovoid-shaped granules were found in the cytoplasm of most Schwann cells (Fig. 4). The homogeneous and highly electrondense content of these granules was bound by a trilaminar unit membrane. According to ultrastructural criteria, these organelles were identified as melanin granules. In some Schwann cells the granules were evenly dispersed throughout the cytoplasm (Fig. 2). Some lipid droplets and dense bodies showing diverse shapes and moderate electrondense content (probably lysosomic in nature), were exceptionally seen. These structures were in close spatial relationship to melanin granules (Fig. 5). On the other hand, in the same cells where lipid droplets and dense bodies were detected, large clusters of melanin granules showing no relation to those structures were also seen (Fig. 6).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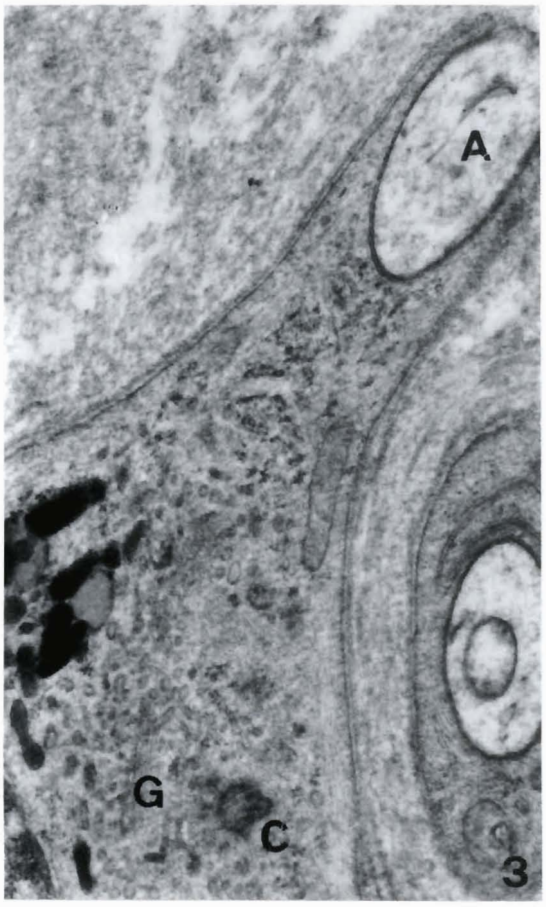
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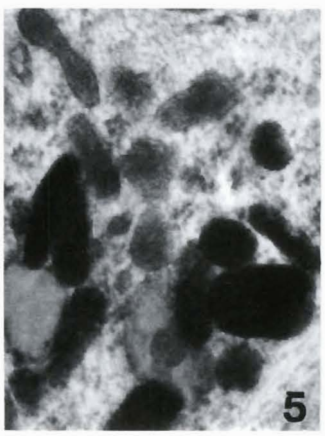
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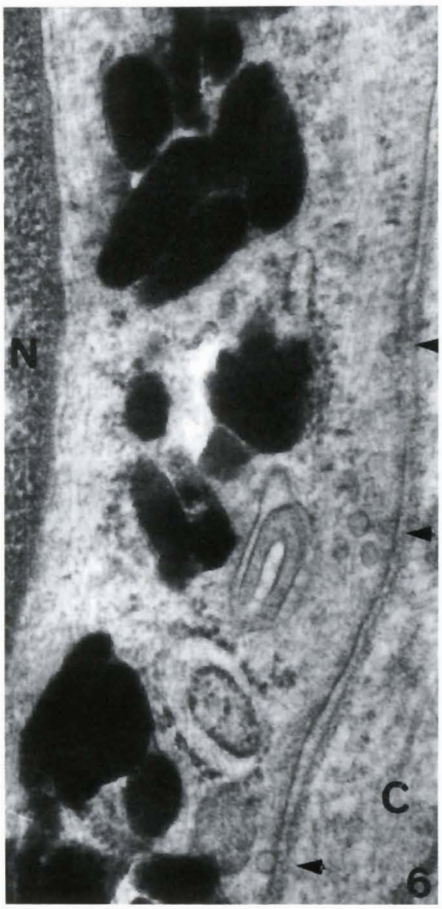
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Fig. 1. Cross-section of a Schwann cell containing several axons. Melanin granules are noted within its cytoplasm. × 11,900

Fig. 2. Schwann cell in the upper dermis surrounded by a basal lamina (arrowheads). Several evenly dispersed melanin granules are observed: E: epithelial cell of the germinative layer. × 7,650

Fig. 3. Schwann cell cytoplasm. The abundance of organelles can be observed,. G: Golgi complex. C: Centriole. A: Axon. × 12,800

Fig. 4. Detail of Fig. 1. The homogeneous and high electrondense content of the melanin granules are noted. × 19,200

Fig. 5. Detail of Fig. 3. Melanin granules are close to dense bodies of lysosomic appearance and lipid droplets. × 24,000

Fig. 6. Detail of a Schwann cell surrounded by basal lamina. Abundant melanin granules are observed. Note pinocytotic-like vesicles on the cell surface (arrowheads). C: Connective tissue. N: Nucleus. × 32,000

Discussion

The present ultrastructural study demonstrates melanin granules in normal human Schwann cells forming typical unmyelinated nerve fibres within dermal connective tissue. Our findings are similar to those reported by García and Szabo (1979). Since both cases correspond to black individuals, the possibility arises that this finding is race-related and could be more frequent in -or even exclusive- to darkly pigmented subjects. Further studies in different races are needed to elucidate this question.

The existence of melanin in Schwann cells or the presence of melanocytic cells exhibiting Schwannoid (neuroid) differentiation has been extensively described in several human and experimental pathological conditions. Thus, ultrastructural studies in human neoplasms have demonstrated neoplastic Schwann cells displaying melanogenesis in melanotic Schwannoma (Mennemeyer et al., 1979; Webb, 1982; Katenkamp et al., 1986), melanotic neurofibroma (Anderson and Robertson, 1979; Payan, 1986), ganglioneuromas and ganglioneuroblastomas (Hahn et al., 1976). Furthermore, neoplastic cells showing ultrastructural features characteristic of both Schwann cells and melanocytes, have been noted in several other tumors including cellular and malignant blue nevus (Merkow et al., 1969; Bruner, 1987), neurotropic melanoma (Warner et al., 1981), malignant melanoma of soft parts (clear cell sarcoma of tendons and aponeuroses) (Azumi and Turner, 1983; Benson et al., 1985) and pigmented dermatofibrosarcoma protuberans (Nakamura et al., 1987). It should be emphasized that spontaneous neuroid transformation is a usual finding in common cutaneous nevi cells located in the deepest regions of the dermis. This fact constitutes the normal sequence in the course of maturation of these lesions (Lever and Schaumburg-Lever, 1983). It should also be noted that melanin-forming Schwann cells have been found in several non-neoplastic human lesions of the oral mucosa, such as lichen planus and sublingual keratosis (El-Labban, 1988). Experimental evidence in animals supports the melanogenic ability of Schwann cells. Thus, melanin-synthesizing cells showing Schwannoid (neuroid) differentiation have been found in experimentally-induced intradermic melanocytic tumors in hamsters and mice after the topical application of chemical carcinogens (Nakai and Rappaport, 1963; Kanno et al., 1986). Finally, melanocyte-like cells were observed in chicken embryo peripheral nervous tissue cultures (Nichols and Weston, 1977; Nichols et al., 1977). Melanin-forming Schwannoid cells have also been detected in experimentally-induced nerve sheath tumors after transplacentaly administration of carcinogens in rats (Spence et al., 1976).

All these findings illustrate the melanogenic ability of Schwann cells. This event may be explained by the common embryonic origin of melanocytes and Schwann cells in the neural crest. In fact, both cell types share an intermediate pluripotential precursor (Le Douarin et al., 1991). Díaz-Flores et al. (1978) have also described the so-called «melanogliocyte» in adult tissues, a cell type that shows ultrastructural features characteristic of both melanocytes and Schwann cells.

The capacity for melanin synthesis in Schwann cells would be either the result of regression states or the response to different stimuli. Schwann cells in our study were totally normal; this could be the reason why melanosomes in different stages of maturation were not found, and only mature melanine granules were present, in contrast to most pathological situations described above.

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