into dopaquinones. Tyrosinase is the enzyme that catalyzes these two reactions. This metabolism is the rate-limiting reaction in the synthesis of melamins (Fig. 1.18).

Dopaquinones are automatically oxidized to become indole compounds that are connected to each other to synthesize eumelans. If cysteins are involved at this stage, dopaquinons connect with cysteins and change into 5-S-cysteinyl dopa (5-S-CD), which polymerizes to synthesize pheomelansins.

3. Melanosome

The melanosome is a subcellular organelle, enclosed by a lipid double membrane, in which melamins are exclusively produced. When tyrosinases, which are synthesized by the Golgi apparatus, are carried to premelanosomes, which are isolated from the agranular endoplasmic reticula, melanin synthesis begins. As the amount of synthesis increases, melanosomes enlarge. The formation of melanosomes is divided into stages I to IV by the degree of melanin deposition (Fig. 1.19). A melanosome in stage IV is 500 nm to 700 nm along its major axis, football shaped, and supplied from the dendrites to the neighboring epidermal keratinocytes.

4. Functions of melanin

The most important role of melanin is protecting the skin from UV rays and preventing the occurrence of malignant tumors and sunlight injury to the skin. The darker the skin of a particular race, the lower is the incidence of skin cancer caused by UV light.

Exposure to sunlight darkens the skin. This darkening may occur immediately after exposure and may be temporary, when melanins are oxidized temporarily, or it may occur after several days of exposure, when there is an increase in melanin synthesis and mature melanosome formation.

Melansins can also act to absorb harmful active enzymes, metals and drugs.

e. Langerhans cell

The Langerhans cell is a bone marrow-derived dendritic cell specific to stratified squamous epithelia such as the skin. Langerhans cells are frequently seen isolated in the middle and upper suprabasal cell layers (Fig. 1.20). The cells are distributed at a density of 400/mm² to 1,000/mm². They lack tonofilaments and cell attachment structures, such as desmosomes, and they migrate. By electron microscopy, a few fibrillary components and Birbeck granules, whose cross-section is a characteristic tennis racquet shape, are observed in the cell cytoplasm (Fig. 1.21a). Birbeck granules are known to be Golgi-apparatus-derived or membrane-derived, and carry antigens in the cells.
Langerhans cells present antigens to T cells (see Chapter 3 for immune reactions in the epidermis). Since the Langerhans cell is ATPase positive, CD1a positive and S-100 protein stain positive, it is easily distinguished from other kinds of cells.

f. **α-dendritic cell**

The α-dendritic cell is found in the epidermis. It resembles a Langerhans cell because of its lack of adhesive intercellular structures such as desmosomes; however, it can be distinguished by its lack of Birbeck granules. Although the origin and function of α-dendritic cells are unknown, these cells may be precursors of Langerhans cells or otherwise related to Langerhans cells.

g. **Merkel cell**

The Merkel cell is a tactile cell found in the basal cell layer. Greater numbers of Merkel cells are seen in the fingers, oral mucosa and trichodis areas (the hair roots). With angular plasma membrane projections, Merkel cells are connected to adjacent keratinocytes by desmosomes (Fig. 1.21b). Multiple dense-core granules called Merkel cell granules are found in Merkel cells, to which the sensory (free) nerve endings are connected by synapses beneath the cell. After physical stimulation, neurotransmitters are secreted from Merkel cell granules, and the tactile information is transmitted to the sensory nerve.

Fig. 1.19 Maturation of melanosomes.

Fig. 1.20 Langerhans cell (immunostaining against CD1a).

Fig. 1.21 Histopathology of Langerhans cell and Merkel cell.

a: Birbeck granules of Langerhans cell (arrows).

b: Dense-core granules of Merkel cell (arrows).

**MEMO**

**Langerhans cell histiocytosis (LCH)**

This used to be called histiocytosis X, a disease in which a malignancy occurs from excess proliferation of Langerhans cell histiocytes.