

ELECTRON MICROSCOPY OF HUMAN EPIDERMAL LANGERHANS CELLS

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Langerhans cells (LCs) are migrating dendritic cells found in the suprabasal part of the epidermis. As the only cells of the epidermis, in which enzyme ATPase is coupled to the cell membrane, they are easily identified by detection of ATPase activity (1). High expression of CD1a and MHC class I and II molecules shows that Langerhans cells are prominent antigen-presenting cells of the skin immune system. Antigens incorporated in cells are degraded by proteolytic enzymes and with adhering MHC class II molecules are presented to T lymphocytes (2).

The most typical organelles of Langerhans cells are Birbeck granules (3). They appear in the cytoplasm of Langerhans cells as rod-shaped bodies with a central zipper-like structure or tennis-racket-shaped bodies with a vesicular dilation at one end. Recent studies have shown that Birbeck granules (Bgs) take part in transfer of molecules entering the cell via receptor-mediated endocytosis and represent a dynamic structure. Nevertheless, the origin of Birbeck granules and their function remain controversial (4).

LCs migrate from the skin to regional lymph nodes where present antigens with adhering MHC class II molecules to T lymphocytes. While migrating, they become mature dendritic cells characterized by lower amounts of Birbeck granules in the cytoplasm with subsequent higher expression of MHC class II molecules on the plasma membrane. These data are based mostly on observations of antigen-presenting Langerhans cells in mice or guinea pigs in which LCs were isolated from skin, lymph nodes, or spleen. Similar data are difficult to obtain on human epidermal Langerhans cells.

Reactivity of Langerhans cells at different time intervals after application of 0.1% 2,4 - dinitrochlorobenzene (DNCB) on the skin of 20 volunteers was studied. Based on the macroscopic findings 30 minutes after DNCB application, these volunteers were divided into group I without erythema (n=12) and group II with erythema (n=8). Skin biopsy specimens were investigated 1, 3, 10, 30 minutes and 72 hours after DNCB application. Morphological changes in the bodies and dendrites of Langerhans cells were studied. The dendrites underwent similar morphological changes as the bodies of Langerhans cells, and the ultrastructural composition of the former also reflected cell activation. Other investigators did not previously pay attention to the dendrites. Our findings confirm formation of Birbeck granules (Bgs) resulting from ligand-receptor mediated endocytosis, most evident in group II where LCs showed more rapid and more vigorous activation and Bgs connected to the plasma membrane were detected in both dendrites and - cell bodies. Furthermore, Birbeck granule-like structures were found in group II LCs dendrites. They reflect enhanced reactivity of these cells that do not represent a different type of LCs. A majority of the intracellular MHC class II molecules were found in vesicular structures, the so-called MHC-II compartment (MIIC). Simultaneously with Bgs, MIIC compartments develop in the cytoplasm and are most abundant at the moment when LCs leave the epidermis.

The skin of eight volunteers was treated with acetone, 60 % alcohol, iodisol, 5 % nickel sulphate. Alcohol and nickel sulphate caused degenerative changes, mainly cytoplasmic vacuolation, in Langerhans cells. Nickel sulphate was even responsible for the disappearance of dendrites. Both chemicals have cytotoxic effects on Langerhans cells: cytoplasmic organelles and Birbeck granules do not proliferate and subsequently, the antigen-presenting activity of epidermal Langerhans cells is inhibited. The reaction of Langerhans cells to iodisol application was surprising. Accumulation of tennis- racket-shaped Birbeck granules is suggestive of increased endocytotic activity. On the other hand, cytoplasmic vacuolation was observed as in the case of alcohol. One possible explanation consists in the composition of the agent used: iodine 450 mg, polyvinylpyrrolidone 2.55 g, and 95 % ethylalcohol per 100 g iodisol. Whether the vacuolation is attributable to alcohol or to hypersensitivity to iodisol is difficult to say, since a similar reaction was observed with the use of DNCB at a toxic concentration. We did not find any morphological changes in LCs after application of acetone. Our results indicate that acetone is more suitable for use, since it does not affect activity of Langerhans cells.

The skin is an important immune organ that can be influenced by external stimuli. Therefore, attention should be focused not only on the immunological responsiveness of epidermal Langerhans cells to different stimuli, but also on its morphological correlates.

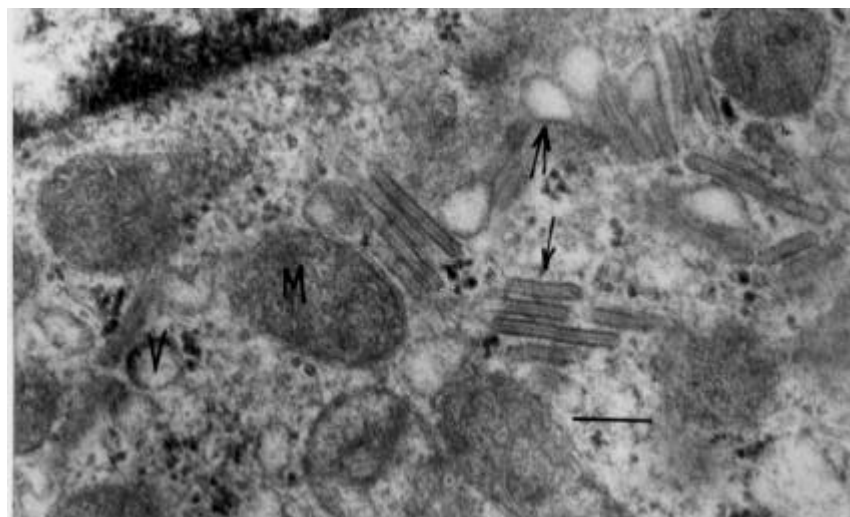


Fig. 1. The cytoplasm of the LCs the rod shaped Bgs (arrow), the tennis-racquet-shaped Bgs (double arrow), bar = 200nm

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