

Langerhans cells differentiation: a three-act play

L. Pieri, L. Domenici, P. Romagnoli

Department of Anatomy, Histology and Forensic Medicine, University of Florence, Florence, Italy

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SUMMARY

Langerhans cells are the dendritic cells typical of stratified squamous epithelia and enjoy an intermediate state of differentiation as dendritic cells, since they are very efficient in uptaking and processing antigens but poor in presenting them to lymphocytes. These cells, and other dendritic cells as well, differentiate from bone marrow precursors, with circulating monocytes as intermediates. Langerhans cells leave the epidermis upon loading with antigen and further differentiate into mature dendritic cells while moving to peripheral lymphoid organs, where they elicit primary immune responses. The signals regulating differentiation of precursors into Langerhans cells and of this latter cells into mature dendritic cells have been unraveled thanks to in vitro studies and include a wide range of cytokines, some of which can actively inhibit this process. Also pro-B cells and thymic precursors can give raise in vitro to mature dendritic cells, but apparently not to Langerhans cells. Keratinocytes, the principal cell type of epidermis and mucosal stratified squamous epithelia, can provide for a wide range of cytokines influencing the differentiation of cells of dendritic lineage, in particular Langerhans cells. These cytokines include GM-CSF and TNF-alpha, that may be relevant also for the maintenance of the differentiated state of Langerhans cells within epidermis. Cell to cell contacts mediated by E-cadherin may also contribute signals from keratinocytes to differentiating Langerhans cells. The epidermis and mucosal squamous epithelia host other cell types, besides keratinocytes, and nerve fibers, that all can contribute signals to differentiating Langerhans cells. The differentiation of Langerhans cells within the epithelial microenvironment of skin and mucosae most probably results from the interaction of several players, that play different roles on this scene in different physiological and pathophysiological conditions.