Langerhans Cells Pathophysiology- An Overview

K. M. K. MASTHAN*, N. ANITHA*, S. HARI PRIYA* and N. ARAVINDHA BABU*

Department of Oral Pathology, Sree Balaji Dental College and Hospital, Bharath University, Pallikaranai, Chennai - 600100, India.

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ABSTRACT

In 1868, Paul Langerhans first described langerhans cell, they are dendritically shaped cells, which were located in epidermis of the squamous epithelia. Langerhans cells are seen in all suprabasal layer of stratified squamous epithelium. They play a vital role in local defense mechanisms in the epithelium. They are bone marrow derived dendritic cell and act as antigen presenting cells (APCs) of immune responses. APCs, the lymphocytes respond to specific microbes. In this article we have reviewed the physiology and mechanism of action of their role in different pathological conditions.

Keywords: Langerhans cells, APCs, Pathological conditions.

INTRODUCTION

Langerhans cells (LC) lack desmosomal attachment and appear as clear cells in histological section, they are characterized by flask shape or rod like granules called birbeck granules. They have immunological function that identifies and process the antigenic material that enter into the epithelium from the external environment. These LC migrate from epithelium to regional lymph nodes. They are present in the suprabasal layer of stratified squamous epithelium.

Morphology and distribution

LCs are flattened disc shaped, which are aligned in a horizontal plane and parallel to the surface of the skin. They possess 5 to 9 dendrites. These dendrites lie in the same horizontal plane. Dendrites from individual cells may overlap, and there is no direct cell-to-cell contact. Dendritic processes can often be observed extending to the level of stratum corneum. In electron microscopy, LCs are 12 microns in diameter and have lobulated nuclei and cytoplasm. Specific cytoplasmic organelles are poor in vacuoles and organelles. Specific cytoplasmic organelles were first described by Birbeck hence called birbeck granules (100 nm to 1 mm in size). Birbeck granules seen in continuity with cytoplasmic membrane and are often clustered near the Golgi apparatus. There is always a conflict that these granules arise from Golgi apparatus as they have secretory function or it may arise from invagination of cytoplasmic membrane. LC are found in the epidermis of skin, in local lymph nodes, thymic epithelium and bronchial mucosa. In the skin they represent 1-2% of the entire epidermal population and seen only in the suprabasal area, with even distribution. The cells have a mean volume of 213µm³ and density about 1.6 x 10⁵ cells per mm² of epidermis. With the dendrites, 25% of the surface area of skin covered by LC. Most of LCs contain one to several Birbeck...
granules in the epidermis some LCs does not possess the birbeck granules which are called “indeterminate cells” these are precursor cells to LCs. Loss of these organelles tend to increase their functional potential of LC.

**Origin of langerhans cells**

The Langerhans cells (LCs) origin from the bone marrow and then travel to the epithelium to perform the function of antigen recognition and presentation. The myeloid and the lymphoid series cell type are CD34+ haematopoietic progenitor cell, which were differentiated into distinct Dendritic Cells (DC) subtypes and perform distinct functions 

Lymphoid progenitors give rise to precursors that differentiate into plasmacytoid DCs, thymic DCs, and interdigitating DCs. Myeloid progenitors give rise to precursors of germinal centre DCs, interstitial DCs, monocyte/macrophage series, LCs, and peripheral blood DCs. This indicates that common precursors give rise to different subtypes DC, under specific environmental conditions.

**Function of langerhans cells**

LCs can present antigen to helper and cytotoxic T-cells.

LCs present

Exogenous antigen

Via MHC class II

Present CD4+helper cells

LCs also possesses the MHC class I restricted cytotoxic (CD8+) T-cell responses, which depend on the expression of costimulatory molecules B7-1. In addition, by the production of cytokines, including IL-12 LCs stimulate NK cells.

LC present in most tissue is unstable “immature” state thus unable to stimulate T-cells. Immature LCs that express surface receptors of various antigens include toll-like receptors, C-type lectin receptors, Fc-g, and complement receptors.

LCs captured these antigen in peripheral tissues and processed to form MHC-peptide complexes. Pathogens and inflammatory cytokines which alter LCs to be mature and mobilized. LCs migrate into the lamina propria and become CD83+ mature LCs are mobilized and matured in response to inflammatory cytokines and pathogen associated molecular patterns from oral mucosal pathogens. LCs migrate into the lamina propria and become CD83+ mature DCs. The maturation and migratory activity regulated by chemokine receptors, inflammatory chemokine/chemoattractants, and integrins.

Bacteria and their cell wall components (Lipopolysaccharides), and cytokines like IL-1b, GM-CSF, and TNF-a, everything stimulate DC maturation and mobilization but IL-10 blocks this process. LCs complete their maturation and attract T- and B-cells by secrete chemokine which maintain the viability of T lymphocytes. Antigen may bind by B-cells, and then both B- and T-cells cluster with mature LCs, but activation in the T-cell area leading the immune responses. B-cell raises humoral immune response and form some antibody-secreting plasma cells but T-cells migrate to the site of antigen deposition, and mediate a cellular response.

**Staining**

**Hematoxylin and eosin staining**

LCs appear as a clear cells - clear halo around their nuclei they present in suprabasal layers are also referred to as ‘high level clear cells

**Special staining**

Osmium iodide, Gold chloride, zinc osmium iodide and uranyl acetate-lead staining. Zinc osmium iodide, gives good staining, can also stains keratinocytes and melanocytes.
Enzyme histochemistry
ATPase, which is an excellent method for the identification of human LCs. Other enzymes5 nucleotidases adenosinediphosphatase (ADPase) and amino-peptidases.

Immunohistochemistry
LCs possess large number of cytoplasmic antigen used of antibodies in different techniques like, immunofluorescence or immunoperoxidase techniques. LCs is the high level of expression of MHC class II antigens also MHC class I antigens. Leukocyte common antigen (CD45) is also expressed by LCs and shows stresses their bone marrow origin. Many other antigens like CD11,CD25, CD29, CD1D and CD83,Fc-IgG, CD54, C3b/C4bare found in trace amount in subpopulations of LCs can detect by sensitive methods.CD1a immunolabeling is considered to be the most reliable method to identify the human LCs. Immunohistochemical markers CD1a, b, c and d express immature DCs.Advance studies shown that Langerin seems to be the more specific marker for LCs.

Electron microscopy
In electron microscope LCs appeared cleaved or folded nucleus and no tonofilaments or desmosomes The Birbeck granules present in their cytoplasm, resemble three-dimensional profile of a disc. The granule with vesicle at one end shows an appearance of ‘tennis racket’.

Langerhans cells in different pathological conditions
Gingivitis and periodontitis9-11
IncreasedLCs in gingival epithelium associated with gingivitis. LCs is five times more in gingivitis than normal gingiva in chronic adult periodontitis.Mature CD83+ DCs form immune conjugates in the oral lymphoid foci with CD4+ T cells.

Human immunodeficiency virus infection
Acquired Immunodeficiency Syndrome and HIV related complex patients have decreased number of LCs.

Oral lichen planus
LCs was increased in lichen planus

Lichenoid drug eruptions
LCs was increased but lower the OLP

Recurrent aphthous stomatitis
LCs are increased in both recurrent aphthous stomatitis and Behcets syndrome.

Contact hypersensitivity
Contact hypersensitivity taking place in the epidermis Haptens-modified LCs can induce sensitization when particular immunizing conditions are applied.

Role of LCs in oral cancer
In oral cancer the increase in the number of LCs and also CD8 + lymphocytes and macrophages and in the epithelium

Radicular granuloma and cyst
Increase in the number of LCs, than other cysts

CONCLUSION
LCs as APCs play an important role in various oral pathologic conditions also initiates immune response. Many concepts about allow us to device specific immunotherapies and treatment modalities.

REFERENCES
1. The Normal Langerhans Cell and the LCH Cellin Macmillan Press Ltd., 1994 'Senior Lecturer/Honorary Consultant Dermatologist, Royal Postgraduate Medical School, Hammersmith Hospital, Ducane Road,London W12 ONN.; Department of Pathology, Childrens Hospital, Fifth Avenue, Pittsburgh PA 15213, USA
2. pathophysiology of Langerhans cells Shweta Jaitely, TR Saraswathi Department of Oral Pathology and Microbiology, K D Dental College and Hospital, Mathura, Uttar Pradesh, India Department of Oral and Maxillofacial Pathology, Vishnu Dental
3. Langerhans cells and their role in oral mucosal diseases. Juhi Upadhyay¹, Ram B Upadhyay¹, Panko Agrawal¹, Shweta Jaitley¹, Rita Shekhar Department of Oral and Maxillofacial Pathology, K.D. Dental College and Hospital, Mathura, India.


