THE ROLE OF LANGERHANS CELLS IN BASAL CELL CARCINOMA AND SKIN MALIGNITY

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Abstract: The Langerhans cells, dermal dendritic cells, and the group of dendritic cells, in which they are included, have as a common activity, the presentation of antigens in the lymph nodes where they are migrating to. The Langerhans cells stimulate the function of cytotoxic T lymphocytes, while the dendritic dermal cells, the function of the B lymphocytes. Recent studies mention the implication of Langerhans cells and of dermal dendritic cells in the antitumor immunotherapy with promising success in the epicutaneous immunization in the carcinoma of the skin.

Keywords: Langerhans cells, dermal dendritic cells, immunotherapy, epicutaneous immunization

Keywords: Celule Langerhans, celule dendritice dermale, imunoterapie, imunizare epicutanată

Rezumat: Celulele Langerhans, celule dendritice dermale din care fac parte au ca activitate comună prezentarea de antigeni limfocitelor la nivelul ganglionilor limfatici unde acestea migrează. Celulele Langerhans stimulează funcția limfocitelor T citotoxice, iar celulele dendritice dermale ale limfocitelor B. Studii recente susțin ideea implicării celulelor Langerhans în a celulelor dendritice dermale în imunoterapia antitumorală, strategii terapeutice de imunizare epicutanate pentru carcinoamele pielei sunt promișcătăre de succes.
The skin immunologic system is made up of LCs (the main immunologic factors) and other cells (keratinocytes, lymphocytes, macrophages and, perhaps, granulocytes), as well as of chemical substances, such as immunoglobulins, cytokines, and immune complexes.

Bos and Kapsenberg (1986) suggested the name of skin immune system (SIS) for the immunologic complex of cells + chemical substances released by them. McArndle et al., in the same year of 1986, asserted that the skin oncogenesis is more specific in the case of basal cell carcinoma regarding the density, morphology, and the pathologic response compared with other premalignant or malignant epidermal tumors, such as squamous cell carcinoma, actinic keratosis and Bowen disease.(15)

Apart from these data on the role of LCs and dermal DCs, recent observations state the existence of another cell subtype in the DCs group, specifically a smaller cellular population located in the superior dermis, named dermal langerin DCs. This cell subtype express the marker of LC langerin CD207, a C-type lectin-receptor, through which these cells take part in the skin immune responses, but have a functional independence.(16)

In vitro, and less often, in vivo studies showed that LCs are equipped with stimulatory mechanisms for cytotoxic T cells. The efficiency of these mechanisms in destroying the malignant cells amplified the investigations regarding the immunization and immune therapy strategies in malignancies.

The LCs and the subset of DCs induce antitumoral responses. The faster these cells are able to migrate from the epidermis/dermis towards peripheral lymphoid organs, the more powerful these responses are. LCs possesses the greatest migration speed, whereas dermal DCs, except langerin+ cells situated in the profound dermis migrate at a much lower speed. Due to the presence of langerin marker at the surface of these cells, which is characteristic to LCs, the two DC types are more potent in inducing the antitumoral immune response.

The immunization strategies through skin-lymph nodes developed lately on the bases of new experimental and practical knowledge on the involvement of DCs in the treatment of malignant tumours.

The aim of the treatment known as epicutaneous immunization is the activation of T lymphocytes and arming them with the power to start the antitumoral attack. Normally, the tumoral antigens are self antigens to which the immune system is tolerant. The immunotherapeutic procedures aim at blocking this tolerance and attacking the tumoral cells.

The increase in numeric density of LCs at the level of the tumour indicates that the malignant cells produce a factor or multiple factors that stimulate the migration of LCs precursors into the epidermis, the increase of mitoses in immunogenetic cells and the decrease of their migration in lymph nodes.(17)

The alternatives for epicutaneous immunization are either the use of antigen protein or peptide antigens conjugated with target antibodies. The objective is to target the tumoral antigen towards the patient’s DCs and to deposit it directly on LCs in order to induce CD4+ and CD8+ T cell responses in lymph nodes.(18)

The peptide or protein antigens are introduced either directly on injured skin, with a broken barrier induced by repeated applications of adhesive bands, or on intact skin (19) in combination with adjuvants such as choleric toxin or ligands that contain imiquimod (Aldara) in the form of creams.(20)

The existing data on these procedures indicate their therapeutic efficiency in stopping malignant tumour growth, especially that of epidermal carcinomas.

An intense stimulating response is obtained by conjugating the antigen with antibodies specifically attached to the surface of DCs, the target conjugates belonging to the family of type C lectin receptors.

The antigen-antibody conjugates are usually administered by intradermic injections.
Nevertheless, these strategies represent the first promising steps in epicutaneous immunization, in which DCs, in particular LCs, are called to exert antitumoral actions. It seems that they can be successfully used for the treatment of malignant skin tumours.

REFERENCES


