COMUNICATION

Immunopathogenesis of psoriasis

Imunopatogênese da psoríase

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Abstract: Psoriasis is a common inflammatory disease affecting 1% of the Brazilian population. Th17 and Th1cells are involved with the immunopathogenisis of psoriasis. In this article it is discussed the interaction between the innate immunity (especially dendritic cells and keratinocytes) and adaptive immunity (T lymphocytes) in the pathogenesis of psoriasis.
Keywords: Allergy and immunology; Cytokines; T- lymphocytes; Psoriasis; Psoriasis/etiology

Resumo: A psoríase é doença inflamatória comum, afetando cerca de 1% da população brasileira. Os linfócito T auxiliares (Th17 e Th1) estão envolvidos na imunopatogênese da psoríase. Neste artigo é discutida a interação entre a imunidade inata (especialmente células dendríticas e queratinócitos) e adquirida (linfócitos T) na patogênese da psoríase.
Palavras-chave: Alergia e imunologia; Citocinas; Linfócitos T; Psoríase; Psoríase/etiologia

IMMUNOPATHOGENESIS OF PSORIASIS

The immunopathogenisis of psoriasis is complex and involves alterations in the innate immunologic system (keratinocytes, dendritic cells – DC, histiocytes, neutrocytes, mastocytes,endothelial cells) and acquired (T lymphocytes).[1] The cells of the innate immunologic system (IIS) when activated produce growth factors, cytokines and chemokines that act upon the cells of the acquired immunologic system (AIS) and vice-versa.[1-5]

Initially there is activation of the cells of the IIS (DC and keratinocytes). Various environmental factors such as mechanical trauma, infections, medications and emotional stress can unleash the disease. Mechanical trauma, e.g., can activate keratinocytes, that begin to release cytokines, (IL-1 and the TNF-α) and proteins of thermic shock. These substances activate the DCs (Langerhans cell - LC – and resident DCs) in the epidermis and dermis. The linkage of antigens of infectious agents to the *toll like* receptors in the DCs and keratinocytes may also lead to the activation of these cells. The DCs and the activated keratinocytes produce inumerous chemokines, cytokines and growth factors. [1-5]

Once activated, the DC processes an antigen (environmental or endogenous, not defined yet) and migrates to the regional where the antigen is presented to the T lymphocytes (TL). In order to activate the TL it is necessary the linkage of the antigen (coupled to the main molecule of histocompatibility on the membrane of DC) to the receptor of the TL, besides the linkage of proteins of the plasmatic membrane of DC (ICAM-1; LFA-3; CD80/CD86) to the proteins of the membrane of TL (respectively LFA-1; CD2; CD28).[3] Therefore, to occur the lymphocyte activation there should be stablished an "immunologic synapse" among proteins of the membrane of the cell that presents the antigen (APC) and of the TL.

The activated TL of patients suffering from psoriasis differ preferentially in LTCD4+ type1 (LTh1; producers of INF-γ, TNF-α e IL-2) and type 17 (LTh17; producers of IL-17, TNF-α, IL-6; IL-22) and LTCD8+ type 1 (LTc1; producers of TNF-α, INF-γ , perforins and granzyme B).[1-5]

The activated TL migrate to the skin through the linkage of molecules of adhesion expressed in its plasmatic membrane (CLA and LFA-1) to the molecules of adhesion present in the membrane of the activated cutaneous endothelial cell (E-selectina and

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ICAM-1). The LTc1 concentrate themselves in the epidermis and the TLh in the dermis.[1,3]

In the dermis the TLh meets and interacts with the DCs and histiocytes forming new "immunologic synapses". The interaction among theses cells leads to the production of inumerous cytokines that keep and amplify the inflammatory process.[1,3]

The activated Dcs and histiocytes produce IL-12 and IL-23.[4] The IL-12 favours the proliferation of the LTh1 and the IL-23 of the LTh17.[4,5] The proliferation of Th17 and Th1 in psoriasis is also attributed to the decrease of regulatory TL (responsible for the suppression of the activation of such lymphocytes).[1,5,6]

In psoriasis the dermal DCs found in greater numbers are of the myeloid type (DC11c+).[1,5] These cells function like APC to the LTs and also as inflammatory cells (DCi), great producers of IL-20, synthetase inducer of the production of nitric oxide (iNOS), as well as of IL-23 and TNF-α. [1,5] The IL-20 stimulates the proliferation of keratinocytes and the nitric oxide the vasodilatation. The IL-23, favours the proliferation of the LTh17 and consequent production of IL22 and IL-6 (that stimulates the proliferation of the keratinocytes), besides of IL-17 and TNF-γ. The IL-17 stimulates the keratinocyte to produce defensins (proteins that impede the infection of the lesions) and IL-8. The TNF-γ stimulates in the keratinocyte the production of IL-8 and IP-10 (chemotatic proteins to neutrocytes and LT respectively), of IL-1 and of TNF-α itself, apart from growth factors that favour the angiogenesis. Therefore, cytokines Th17 stimulate the keratinocytes to proliferate and to produce inumerous inflammatory proteins **(Pic.1).** [1,5,7,8]

The proliferation of LTh1 induced by IL-12 leads to the production of TNF-α and INF-γ. The INF-γ also stimulates the production of IL-12, IL-8, IP-10, IL-23, defensins and iNOS by the keratinocytes and DC. [7-8]

Interferons, TNFs and IL-20 are activators of transcription factors (STAT-1, STAT-3 and nuclear factor κB) that, in their turn, control various groups of genes that codify various inflammatory mediators in psoriasis. [1,5,9]

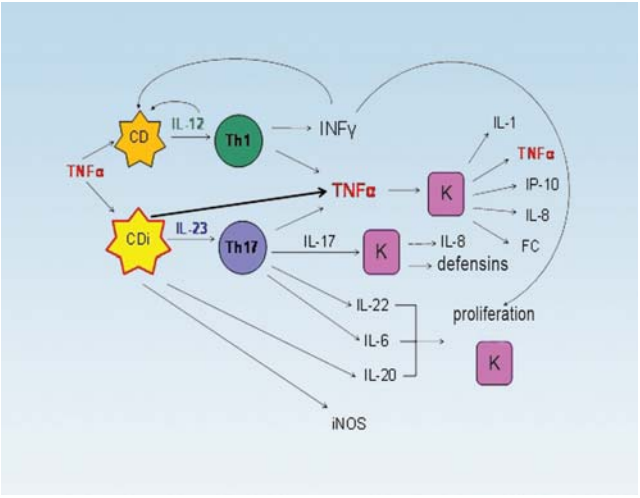

Figure 1: Main proteins produced by denditric cells (Dci) and myeloid denditric cells of the inflamatory type (DCi), auxiliary T lymphocytes type 1 (Th1), auxiliary T lymphocytes type 17 (Th17) and keratinocytes (Q) in psoriasis. FC: growth factors; iNOS: synthetase inducer of production of nitric oxide

Recent studies in patients treated with etanercept reveal that the TNF modulates the activation and maturation of the DCs in psoriasis.[7,8] The blocking of TNF by this therapeutic agent decreases the activation and maturation of the Dcs and consequently inhibts the activation of the lymphocytes and the production of cytokines, chemokines and growth factors by LT, DC keratinocytes [7,8]

It is worth mentioning that the IL-6, the TNF-· and the IL-17 are cytokines involved in the pathogenesis of the atherosclerosis, what justifies a higher incidence of cardiovascular diseases and of the metabolic syndrome in patients with psoriasis. [2,10]

Concluding this study, the knowledge of the main alterations between the SII and the SIA is essential for a better understanding of the immunopathogenesis of psoriasis, as well as of the mechanisms of action of the immunosupressive and biological medications used in its treatment. ❑

REFERENCES

1. Lowes MA, Bowcock AM, Krueger JG. Pathogenesis and therapy of psoriasis. Nature. 2007;445:866-73.
2. Menter A, Gottlieb A, Feldman SR, Van Voorhees A, Leonardi CL, Gordon KB, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis: Section 1. Overview of psoriasis and guidelines of care for the treatment of psoriasis with biologics. J Am Acad Dermatol. 2008;58:826-50.
3. Nickoloff BJ, Nestle FO. Recent insights into the immunopathogenesis of psoriasis provide new therapeutic opportunities. J Clin Invest. 2004;113:1664-75.
4. Mackenzie B, Kastelein RA, Cua DJ. Understanding the IL-23 – IL-17 immune pathway. Trends Immunol. 2006;27:17-23.
5. Guttman-Yassky E, Krueger JG. Psoriasis: evolution of pathogenic concepts and new therapies through phases of translational research. Br J Dermatol. 2007;157:1103-15.
6. Sugiyama H, Gyulai R, Toichi E, Garaczi E, Shimada S, Stevens SR, et al. Dysfunctional blood and target tissue CD4+CD25high regulatory T cells in psoriasis: mechanism underlying unrestrained pathogenic effector T cell proliferation. J Immunol. 2005;174:164-73.
7. Gottilieb AB, Chamian F, Masud S, Cardinale I, Abello MV, Lowes MA, et al. TNF inhibition rapidly down-regulates multiple proinflamatory pathways in psoriasis plaques. J Immunol. 2005;175:2721-9.
8. Zaba LC, Cardinale I, Gilleaudeau P, Sullivan-Whalen M, Suárez-Fariñas M, Fuentes-Duculan J, et al. Ameriolation of epidermal hyperplasia by TNF inhibition is associated with reduced Th17 responses. J Exp Med. 2007;204:3183-94.
9. Loyola AJC, Castro LCM, Chaibub SCW, Ximenes AC. Infliximab no tratamento da artrite psoriásica grave. An Bras Dermatol. 2005;80:535-7.
10. Kourosh AS, Miner A, Menter A. Psoriasis as the marker of underlying systemic disease. Skin Theraphy Lett. 2008;13:1-5.

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