Pathogenesis of Psoriasis

Psoriasis has been regarded as T-cell specific autoimmune disease mediated by Th-1 and Th-17 lymphocytes. In this paper Maria Salskov-Iversen discovered that a component of inflammasome, caspase-5 is upregulated in psoriasis lesions. This finding suggests a major role of the innate immune response in the pathogenesis of psoriasis. Treatment targeting the T-cell-independent inflammation may provide a new approach to psoriasis therapy.

This is a summary of a paper recently published by Salskov-Iversen et al. The full reference for the article is: *Salskov-Iversen M, Johansen C, Kragballe K, Iversen L. Caspase-5 expression is upregulated in lesional psoriasis skin. J Invest Dermatol 2011; 131: 670–676.*

Our understanding of the pathogenesis of psoriasis has undergone amazing changes over the last 30 years. Psoriasis was initially considered as a disease of the epidermis. This view changed radically in 1979, when the potent immunosuppressive drug, cyclosporine, was shown to be an effective treatment. Since then, psoriasis has been considered an autoimmune disease of the adaptive immune system.

This view is about to change gradually. The findings of Maria Salskov-Iversen, working in a dynamic research group headed by Professor Lars Iversen (not a family relation) in Aarhus point at a role of innate (non-specific) immunity in the pathogenesis of psoriasis.

Maria Salskov-Iversen studied the expression of the components of inflammasome, with a particular focus on caspase-5 in psoriasis lesions. Inflammasome is a multiprotein complex, which precipitates the inflammatory reaction by activating interleukin-1-beta. Inflammasome, in turn, can be activated in an antigen-non-specific manner by sensing cytosolic pathogen-associated molecular patterns (e.g. lipopolysaccharides in bacterial walls, released DNA, etc). Caspase-5 is a known, but poorly studied, component of inflammasome.

Salskov-Iversen has shown that caspase-5 is heavily upregulated in lesional psoriasis skin, to a much higher degree than other known inflammasome components. Caspase-5 was not increased in biopsies from other inflammatory skin diseases, suggesting that it may play a quite specific role in psoriasis. Caspase-5 could also be upregulated in keratinocytes by interferon-gamma, a known pathogenic cytokine in psoriasis. Taken together, these findings indicate that a non-specific auto-inflammatory response is an important component of the pathogenic cascade of events in psoriasis.

Maria Salskov-Iversen gained her MD degree from the University of Aarhus in 2005. She was active in research during her studies, and was involved in scientific project at the Department of Medical Microbiology and Immunology in Aarhus, and spent 7 months at the Department of Dermatology in Yale University in the USA, under the supervision of Carole Berger and Richard Edelson, working on dendritic cell vaccination in cutaneous lymphoma. Maria has started her specialist training in dermatology at the department at Marselisborg Hospital, Aarhus, and has recently defended her PhD on inflammatory caspases in psoriasis.

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