Experimental and Clinical Studies of Psoriasis

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A generous donation to Linköping University made possible the establishment of the Foundation for Psoriasis Research to strengthen, broaden and deepen the research about psoriasis. As a result of this, the Ingrid Asp Psoriasis Research Center was inaugurated in the spring of 2012. The present group includes Charlotta Enerbäck, Professor of Dermatology and Cecilia Bivik, Anna-Karin Ekman, Charlotta Sandin, Deepti Verma, all principal research engineers, and Gunnthorunn Sigurdardottir and Ines Köhler, both PhD students and dermatologists.

Psoriasis is a common skin disease affecting about 3% of the population. It is an immunologically mediated disorder occurring in genetically predisposed individuals. It is sometimes associated with conditions affecting other organ systems, notably arthritis. Psoriasis is also to a certain extent associated with other serious medical conditions such as diabetes and coronary heart disease. The relationships to these conditions, often referred to as comorbidities, are not well understood and needs further study.

The psoriatic skin lesion shows an excessive proliferation and disturbed differentiation of epidermal cells and new vessel formation in the underlying dermis, a combination of changes reminiscent of those seen in cancer. Importantly however, the epithelial proliferation in psoriasis remains under strict control while the hallmark of cancer is its lack of epithelial growth control.

Our ultimate goal is to obtain an improved understanding of the pathogenesis of psoriasis and to find new modalities for its therapy. It is devoted to 3 major areas:

The role for psoriasin in psoriasis

We are studying the pathogenesis of the disease in experimental systems using broad cell biological techniques. Special interest is devoted to psoriasin which is a small protein belonging to the S100 gene family, first identified in psoriatic epithelium and strongly expressed in psoriasis, but also and in early stages of breast cancer. We investigate the importance of angiogenesis in the development of the psoriatic lesion and the role of psoriasin and related proteins in its regulation. We have demonstrated that the expression of psoriasin triggers an amplified response towards reactive oxygen species which lead to increased angiogenesis. Moreover, the role of psoriasin in the differentiation process in the skin is explored.

Immunological and clinical studies

The psoriatic skin lesion is the site of a strong chronic inflammatory response that is initiated and maintained by a variety of cytokines. Many of the cytokines that contribute to the inflammation in the skin are known to be released into the circulation. Circulating cytokines may thus contribute to the development of the comorbidities of psoriasis, such as coronary heart disease. We study circulating cytokines, chemokines and antibodies in the serum and skin of psoriasis patients in relation to the degree of skin symptoms, presence of comorbidities and response to therapy. We have demonstrated that psoriasis patients have increased levels of cardiovascular risk markers and that these levels diminish by systemic therapy but not by UV therapy. This means that systemic treatment is the preferred therapy in patients with increased cardiovascular risk.

Genetic studies

Psoriasis has a strong genetic component. We study the genetics of psoriasis in a large group of patients collected in collaboration with the Swedish Psoriasis Association. We analyze the association between certain gene variants with the risk of developing psoriasis and relate them to various aspects of the disease, such as age at onset, severity and comorbidities. We focus on inflammasome-related genes and have found association to the gene variants in NLRP1 and 3. New studies aim to identify the functional consequences of these associated gene variants. We also take part in an international collaboration to identify the genetic contribution to psoriasis pathogenesis. In collaboration with a research team at Michigan University Medical School, we explore the functional relevance for several genetic variants that have shown strong genetic association with psoriasis. We currently perform a genome-wide epigenetic study of more than 4 million methylation sites. We have among other things found interesting aberrations in the normal appearing skin of psoriasis patients.

Methods

The studies involve culture of cell lines and primary cells such as endothelial cells, normal epidermal cells and psoriatic epidermis. Upregulation of genes is studied using adenoviral and retroviral vectors and downregulation of genes using siRNA and shRNA. Gene expression is being studied on the protein level by use of Western blotting and ELISA and on the mRNA-level using RT-PCR (TaqMan analysis). Cell cycle progression and expressions of cellular surface molecules as well as intracellular proteins are analyzed using flow cytometry. Protein expression in tissues is studied using immunohistochemistry on paraffin-embedded biopsy samples. Microarray analysis of mRNA-expression is performed using the Affymetrix microarray instrument. Analysis of cytokines and antibodies is carried out using array-based methods (Luminex). Genotyping is performed by the aid of allelic discrimination with Applied Biosystems TaqMan-based procedures (7900HT permanent Real-Time PCR systems).

Selected publications

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