The Role of Microbial Influence on Atopic Dermatitis and Inflammatory Skin Diseases – From Molecular Mechanisms to Therapy

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Atopic dermatitis (AD) is characterized by chronic inflammation, dysfunctions of the skin barrier, dysregulations of innate and adaptive immunity, and a high susceptibility for bacterial colonization and infections. Microbial pathogens and their products play an influential role and are potential triggers for the maintenance of the inflammatory processes. Several pro-inflammatory cytokines and other molecules are interesting candidates for discovery of new inflammatory and disease severity markers in AD.

The general aim of the research project is to generate new understanding of the microbial influence on inflammatory skin disease and to explore mechanisms involved in microbial impact on the skin contra host defense and inflammation.

Specifically, this project may lead to new understanding of the role of *Staphylococcus aureus* and other skin-associated microbial pathogens in the pathogenesis of AD. In AD, *S. aureus* infects or colonizes lesional skin in about 90% of the patients. Defective bacterial clearances because of defects in the innate immune response contribute to the high density of *S. aureus* colonization in AD skin. Knowledge of interactions between components of host defense and microbial pathogens can potentially facilitate development of strategies to control the microbial impact in skin infection and inflammation. In the present investigation we plan to investigate these aspects, both in clinical studies and in *in vtro* experiments. We will in the project focus on clinical studies in patients with AD and inflammatory skin diseases, microbial colonization, infection and sensitization to skin-associated microorganisms. AD skin is characterized by overexpression of T-helper type 2 cytokines, but several novel inflammatory pathways are recently discovered in AD mediated, for example, by thymic stromal lymphopoietin (TSLP). TSLP is up-regulated in direct response to microbial stimuli of the skin, and an antimicrobial function of TSLP has recently been discovered.

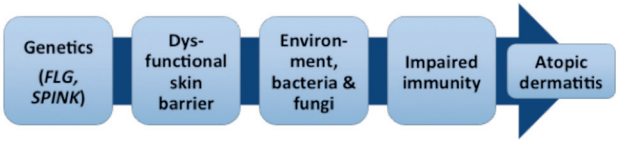

Fig. 1. AD is a chronic inflammatory skin disease. It is a multifactorial disease based on a strong genetic predisposition, and a dysfunctional skin barrier. Environmental factors such as microbial infections, and alterations in innate and adaptive immunity are important in the pathogenesis of AD.

The interaction of skin barrier dysfunction, genetics, and innate and adaptive immunity, in combination with the influential role of microorganisms in AD make this inflammatory skin disease a challenging field for further research. The barrier disruption in AD skin favors colonization and penetration of molecules from bacteria, fungi and viruses, including allergens and proteases. Over-expression of several enzymes and defects in endogenous enzyme regulatory mechanisms are present in AD, which all will contribute to a high enzymatic activity in AD skin. In this context, the expression, production and degradation of antimicrobial peptides (AMPs) and other molecules including TSLP, in AD skin are of fundamental interest. Moreover, knowledge of interactions between the innate immune system and microbial strategies to overcome, evade or take advantage of the system will probably facilitate development of strategies to control the microbial impact in skin diseases. Increased understanding of these mechanisms is expected to lead to development of novel strategies for prevention and treatment of AD and other inflammatory skin diseases.

Recent publications

1. Ling Jinnestål C, et al. Skin barrier impairment correlates with cutaneous Staphylococcus aureus colonization and sensitization to skin-associated microbial antigens in adult patients with atopic dermatitis. Int J Dermatol 2014; 53: 27–33.
2. Sonesson A, et al. Sensitization to skin-associated microorganisms in adult patients with atopic dermatitis is of importance for disease severity. Acta Derm Venereol 2013; 93: 340–345.
3. Sonesson A, et al. Thymic stromal lymphopoietin exerts antimicrobial activities. Exp Dermatol 2011; 20: 1004–1010.