The role of innate immunity in polymorphic light eruption

Background: A failure to induce immune suppression after UV exposure (e.g., as measured by standardized contact hypersensitivity assay) has been implicated in the pathogenesis of polymorphic light eruption (PLE). This immunological resistance has been linked to an impaired neutrophil infiltration into the skin following UV exposure. Therapeutic photohardening can restore this abnormal neutrophil infiltration in PLE skin and is thought to be responsible for prophylactic efficacy. We have previously disclosed a significantly reduced neutrophil responsiveness to the chemoattractants LTB(4) and fMLP in PLE patients and cytokine abnormalities that normalized after phototherapy. This suggests an involvement of the innate immune system in the pathogenesis of the disease. We also found that PLE patients have reduced mast cell numbers in the skin that were restored upon photohardening (unpublished data). We are currently employing mast cell-deficient mice as a model for PLE, in which animals exhibit an abnormal scratching behaviour upon UV exposure, similar to PLE patients. Neutrophils and mast cells are important components of innate immunity but the causes and mechanisms of their abnormal status in PLE are unknown. UV exposure is known to upregulate certain antimicrobial proteins (AMPs) in the skin. AMPs have immunomodulating properties and may induce the infiltration of the skin by neutrophils and mast cells, as evident from the inflammatory skin disease psoriasis. We therefore hypothesize that an abnormal regulation of innate immunity and expression of pro-inflammatory AMPs may be crucial in the resistance of PLE patients to UV-induced immune suppression. This hypothesis goes well in line with a reduced skin cancer incidence reported for PLE patients.

Objectives: To investigate the significance of innate immunity and expression of AMP ii) in PLE patients and control subjects and ii) mouse models in the pathophysiology of resistance to UV-induced immune suppression after defined exposures to UV radiation. The role of AMPs, such as human beta defensin (hBD)-2, hBD3, ribonuclease 7 (RNase 7), and S100 (psoriasin), cathelicidin will be addressed.

Methods: The PhD candidate will learn how to perform the assays and methods necessary to study the objectives above. She/He will learn how to use disease mouse models, including mast cell deficient mice to investigate photodermatoses and study immune function by contact hypersensitivity assay(s). Blood and skin samples will be provided from an ongoing clinical study. The techniques employed by the student include photobiologic methods such as UV light treatment and dosimetry, flow cytometry, RT-PCR, western blot, multiplex ELISA, immunobead technology, immunohistochemistry, immunofluorescence microscopy, and microarray.

References:


