

## Dermatology

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### Research Highlights 2012 / Outlook 2013

#### Allergies

Thymic stromal lymphopoietin (TSLP) is a cytokine released by epithelial cells upon stimulation by various environmental stresses (e.g., viruses, bacteria, allergens) and one of the major culprits in the allergic inflammatory diseases asthma, allergic rhinitis, and atopic dermatitis. In collaboration with the research groups of H.-U. Simon and S. Yousefi (Institute of Pharmacology), we demonstrated that TSLP triggers the release by eosinophils of extracellular DNA in association with eosinophilic cationic protein, termed eosinophil extracellular traps (EETs). This release of EETs was dependent on integrin-mediated adhesion or production of reactive oxygen species, and exhibited antimicrobial activity against *Staphylococcus aureus* and *S. epidermidis*. This mechanism provides a link between the injury to an epithelial barrier and increased TSLP expression, with subsequent pathogen defense response by eosinophils and eosinophilic inflammation.

#### Psoriasis

Innate immune responses play a central role in psoriasis. Our investigations showed that a new retinoid named alitretinoin leads to clinical amelioration and abrogates innate inflammation in palmoplantar pustular psoriasis. Heat shock proteins may play an important part in plaque psoriasis. The expression of these proteins in psoriasis and their regulation through proinflammatory cytokines is currently being investigated.

#### Hidradenitis Suppurativa (HS)

Antimicrobial peptide cathelicidin expression was found to be significantly increased in lesional HS skin at the mRNA and protein level. Using immunofluorescence double staining we could demonstrate that neutrophils and dendritic cells expressing cathelicidin are present in the lesions. By analysing freshly isolated cells from lesional skin by flow cytometry, we could further confirm the expression of cathelicidin on CD15-positive neutrophils and CDD4+CD3-infiltrating cells.

#### Malignant Melanoma

We investigated the role of various immunohistochemical markers in predicting disease progression and showed that high expression of the T cell marker FoxP3 is associated with bad prognosis in melanoma patients.

#### Plakins

Plectin is a cytolinker of the plakin family with intermediate filaments (IFs) that is important for cell cytoarchitecture, and for cell and tissue resilience to mechanical stress, especially in the skin and skeletal muscle. Investigation of the interaction of plectin with IFs revealed much more complex binding than previously published, thanks to a new method to test and quantify protein-protein interactions. Moreover, we found that phosphorylation of a serine residue in the carboxyl tail of plectin inhibits its interaction with IFs, and identified two protein kinases catalysing this phosphorylation in vivo. Our data provide insights into the molecular basis of plectin- and IF-related human diseases associated with pathogenic mutations affecting functionally relevant sites within these molecules.



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Studied medicine at Universities of Fribourg and Bern (1984-1990); MD-PhD at University of Bern (1996); board certified in Dermatology (2001). Postdoc in USA at University of California, Los Angeles (2001-2003). Since 2011, Associate Professor, Department of Dermatology, Inselspital.



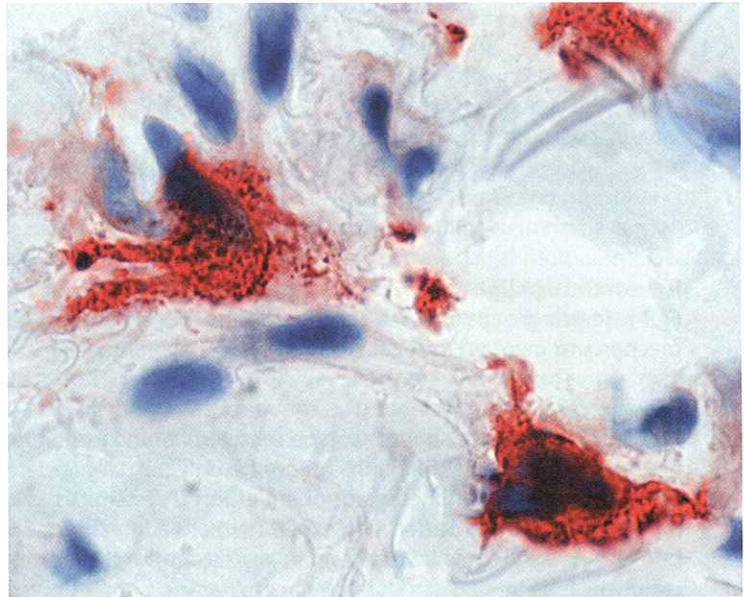
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### Group Members

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### Collaborators

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### Grants

Amounts allocated for 2012:

- SNF: Analysis of molecular and cellular mechanisms in immune-mediated tissue damage of the skin: Hidradenitis suppurativa as a model disease (R. Hunger, N. Yawalkar) CHF 70,000
- OPO Foundation, Zurich: The effects of thymic stromal lymphopoietin (TSLP) on eosinophil extracellular DNA release (D. Simon) CHF 32,000

### Five Selected Publications

Endemic pemphigus foliaceus: towards understanding autoimmune mechanisms of disease development. Di, ZG; Zambruno, G; Borradori, L (2012) in: *J Invest Dermatol*, 132(11), p. 2499-2502.

Alitretinoin abrogates innate inflammation in palmoplantar pustular psoriasis. Irla, N; Navarini, AA; Yawalkar, N (2012) in: *Br J Dermatol*, 167(5), p. 1170-1174.

Thymic stromal lymphopoietin stimulates the formation of eosinophil extracellular traps. Morshed, M; Yousefi, S; Stockle, C; Simon, HU; Simon, D (2012) in: *Allergy*, 67(9), p. 1127-1137.

The role of androgens on hypoxia-inducible factor (HIF)-1alpha-induced angiogenesis and on the survival of ischemically challenged skin flaps in a rat model. Shafighi, M; Olariu, R; Brun, C; Fathi, AR; Djafarzadeh, S; Jakob, SM; Hunger, RE; Banic, A; Constantinescu, MA (2012) in: *Microsurgery*, 32(6), p. 475-481.

Eosinophil extracellular DNA traps: molecular mechanisms and potential roles in disease. Yousefi, S; Simon, D; Simon, HU (2012) in: *Curr Opin Immunol*, 24(6), p. 736-739.