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**Serfling E**

University of Würzburg, Germany

**NFATC1 ENHANCES IMIQUIMOD-INDUCED SKIN INFLAMMATION BY INHIBITING IL-10 EXPRESSION IN B LYMPHOCYTES**

Psoriasis is a chronic inflammatory skin disease that affects 2-3% of population in Western countries. Since B cells are hardly detected in psoriatic skin, until recently their role in psoriasis remained un-regarded. We show here that the repetitive epicutaneous application of Aldara®, a cream containing the toll-like receptor (TLR) 7-agonist imiquimod (IMQ), to mice induces skin inflammation that exhibits many aspects of early stages of human psoriasis. Mice depleted of B cells or bearing IL-10-deficient B cells show an even more fulminant inflammation upon IMQ exposure indicating that IL-10 synthesized in B cells controls skin inflammation. In contrast, ablation of NFATc1 in B cells results in depressed IMQ-induced skin inflammation. Aldara® cream application to the skin leads to the differentiation of splenic B cells to plasmablasts and IL-10-producing B cells. In vitro, IMQ induces the proliferation and IL-10 expression of splenic B cells. The induction of IL-10 RNA by IMQ can be blocked by a-IgM-mediated B cell receptor signals that, on the other hand, induce NFATc1. By binding to HDAC1, NFATc1 suppresses IL-10 expression, which, otherwise, dampens the production of inflammatory cytokines by T cells, including TNF $\alpha$  and IL-17. These data indicate a close link between NFATc1 and IL-10 expression in B cells during IMQ-mediated skin inflammation and suggest that the suppression of NFATc1 activity might be of benefit to treat human psoriasis and, possibly, other autoimmune diseases as well.

**Biography**

Edgar Serfling has been graduated from the University of Halle/Wittenberg as PhD and of University of Wuerzburg (Habilitation), with the specialties in Biochemistry and Molecular Pathology. Later on, he obtained his post-graduation from University of Wuerzburg and then started working at the Institutes of Virology and Immunobiology, and of Pathology where he has continued his research. Presently he has been working at the Institute of Pathology, Wuerzburg, Germany.

[Serfling.e@mail.uni-wuerzburg.de](mailto:Serfling.e@mail.uni-wuerzburg.de)