



University of  
Zurich<sup>UZH</sup>

Institute for Regenerative  
Medicine (IREM)



Colloquium

## Clinical Colloquium Regenerative Medicine

Thursday, 27<sup>th</sup> Sept 2018 at 1–2pm,  
Institute for Regenerative Medicine (IREM),  
University of Zurich, Wagistrasse 12,  
WAD-904 (Founders Lab), 8952 Schlieren

**Prof. Dr. Sabine Werner**

Institute of Molecular Health Sciences, ETH Zurich

## Regulation of Skin Inflammation and Repair by Genetic and Environmental Cues

Injury to adult tissues initiates a well-coordinated series of events, which results in at least partial reconstruction of the damaged site. Fibroblast growth factors (FGF) are master regulators of tissue repair through controlling migration, proliferation and survival of different cell types. We recently showed that loss of FGF receptors 1 and 2 in keratinocytes causes a severe defect in the epidermal barrier, resulting in the development of a chronic inflammatory skin disease with similarities to Atopic Dermatitis in humans. Interestingly, the inflammatory response was strongly reduced upon exposure of the mice to high environmental humidity, demonstrating a novel role of osmo-regulated gene expression in the control of inflammation. We also showed that loss of FGF receptors in keratinocytes affects innate immune responses in the skin, unravelling a novel role of FGFs as counterplayers of inflammatory cytokine signaling.

A major FGF target is the Nrf2 transcription factor, a master regulator of the antioxidant response. Since pharmacological activation of Nrf2 is a promising strategy for tissue protection under various stress conditions, we developed a genetic mouse model to activate Nrf2 in a tissue-specific manner. We show that activation of Nrf2 in fibroblasts promotes cutaneous wound healing, but also cancer development. This was caused by Nrf2-mediated alterations in the matrisome, which promoted fibroblast senescence and subsequent release of wound healing- and cancer-promoting cytokines.

Overall, our work identified new players in tissue protection, inflammation and repair and highlights the cross-talk between genetic and environmental control of tissue repair and inflammation.

**Organiser:** Prof. Dr. Dr. Simon P. Hoerstrup / Prof. Dr. Roger M. Nitsch

**Execution/Chair:** Dr. Steffen M. Zeisberger / Dr. Christian Tackenberg

IREM, University of Zurich

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