

Project 3:**The role of Wnt signaling in tumor-initiating cells and tumor progression in cutaneous SCC****Principal Investigator:****Dr. Iris Augustin, Prof. Dr. Michael Boutros, Div. of Signaling and Functional Genomics DKFZ, and Dept. Cell and Molecular Biology, Medical Faculty Mannheim, Heidelberg University****London Project Partner:****Prof. Fiona Watt, Centre for Stem Cells and Regenerative Medicine, King's College, London**

Developmental programs such as the Wnt signaling pathway are often hijacked in cancer. The Wnt pathway is not only involved in self-renewal of normal stem cells, but also often deregulated in tumor-initiating cells. For normal skin homeostasis as well as skin pathology of both neoplastic as well as non-neoplastic nature, the importance of Wnt signaling is well established and widely recognized. As the signaling pathway with its multiple ligands and receptors is quite complex and the outcomes of Wnt signaling are known to be highly context-dependent, Wnt signaling continues to be a conceptually difficult field of research. Evi, a protein necessary for the secretion of Wnt proteins, has a pivotal role in maintaining normal skin homeostasis. Mice lacking Evi expression in the epidermis lose hair during the first hair cycle and suffer from impaired skin barrier function, up-regulation of inflammation-associated genes, immune cell infiltration and skin lesions that resemble human psoriasis.

As the best way of developing novel therapeutic strategies is to better understand the underlying cellular and molecular mechanisms, I aim to investigate the role of autocrine and paracrine Wnt signaling in skin carcinogenesis and to compare these findings to human disease. The contribution of Wnt signaling to tumor initiation and malignancy will be dissected. My findings will enhance our understanding tumor development and the mechanisms that contribute to invasion and metastasis of tumor cells, thereby providing insights in cellular signal transduction controlling skin carcinogenesis.