WNT AND HEDGEHOG SIGNALLING IN COLORECTAL CANCER

Prof. Dr. Konrad Basler

Department of Molecular Life Sciences
University of Zurich
Winterthurerstr. 190, 8057 Zurich

konrad.basler@imls.uzh.ch
www.imls.uzh.ch/en/research/basler.html

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SUMMARY & MISSION STATEMENT

The central theme of our research is to understand how cell-to-cell communication controls growth and patterning in development and disease. The course of tumour progression is dictated by the dialogue between the cancer cells and tumour stroma. We want to understand the nature of this communication in the case of colorectal cancer.

OVERVIEW

Colorectal cancer (CRC) is the third leading cause of cancer death. Most cases arise as a consequence of the hyperactivation of the Wnt signaling pathway. This hyperactivation leads to deregulation of the stem cell pool. During normal epithelial homeostasis, stem cell differentiation and renewal are controlled by signals, such as Wnts, that are emitted from the stem cell niche. In the colon Gli1-expressing mesenchymal cells form the Wnt-producing niche; Gli1 expression is a marker of Hedgehog pathway activity. Underscoring the two-way nature of the conversation between the epithelium and mesenchyme, the Hedgehog source appears to be the intestinal epithelial cells. We are analyzing the roles of both Hedgehog and Wnt signaling during intestinal epithelium homeostasis, during injury-induced regeneration, and during CRC progression. The aim is to understand how they contribute to the malignant growth of CRC.

SELECTED CANCER RELATED PUBLICATIONS

GLI1-expressing mesenchymal cells form the essential Wnt-secreting niche for colon stem cells. B. Degirmenci, T. Valenta, S. Dimitrieva, G. Hausmann and K. Basler (2018). **Nature**, doi: 10.1038/s41586-018-0190-3.

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Wnt Ligands as a Part of the Stem Cell Niche in the Intestine and the Liver. B. Degirmenci, G. Hausmann, T. Valenta and K. Basler. **Prog Mol Biol Transl Sci.** 2018; 153, 1-19.

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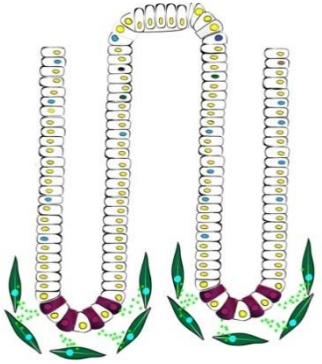
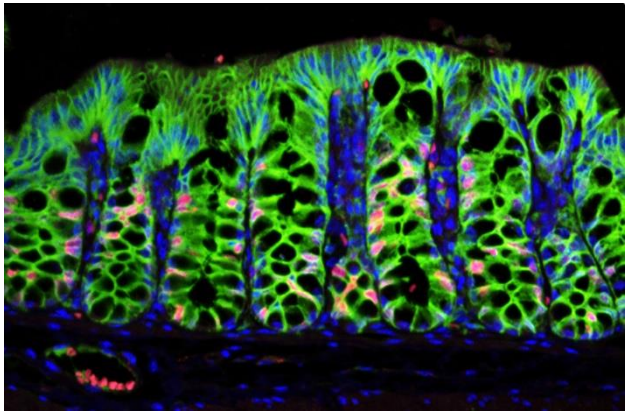
Probing transcription-specific outputs of β-catenin in vivo. T. Valenta, M. Gay, S. Steiner, K. Draganova, M. Zemke, R. Hoffmans, P. Cinelli, M. Aguet, L. Sommer and K. Basler. **Genes Dev.** 2011;25, 2631-2643.





Left: Schematic representation of the colonic epithelium, indicating mesenchymal niche cells secreting Wnt proteins. Right: Cross section through a wild-type murine colonic epithelium