Dipl. Biol. Gnad, Thorsten

PhD-Thesis:

“Modulation of the canonical Wnt/β-catenin signaling pathway in *H. pylori* infection”

Summary

The human pathogen *H. pylori* colonizes the antrum and corpus region of the gastric mucosa and is identified as the main course for the development of chronic gastritis, peptic ulcer and in rare cases, gastric cancer. The canonical Wnt/β-catenin signaling pathway has important roles in the regulation of distinct cellular processes like proliferation, migration, differentiation, apoptosis, or in the regulation of stem cell differentiation. Central player of the signaling pathway is β-catenin, a protein with a dual role. On the one hand it mediates cell-cell adhesion and on the other hand it acts as transcription factor and regulates over 100 different target genes. Constitutive activation of the β-catenin is described in many human cancer diseases, including gastric cancer. *H. pylori* is able to regulate β-catenin and the content of this PhD-thesis comprises the characterization of components of the canonical Wnt/β-catenin signaling pathway involved in this regulation.

Within this PhD-thesis the following important results were obtained:

I. Infection of gastric epithelial NCI-N87 cells with *H. pylori* results in activation of β-catenin. Besides nuclear accumulation of β-catenin, this activation could be shown by Lef/Tcf transactivation and upregulation of target gene expression on the mRNA and protein level.

II. *H. pylori* infection results in increased phosphorylation of the Wnt co-receptor LRP6, which depends on a functional T4SS.

III. *H. pylori*-mediated activation of β-catenin is dependent on LRP6, Dvl2 and Dvl3