

The role of epigenetic changes in *Helicobacter pylori*-induced gastric carcinogenesis

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Recent research has revealed that microbial pathogens can influence the host cells' epigenome in order to modulate host cell functions to the benefit of the pathogens' colonization and persistence. For the carcinogenic bacterium *Helicobacter pylori* it was shown that this bacterium drastically alters the histone code and thereby influences critical cell fate decisions. Another key component of the epigenetic landscape, DNA methylation, is currently in the center of interest in molecular biology research. Aberrant promoter hypermethylation is causally linked with the inactivation of several tumor suppressor genes. For *H. pylori* infections, it has been shown that the presence of *H. pylori* positively correlates with aberrant DNA methylation of certain CpG islands in gastric cancer. We performed a genome-wide DNA methylation analysis using the MeDIP (methylated DNA immunoprecipitation)-on-Chip approach to identify genes with altered methylation patterns in gastric epithelial cell lines upon *H. pylori* infection. We found numerous genes and gene promoters that are either hyper- or hypo-methylated after infection. Some of these genes have already been described as oncogenes or tumor-suppressor genes; for others, the functional assignment is incomplete.

This project aims at the validation and functional characterization of *H. pylori*-induced DNA methylation changes and at the determination of its consequences with regard to malignant cell transformation. In-depth studies of selected individual gene targets will be carried out; for validation, approaches including methylight and bisulfite conversion and next-generation sequencing will be used. Functional characterization of confirmed targets include transcriptional analyses, knock-down studies, the investigation of associated cellular signalling pathways, and the analyses of clinical gastric cancer samples. To further investigate the correlation between persistent infection, site-specific methylation changes and transcriptional silencing, we will extend our study to long-term and stem cell infection models. The ultimate goal is to unravel *H. pylori*-employed mechanisms to induced tumorigenesis; altered DNA methylation may thereby predispose for the malignant transformation of gastric cells.