

## IGS-DHD Project

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### **Role of LuxR-type transcription factors and H-NS in pathogenic *Escherichia coli***

*Escherichia coli* include commensal strains residing in the intestine of vertebrates and pathogenic strains which cause various intra- and extraintestinal diseases. The nucleoid-associated protein H-NS is a global repressor (silencer protein) in *Enterobacteriaceae* and a regulator of genes for pathogenicity, biofilm formation and stress responses. Repression by H-NS is relieved gene-specifically, and in most cases this involves specific transcription factors. Up to date little is known about transcription factors required for de-repression of pathogenicity genes and the signals and pathways activating them. We study transcription factors of the so-called LuxR-family which include 'master' regulators of pathogenicity genes.

In one project the role of selected LuxR-type transcription factors will be analyzed in commensal and pathogenic *E. coli*. The aims are: (i) to analyze the induction of the genes encoding the LuxR-type transcription factors, which will include co-cultivation of pathogenic *E. coli* with eukaryotic cell lines (with focus on uropathogens); (ii) to identify levels of post-translational control such as proteolysis and protein-protein interaction of the selected LuxR-type transcription factors; and (iii) to characterize the direct target genes of these LuxR-type transcription factors by genetic screens and by microarray analyses, followed by molecular analysis. The aim of the project is to identify novel regulatory signaling cascades in pathogenicity of *E. coli*.

In another project the mechanism of repression by H-NS and the role of transcription in de-repression will be addressed. H-NS represses transcription by formation of extended H-NS-DNA complexes, which prevent initiation of transcription by RNA polymerase. RNA polymerase, once it is engaged in transcription, is a powerful enzyme. Our unpublished data indicate that RNA polymerase when transcribing across H-NS nucleoprotein complexes remodels the complex or even removes H-NS from the DNA and thus abrogates repression by H-NS. The aim of the project is to analyze the interference of transcription and H-NS mediated repression qualitatively and quantitatively *in vivo* and *in vitro*, to elucidate a general mechanism which links the efficiency of repression by H-NS to the transcription rate.