SCHOOL OF LIFE SCIENCES / FACULTE DES SCIENCES DE LA VIE

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ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

GHI Seminar – May 19th, 12h15, SV 1717a

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Regulatory RNAs in the pathogenic Epsilonproteobacteria *Helicobacter* and *Campylobacter*

Small regulatory RNAs (sRNAs) are an emerging class of posttranscriptonal gene expression regulators that have been implicated in bacterial stress response and virulence control. The majority of the functionally characterized sRNAs act as antisense RNAs on mRNAs. Although genome-wide approaches have revealed hundreds of sRNA candidates in diverse prokaryotes, most of the mechanisms and functions are based on work in enterobacteria, such as *Escherichia coli* or *Salmonella*. In contrast, little is known about posttranscriptional regulation in Epsilonproteobacteria, including the gastric pathogen *Helicobacter pylori* and the emerging food-borne pathogen *Campylobacter jejuni*. *Helicobacter* and *Campylobacter* lack, like 50% of all bacteria, a homolog of the RNA chaperone Hfq, a key player in sRNA-based regulation in enterobacteria. Thus, we are interested whether they use other auxilliary proteins that replace the functions of Hfq or whether their sRNAs act independently by novel mechanisms.

Our differential RNA-sequencing approach (dRNA-seq) allowed us to define a genome-wide map of transcriptional start sites (TSS) and revealed >60 sRNAs in *H. pylori* [1]. To understand how transcriptome differences could contribute to phenotypic differences among strains, we recently applied a comparative dRNA-seq to multiple *C. jejuni* strains [2]. Our study revealed that the majority of TSS is conserved among strains, but we also observed strain-specific promoter usage and sRNA repertoires, which might underlie strain-specific gene regulation and phenotypic differences among strains. Based on our transcriptome datasets, we are now using *Helicobacter* and *Campylobacter* as new model organisms for riboregulation in bacterial pathogens and bacteria without Hfq. We are functionally characterizing abundant sRNAs and are especially interested in the roles and underlying molecular mechanisms of sRNAs in stress response and virulence control as well as the identification of associated RNA-binding proteins. For example, we could recently show that the highly abundant and conserved sRNA, RepG, from *H. pylori* directly base-pairs with a homopolymeric G-repeat in the mRNA leader of the chemotaxis receptor TlpB and that length variation of this G-repeat determines the outcome (repression or activation) of RepG-mediated post-transcriptional regulation [3]. We have also identified a first potential virulence regulating sRNA that directly represses multiple virulence factors. These examples show that identifying and studying sRNAs in bacteria without Hfq can reveal new twists in RNA-mediated regulation and will provide new insight into mechanisms of gene regulation and virulence control of bacterial pathogens.

References:

[1] Sharma, C.M., Hoffmann, S., Darfeuille, F., Reignier, J., Findeiss, S., Sittka, A., Chabas, S., Reiche, K., Hackermüller, J., Reinhardt, R. Stadler,P. F., Vogel, J. (2010) *The primary transcriptome of the major human pathogen Helicobacter pylori.* Nature, 464, 250-255

[2] Dugar G, Herbig A, Förstner KU, Heidrich N, Reinhardt R, Nieselt K, Sharma CM (2013) *High-resolution transcriptome maps reveal strain-specific regulatory features of multiple Campylobacter jejuni isolates.* PLoS Genetics 9(5):e1003495

[3] Pernitzsch SR, Tirier S, Beier D, Sharma CM (2014) *A variable homopolymeric G-repeat defines small RNA-mediated post-transcriptional regulation of a chemotaxis receptor in Helicobacter pylori.* PNAS 111(4) E501–E510

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