Stefan SCHILD (ORCID: 0000-0001-7842-0177): Adaptation strategies of the facultative pathogen *Vibrio cholerae* to its lifecycle

Research interest and scientific background: The facultative human pathogen *V. cholerae* is the causative agent of the severe diarrheal disease cholera. Its lifecycle is characterized by constant transition between two very different lifestyles: As a natural inhabitant of the aquatic environment and as a pathogen in the human gastrointestinal tract. One focus of our lab is the elucidation of *V. cholerae*'s adaptational strategies to different conditions faced by the pathogen along its lifecycle.

We are using a temporally controlled single-cell based reporter of transcription to investigate differences in gene regulation under environmental and host conditions [e.g.: during colonization and transmission of *V. cholerae* in the gastrointestinal tract (including mouse models), biofilm formation, persistence in the aquatic reservoirs, survival in the presence of natural predators using the *C. elegans* model], which already yielded in several publications [1-5]. Besides others, differentially regulated genes were linked to degradation of extracellular DNA, neutrophil escape, second messenger cascades, controlled proteolysis, protein glycosylation as well as to the phosphate metabolism and storage. The identified factors seem to be important for several stages in the lifecycle of *V. cholerae* [e.g.: virulence, colonization fitness and transmission of *V. cholerae* in the gastrointestinal tract (including mouse models), biofilm formation, survival in the aquatic reservoir].

Within the doc.funds project the student will focus on the comprehensive characterization of selected genes and their gene products to unravel their physiological role for *V. cholerae*. For two candidates we have already loss-of-function mutants and distinct phenotypes available, which allowed us to get first inisghts in their potential role/ function.

Approach and methods: Besides standard techniques in molecular biology and microbiology, the student will learn cultivation and genetic engineering of bacterial pathogens as well as their phenotypic characterization. A non-exhaustive list of methods includes various transcriptional reporter assays, protein-protein interaction assays, bacterial cell fractionation, static and dynamic biofilm assays, motility assays, variety of assays to analyze nutrient acquisition and in vivo competition assays (mouse model, but animal handling is not compulsory for this position). Naturally, the student will strongly interact with other research groups of the doc.fund Molecular Metabolism and the research & training networks NAWI Graz and BioTechMed Graz.

Affiliation: The student will work at the Institute of Molecular Biosciences at the University of Graz. This project is directly connected to the doc.fund Molecular Metabolism.

References:

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[4] Cakar, F., Zingl, F.G., Moisi, M., Reidl, J., Schild, S. In vivo repressed genes of *Vibrio cholerae* reveal inverse requirements of an H(+)/Cl(-) transporter along the gastrointestinal passage ***Proc Natl Acad Sci U S A*** 2018, *115* (10), E2376-E2385. 10.1073/pnas.1716973115

[5] List, C., Grutsch, A., Radler, C., Cakar, F., Zingl, F.G., Schild-Prufert, K., Schild, S. Genes Activated by Vibrio cholerae upon Exposure to *Caenorhabditis elegans* Reveal the Mannose-Sensitive Hemagglutinin To Be Essential for Colonization ***mSphere*** 2018, *3* (3). 10.1128/mSphereDirect.00238-18