Available online at www.sciencedirect.com

ScienceDirect

Current Opinion in Microbiology

Editorial overview: Bacterial systems biology

Christoph Dehio and Dirk Bumann

Current Opinion in Microbiology 2017, **39**:viii–xi

For a complete overview see the Issue

https://doi.org/10.1016/j.mib.2017.11.024

Christoph Dehio

Focal Area Infection Biology, Biozentrum, University of Basel, Klingelbergstrasse 70, CH-4056 Basel, Switzerland
e-mail: christoph.dehio@unibas.ch

Christoph Dehio is a professor of Molecular Microbiology at the Biozentrum of the University of Basel, Switzerland. His longstanding interest is the molecular analysis of pathogenicity mechanisms of *Bartonella* spp., and more recently also of *Brucella* spp. In particular, he is studying structure/function aspects and the evolution of bacterial effector proteins translocated by the type IV secretion process and their molecular interactions with target proteins that result in subversion of central host cellular processes in the course of infection. In earlier work, he has been studying bacterial pathogenesis mechanisms of other Gram-negative pathogens, including *Shigella flexneri and Neisseria gonorrhoeae*.

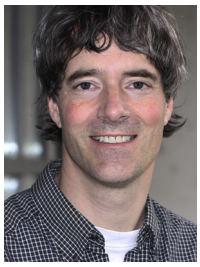
Bacterial systems biology represents a large and diverse research field studying the functions and properties of bacteria in an integrative, systematic way, based on the analysis and modelling of large data sets. The field has advanced considerably over the past decade based on methodological and conceptional advances in several fundamental enabling technologies and computational analysis of their results, including next generation sequencing at the DNA and RNA levels, proteomics, metabolomics and genome-wide genetic approaches. These diverse systems-level approaches have revealed fascinating new insights into diverse fundamental processes in bacteria. Those include the mapping and characterization of basic regulatory principles on the DNA, RNA, protein and metabolic level, physiological processes such as chemotaxis, drug mode of action, phenotypic heterogeneity, host–pathogen interaction, and interbacterial interactions in polymicrobial communities. This special issue of Current Opinions in Microbiology represents a collection of short reviews that provides selected examples of state-of-the-art applications of systems biology approaches in diverse research areas of bacteriology.

Genome-wide studies of RNA regulation

Transcription is a core process of gene expression and as such is tightly controlled. While transcription factors serve as major transcriptional regulators, genome-reduced bacteria with just a few of these proteins show still a remarkably flexible adaptation to changing environments. Alternative mechanisms of transcriptional control may thus orchestrate RNA levels in these microorganisms. These alternative mechanisms rely on intrinsic features within DNA and RNA molecules, suggesting that they are ancestral to transcription factors and possibly still shared among bacteria with larger genomes and large sets of transcription factors. Serrano *et al.* review the alternative elements that can regulate transcript abundance in genome-reduced bacteria and how they contribute to the RNA homeostasis at different levels.

The identification of new RNA functions and the functional annotation of transcripts in genomes represent challenging endeavors of modern biology. Crucial insights into the biological roles of RNA molecules can be gained from the identification of the proteins with which they form specific complexes. State-of-the-art interactome techniques facilitate the genome-wide profiling of RNA–protein interactions and the identification of novel RNA classes associated with globally acting RNA-binding proteins. Such methods are already revolutionising our understanding of RNA-mediated biological processes. The review by Smirnova *et al.* focuses on one such approach — Gradient sequencing or Grad-seq — which has recently guided

Dirk Bumann



Dirk Bumann is professor of Infection Biology at the Biozentrum of University of Basel, Switzerland. His lab focusses on pathogen–host interactions in host tissues. Specific goals include (i) elucidation of metabolism networks that drive *in vivo* growth of *Salmonella enterica*, *Shigella flexneri*, and *Pseudomonas aeruginosa*, and (ii) determination of single-cell properties and fates of *Salmonella enterica*, and their impact on disease progression and antimicrobial chemotherapy, in complex host microenvironments. The research combines molecular biology, flow cytometry, proteomics and 3D microscopy at various scales. Previously, he was involved in research on the infection biology of *Helicobacter pylori* and vaccine development.

the discovery of protein ProQ and its associated large set of small RNAs as a new domain of post-transcriptional control in bacteria.

Systems-level proteomics approaches

The quickly evolving proteomics methodologies are revolutionizing many research domains in bacteriology. Three reviews of this issue highlight different applications of proteomics for systems-level studies.

Classical research approaches have already identified important molecular mechanisms underlying infection. However, it is increasingly recognized that many pathogens use a whole complex network of diverse molecular mechanisms to manipulate and interfere with the biochemical processes of the host. Therefore, systems-level approaches can complement the standard molecular biology techniques to investigate more comprehensively pathogen molecular mechanisms and their interactions with the host. Banaei-Esfahani *et al.* review omic studies in *Mycobacterium tuberculosis*, the causative agent of tuberculosis, with a focus on proteomic methods and their application to this particular pathogen. However, the discussed methods are directly portable also to any other bacterial pathogen.

Infectious diseases are the result of molecular cross-talks between hosts and their pathogens. These cross-talks are in part mediated by host–pathogen protein–protein interactions, which play crucial roles in infections as they may tilt the balance either in favor of the pathogens' spread or their clearance. The identification of host proteins that bacterial pathogens target with their effector proteins, can provide insights into their underlying molecular mechanisms of pathogenicity, and potentially even single out pharmacological intervention targets. Nicod *et al.* review the available methods to study host–pathogen protein–protein interactions, with a focus on recent mass spectrometry-based methods to decipher bacterial infections, and examine their utility for uncovering host cell rewiring by pathogens.

Small proteins comprising 50 amino acids (aa) or less have been overlooked in many genome annotations, but they are increasingly recognized as important regulators in bacteria. They are involved in a wide range of processes, including the sensing and response to stresses, interbacterial communication, and the modulation of infection. Bacteriophages can produce small proteins to influence lysogeny/lysis decisions. The review by Duval and Cossart presents experimental strategies for the genome-wide identification of small proteins, examples of their functions, and possible applications.

Comprehensive mapping of the protein–metabolite interaction space

New experimental approaches using mass spectrometry and nuclear magnetic resonance spectroscopy (NMR) have greatly expanded our view on the cellular landscape of protein–metabolite interactions. These methods either identify proteins interacting with a given metabolite, or metabolites that bind to a particular protein of interest. Diether and Sauer review recent developments that might eventually enable comprehensive mapping of the protein–metabolite interaction space. In particular, proteomics techniques to assess cell wide protein property changes in response to metabolite treatment are highly promising. Since we expect major advances in mapping protein–metabolite interactions in the near future, the challenge shifts to the determination of their functional relevance. However, currently only few specialized methods are available to achieve this goal on a system-level.