Editorial for Article Collection on “Bacterial Survival Strategies”

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The question of how bacteria cope with harmful conditions and which strategies they employ to maintain viability in unfavorable environments represents one of the most fundamental issues in microbiology. In an ideal environment, where substrates and nutrients are abundantly available and metabolic end-products are constantly removed, bacterial populations grow exponentially. Research in classical microbial physiology has for long focused on deciphering cellular processes during this phase of a bacterial life. However, in most natural environments, bacteria face – at least temporarily – adverse conditions, which limit their growth or where the viability of bacteria is challenged. Abiotic conditions stressing viability could be severe lack of essential nutrients, the presence of toxic compounds or unfavorable physicochemical environmental conditions. Moreover, the surrounding organisms challenge bacterial survival as predators or competitors for resources and niche occupation.

Bacteria have been subjected to these selective pressures during their entire evolution. As a result, they acquired elaborate strategies that allow them to cope with such challenges. Thus, bacterial survival strategies are fundamental to understand key aspects of bacterial behavior, from the long-term survival of nutrient-starved cyanobacteria and their stunning recovery capabilities to the strategies of pathogenic bacteria to survive and resist host defense or to withstand competing microorganisms. We can assume that the survival strategies of bacteria are

based on fundamental principles acquired early in evolution and therefore common in most bacteria, as well as on lifestyle specific and highly adapted programs, acquired during niche evolution of the various bacterial genera. These manifold survival strategies are essential to successfully compete in the various ecological niches and to colonize new habitats and hosts. Therefore, this topic is of greatest relevance for bacterial ecology and physiology, for the spread of bacterial pathogens, and for the development of antibacterial compounds and, hence, it is a central area of microbiological research.

Nine years ago, the DFG-funded research training group “Molecular Principles of Bacterial Survival Strategies” (RTG1708) was initiated at the University of Tübingen with the aim to elucidate fundamental and niche specific principles of bacterial survival strategies in an interdisciplinary research group, by combining the expertise of research teams with a strong background in molecular physiology, genetics, chemical analytics, environmental microbiology or medical microbiology. On the occasion of the end of the RTG1708 program, a final symposium on “bacterial survival strategies” was organized from October 7 to 9, 2020, together with invited international guests included via remote video access. The present article collection on bacterial survival strategies includes both primary research papers as well as review articles from contributors of this symposium.

The papers in this article collection reflect the breadth of the research spectrum. A fundamental challenge to

bacterial survival, frequently occurring in natural habitats, is the lack of essential nutrients. Successful survival requires an ability to persist for potentially long periods of time in growth-arrested states. The invited contribution by Bergkessel and Delavaine provides a comprehensive review on the diversity in carbon starvation survival strategies imposed by the limited availability of substrates for biosynthesis and for energy metabolism and the corresponding outcomes among heterotrophic Proteobacteria [Bergkessel and Delavaine, 2021]. The following review summarizes research on the response of unicellular cyanobacteria towards long-term nitrogen starvation (chlorosis). Within the RTG program, the resuscitation of strain *Synechocystis* sp. PCC 6803 from long-term nitrogen chlorosis could be established as a powerful research model system to investigate the awakening of dormant bacteria [Neumann et al., 2021]. In filament-forming cyanobacteria of the order *Nostocales*, the lack of essential nutrients such as phosphorus leads to a cell differentiation process culminating in the formation of spore-like cells termed akinetes, a process reviewed by Garg and Maldener [2021].

Starvation causes the induction of various specific cellular processes, often involving the accumulation of cellular reserve materials. Many bacteria are able to accumulate the carbon polymer polyhydroxybutyrate, when nutrients other than carbon become growth limiting. The physiological implications of the formation of polyhydroxybutyrate in cyanobacteria is still poorly understood, an aspect that is highlighted by Koch and Forchhammer [2021]. Polyphosphate accumulation occurs frequently in response to growth imbalances or entry into a stationary phase. In their research article, Rosigkeit et al. [2021] report about the multiple roles of polyphosphate in *Ralstonia eutropha* and other bacteria.

A strategy to cope with nutrient limitation is the induction of special catabolic pathways enabling the use of unfavorable compounds. Krysenko et al. [2021] provide a review article on the new role of glutamine synthetase-like enzymes in the survival under environmental stress, by catalyzing the first step in poly- and monoamine catabolism in *Streptomyces coelicolor*.

Chemoautotrophic bacteria such as iron-oxidizing bacteria gain their energy by catalyzing redox reactions coupled to an oxygen-dependent respiratory chain. Under anoxic conditions, a bacterial enrichment culture was obtained capable of autotrophic growth. Huang et al. [2021] report an investigation describing core features of microbial networks contributing to autotrophic Fe(II) oxidation coupled to nitrate reduction.

The ability of microbial communities to colonize diverse habitats typically depends on the concerted action of multiple members of the community using common goods. Of particular importance in the case of plant surface colonization is the synthesis and excretion of amyloid proteins. They allow surface adherence and creation of a protective coating and the formation of hydrophobic surface layers, which play a pivotal role in the survival of plant-associated microbes. A comprehensive state-of-the-art review on this topic is provided by Gómez-Pérez et al. [2021].

The oral cavity is colonized by a highly specialized microbial community, with the strain *Tannerella forsythia* being a causative agent of periodontitis. To survive in the oral habitat, *T. forsythia* depends on cohabiting bacteria providing them with N-acetylmuramic acid derived from their cell wall. How *T. forsythia* uses peptidoglycan salvage to survive within the oral microbial community is described in the paper by Hottmann et al. [2021].

Successful colonization of niches also depends on the ability to recognize and degrade malfunctioning or waste proteins. Several bacteria make use of this dependence by modulating the proteolytic machinery of competitors. The review by Illigman et al. [2021] focuses on the contribution of the Clp protease system to prokaryotic survival and summarizes the current state of knowledge for exemplary bacteria in an increasing degree of interaction with eukaryotic cells.

Staphylococcus aureus is an opportunistic pathogen of humans and animals, which asymptotically colonizes the nasal cavity from where it can spread out to cause life-threatening acute or chronic infections. When colonizing new hosts, modulation of the genome by insertion of mobile genetic elements like prophages plays an important role, as detailed in the review article by Rohmer and Wolz [2021]. In the nasal cavity, different *Staphylococcus* strains compete for colonizing this niche. Recent studies in the RTG program highlighted that secondary metabolites produced by the various strains are thereby a major factor for microbiome interactions, in particular of staphylococcal pathogens and commensals [Torres Salazar et al., 2021]. In general, the chemical warfare between bacteria involves the synthesis of a large variety of secondary metabolites. In Firmicutes, these are frequently derived from peptides. The eipeptide biosynthesis locus *epeXEPAB* encodes a minimalistic biosynthetic pathway for a linear antimicrobial eipeptide, EpeX. The invited contribution by Popp et al. [2021] reports the mechanism of immunity against self-produced EpeX, triggered by intrinsic envelope stress. The Actinobacteria harbor a particularly rich

arsenal of secondary metabolites. Engelbrecht et al. [2021] provide a review on natural products from *Nocardia* and their role in pathogenicity.

RTG research discovered that the unicellular cyanobacterium *Synechococcus elongatus* produces an unusual sugar, 7-desoxy-sedoheptulose that acts against other photoautotrophic organisms. Synthesis does not require a secondary metabolite gene cluster but is derived from desoxyadenosine salvage metabolism, reviewed by Rapp and Forchhammer [2021]. As primary producers, cyanobacteria have also to cope with predation. Whereas protozoa are well known grazers of cyanobacteria, knowledge on bacterial predators on cyanobacteria is still in its infancy, as reported by Bauer and Forchhammer [2021]. Myxobacteria are perhaps the best studied bacterial predators. In their invited review article, Whitworth and colleagues provide a review on the genetics of prey susceptibility to myxobacterial predation [Swain et al., 2021].

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