RiM2024 Michelsberg Registration Form

Name, surname:

Email:

Participant status

Academia ☐
Industry ☐

I would like to attend the conference without contribution ☐

I would like to present my research…

…in a talk ☐
…on a poster ☐

Presenter status

M.Sc. ☐
PhD student ☐
Postdoc ☐
other ☐

Food preferences

No preferences ☐
Vegan ☐

Abstract instructions
The deadline for registration and abstract submission: **August 15, 2024**. Please use the template on the next page to create your abstract. The abstract has a word limit of 300 words. Please overwrite the attached template.

When completed, save the registration form as follows (example):
RiM2024_registration_form_Commichau

Send it to: rim2024@uni-hohenheim.de

Please address any question to Fabian.commichau@uni-hohenheim.de

Adaptation of *Listeria monocytogenes* to perturbation of c-di-AMP metabolism underpins its role in osmoadaptation and identifies a fosfomycin uptake system

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c-di-AMP controls osmolyte homeostasis in several bacteria, including *Listeria monocytogenes* (1,2). c-di-AMP also indirectly stimulates the DNA-binding activity of CodY, which negatively controls the expression of genes required for adaptation to nutrient limitation (3). In *L. monocytogenes*, c-di-AMP is synthesized by the diadenylate cyclase CdaA and degraded by the phosphodiesterases GdpP and PgpH (4). c-di-AMP is essential for growth because it prevents uncontrolled uptake of osmolytes. Elevated cellular c-di-AMP concentrations are also often associated with increased resistance of bacteria to cell wall-targeting antibiotics (2). To get further insights into the cellular role of c-di-AMP in *L. monocytogenes*, we studied the phenotypes of Δ*cdaA* and Δ*gdpP* Δ*pgpH* mutants and characterized suppressor mutants derived from them. We identified Δ*cdaA* suppressor mutants that can be assigned to two different classes. In the first class of mutants carrying mutations in the *relA* (p)ppGpp synthase gene, the CodY regulon was affected. These mutants turned out to be sensitive to fosfomycin, which inhibits peptidoglycan biosynthesis. In the second class of mutants, the *opp* oligopeptide transporter genes were inactivated, resulting in a fosfomycin-resistant phenotype. Thus, the suppressor analysis identified a major route for fosfomycin uptake. We also observed that casamino acids and isoleucine are toxic for the Δ*cdaA* mutant. A subsequent suppressor screen revealed that isoleucine toxicity is readily relieved by mutations in the *codY* gene. The encoded CodY variants are less responsive to isoleucine and have reduced DNA binding activity. Thus, a c-di-AMP-free strain shows increased uptake of isoleucine, which in turns leads to CodY hyperactivity. The characterization of the Δ*gdpP* Δ*pgpH* mutant revealed that the bacteria are osmosensitive, a phenotype that is invariably suppressed by the acquisition of loss-of-function mutations in the *cdaA* diadenylate cyclase gene. The current status of the project will be presented (5).

(1) Stülke, J. and L. Krüger (2020) Annu. Rev. Microbiol. 8: 159-179.
(2) Commichau, F.M., et al. (2018) Trends Microbiol. 26: 175-185.
(3) Peterson, B. N., et al. (2020) MBio. 11: e01625-20.
(4) Commichau, F. M., et al. (2019) J. Bacteriol. 201: e00462-18.
(5) Wang, M., et al. (2022) Environ. Microbiol. 24: 4466-4488.