

LS24-009 - Engineering enhanced microbiome function using synthetic ecology

Zusammenfassung

The gut microbiota is essential for developing, regulating and maintaining human health. Microbial metabolite production is important for limiting inflammation but can derail during dysbiosis, with a disbalance between pro- and anti-inflammatory metabolites contributing to acute and chronic inflammatory diseases. A targeted repair of microbiome function to promote health is currently limited by our lack of understanding of context-dependent microbial activity and community interactions. Furthermore, high inter-person variability of the microbiota precludes a one-size-fits-all solution. We propose a rational design of anti-inflammatory consortia by engineering the production of the key metabolites short chain fatty acids (SCFAs). We aim for a personalized modification strategy by mimicking the architecture of the most similar high-performing communities. To distil rules that govern metabolic production, we will first analyze SCFA production, co-expression of metabolic pathways with RNAseq, and ecological community structure of natural and synthetic gut communities (n=1000). We will employ machine learning and network reconstruction to reveal cooperating strains and interaction motifs that determine SCFA production. In order to guide engineering, we will use community metabolic modeling for the identification of metabolic bottlenecks and essential pathways. For simulating the effects of molecular interventions, we will extend an existing heuristic ODE model of butyrate production. To engineer high-performing communities, we will redesign natural communities by adding genetically-modified and native strains that enhance beneficial and stabilizing interactions, and releasing molecular bottlenecks. By leveraging the tools of synthetic biology and ecology and performing modeling on multiple scales from genes to communities, this project will provide a valuable framework for effective microbiome engineering in diverse applications.

Wissenschaftliche Disziplinen:

Microbiome research (50%) | Mathematical modelling (40%) | Bioinformatics (10%)

Keywords:

Gut microbiome
Microbial community modeling
Synthetic ecology of microbial communities
Engineering complex community function

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Status: Vertrag in Vorbereitung

Weiterführende Links zu den beteiligten Personen und zum Projekt finden Sie unter

<https://wwtf.at/funding/programmes/ls/LS24-009/>