Jena School for Microbial Communication
Graduate School of Excellence

PhD project title
Deciphering microbiome-enteric nervous system interactions in sepsis

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Abstract:
Sepsis is a complex, life-threatening syndrome in which infection triggers a dysregulated host response, profound gut dysbiosis, and, in many patients, acute neurological complications such as delirium. However, the biological mechanisms that distinguish sepsis-associated delirium from sepsis without delirium remain poorly understood. Because the gut microbiome is a key regulator of gut–brain communication and the enteric nervous system (ENS) directly interfaces with microbial, metabolic, and immune signals, the ENS may represent an early site at which sepsis-induced dysbiosis contributes to neurological dysfunction.

This project aims to determine how alterations in the gut microbiome and microbial metabolic pathways contribute to ENS dysfunction during sepsis and whether these mechanisms differ between patients with and without delirium. Using an integrated computational and experimental strategy, defined synthetic microbial communities (SynComs) will be designed to capture key functional features of the human gut microbiota associated with these two clinical phenotypes. Genome-scale metabolic models (GEMs) will be reconstructed for the selected microbial members to predict community-level interactions, including metabolic cross-feeding, competition, and the production of neuroactive or immunomodulatory metabolites.

These computational predictions will guide the assembly of the SynComs and their incorporation into immunocompetent gut-on-chip models integrated with enteric neurons and glia. These models will be used to investigate local neuro–immune–microbe interactions and their effects on ENS structure and function, including mechanisms that may precede or contribute to central nervous system dysfunction. By identifying microbiome-derived metabolites, microbial interactions, and host pathways associated with sepsis-related neurological dysfunction, this study will provide a foundation for microbiome-targeted strategies to prevent or mitigate delirium and longer-term cognitive impairment.