



CAIRIBU UROBIOME RESEARCH INTEREST GROUP (U-RIG)

CAIRIBU U-RIG KNOWLEDGE EXCHANGES

EXECUTIVE SUMMARY 12/19/2025 U-RIG KNOWLEDGE EXCHANGE

U-RIG RESEARCH HOUR

FEAT: MEGAN BEHRINGER, PHD



Goal: Facilitate knowledge exchange and spur collaborations in the urobiome and adjacent fields

Summary

Experimental evolutionary approaches to understanding the Urobiome

Introduction to the Urobiome and Experimental Evolution

- **Dr. Megan Behringer** introduced herself as an assistant professor at Vanderbilt University, focusing on eco-evolutionary feedbacks. **She studies how the environment influences microbial evolution and how microbial evolution alters the environment in a cyclical way.**
- The five forces of evolution are mutation, recombination, migration, genetic drift, and natural selection.
- To study non-adaptive microbial evolution, **Dr. Behringer** uses the approach of mutation accumulation. Within the lens of experimental evolution, this approach focuses on **mutation as a key force.**
- The mutation accumulation approach involves minimizing the effective population size to isolate true mutation rates.
- Streaking bacteria on a plate creates single colonies, which allows for the random selection of a single colony for further study.

Influence of Oxygen Conditions and Carbon Sources on Mutation Rates

- Aerobic conditions generally led to higher mutation rates compared to anaerobic conditions. This was shown in prior experiments in *E. coli*.
- **Dr. Behringer** noted that the difference in mutation rates has varied depending on the primary carbon source, with glucose showing comparable rates in both aerobic and anaerobic conditions.
- She speculated that the metabolism of glucose might be overwhelming mutation rates, regardless of oxygen conditions.
- She discussed the implications of these findings for understanding mutation rates across the bacterial tree of life and their relevance to biomedicine. **Early evolution occurred in an anaerobic environment.** In the GI and urinary tracts, oxygen levels vary greatly. Therefore, it is critical to understand bacteria mutation rates in different levels of oxygen.

Mutation Rates in Lactic Acid Bacteria

- **Dr. Behringer's** study focused on the mutation rates of three species of lactic acid bacteria: *Lactobacillus crispatus*, *Lactobacillus acidophilus*, and *Lactococcus lactis*.
- Her lab observed extremely high mutation rates in *Lactobacillus acidophilus*, particularly in anaerobic conditions.
- Compared to aerobic *E. coli*, anaerobic *Lactobacillus* mutation rates are higher.
- **For all three species, the highest mutation rates were observed in the G:C to A:T mutations.**

Comparative Genomic Analysis and Implications for Probiotics

- In addition to extremely high mutation rates, *Lb. acidophilus* exhibited a strong positional bias in mutation frequency near the origin of replication.
- A comparative genomic analysis of *Lactobacillus acidophilus* genomes revealed widespread loss of mismatch repair proteins.

- **Elevated mutation rates in *L. acidophilus* may reflect its domestication history.** Repeated population bottlenecks during industrial propagation, such as in probiotic development, could promote genetic drift, allowing deleterious or unintended mutations to become fixed. This could be a potential concern for probiotic strain stability and should be considered in maintaining the genetic integrity of the strains to preserve consistency in probiotics and in experiments.
- **Dr. Behringer** observed high rates of structural variation, particularly in large deletions or in transposition in *Lactobacillus crispatus*. For this reason, she suggested that *Lactobacillus crispatus* could be a unique model species for studying the evolution of CRISPR loci, especially in a spontaneous mutation context.

Summary of Mutation Rates in Lactic Acid Bacteria

- Mutation rates are heavily influenced by diet, environment, and demography.
- LAB have uniquely elevated mutation rates, which can contribute to rapid evolution but is concerning in the context of genetic load.
- **Domestication and industrialization of species can result in increased mutation rates.**
- *Lactobacillus crispatus* exhibits elevated structural variation rates. Spontaneous mutations of the CRISPR locus inspires questions of the urobiome.

Infection as an Evolutionary Biology Problem

- **Dr. Behringer** views infection as an invasive species problem, using the analogy of a river flowing into a lake. Ecology disruptions may occur if microbes flow from the river to the lake as each body of water has its own biological and physical properties based on pH, flow rates, biological makeup, metabolites, etc.
- Similarly, bacterial strains may disrupt the ecology of a healthy bladder.
- Looking at the Amazon River confluence, the biota and properties of the rivers (Rio Negro and the Amazon River) significantly impact the health and conservation of the region.
- It is important to understand these ecological interactions to inform biomedical research and predict future outcomes.

Megan Behringer, PhD is an Assistant Professor of Biological Sciences and Associate Director of the Vanderbilt Microbiome Initiative at Vanderbilt University. Her laboratory employs experimental evolution combined with genomic analysis to study how environmental factors affect the creation of genetic variation (i.e. mutation) and influence how microbes adapt and diversify in novel complex environments.