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“Atlas” of mouse microbiome strengthens reproducibility of animal testing

Researchers from the University of Bern and Inselspital, Bern University Hospital, in collaboration with over 50 global institutions, have launched the first comprehensive atlas of the mouse gut microbiome. This landmark study synthesizes data from mouse microbiomes across six continents, revealing that metabolic functions remain relatively stable despite microbial diversity. These findings enhance the reliability of biomedical research using mouse models, highlighting the importance of microbial function in experimental outcomes.

Laboratory mice are indispensable for biomedical discovery, yet even genetically identical mice can yield conflicting experimental results depending on their resident microbiota. The complex interplay between microbial communities and their associated metabolic functions in the intestine can profoundly influence experimental results, therapeutic interventions, and our understanding of various biological processes. Understanding the dynamics of the gut microbiome is therefore of paramount importance for biomedical research, as it plays a vital role in shaping health and disease outcomes. This groundbreaking study addresses a fundamental question in microbiome science: how does the composition of microbial communities affect their metabolic function? By exploring this relationship, the research aims to provide insights that could lead to more effective strategies for utilizing mouse models in biomedical studies.

Led by researchers from the Department of Biomedical Research of the University of Bern and the Department of Visceral Surgery and Medicine from the Inselspital, Bern University Hospital, this collaborative effort involved a vast global consortium, that meticulously analyzed approximately 4,000 intestinal samples from mice. The study forms the geographically most comprehensive mouse microbiome dataset to date and revealed that, despite immense differences in bacterial species across facilities, metabolic outputs in the intestine are strikingly consistent. The findings represent a significant milestone in microbiome research and were recently published in the scientific journal *Cell Host & Microbe*.

Bern as international reference center for microbiome systems biology

The research project united more than 50 institutions across Europe, the Americas, Asia, and Africa, with each partner contributing samples under standardized protocols. In total, the global consortium encompassed 51 mice facilities and 12 wild-mouse colonies, producing roughly 4,000 intestinal samples. “By employing a suite of cutting-edge techniques, including strain-resolved metagenomics, metabolomics, and advanced structural modeling, we were able to conduct a thorough analysis of the mouse gut microbiome, facilitating the reconstruction of 98 complete bacterial genomes”, says first

and co-corresponding author, Bahtiyar Yilmaz from the Department of Biomedical Research of the University of Bern and the Department of Visceral Surgery and Medicine from the Inselspital, Bern University Hospital. He adds: "All samples were received, curated, sequenced, annotated, and analyzed in our laboratories, positioning Bern as a global hub for mouse microbiome systems biology." This centralized, multi-omics approach enabled an unprecedented integration of microbial community structure, genetic diversity, and metabolic function.

New foundations to enhance reproducibility in microbiome research

The findings from this extensive study indicate that core metabolic functions remain remarkably stable across diverse microbial communities. "To our surprise, our analysis revealed a universal ecological principle: diversity and stability coexist. Just as ecosystems and the human gut maintain balance amid change, mouse microbiomes adapt their composition while preserving core functions, underscoring the resilience and adaptability of microbial life", explains Bahtiyar Yilmaz. Co-lead researcher Prof. em. Dr. Andrew Macpherson from the Department of Biomedical Research of the University of Bern and the Department of Visceral Surgery and Medicine from the Inselspital, Bern University Hospital highlights: "These results challenge previous assumptions that taxonomic composition alone dictates microbiome function. It shows that by focusing on metabolic functionality, rather than on species identity, one may significantly enhance the reproducibility of biomedical studies." The study further shows that each bacterial species consists of various sub-species, which are all essential for a functioning microbiota. In many diseases, the diversity of microbial specialists is however reduced. MacPherson explains: "The challenge is to ensure that enough healthy bacteria and their subspecialists are always present to keep their home, the intestine, and us healthy". Two interactive online resources developed within the context of this study will allow researchers worldwide to contextualize their data and evaluate potential metabolic biases affecting experimental outcomes, establishing a foundation for enhanced reproducibility in microbiome research.

Unprecedented level of international collaboration

The implications of this research extend well beyond academia, as it provides a valuable reference framework for interpreting microbiome-driven variations in mouse models that are commonly used to study human diseases. "The unprecedented level of international collaboration underscores the global scope of the study and the University of Bern's central role in coordinating the world's most comprehensive analysis of mouse microbiome diversity and function," emphasizes Yilmaz. By establishing a robust foundation for understanding the functional attributes of microbial communities, the study opens new avenues for translational research and the development of targeted microbiome interventions. This ultimately paves the way for more reliable disease models, accelerating the discovery of new therapies for conditions like inflammatory bowel disease, obesity, and infections that affect millions worldwide.

Future research will focus on experimentally validating how specific strain variants influence host physiology, as well as conducting microbiota transfer experiments to assess the impact of microbial exchange on metabolic and immune outcomes. "The insights gained from this study enable a more nuanced approach to microbiome research, promoting a shift toward function-based frameworks that could lead to improved experimental design and interpretation", concludes Yilmaz.

Publication details

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Contact

Prof. Dr. Bahtiyar Yilmaz

Department of Biomedical Research (DBMR) of the University of Bern and Department of Visceral Surgery and Medicine – Gastroenterology, Inselspital, Bern University Hospital

Tel: +41 31 684 16 44

E-Mail: bahtiyar.yilmaz@unibe.ch

Prof. Dr. Andrew Macpherson

Department of Biomedical Research (DBMR) of the University of Bern and Department of Visceral Surgery and Medicine – Gastroenterology, Inselspital, Bern University Hospital

Tel: +41 31 632 80 25

E-Mail: andrew.macpherson@unibe.ch

Department for BioMedical Research (DBMR)

The Department for BioMedical Research (DBMR) of the Faculty of Medicine of the University of Bern was founded in 1994 by the University of Bern and the Inselspital, University Hospital Bern. The DBMR is divided into 13 research programmes with around 100 participating individual laboratories and several independent research laboratories whose research spans all biomedical areas. To bridge the gap between the laboratory and the bedside, the DBMR promotes clinical research with a strong emphasis on the development of translational approaches, the use of "omics" and other cutting-edge technologies, and extensive collaboration between laboratory-based and patient-centered clinical research. The DBMR is also committed to the promotion of young scientists.

Further information: https://www.dbmr.unibe.ch/index_eng.html