


The microbiome and aging: Unlocking new frontiers in healthy longevity

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Research conducted by the USF Microbiomes Institute and the MiaGB Consortium is uncovering the significant link between microbial communities and host biology. This understanding could lead to new therapies for age-related conditions. Shalini Jain, Christian Brechot, and Hariom Yadav provide further insights

Aging is often called a “silver tsunami” due to its overwhelming and rapidly approaching impact. By 2050, the global population aged 65 and older is expected to exceed 1.6 billion, doubling from current numbers. In the United States alone, 16% of the population (54 million individuals) is aged 65 or older, projected to rise to 22% by 2040. This demographic shift poses many challenges for individuals, families, and healthcare systems.

THE MICROBIOME: A New Frontier in Aging Research

The microbiome consists of trillions of microorganisms residing primarily in the gut, including bacteria, viruses, fungi, and archaea. These microorganisms are essential in digestion, immune modulation, and metabolic regulation.

Studies increasingly suggest that the microbiome undergoes significant changes with age. These changes can disrupt the delicate balance of microbial communities, leading to dysbiosis—a condition where harmful microorganisms outnumber beneficial ones. Dysbiosis has been linked to a range of age-related conditions, including neurodegenerative diseases, muscle loss, cardiovascular diseases, and immune dysfunction.

However, while observational studies have identified associations between the microbiome and aging, the causal and consequential links remain poorly understood. This lack of clarity highlights the need for focused research efforts to elucidate these interactions and develop targeted interventions.

How the Microbiome Contributes to Aging-Related Disorders

1. Alzheimer's Disease.

Neurodegenerative diseases, particularly Alzheimer's disease (AD), are among the most devastating age-related conditions. Emerging evidence suggests that the gut microbiome is critical in neuroinflammation and cognitive decline. Dr. Yadav's research at Wake Forest University and University of South Florida (USF) demonstrated that gut dysbiosis exacerbates amyloid-beta accumulation and neuroinflammation in animal models of Alzheimer's. By introducing specific probiotics and dietary interventions, his team was able to mitigate these effects, improving cognitive function in these models. These findings are now being translated into human clinical trials to explore microbiome-based therapies for AD.

2. Sarcopenia and Muscle Health.

Sarcopenia, or age-related muscle loss, is a major contributor to frailty and falls in older adults. Research indicates that the gut microbiome influences muscle health by modulating inflammation and protein metabolism. Studies conducted at USF have identified specific probiotic strains that improve muscle strength and reduce inflammation in aging animal models. These findings open the door to microbiome-targeted therapies to preserve muscle health and reduce the risk of sarcopenia.

3. Cardiovascular Health.

Cardiovascular diseases remain a leading cause of morbidity and mortality among older adults. Microbiome-derived metabolites, such as trimethylamine-N-oxide (TMAO), butyrate, and others, have been implicated in cardiovascular disease risk. Dr. Yadav's lab has explored strategies to modulate gut bacteria to lower TMAO levels and increase butyrate levels, demonstrating that dietary and probiotic interventions can significantly reduce cardiovascular risks associated with aging.

USF MICROBIOME INSTITUTE: Advancing Microbiome and Aging Research

The University of South Florida Microbiomes Institute, led by Drs. Christian Brechot and Hariom Yadav, is a pioneering force in microbiome and aging research. Its flagship program investigates the microbiome's role across the lifespan, emphasizing that aging begins at the embryonic stage. The institute highlights that while aging is often associated with older adults, the process starts early in life as the body accumulates abnormalities in biological pathways over time. The microbiome, which is highly dynamic and evolves throughout life, plays a crucial role in this process.

Early-life microbial interactions shape immune memory, influencing childhood, adulthood, and later life health. By studying these interactions, the USF Microbiomes Institute aims to uncover how microbial imbalances contribute to aging-related conditions and develop interventions to restore harmony in these pathways.

THE MICROBIOME IN AGING GUT AND BRAIN (MiaGB) Consortium

The MiaGB Consortium, led by Dr. Yadav, is a Florida state-wide initiative funded by the Florida Department of Health and the National Institutes of Health. This consortium has created a unique dataset comprising microbiome samples from over 500 older adults.

Key Features of the MiaGB Consortium:

- **Cross-Sectional and Longitudinal Data:**
MiaGB collects and analyzes microbiome data over time, providing insights into how microbial communities change with age.
- **Brain, Muscle, and Immune Health:**
The consortium examines the links between microbiome changes and cognitive decline, muscle loss, and immune dysfunction.
- **Microbial Biomarkers:**
MiaGB aims to identify microbial signatures that predict the risk of age-related conditions, paving the way for early detection and intervention.

The consortium's findings have far-reaching implications for understanding the biological underpinnings of healthy ageing, as well as training young investigators in this area of research/ science. By developing microbial biomarkers, MiaGB lays the foundation for personalized strategies to prevent and treat age-related disorders.

LEAKY GUT AND INFLAMMAGING

Leaky gut is an understudied phenomenon characterized by increased gut permeability. This condition allows pro-inflammatory molecules to enter the bloodstream, triggering systemic inflammation known as inflammaging. Chronic inflammation accelerates the progression of age-related diseases, including dementia and cardiovascular disorders. Dr. Yadav's lab at USF has made significant strides in addressing leaky gut. One of the lab's most notable innovations is PoZibio®, a postbiotic derived from *Lactobacillus paracasei* D3.5. This heat-inactivated probiotic has been shown to:

- **Reduce Gut Permeability:**
Strengthening the gut barrier to prevent unwanted molecule leakage.
- **Lower Inflammation:**
Mitigating chronic inflammation associated with aging.
- **Promote Healthy Aging:**
Improving overall health and longevity in clinical trials.

PoZibio® represents a promising therapeutic approach for combating leaky gut and inflammaging, and its successful commercialization underscores its potential for widespread impact.

CONCLUSION: The Promise of Microbiome Research

The microbiome represents a transformative frontier in aging research. Pioneering studies from the USF Microbiomes Institute and the MiaGB Consortium are unraveling the complex interplay between microbial communities and host biology.

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