

# Youth-associated signatures in the gut microbiome of centenarians

We characterized the enterotypes of a large cohort of individuals of 20–117 years of age and found that the gut microbiome of centenarians has features that are usually associated with gut microbiomes of young individuals: dominance of *Bacteroides* spp., increase in species evenness, enrichment of potentially beneficial Bacteroidetes and depletion of potential pathobionts.

## This is a summary of:

Pang, S. et al. Longevity of centenarians is reflected by the gut microbiome with youth-associated signatures. *Nat. Aging*, <https://doi.org/10.1038/s43587-023-00389-y> (2023).

## Publisher's note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Published online: 6 April 2023

## The question

The human gut microbiota has important roles in the aging process as well as the cause and development of aging-related diseases<sup>1</sup> (for example, diabetes mellitus and cancers). Centenarians, who usually exhibit a reduced susceptibility to chronic diseases, are an exemplary model for studying how the gut microbiota contributes to healthy aging. An enrichment of certain gut bacteria that are associated with aging (for example, *Akkermansia* spp. and the Christensenellaceae family) has been identified in centenarians<sup>2</sup>. Yet limited sample sizes and lack of a longitudinal design in these previous investigations might undermine their conclusions and explanations. Additional evidence is needed to understand how the gut microbiota is linked with longevity. We conducted a longitudinal study of the gut microbiome in a large cohort of 1,575 individuals, including 297 centenarians, from Guangxi, South China. We sought to explore the aging pattern of the gut microbiota in centenarians and provide insights into whether the gut microbiota is associated with the healthy aging of these individuals.

## The discovery

We collected fecal samples and health information from the centenarians and four other control groups of individuals of 20–85 and 90–99 years of age, and performed 16S ribosomal RNA sequencing to identify and characterize the signatures of gut microbiomes. To further explore how the gut microbiome of centenarians developed as the individuals aged, we designed a longitudinal study of 45 centenarians randomly selected from the 297-individual cohort and collected fecal samples 1.5 years apart to compare their microbial structure, composition and diversity.

Four distinct enterotypes were identified from the gut microbiomes of the study population, and the centenarians exhibited a unique enterotype pattern characterized by the combination of *Bacteroides* spp. and *Escherichia–Shigella* (*Escherichia* and/or *Shigella*) spp. (Fig. 1), which were dominant in the young adults (20–44 years of age) and other groups of older individuals, respectively. We discovered that the gut microbiome signature in centenarians has a structure that resembles that in young adults: an over-representation of *Bacteroides* spp., an increase in species evenness (a measure of how close in numbers each species in a community is (high evenness indicates that the species have similar abundance)), an enrichment of potentially beneficial species from the Bacteroidetes (now Bacteroidota)

phylum and depletion of potential pathobionts (harmless commensals that can become pathogenic under certain circumstances). Our findings also suggest that the enterotype dominated by *Bacteroides* spp. (in particular, the enterotypes enriched in beneficial *Bacteroides* spp.) could serve as a hallmark to distinguish centenarians from other older individuals. For example, *Bacteroides thetaiotaomicron*, which is crucial for maintaining intestinal homeostasis and symbiosis, is enriched in centenarians. In contrast with a previous study<sup>3</sup>, health status may bring some variation, but has no significant effect on the direction of the changes in the microbiome signatures between centenarians and other age groups. Our longitudinal study further revealed a microbiome pattern in centenarians that maintains or enhances youth-associated features of the gut microbiota signature during aging. Our large-scale cross-sectional and longitudinal study has identified unique gut microbial signatures for centenarians and suggests that these youth-associated features may contribute to healthy aging and longevity.

## The implications

The similarity of gut microbial hallmarks, such as high species diversity and the over-representation of *Bacteroides* spp. and microorganisms with beneficial potential, shared by centenarians and young adults is very intriguing. Because the longitudinal data suggest that these youth-associated signatures were enhanced in centenarians during aging, we propose that this microbiome signature is associated with longevity and may counteract the senescence or chronic diseases that generally accompany aging.

Our study highlights links between gut microbiota patterns and extreme longevity, but how the aging pattern of the gut microbiota contributes to healthy aging or longevity is unclear. Longitudinal data on other age groups (especially other older adults) might help in our understanding of this issue, which must be considered in future aging studies. Another question is how the gut microbiota helps centenarians to have a reduced susceptibility to aging-related chronic diseases. The identification and functional exploration of youth-related bacteria in centenarians in either animal models or humans could shed light on this issue.

## Shuai Wang<sup>1</sup> & Weifei Luo<sup>2</sup>

<sup>1</sup>Lanzhou University, Lanzhou, China.

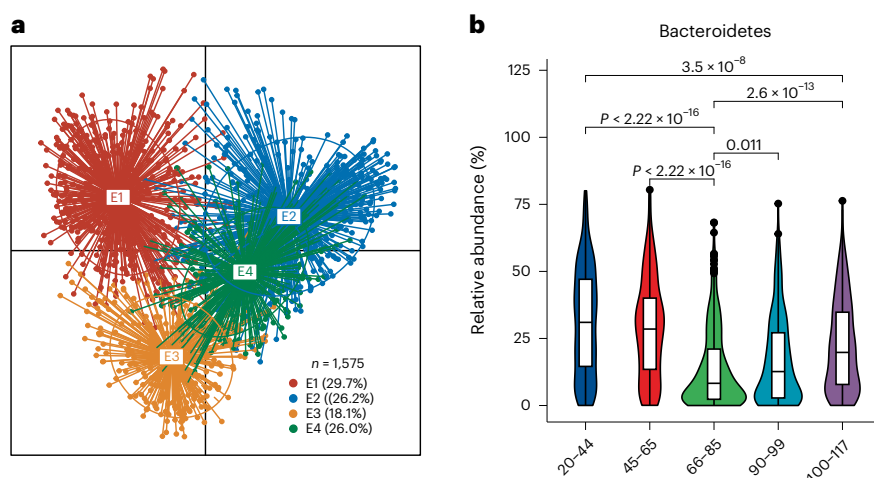
<sup>2</sup>Guangxi Academy of Sciences, Nanning, China.

## EXPERT OPINION

“The authors explored the gut microbiome of centenarians and compared it to the gut microbiomes of young and older individuals in a large cohort of Chinese people. Given that the study is focusing on a completely distinct geographical cohort, it may add

towards a universal model of microbiome alterations associated with healthy aging, which makes the study interesting and important.” **Paul O’Toole, University College Cork, Cork, Ireland.**

## FIGURE



**Fig. 1 | Youth-associated gut microbial signatures in centenarians. a**, The enterotypes (E) identified are characterized by the predominance of the genera *Bacteroides* (E1), *Escherichia-Shigella* (E2), *Prevotella* (E3), and *Blautia* (E4). In each cluster, the ellipse includes two thirds of the samples. The enterotypes of centenarians are distinct from those of other older adults (66–85 years of age), and characterized by the combination of *Bacteroides* spp. and *Escherichia-Shigella* spp. **b**, Violin plots of the relative abundance of Bacteroidetes; compared with older adults, both the centenarian and young (20–44 years of age) groups possessed higher abundances of Bacteroidetes. © 2023, Pang, S. et al.

## BEHIND THE PAPER

The gut microbiota has been proposed as a possible determinant of healthy aging, as increasing evidence<sup>4</sup> shows its effect on human metabolism and immunology. At the beginning of this project, we hypothesized that studying the gut microbiome of long-lived people could provide an improved understanding of how the gut microbiota is linked with longevity. One of the main challenges was collecting the samples and information from people with extreme longevity, which became much more

difficult under the COVID-19 pandemic. We were excited to discover youth-associated gut microbial signatures in our cohort of centenarians. These findings give us confidence that studies on centenarians would be of high value in aging research. We are now isolating thousands of bacteria strains from the centenarians and testing their benefits on animal models. We hope to find microorganisms that are able to extend the human lifespan or promote health. **S.W.**

## REFERENCES

1. Lopez-Otin, C. et al. Hallmarks of aging: an expanding universe. *Cell* **186**, 243–278 (2023).  
**This review summarizes 12 hallmarks of aging and their interconnections.**
2. Biagi, E. et al. Gut microbiota and extreme longevity. *Curr. Biol.* **26**, 1480–1485 (2016).  
**This paper reports gut microbiome signatures of individuals with extreme longevity, including centenarians and semi-supercentenarians (individuals 105–109 years old).**
3. Wilmanski, T. et al. Gut microbiome pattern reflects healthy ageing and predicts survival in humans. *Nat. Metab.* **3**, 274–286 (2021).  
**This paper reports the relationship between gut microbiome pattern and healthy aging.**
4. Ghosh, T. S., Shanahan, F. & O’Toole, P. W. The gut microbiome as a modulator of healthy ageing. *Nat. Rev. Gastroenterol. Hepatol.* **19**, 565–584 (2022).  
**This review paper summarizes the roles of the gut microbiota in healthy aging.**

## FROM THE EDITOR

“The gut microbiota affects health and disease. In this study, the authors describe gut microbiome profiles of a large group of centenarians and compare them to those of individuals of different ages.” **Editorial Team, Nature Aging.**