

Increased life expectancy has led to a rise in age-related diseases. Hippuric acid (HPA) is a potential biomarker for aging. We aim to examine the associations between plasma HPA and biological aging of different organs, and identify the influence factor by integrating genetic and metabolomic data. In 777 healthy participants, Klemmer-Doubal method was used to estimate biological aging and the discrepancy (Δ age) between biological age and chronological age. Multiple linear regression was used to assess the relationship between plasma HPA and organ age or Δ age (heart, kidney, liver, vascular). Genetic and metabolomic data were integrated to identify factors influencing HPA and kidney aging, and Mendelian randomization (MR) analysis was performed to examine causality. Plasma HPA levels were positively associated with chronological age and liver Δ age, but negatively correlated with Δ age of heart, kidney (β : -0.794, 95% CI: -1.352, -0.235), and vascular. The MR analysis further support a causal relationship between the HPA and kidney Δ age (β : -0.009, 95% CI: -0.015, -0.003). What's more, the INPP4B and STEAP2 gene regions were identified as modulating HPA's effects on kidney aging. Metabolomic analysis showed that specific pathways, including alanine, aspartate, and glutamate metabolism; arginine biosynthesis; and glyoxylate and dicarboxylate metabolism, may play a role in HPA against kidney aging. In conclusion, HPA has distinct associations with different organic aging, especially acting as a protective biomarker for kidney aging. The association is influenced by both genetic and metabolic factors. HPA may provide for early intervention in kidney aging.

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INTEGRATING GENETICS AND METABOLOMICS REVEALS PUTATIVE MECHANISMS FOR HIPPURIC ACID DELAYING KIDNEY AGING

Yaxin Li¹, Bangwei Chen¹, Li Luo¹, Shengyin Zeng¹, Lei Ruan⁴, Shida Zhu¹, Cuntai Zhang⁴, and Tao Li¹, 1. *BGI Genomics, Shenzhen, Guangdong, China (People's Republic)*, 3. *Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, China (People's Republic)*, 4. *Huazhong University of Science and Technology, Wuhan, Hubei, China (People's Republic)*