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Phenome-wide associations of human aging uncover sex-specific dynamics

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Abstract

Aging varies significantly among individuals of the same chronological age, indicating that biological age (BA), estimated from molecular and physiological biomarkers, may better reflect aging. Prior research has often ignored sex-specific differences in aging patterns and mainly focused on aging biomarkers from a single data modality. Here we analyze a deeply phenotyped longitudinal cohort (10K project, Israel) of 10,000 healthy individuals aged 40–70 years that includes clinical, physiological, behavioral, environmental and multiomic parameters. Follow-up visits are scheduled every 2 years for a total of 25 years. We devised machine learning models of chronological age and computed biological aging scores that represented diverse physiological systems, revealing different aging patterns among sexes. Higher BA scores were associated with a higher prevalence of age-related medical conditions, highlighting the clinical relevance of these scores. Our analysis revealed system-specific aging dynamics and the potential of deeply phenotyped cohorts to accelerate improvements in our understanding of chronic diseases. Our findings present a more holistic view of the aging process, and lay the foundation for personalized medical prevention strategies.

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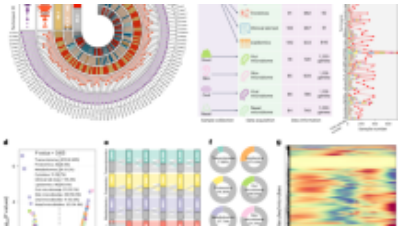

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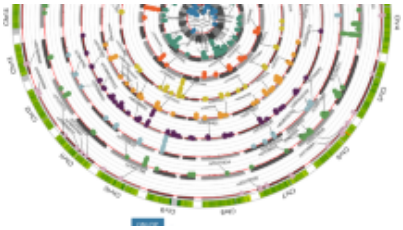

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Data availability

Data in this paper are part of the Human Phenotype Project and are accessible to researchers from universities and other research institutions at https://humanphenotypeproject.org/. Interested bona fide researchers should contact info@pheno.ai to obtain instructions for accessing the data.

Code availability

Analysis source code is available at https://github.com/noambar/BiologicalAge.

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Contributions

L.R. and N.B. conceived the project, designed and conducted all analyses, interpreted the results and wrote the manuscript. Y.R. developed protocols, interpreted the results and wrote the manuscript. A.G. and L.Z. performed data analysis. N.S. developed lipidomics processing, performed lipidomics analyses and wrote the manuscript. A.W. designed the project, developed protocols, and oversaw sample collection and processing. E.S. conceived and directed the project and analyses, designed the analyses, interpreted the results and wrote the manuscript.

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Ethics declarations

Competing interests

The authors declare no competing interests.

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Extended data

Extended Data Fig. 1 Dispersion of biological aging scores from a model based on bone density parameters.

A Ridgeline plot showing the distribution of the BA scores (x-axis) from a model of CA based on bone density parameters. Distributions are separated into CA groups (40-45, 45-50, 50-55, 55-60, 65-70, 70-75; y-axis) and to males and females.

Extended Data Fig. 2 Dispersion of biological aging scores from a model based on diet parameters.

A Ridgeline plot showing the distribution of the BA scores (x-axis) from a model of CA based on diet parameters. Distributions are separated into CA groups (40-45, 45-50, 50-55, 55-60, 65-70, 70-75; y-axis) and to males and females.

Extended Data Fig. 3 Distribution of sample sizes grouped by age is similar across profiled systems.

Figure panels show the normalized distribution of sample sizes of each profiled system (y-axes) grouped by CA (x-axes). **a**–**n**, Blood lipids system (**a**), cardiovascular system (**b**), immune system (**c**), liver health system (**d**), renal function (**e**), bone density (**f**), gut microbiome (**g**), body composition (**h**), frailty (**i**) lifestyle (**j**), diet (**k**), hematopoietic system (**l**), insulin resistance (**m**) and sleep characteristics (**n**).

Supplementary information

Reporting Summary

Supplementary Table 1

Blood lipids system parameters. The full list of parameters within blood lipids category, along with the number of participants (males and females) for which each parameter was available.

Supplementary Table 2

Cardiovascular system parameters. The full list of parameters within cardiovascular system, along with the number of participants (males and females) for which each parameter was available.

Supplementary Table 3

Immune system parameters. The full list of parameters within Immune system category, along with the number of participants (males and females) for which each parameter was available.

Supplementary Table 4

Liver health system parameters. The full list of parameters within liver health category, along with the number of participants (males and females) for which each parameter was available.

Supplementary Table 5

Renal function parameters. The full list of parameters within renal function, along with the number of participants (males and females) for which each parameter was available.

Supplementary Table 6

Bone density parameters. The full list of parameters within bone density, along with the number of participants (males and females) for which each parameter was available.

Supplementary Table 7

Gut microbiome parameters. The full list of parameters within gut microbiome, along with the number of participants (males and females) for which each parameter was available.

Supplementary Table 8

Body composition parameters. The full list of parameters within body composition, along with the number of participants (males and females) for which each parameter was available.

Supplementary Table 9

Frailty parameters. The full list of parameters within frailty category, along with the number of participants (males and females) for which each parameter was available.

Supplementary Table 10

Lifestyle parameters. The full list of parameters within lifestyle category, along with the number of participants (males and females) for which each parameter was available.

Supplementary Table 11

Diet parameters. The full list of parameters within diet category, along with the number of participants (males and females) for which each parameter was available.

Supplementary Table 12

Hematopoietic system parameters. The full list of parameters within hematopoietic system, along with the number of participants (males and females) for which each parameter was available.

Supplementary Table 13

Insulin resistance parameters. The full list of parameters within insulin resistance category, along with the number of participants (males and females) for which each parameter was available.

Supplementary Table 14

Sleep characteristics parameters. The full list of parameters within sleep characteristics, along with the number of participants (males and females) for which each parameter was available.

Supplementary Table 15

Number of self-reported medical diagnoses by profiled system and sex.

Supplementary Table 16

Medical diagnoses associated with biological aging scores. Two-sided odds ratios computed with logistic regression.

Supplementary Table 17

Medical diagnoses associated with biological aging scores. Two-sided odds ratios computed with logistic regression.

Supplementary Table 18

Medical conditions of similar physiological characteristics.

About this article

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