

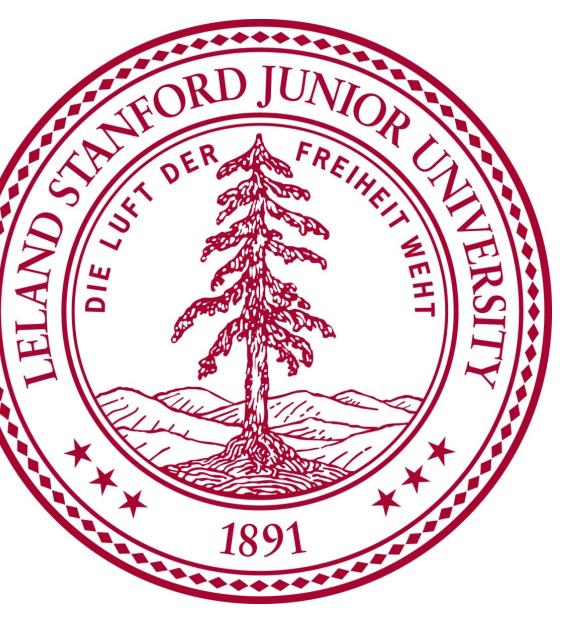
Nonlinear Dynamic Changes During Human Aging Revealed in Multi-omics Profiles

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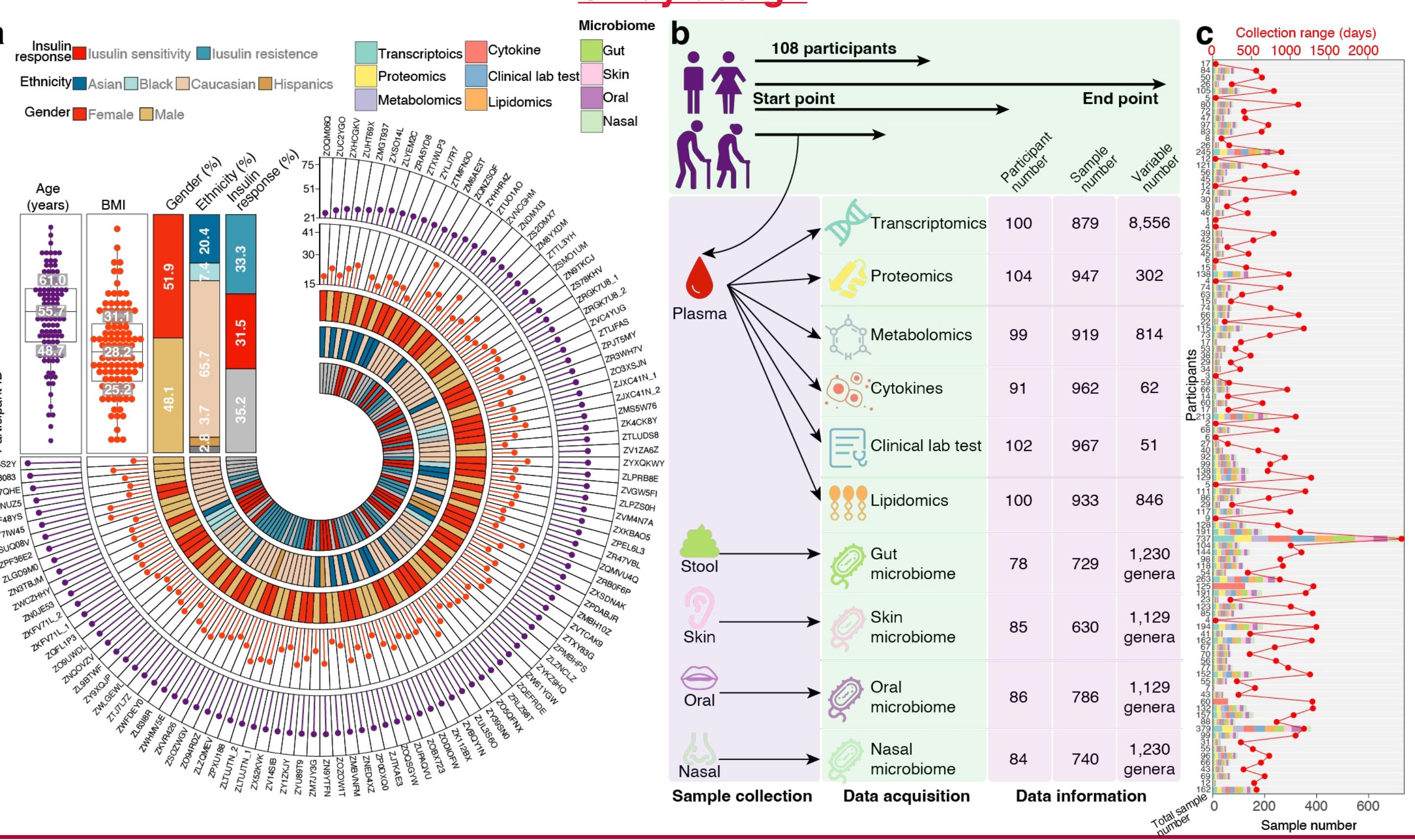
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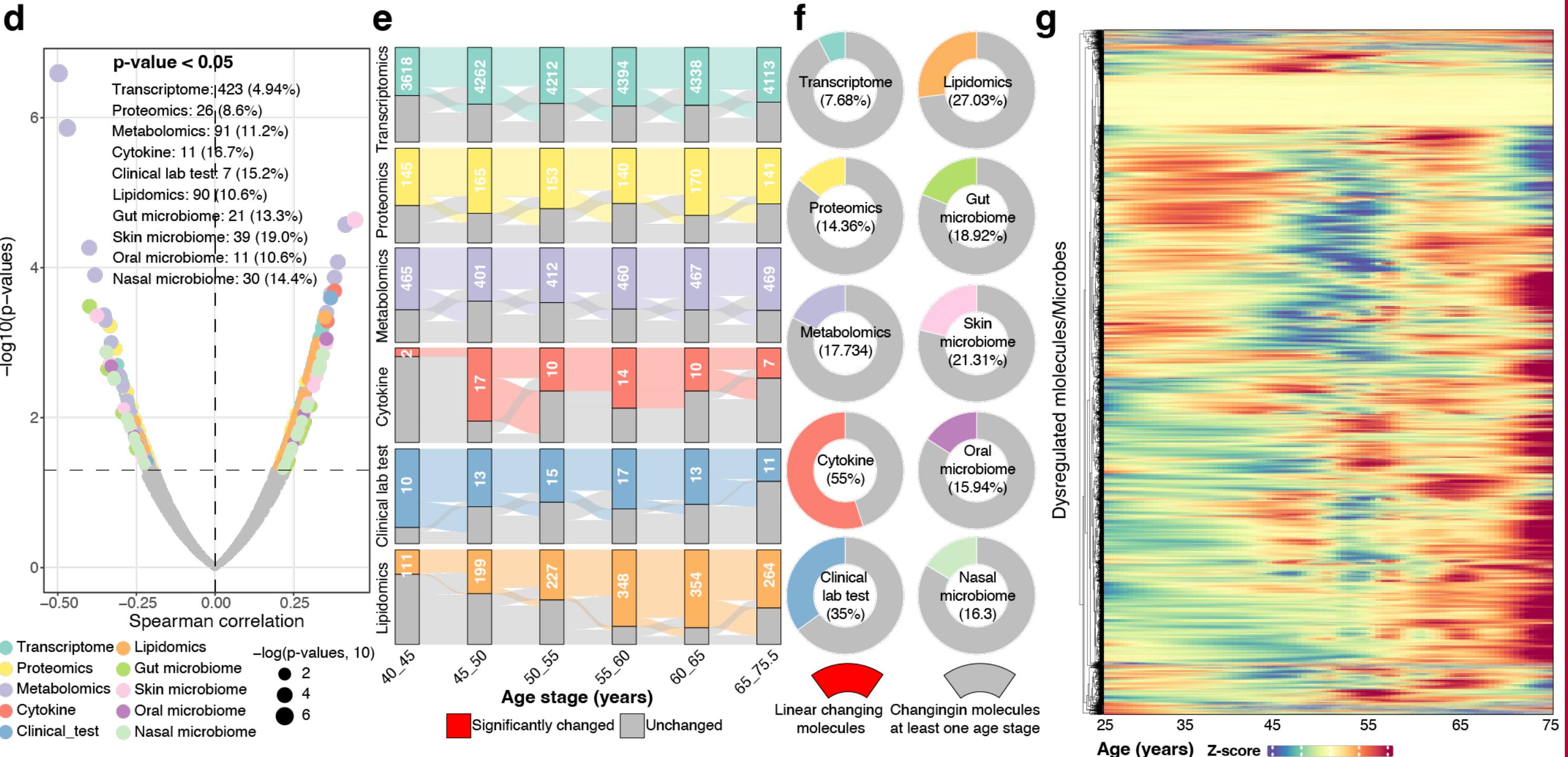
Abstract

Understanding the molecular changes underlying aging and identifying therapeutic targets for aging-related diseases is crucial for increasing health span. While many studies have explored linear changes during aging, the prevalence of aging-related diseases and mortality risk accelerates after specific time points, indicating the importance of studying nonlinear molecular changes. We conducted deep multi-omics profiling of a longitudinal human cohort aged 25 to 75 years. The analysis revealed consistent nonlinear patterns in molecular markers of aging, with significant dysregulation occurring at two major periods occurring at approximately 40 and 60 years of chronological age. Functional pathways associated with these nonlinear changing molecules, such as immune regulation and carbohydrate metabolism, were also identified during the 60-year transition, indicating that functions and risks of aging-related diseases change nonlinearly across the human lifespan. Overall, this research provides significant biological insights through the global monitoring of nonlinear molecular changes during human aging.

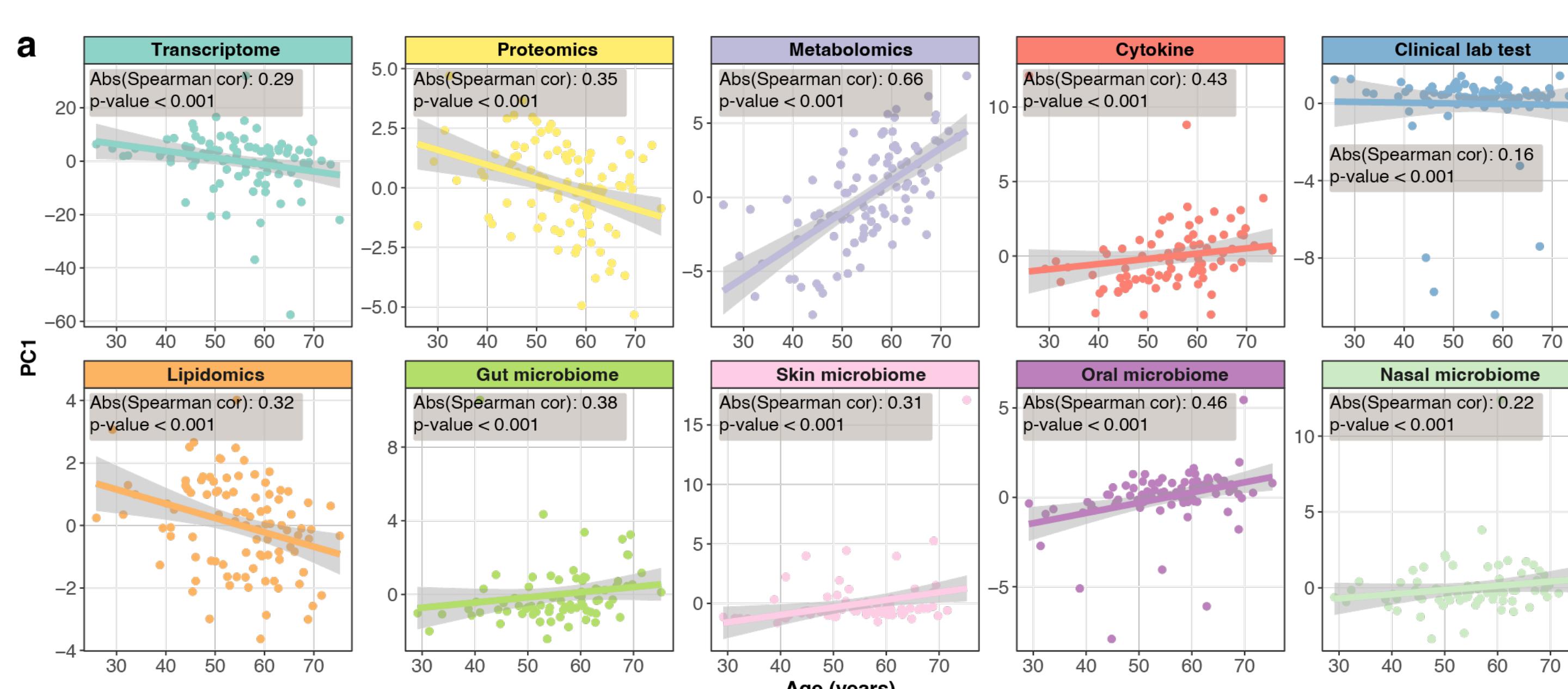
Study design



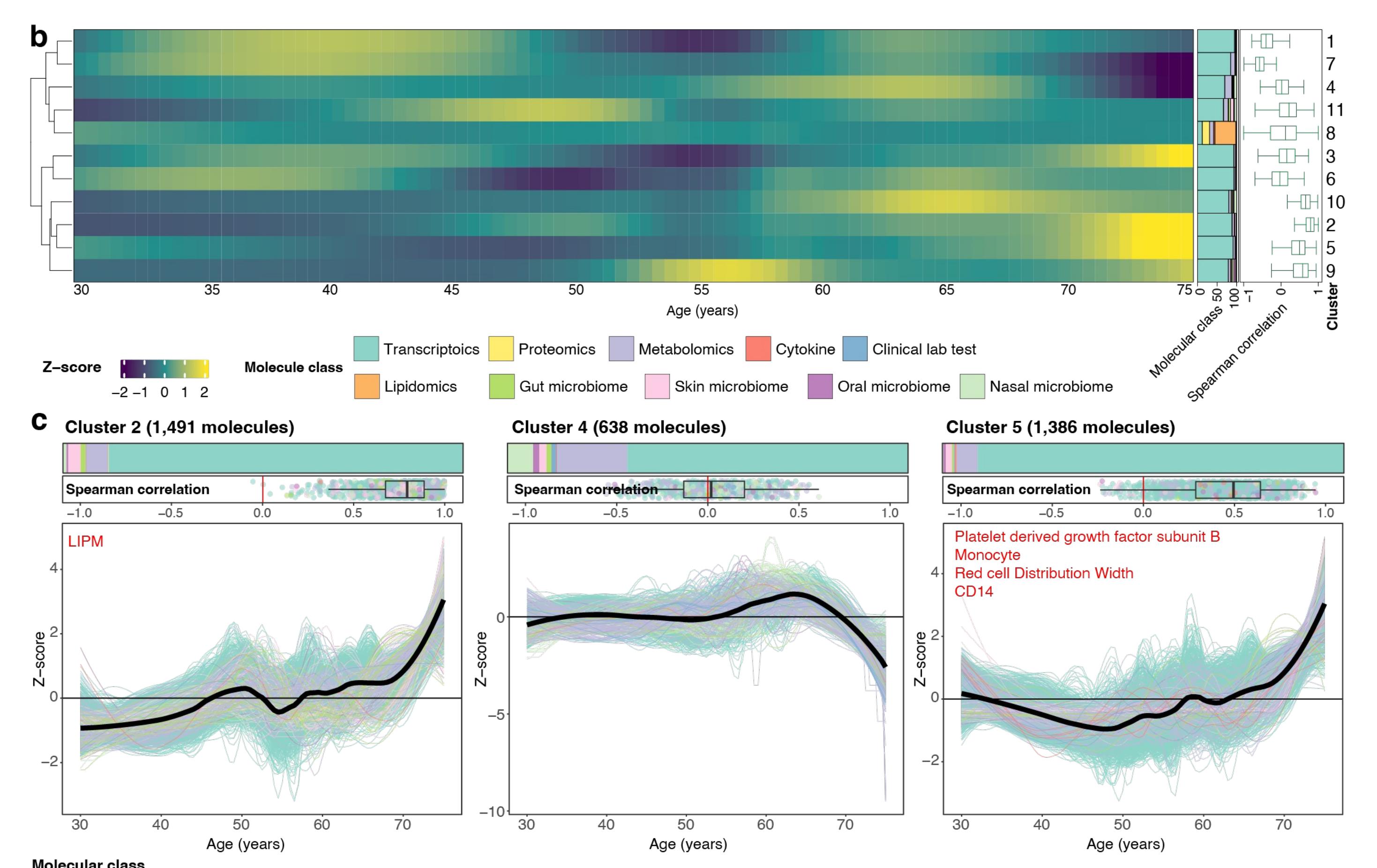
Most of the molecules/microbes change nonlinearly during human aging



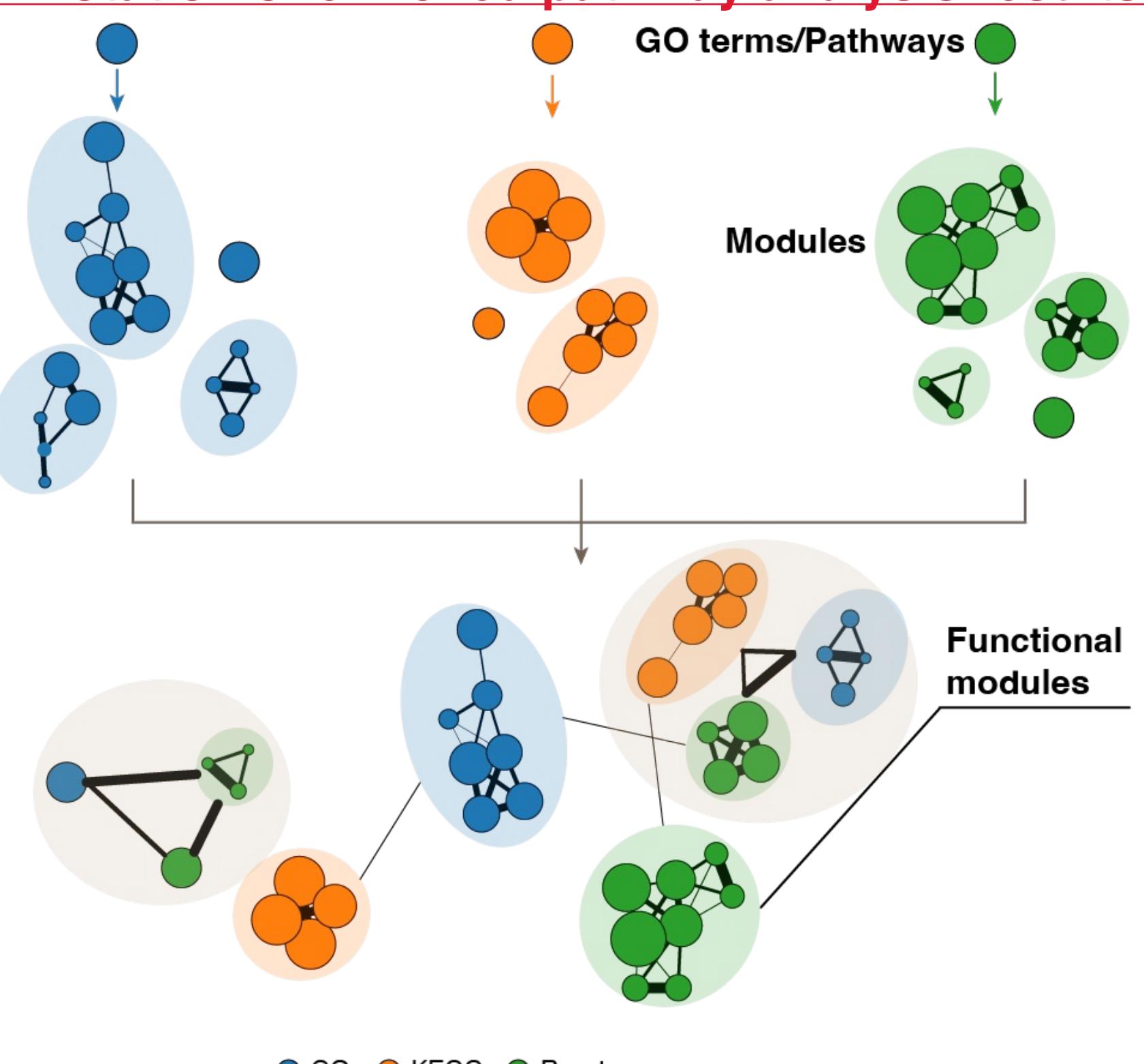
Multi-omics data could serve as reliable indicators of the aging process



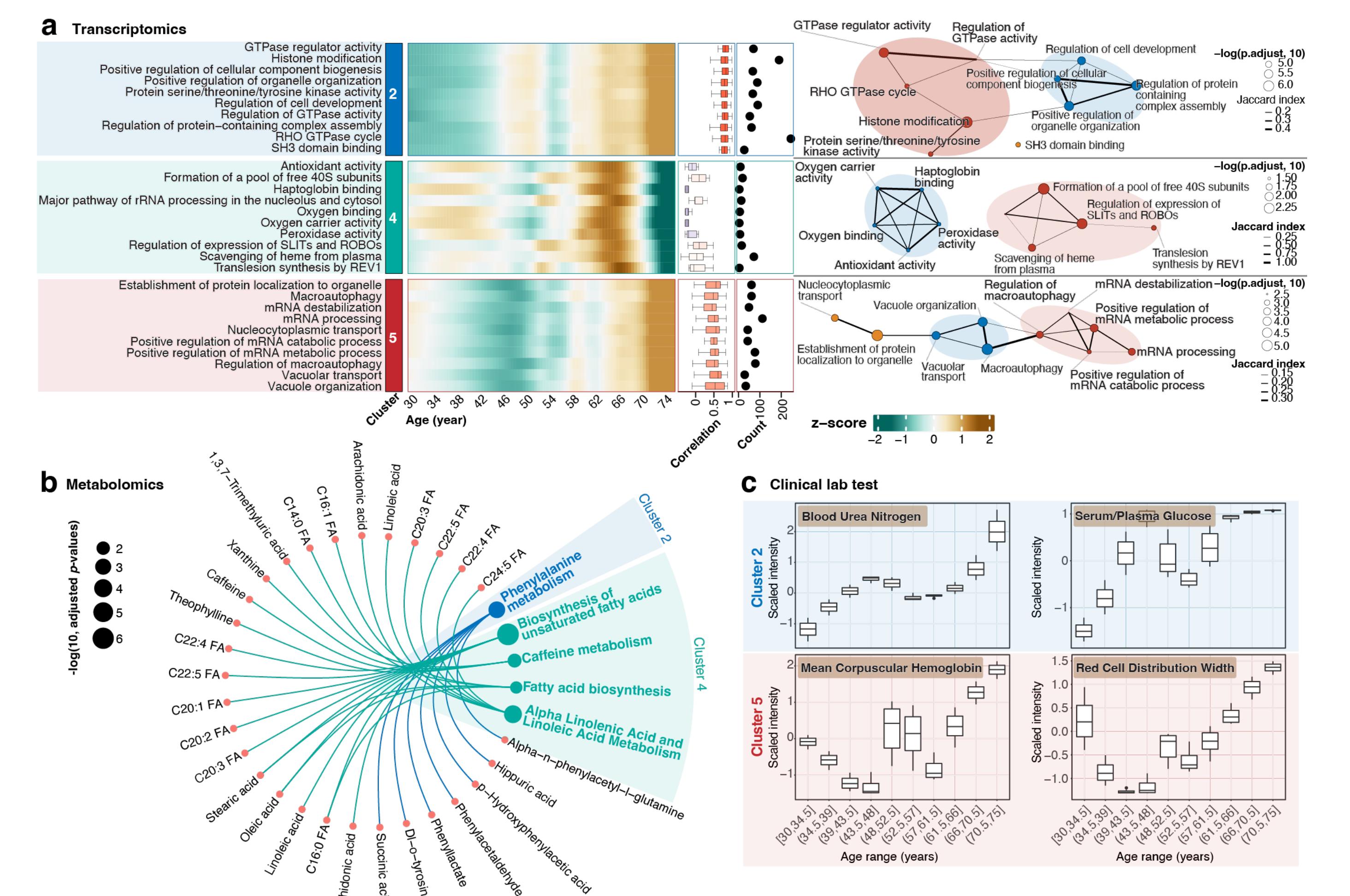
Clustering reveals nonlinear changes in multi-omics profiling during human aging



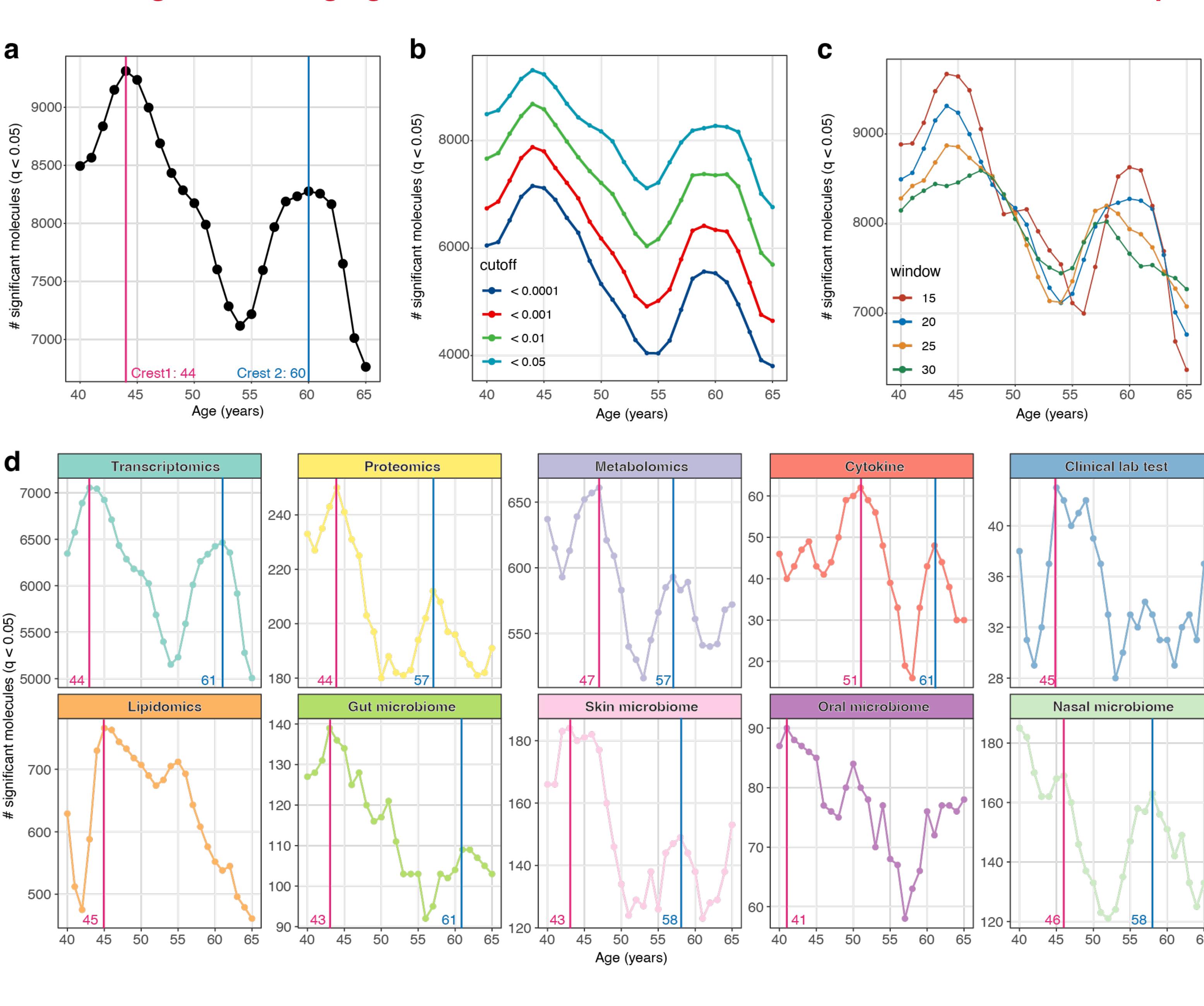
Module annotation of enriched pathway analysis results (MAPA)



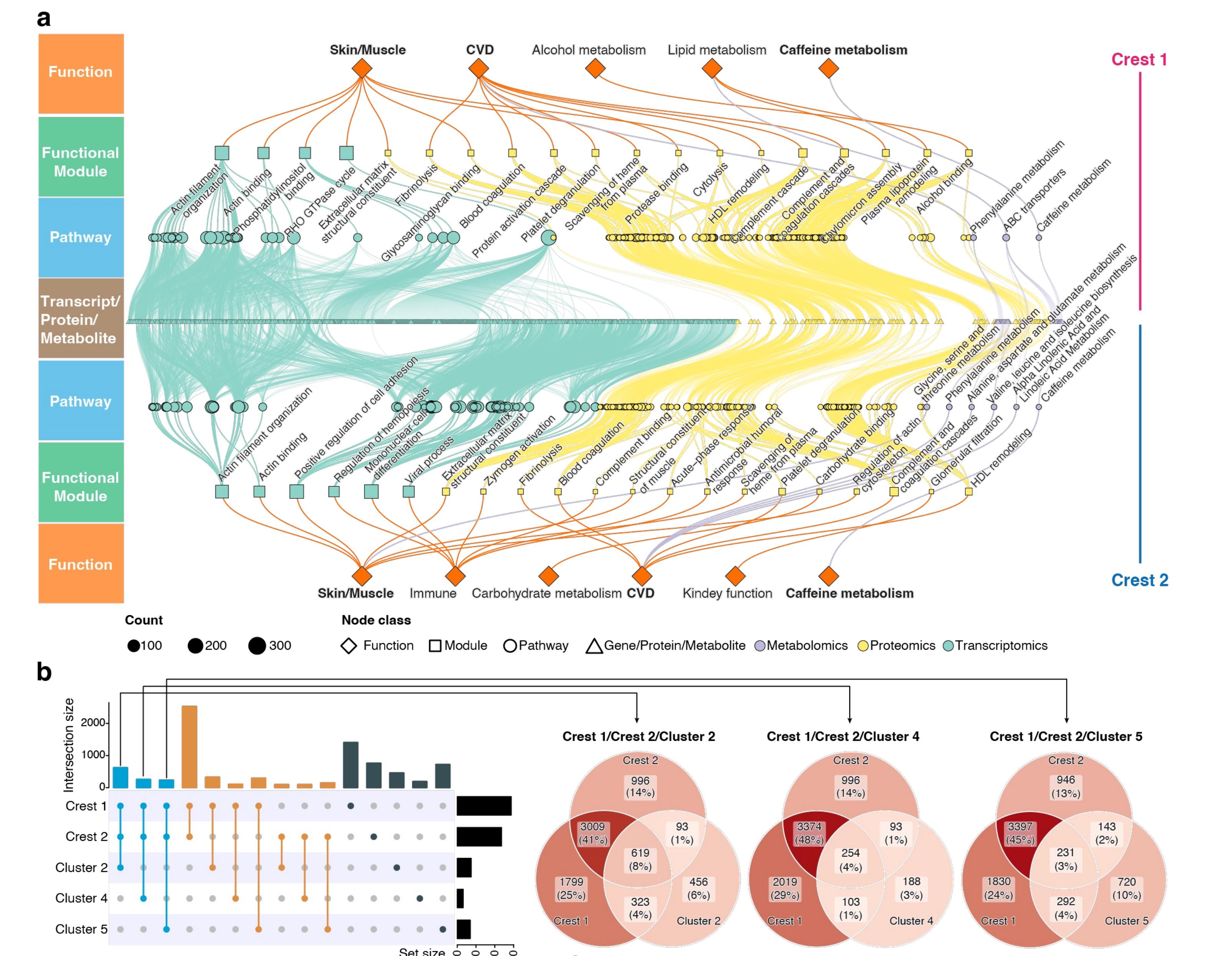
Nonlinear alterations in function and disease risk during the aging process



Uncovering waves of aging-related molecules and microbes across the human lifespan



Functional analysis of aging-related waves of molecules across the human lifespan



Acknowledgments

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