New study reveals molecular fingerprint of biological aging

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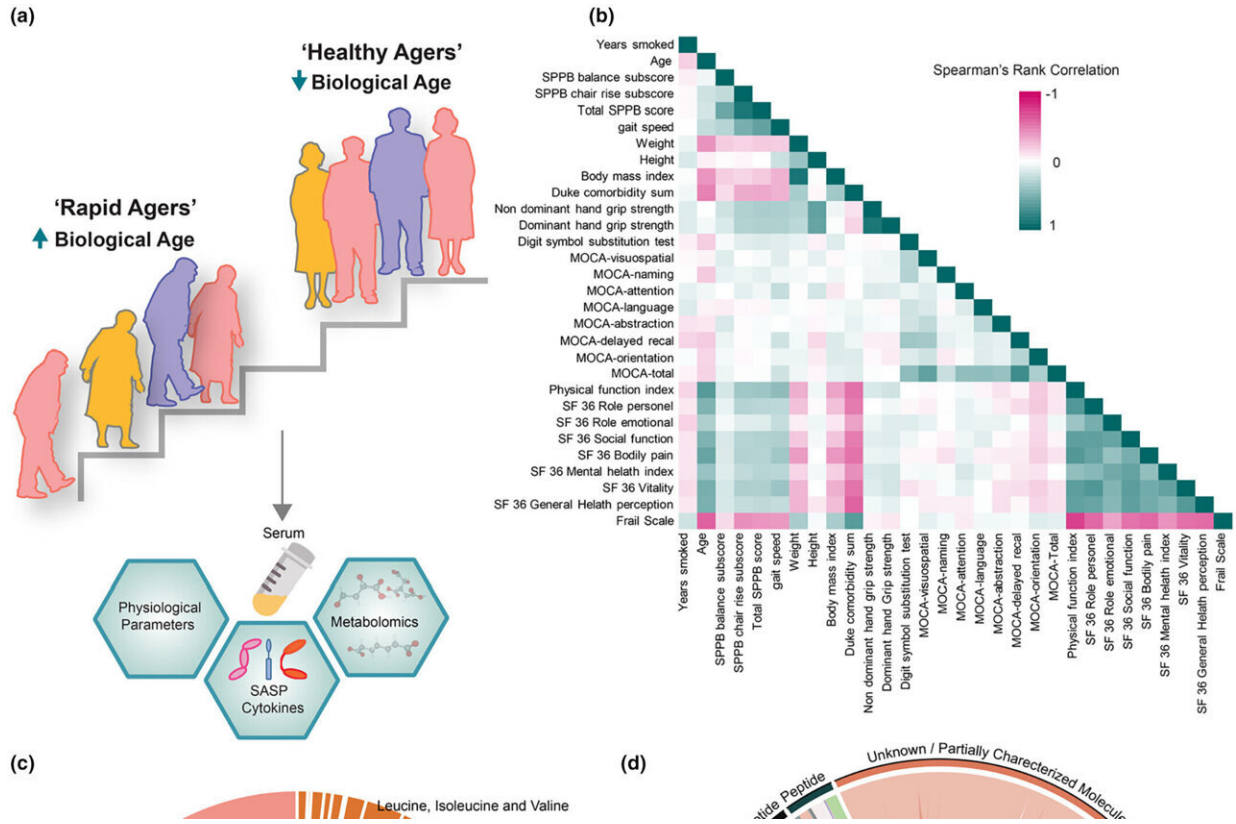

Global metabolic profiling of SOLVE-IT study cohort. Credit: *Aging Cell* (2024). DOI: 10.1111/acel.14104

University of Pittsburgh researchers have uncovered blood-based markers linked with healthy and rapid aging, allowing them to predict a

person's biological age—how fast a person's cells and organs age regardless of their birthdate.

The new research, published in *Aging Cell*, points to pathways and compounds that may underlie biological age, shedding light on why people age differently and suggesting novel targets for interventions that could slow aging and promote healthspan, the length of time a person is healthy.

"Age is more than just a number," said senior author Aditi Gurkar, Ph.D., assistant professor of geriatric medicine at Pitt's School of Medicine and member of the Aging Institute, a joint venture of Pitt and UPMC. "Imagine two people aged 65: One rides a bike to work and goes skiing on the weekends, and the other can't climb a flight of stairs. They have the same chronological age, but very different biological ages. Why do these two people age differently? This question drives my research."

Towards answering this question, Gurkar and her team compared 196 older adults who they classified as healthy or rapid agers by how easily they completed simple walking challenges. Because walking ability is a holistic measure of cardiovascular fitness, physical strength and neurological health, other studies have shown that it's the single best predictor of hospitalization, disability, functional decline and death in older adults.

Healthy agers were 75 years or older and could ascend a flight of stairs or walk for 15 minutes without resting, and the rapid agers, who were 65 to 75 years old, had to rest during these challenges.

According to Gurkar, this study is unique because the rapid agers were chronologically younger than the healthy agers, allowing the researchers to home in on markers of biological—not chronological —aging, unlike other studies that have compared young adults with older people.

To define a molecular fingerprint of biological aging in blood samples from participants, they performed metabolomics—an analysis of metabolites, molecules that are produced by chemical pathways in the body—with blood samples from the two groups.

"Other studies have looked at genetics to measure biological aging, but genes are very static: the genes you're born with are the genes you die with," said Gurkar. "We chose to look at metabolites because they are dynamic: They change in real time to reflect our current health and how we feel, and we have the power to influence them through our lifestyles, diet and environment."

Healthy and rapid agers showed clear differences in their metabolomes, indicating that metabolites in the blood could reflect biological age.

Gurkar and her team next identified 25 metabolites that they termed the Healthy Aging Metabolic (HAM) Index. They found that the HAM Index was better than other commonly used aging metrics—including the frailty index, gait speed and the Montreal Cognitive Assessment test—at distinguishing healthy and rapid agers.

To validate their new index, the researchers analyzed a separate cohort of older adults from a Wisconsin-based study. The HAM index correctly predicted whether individuals could walk outside for 10 minutes without stopping with accuracy of about 68%.

"We took a very different cohort of people from a different geographical region, and we saw the same metabolites were associated with biological aging," said Gurkar. "This gives us confidence that the HAM Index can truly predict who is a healthy ager versus a rapid ager."

Using an artificial intelligence model that can predict potential drivers of biological traits, the team identified three main metabolites that were

most likely to promote healthy aging or drive rapid aging. In future research, they plan to delve into how these metabolites and molecular pathways that produce them contribute to biological aging and explore interventions that could slow this process.

Gurkar is also planning more research to evaluate how the metabolome of younger people shifts over time. Eventually, she hopes to develop a blood test that could estimate biological age in young adults or predict those who might go on to develop diseases of aging.

"While it's great that we can predict biological aging in older adults, what would be even more exciting is a blood test that, for example, can tell someone who's 35 that they have a biological age more like a 45-year-old," Gurkar said. "That person could then think about changing aspects of their lifestyle early—whether that's improving their sleep, diet or exercise regime—to hopefully reverse their biological age."

"Today, in medicine, we tend to wait for a problem to occur before we treat it," she added. "But aging doesn't work that way—it's about prevention. I think the future of medicine is going to be about knowing early on how someone is aging and developing personalized interventions to delay disease and extend healthspan."

Other authors on the study were Shruthi Hamsanathan, Ph.D., Tamil Anthonymuthu, Ph.D., Denise Prosser, Anna Lokshin, Ph.D., Susan L. Greenspan, M.D., Neil M. Resnick, M.D., Subashan Perera, Ph.D., and Satoshi Okawa, Ph.D., all of Pitt or UPMC; and Giri Narasimhan, Ph.D., of Florida International University.

More information: Shruthi Hamsanathan et al, A molecular index for biological age identified from the metabolome and senescence-associated secretome in humans, *Aging Cell* (2024). DOI: 10.1111/acel.14104

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