The dawning science of age reversal

Anti-aging science is coming of age. Intuitively, we've long surmised that a healthy diet, exercise, stress reduction techniques like meditation, avoidance of environmental toxins, and certain supplements can slow aging, and even rejuvenate us.

But until recently we had to rely on subjective measures (feeling "younger"), or functional markers of physical prowess like body composition, endurance, VO2 max, strength, lung capacity, or brain performance like memory, reflexes, visual and auditory acuity, balance, etc.

The condition of our arteries, kidneys, liver, bones and joints can be measured, too. And freedom from diseases or reliance on medications can be hallmarks of "youth".

But can we pinpoint the biological age of humans, much as we carbon date fossils with precision? How can we prove that "60 is the new 40"?

First came the promise of measuring telomeres, which are the structures that keep chromosomes from unraveling. Telomeres shorten with aging and disease. When they cease to protect our genetic material it's game over for our repair processes, and debility and death ensue. They've been analogized to the plastic sheaths that keep the ends of our shoelaces from fraying. (Fun fact for crossword puzzle and Scrabble

enthusiasts: they're called "aglets").

Commercial tests for measuring telomeres have been around for a while, and certain supplements claim the ability to forestall telomere shortening. But while popular, doubts have arisen over the accuracy of telomere testing. One comprehensive review states, *"In many studies, telomere length was not a better predictor of age-dependent functional declines, morbidity and mortality than chronological age."*

Along came epigenetic markers in the 2000s. They leverage new technology that enables researchers to map modifications to binding sites on DNA strands. Attachment of methyl groups act as red lights/green lights to turn on or turn off certain regulatory functions of DNA. Epigenetics is the science that seeks to explain how environmental influences selectively modify DNA *expression.*

While your DNA remains essentially unchanged from conception to death (with the exception of rare mutations), epigenetics accounts for how diet, sleep, stress, exercise, supplements—even our microbiome—can modify your inherited traits. Hence, identical twins, when separated at birth, possessing exactly the same DNA, can be shaped by divergent environmental factors to take on distinct traits—even appearance.

Various "aging clocks" based on methylation are now routinely used by researchers to study aging. They do a better job of predicting the risk of dying than chronological age alone.

I took such a test when I was 65, and was slightly disappointed that my epigenetic age was 56 (why not 40!). I'm now offering these tests to patients, excited that their costs have come down considerably, and their accuracy improved, as the technology has advanced.

Those of you who are familiar with the term "methylation" are probably aware that certain nutrients—like B6, folate, methylcobalamin, B2, and TMG—are methyl donors. They can be used to lower homocysteine, which is elevated in certain persons who possess a genetic propensity to impaired methylation, like the MTHFR c677 or c1298 single nucleotide polymorphisms (SNPs), among others.

So, logically, why not just take a bunch of B vitamins to attain the Fountain of Youth? The answer is that methylation is a two-way street. Methylation can turn on helpful genes and mute harmful ones, but the converse is true; it may downregulate certain tumor suppressor genes, lowering immune vigilance against cancer. *Hyper-*methylation has recently been suggested to be contributory to Parkinson's Disease risk.

Certain studies have suggested that B vitamin supplementation slightly increases the risk for certain cancers, like colon cancer; other studies exonerate supplements, and even that deficiency of, for example, folate, is associated with risk of progression of precancerous esophageal and cervical lesions.

Therefore, the relationship between methyl donor supplements and disease is not straightforward. The benefits may outweigh the risks, because different tissues respond heterogeneously. I use folate for cancer prevention, and withhold B vitamins for patients who have been diagnosed with cancer, but that's only a conjecture based on incomplete research findings.

A recent podcast I did with Dr. Kara Fitzgerald, a methylation expert, explores the notion of "methylation balance". She advanced the notion of a "methylation lifestyle" comprising diet, exercise, stress reduction, sleep and certain "methyl

adaptogen" supplements to optimize– not simply boost–methylation status, and hence slow and even reverse aging.

These supplements include many familiar dietary polyphenols like curcumin, lycopene, resveratrol, quercetin, genistein, sulforaphane, and EGCG, as well as non-B vitamins and minerals like A, D, selenium and zinc, and the omega-3 DHA.

Excitingly, Dr. Fitzgerald has published a landmark research study documenting the anti-aging effects of a concerted diet, lifestyle and supplemental program. She has also authored a book for the lay public summarizing her findings called *Younger You.*

Close on the heels of her publication in the journal *Aging* came two related papers, "Healthy eating patterns and epigenetic measures of biological age" and "Higher diet quality relates to decelerated epigenetic aging" in the January '22 *American Journal of Clinical Nutrition (AJCN).*

An editorial in that issue posited, "Is high dietary quality the real fountain of youth?" The reviewers concluded: *"Recent work suggests that diet can have a major impact on an individual's epigenome . . . These sensitivity analyses strengthen the argument that there is a strong relation between overall dietary quality and markers of epigenetic aging."*

Finally, there's this, also in the *AJCN:* "A proinflammatory diet is associated with increased odds of frailty after 12-year follow-up in a cohort of adults."

These are all about simple lifestyle measures, not invoking drastic solutions like challenging fasting regimens, or medications (listen to my recent podcast on the anti-aging drug Rapamycin here).

And despite promising research into anti-aging drugs, called senolytics, the latest studies suggest that lifestyle measures still outperform pharmaceuticals.

Which all goes to demonstrate that science is finally catching up with common sense .