"Deep biomarkers of aging developed from various types of aging data are rapidly advancing the longevity biotechnology industry. The use of biomarkers of aging to improve human health, prevent age-related diseases, and extend healthy life spans is now being facilitated by rapidly increasing data acquisition capacity and recent advances in AI. They offer great potential to change not only aging research, but healthcare in general," said Polina Mamoshina, a scientist at Insilico Medicine.

Theme of the month: Biomarkers and longevity

A biomarker is a measurable biological characteristic related to a normal or abnormal process.

In the medical field, a biomarker can be any measurable biological indicator. They can be quantitative or qualitative. Qualitative biomarkers could be involved in detecting a disease process in a yes/no analysis, while quantitative biomarkers are involved in detecting a disease process with a threshold effect. Most diagnoses are based on biomarkers.

Biomarkers and aging

Biomarkers are of growing interest, as they allow the measurement of aging, not on a one-off basis (as is the case with biological age), but on a continuous basis, resulting in a new measure: the rate of aging. Researchers have summarized the biomarkers of aging into different subcategories:

Biomarkers known as"genetic criteria"

The appearance of somatic DNA mutations during aging suggests that the measurement of genomic instability (the loss of the ability to repair DNA during cell divisions) could be a biomarker of aging.

With regard to telomere length, this is decreased with aging. Telomere shortening is explained by a decrease in telomerase activity. The measurement of telomerase enzymatic activity in human cells could be informative to assess aging.

Cellular senescence, the "pausing" of certain cells in response to cellular damage, is a protective mechanism that is increasingly used throughout the aging process. The measurement of cellular senescence is reliable and informative for assessing biological aging.

The increase in the number of epigenetic modifications such as DNA methylation, histone modification, the presence of non-coding RNA, appear during aging. These measurements, known as "epigenetic clocks" have been studied in particular by Steve Horvath.

Repair of cellular damage (damaged macromolecules, organelles) is a key process in maintaining cellular integrity and function. Autophagy capacity decreases with age, resulting in the accumulation of non-functional damaged proteins. Assessing the mechanisms of repair, recycling, and removal of damaged macromolecules could be a measure of biological aging.

Mitochondrial dysfunction, i.e. a weakening of the energy production mechanisms in our cells and of the capacity to manage oxidative stress by the mitochondria, are other interesting markers.

Finally, the evaluation of stem cell depletion, of nutrient sensing dysfunction, and alteration of intercellular communication could also be useful biomarkers to evaluate the aging of an individual.

Biomarkers known as "biological criteria"

Abnormal levels of these "markers" indicate an accentuated aging of the organism, and they are, for the most part, linked to a shorter lifespan and a higher risk of disease.

With an anti-aging evaluation, it is possible to evaluate the stage of aging. These biomarkers are classified according to the functions most often altered in aging:

- Glycemia and insulin resistance

Aging is associated with a disturbance in glucose metabolism. Disturbances in the regulation of blood sugar levels and insulin spikes are often present in aging-related phenomena.

Biomarkers such as glycated hemoglobin (HbA1c), fasting insulin level and the HOMA index (= insulin*glucose / 22.5)... are indicators reflecting the general state of glycation of tissues, a major phenomenon of aging.

Adiponectin: this recently discovered hormone is correlated with the mechanisms of inflammation. Studies have shown that it steadily decreases with advancing age and has strong links with the onset of metabolic syndrome, diabetes, atherosclerosis and non-alcoholic fatty liver disease.

- Vitamins and minerals

Vitamin D: A study of 10 different populations showed that relatively high levels of vitamin D were associated with a decreased risk of all-cause mortality. Diseases related to aging and vitamin D include osteoporosis and Alzheimer's.

Vitamin B12: Vitamin B12 levels often decline after age 50. Low levels are correlated in various studies to a higher risk of cognitive dysfunction, dementia and coronary artery disease.

Calcium: it has been shown that advancing age is often linked to a calcium deficit (leading to osteoporosis, among other things). This deficiency is thought to be due to vitamin D deficiency and also to a decrease in intestinal calcium absorption.

Zinc: Zinc deficiency is common in the elderly, due to dietary deficiencies and/or poorer intestinal absorption. It leads to phenomena similar to those observed with the oxidative inflammation of age and immunosenescence (degradation of defenses).

Selenium: A high blood level of selenium is generally correlated in studies with decreases in cancer risk.

Albumin: best known as a biological marker of protein-energy malnutrition, it is also a marker of aging that tends to decrease with age.

Creatinine and urea: they allow the evaluation of a weakening of the renal function.

Chronic inflammation, which generally increases with age, is the best-studied field in immunosenescence. Elevated plasma levels of leukocytes, interleukin 6 (IL-6), and TNF-α (tumor necrosis factor) correlate with loss of grip strength.

Ultra-sensitive C-reactive protein (CRP): this marker of inflammation is correlated with lifespan according to a study of 90,000 people. Lower levels of CRP are associated with greater longevity.

- Hormones

Testosterone: Testosterone levels decline steadily with age.

IGf-1 (insulin-like growth factor 1): the marker for growth hormone. Its decline is associated with aging, called "somatopause".

Sex Hormone-Binding Globulin (SHBG): as we age, SHBG levels increase by about 1% per year. The decrease in androgens and the excess of estrogens increase the production of SHBG by the liver.

Cortisol: The level of cortisol, the stress hormone produced by the adrenal glands, is correlated with age-related diseases. The more abnormal its secretion, the more glucose metabolism is disturbed.

Dehydroepiandrosterone (DHEA): DHEA sulfate is well known to decrease in blood levels with age in both sexes from the age of 30. One study reported an average decrease of 5.2% per year.

Pregnenolone: generally decreases with age, especially between the ages of 35 and 50 where its level frequently drops by 60% or more. Pregnenolone allows better resistance to stress and is very much involved in cognitive functions and memory.

- Lipids and fatty acids

Disturbances in blood lipids are among the most reliable markers of cardiovascular risk and mortality. Triglycerides and cholesterol will therefore be classic markers in the monitoring of aging.

Free radicals can damage our DNA by oxidizing nucleic bases. These reactions leave traces: a fragment of oxidized base called 8-hydroxy-2-deoxy-guanosine (8-OHdG).

Biomarkers called "physical criteria"

You don't wake up one morning with gray hair and a cane. Old age is a long process of biological changes.

- The senses

The loss of autonomy generally occurs after the age of 70. It is explained by cognitive, physiological, muscular and articular changes, the first symptoms of which appear between the ages of 40 and 50.

The first sign is presbyopia. At an average age of 44, vision is affected by a loss of accommodation between distance and near vision. Around the age of 60, it is hearing that is affected: presbycusis. 34% of people over 60 have difficulty hearing. The three other senses are then affected: touch, taste and smell.

- The physical and the mental

With old age, the structure of the brain and nervous system changes. With age, these cognitive changes lead to psychomotor slowing down, an alteration of attention or of short-term memory.

The decrease in physical capacities (gripping strength, speed of movement, etc.) are simple and fairly reliable indicators of aging.

Old age brings about other physiological changes such as weight gain, changes in the hair system (gray hair and baldness), drying and degradation of the skin (wrinkles), a decrease in immune resistance or even the loss of teeth. Even the percentage of water in our body decreases.

Is it useful to improve the indicators?

Many therapies aim to improve certain biomarkers. For example, gene therapies for telomerase or hormone cocktails to compensate for age-related decreases.

However, it is not necessarily established that the indicators of aging are also influencers. In some cases, it is very likely that they are mainly an effect (e.g. gray hair). In many other cases, therapies aimed at influencing the indicator should have therapeutic effects. If an indicator changes favorably, the impact will be to some extent favorable to healthy longevity.

We have more and more information about biomarkers and how our actions, therapies etc. influence them. New experiments are not always needed to understand them better. We can use the immense resources of health measures already available through retrospective studies and through the monitoring of ongoing therapies. The more rigorously we use them, the easier it will be to assess and to achieve progress towards longevity.

Many good news this month.

Aubrey de Grey, the iconic leader of SENS, the most renowned and probably the most effective organization in the fight against aging, has announced the receipt of donations totaling approximately $20 million, several times the organization's annual budget.

Laurent Simons, a gifted Belgian who recently graduated from university at the age of 11, has one ultimate goal: to enable the "immortality" of his grandparents, among others. And that's why he studies!

Vitalik Buterin, developer of the Ethereum crypto-currency and a young, gifted billionaire, publicly announces his passion and investments in longevity.

The BioViva organization, presented by Elisabeth Parrish, announces a gene therapy experiment giving excellent results for longevity in mice.

The United Kingdom announces in an official document entitled "Life Science Vision": <<[...] there is now a wealth of literature on potential pathways and targets that could be used to address the most inevitable cause of disease in human populations.>> (translation)"

The United States clarifies Joe Biden's stated goal of developing an agency that will address diseases in innovative ways. The name of this future organization is ARPA-H (Advanced Research Projects Agency for Health).

For more information:

- See in particular: heales.org, sens.org, longevityalliance.org and longecity.org.
- Source of the image