

infoaging guides

BIOLOGY OF AGING



BIOMARKERS OF AGING

An introduction to aging science brought to you by the
American Federation for Aging Research



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WHAT ARE BIOMARKERS OF AGING?

Aging is a process that can affect almost all the systems in the body. With increasing age, physically and mentally healthy adults gradually become less fit and more vulnerable to illness and death. However, these changes happen at different rates in different people.

Scientists are looking for a more complete understanding of the mechanisms of aging, to answer questions about the biological processes that account for an inevitable decline in physical vitality. For example, is there an underlying process that accounts for grey hair, wrinkled skin, decreased muscle strength, increased susceptibility to disease, and all the other consequences of aging?

In other words, is aging a single process that affects many of the body's systems, or are separate processes going on within each system? For example, one theory suggests that oxidative damage may be an underlying cause of many aspects of aging. Over the course of a lifetime, free radicals in the body damage tissue in various organs, which eventually leads to aging. This would be a single process model.

Current research is looking closely into the process of aging and seeking ways to slow it down. In order to test new interventions (i.e., drugs, vitamins, etc.), there has to be a way to determine if the intervention is having an impact on the underlying process of aging—not just whether it has an effect on one of the body's systems, such as affecting blood pressure or cholesterol levels, but whether it slows down the actual aging process.

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Currently, the only way to test interventions that are aimed at extending life is to conduct studies that follow subjects to the end of their lives. This can take an impractically long time. What's needed are biomarkers of the aging process that could help determine a person's life expectancy, making it unnecessary to wait many years for the results of studies.

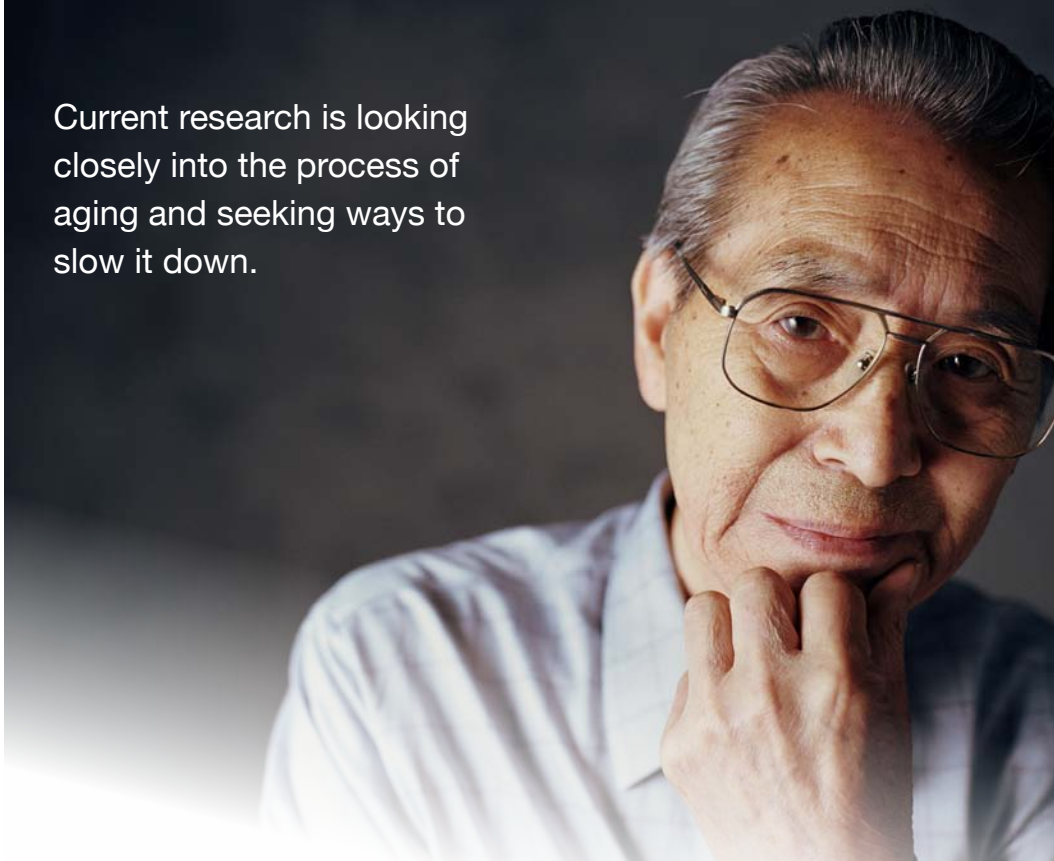
Ideally, there would be a set of these biomarkers that would identify biological age. These could be used to test whether a behavior (such as exercise), drug, or dietary additive slowed down the aging process.

If a set of biomarkers of aging were identified, it would also have the effect of demonstrating that there actually is an underlying mechanism of aging that coordinates changes across the body's systems.

CRITERIA FOR BIOMARKERS OF AGING

While there are several candidates for biomarkers of aging, none have so far proven a true measure of the underlying aging process. A true biomarker of aging must meet certain criteria in order to be both accurate and useful:

- It must predict a person's physiological, cognitive, and physical function in an age-related way. In other words, it must predict the future onset of age-related conditions and diseases, and do so independently of chronological age.
- It must be testable and not harmful to test subjects. For example, it could be a blood test or an imaging technique. It must also be technically simple so that most clinical laboratories could perform the test accurately and reproducibly without the need for specialized equipment or techniques.



- It should work in laboratory animals as well as humans, since preliminary testing is always done in non-human subjects.

Simply put, biomarkers need to be simple and inexpensive to use. They should cause little or no pain and stress. And they must measure aging accurately.

CRITICS OF BIOMARKERS OF AGING

Not everyone is convinced that biomarkers of aging actually exist. Some critics doubt that there is an underlying aging process at all. Therefore, there can be no marker for it.

Some scientists believe that as people age, deleterious physiological processes can occur that may lead to cancer, heart disease, dementia, or other diseases. These processes can overlap, but there is no single, underlying biological process driving them all.

Critics also argue that aging doesn't occur at a single rate, and therefore the rate of aging can't be measured. Different body functions can change at different rates over time. A person may lose muscle strength faster than his or her eyesight deteriorates. And there can be different reasons for the deterioration. For example, a person may lose muscle strength faster because he or she never had much strength to begin with.

Despite these criticisms, many researchers still believe aging

takes place at a measurable overall rate. The goal for these scientists is to find the biomarkers and convince the doubters.

HURDLES TO IDENTIFYING BIOMARKERS OF AGING

Although scientists have been interested in finding biomarkers of aging since the National Institute on Aging organized its first conference on the subject in 1981, none have yet been identified. One difficulty has to do with the overlap between aging and disease. Both the aging process and diseases can cause changes in the body, which affect lifespan.

It has been difficult, however, to separate out the aging process from conditions that precede the onset of disease, as growing older predisposes a person to many illnesses. Arguably, markers in the blood, such as cholesterol and C-reactive protein levels, both measure some aspects of aging and predict the onset of certain age-related diseases.

Another obstacle lies in the fact that some age-related changes cause no harm, while others do—and medical science doesn't always know which is which. This makes it more difficult to pinpoint exactly what to look for.

From 1988 to 1998, the National Institute on Aging sponsored a 10-year initiative encouraging research into biomarkers of aging. Although researchers explored many interesting candidates for possible biomarkers and

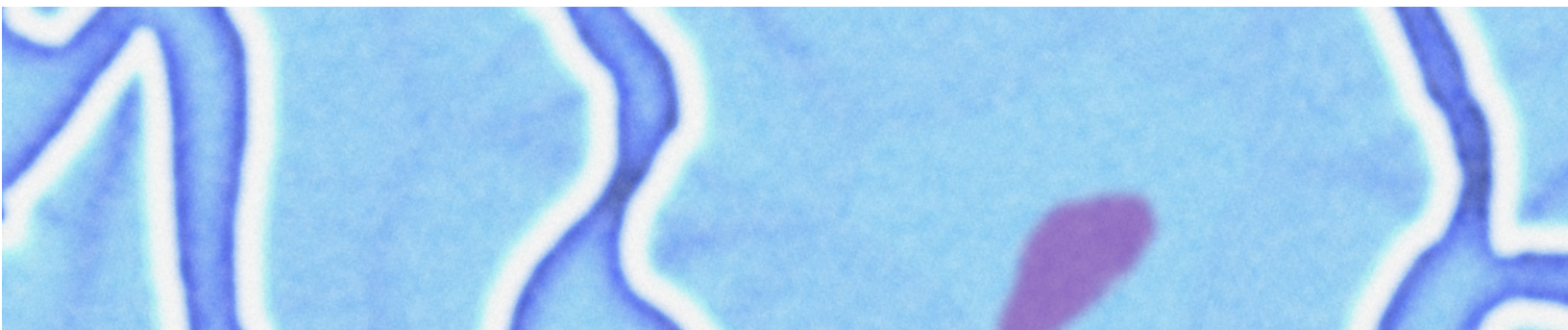
contributed to the body of knowledge on aging, no biomarkers were successfully identified and validated. Since then, obtaining funding for biomarkers research has become more difficult.

TARGETS FOR BIOMARKERS OF AGING

Studies on biomarkers of aging have looked for changes in cells, hormones, genes, and even behaviors to find a predictor of the rate of aging.

One target that has been looked at is the central nervous system (consisting of the brain and spinal cord). Computerized tomography (CT) scans can be used to look for changes in the brain that may serve as biomarkers of aging. For example, the brain shrinks with age. This does not mean that brain cells necessarily die, but rather that they become smaller in size and volume. Some research has been done to find out if brain shrinkage in certain areas may underlie the changes in function that occur with age. So far, brain function and age have proved too complex to produce reliable biomarkers.

Age at menopause has been suggested as a possible biomarker of aging in women. One study showed that women who had early menopause (before age 44) had shorter lifespans than women who experienced menopause at ages 50 to 54. This suggests that ovarian function is related to the overall aging process, but the mechanistic links for this require further study.



Other possible biomarker targets include cell replication rate and immunological markers.

THE FUTURE OF BIOMARKERS OF AGING RESEARCH

At the level of cells, a potential biomarker of aging may be the presence of senescence. Senescence is a condition in which old or damaged cells remain alive but cease to reproduce. This

is an important tool in the body's ability to prevent cancerous tumors from developing. The older a person becomes, the more senescent cells he or she accumulates. Several markers of senescence in humans have been suggested as biomarkers of aging.

On November 10, 2011, researchers at the [Mayo Clinic](#) published a study in the journal Nature showing that an accumulation of senescent cells may lead

to age-related diseases, at least in animals. By removing most of these cells from several organs (body fat, eye, and skeletal tissue) of lab mice, the investigators were able to significantly delay the onset these diseases, or stop their progression if they had already become established.

The study suggests what may prove fruitful areas for future researchers to explore in the search for true biomarkers of aging.

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