HEALTHY INTO OLD AGE

Healthy aging medicine is a new form of preventative medicine and is in contrast to repair medicine.

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The focus is on the early detection of risks and predispositions, on the basis of which diseases can develop, with the aim of maintaining biological age, promoting physical and mental health in order to reduce the risk of chronic diseases. Premature aging or disease is determined by genetics and epigenetics. The human epigenome is changeable and plays an important role in controlling the genetic material. It is influenced by environmental as well as lifestyle factors. Healthy aging medicine aims to influence the epigenome by changing and optimizing lifestyle factors. Studies show that epigenetic processes can still be changed in adulthood (Sweatt, 2009), since the enzymes required for methylation (methyltransferases) are still active in the adult brain (Feng et al., 2010).

Longevity research defines hallmarks of aging, multiple factors that accelerate the aging process. Hallmarks of aging are genomic instability, telomere shortening, epigenetic changes, loss of proteostasis, altered nutrient recognition, mitochondrial dysfunction, cellular senescence, stem cell depletion, and altered intercellular communication.

„The Hallmarks of Aging“, Carlos López-Otín, Maria A. Blasco, Linda Partridge, Manuel Serrano, Guido Kroemer, J.-cell.2013.05.039 June 06, 2013 Volume 153, ISSUE 6, P1194-1217

Genome instability and telomere shortening

The genome encodes all the possibilities open to a cell. Impaired repair processes of the genome due to irreparable DNA damage lead to genome instability. People with impaired DNA repair processes show several signs of accelerated aging.

Telomeres are repeated sequences of DNA that protect the ends of chromosomes and prevent them from being mistaken for broken strands of DNA. Telomere shortening denotes a decrease in the structural element in our DNA, which is normal during the aging process. Short telomeres put you at risk for degenerative diseases. Critically short telomeres or breakdown of telomere structure caused by displacement of the telomere-binding protein complex shelterin triggers a DNA damage response and leads to senescence or apoptosis. Glucocorticoids, reactive oxygen species (ROS), mitochondria, and inflammation are important factors in telomere maintenance.

Epigenetic changes
The epigenome is understood to be the chemical modification of the organism's DNA and histone proteins. Changes in the epigenome can change the structure of the chromatin and affect the function of individual sections in the genome. The epigenome is a type of molecular memory that influences the way the genome is read. It is changeable and can be corrected by adjusting environmental and lifestyle factors. These changes can be passed on to offspring. Therefore, analysis of DNA sequences alone will not answer all questions - knowledge of epigenetics will be crucial.

Deregulated nutrient recognition
The task of the proteostasis is to stabilize or restore the correct folding of the proteins. With increasing age, however, proteins are damaged by normal cellular processes and thus no longer folded correctly. Studies have shown that proteostasis changes with age. The chronic accumulation of misfolded or unfolded proteins contributes to the development of some age-related diseases. Increased metabolic activities can stress the cells and cause the cells to age faster due to a change in the availability and composition of nutrients.

Metabolism and its byproducts over time can damage cells through oxidative stress, ER stress, calcium signaling, and mitochondrial dysfunction. Age-related obesity, diabetes and other metabolic syndromes can result from deregulated nutrient recognition. Chronic inflammation associated with obesity and diabetes, acting via JNK and IKK crosstalk, may further deregulate nutrient recognition. Intermittent calorie restriction - that is, fasting - is the only measure that can counteract this and extend human lifespan.

cellular senescence

Cellular senescence describes the termination of cell division. With increasing age, senescent cells accumulate and persist, excreting harmful molecules into the environment. Cellular senescence can be triggered by a variety of stress-inducing factors. These stressors include environmental factors, abnormal cellular growth, oxidative stress, autophagy factors, as well as immunosenescence. Chronic inflammation of SASP from senescent cells can reduce the immune system's ability to clear senescent cells.

depletion of stem cells

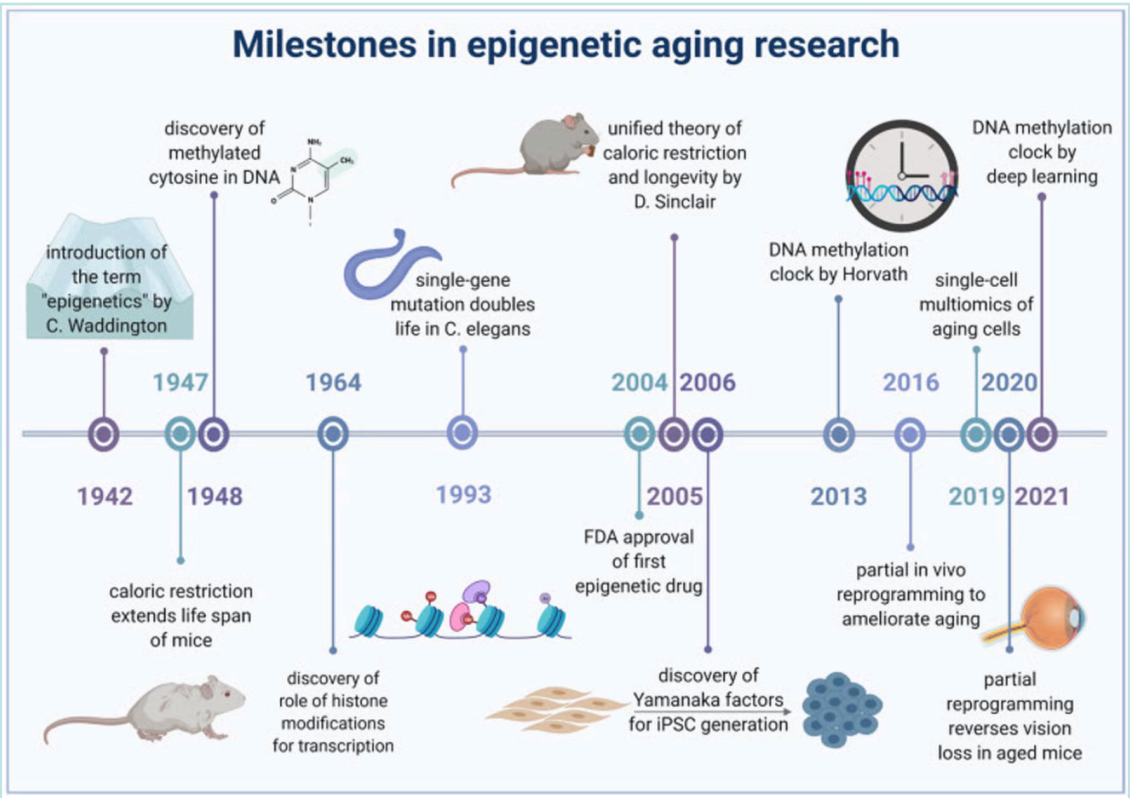
The body's ability to regenerate tissues and organs depends on healthy stem cells in each tissue. The ability of stem cells to replicate decreases with age. USC researchers found that fasting-like diets reduced gut inflammation and increased intestinal stem cells, in part by promoting the expansion of beneficial gut microbiota. The specific, calorie-restricted diet enabled increased growth of microbes in the gut, which was crucial for rebuilding and regenerating stem cells.

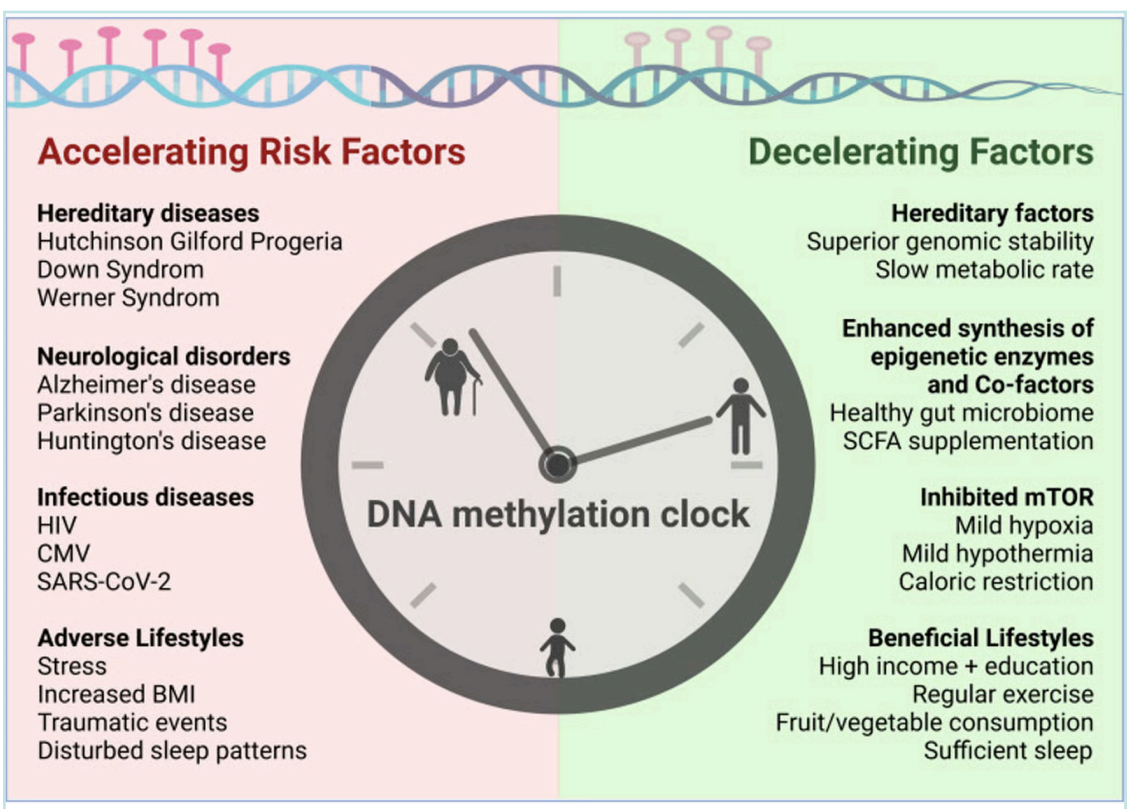
Altered intercellular communication

As cells age, they exhibit an increase in self-sustaining signals that lead to damage elsewhere and a chemical message signaling environment throughout the body that tends to become more inflammatory. In particular, senescent cells trigger chronic inflammation that can further damage aging tissue.

Senescent cells are known to secrete an inflammatory, immunosuppressive and harmful compound that has been shown to stimulate neighboring cells to become senescent and may contribute to several age-related diseases. This mix is known as the senescence-associated secretory phenotype (SASP). Restoring proper intercellular communication could prolong health by reducing chronic age-related inflammation.

In addition to the classic comprehensive check-up, age-related physical changes and signs of aging can be detected by examining blood vessels, hormone levels, functions of the sensory organs, gait analysis, proprioceptor analysis, balance between active oxygen and antioxidant potential, HRV measurements, metabolic measurements and bone density measurement. Additional genetic tests can also be used to determine predisposing factors. These examinations enable early detection and treatment as well as lifestyle advice to prevent age-related diseases. It is crucial to recognize the signs of aging as early as possible and take appropriate action. The basic elements of clinical healthy aging medicine consist of measures to improve the patient's lifestyle by identifying the weakest pillars.


Milestones in epigenetic aging research
introduction of the term "epigenetics" by C. Waddington
1942
discovery of methylated cytosine in DNA
1947
1948
caloric restriction extends life span of mice
single-gene mutation doubles life in C. elegans
1964
1993
discovery of role of histone modifications for transcription
unified theory of caloric restriction and longevity by D. Sinclair
2004
2006
2005
FDA approval of first epigenetic drug
discovery of Yamanaka factors for iPSC generation
DNA methylation clock by Horvath
2013
single-cell multiomics of aging cells
2016
2020
2019
partial in vivo reprogramming to ameliorate aging
DNA methylation clock by deep learning
2021
partial reprogramming reverses vision loss in aged mice


Accelerating Risk Factors
Hereditary diseases
Hutchinson Gilford Progeria
Down Syndrom
Werner Syndrom
Neurological disorders
Alzheimer's disease
Parkinson's disease
Huntington's disease
Infectious diseases
HIV
CMV
SARS-CoV-2
Adverse Lifestyles
Stress
Increased BMI
Traumatic events
Disturbed sleep patterns
DNA methylation clock
Decelerating Factors
Hereditary factors
Superior genomic stability
Slow metabolic rate
Enhanced synthesis of epigenetic enzymes and Co-factors
Healthy gut microbiome
SCFA supplementation
Inhibited mTOR
Mild hypoxia
Mild hypothermia
Caloric restriction
Beneficial Lifestyles
High income + education
Regular exercise
Fruit/vegetable consumption
Sufficient sleep

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