ОГЛЯДИ

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Potential prognostic markers of cellular senescence in age-associated cardiovascular pathology

V. Kyryk[1,2], O. Parkhomenko[1]

[1]M. D. Strazhesko National Scientific Center of Cardiology, Clinical and Regenerative Medicine, National Academy of Medical Sciences of Ukraine, Kyiv;
[2]D. F. Chebotarev State Institute of Gerontology, National Academy of Medical Sciences of Ukraine, Kyiv; e-mail: labcellculture@gmail.com

The review addresses the issue of cellular senescence, its impact on the development of age-associated cardiovascular diseases, and its prognostic perspective. We appreciated the relationship between cellular senescence and overall organismal aging, focusing on endothelial dysfunction in cardiac patients. The review also discusses the manifestations of cellular aging and highlights their markers that can be used for comprehensive diagnosis and prediction of the risk of acute cardiovascular events. The potential and limitations of senolytic therapy for eliminating senescent cells and reducing systemic inflammation are discussed. The review emphasizes the importance of developing new methods for identifying markers of cellular senescence and implementing personalized approaches in the treatment of age-associated cardiovascular diseases within the framework of modern precision medicine.
Key words: cellular senescence; aging; cardiovascular diseases; endothelial dysfunction; senolytics.

Age and cardiovascular diseases

The challenges of aging and the potential for age correction have long intrigued humanity. However, it was only recently, in the early 1980s, that a methodology was developed, providing a scientifically grounded assessment of the influence of various environmental factors on the human genome, including dietary habits, smoking, physical activity, obesity, stress, and their impact on major cardiovascular diseases (CVD) [1, 2]. This impact is mediated without altering the DNA sequence through two mechanisms of epigenetic gene activity regulation: DNA methylation (involving the addition or removal of methyl groups to/from the DNA sequence) and the action of short- and long-chain RNAs. These RNAs are non-coding for protein structures but regulate the activity of various genes [3]. Based on these principles, several models for determining biological age have been developed, which can differ significantly from chronological age [4].

However, the proposed definition should be used solely as an indicator of a person's health status before the onset of any pathological conditions. For instance, DNA methylation in specific regions can reflect the cumulative risk of numerous factors involved in the pathogenesis of complex age-related conditions, including CVD [5, 6]. Notably, this mechanism is the most thoroughly studied and has led to the development of the so-called "biological clock" (epigenetic biological age clocks). In recent decades, significant progress has been made in developing and applying algorithms based on DNA methylation to predict chronological age, disease risk, mortality, and aging rate. It is important to note that the aging rate varies across different cells and tissues, necessitating the creation of a comprehensive "clock" model for each individual. Scientific research has resulted in the development of several calculators, such

as GrimAge (2019), GrimAge2 (2022), and DunedinPACE (2022) [7, 8]. One of the most widely used tools, PhenoAge (2018), estimates the aging rate of all body tissues based on an individual's phenotype. These calculators were created using machine learning algorithms and clinical blood biomarkers, enabling the assessment of biological age solely through biomarkers, without requiring DNA methylation measurements [9].

As noted above, the described approaches for assessing biological age are primarily applicable to individuals before the onset of chronic diseases. These methods have limited utility in evaluating cardiovascular system aging in the context of established pathology, though scientific advancements in this area are ongoing. It is important to recognize that the DNA age serves as a marker of cellular senescence. However, DNA methylation patterns are influenced by the chronological age of so-called "immortal" or inactive cells [10]. While this process is a natural aspect of aging that prevents the accumulation and transmission of damage, it can be triggered by various factors, including DNA damage, oxidative stress, telomere shortening, and others.

During acute disease conditions involving tissue damage (e.g., myocardial infarction or stroke) or under the influence of acute stress (e.g., post-traumatic stress disorder, particularly relevant in wartime), metabolic maladaptation processes accelerate. This acceleration can worsen cell survival and impair the body's tissues' ability to recover [11, 12].

Aging and cellular senescence

The aging of the organism occurs through three primary pathways: telomere-dependent replicative senescence, oncogene-induced senescence, and stress-induced premature senescence [13, 14].

Replicative cellular senescence is a biological process in which cells cease to divide after reaching a certain number of divisions. This phenomenon was first described by Leonard Hayflick in the 1960s and is known as the Hayflick limit. It is primarily driven by telomere shortening, along with the activation of molecular signaling pathways, including the proteins p53 and $p16^{INK4a}$ [15]. Replicative senescence prevents uncontrolled cell division and tumor formation, while also playing a role in physiological aging and maintaining tissue homeostasis [16].

Oncogene-induced senescence is a stable antiproliferative response triggered by the activation of oncogenic signaling due to activating mutations in an oncogene or the inactivation of a tumor suppressor gene. Oncogene-induced senescence is hypothesized to have evolved as an alternative to apoptosis, particularly for long-lived cell types that cannot be readily replaced in large numbers [17].

Stress-induced premature senescence, more frequently observed during acute cardiovascular events, arises from exposure of normal, immortal, or transformed cells to chemical or physical stressors. These stressors induce oxidative stress and/or DNA damage, leading to cellular senescence [18]. All cell types undergoing stress-induced senescence *in vivo* likely contribute to tissue changes observed during aging. For example, human diploid fibroblasts exposed *in vivo* and *in vitro* to pro-inflammatory cytokines exhibit senescence biomarkers and may participate in the degradation of the extracellular matrix commonly observed with aging. Even a small proportion of senescent cells in tissues can disrupt tissue renewal and homeostasis, impair organ function, and promote the development of a senescence-associated phenotype [19].

Manifestations of cellular senescence and their markers

Cellular senescence is characterized by a range of interrelated features, including altered morphology, structural remodeling of organelles, expression of specific surface markers on the membrane, DNA damage with chromatin reorganization in the nucleus, cell cycle arrest,

metabolic dysfunction, and the secretion of numerous pro-inflammatory cytokines, chemokines, and growth factors (Fig. 1) [14, 20].

In *in-vitro* cultures, senescent cells exhibit a significant increase in surface area, often associated with disruptions in the normal cell cycle and the accumulation of metabolic damage [21, 22]. In senescent cells, membrane permeability is altered, likely due to imbalance in ion channels and impaired molecular transport [23]. Similar manifestations occur *in vivo*, leading to alterations in tissue cytoarchitecture and the progression of dysfunction. Additionally, degradation products from dead cells within the tissue microenvironment may act as triggers for autoimmune processes. In the nuclei of senescent cells, micronuclei are formed as a result of DNA fragmentation or chromosomal missegregation, stemming from prolonged stress and activation of repair mechanisms that fail to fully restore the damage [24].

On the membrane of senescent cells, certain molecules may be overexpressed, serving as indicators of pathological functional changes. For instance, the urokinase plasminogen activator receptor (uPAR), also known as CD87, modulates intracellular signaling pathways, altering cell adhesion and migration. It also activates plasminogen to form plasmin, which degrades fibrin, dissolves thrombi, and activates matrix metalloproteinases, leading to connective tissue lysis, immune and cancer cell invasion, and growth factor release. uPAR functions as a key regulator of inflammation, maintaining a stem-like phenotype or driving the differentiation of various cell types [25, 26].

The programmed death-ligand 1 (PD-L1), or CD274, plays a role in regulating immune responses, enabling evasion of immune surveillance [27]. The intercellular adhesion molecule ICAM-1 (CD54) is involved in biological processes such as cellular adhesion and interactions with viruses [28]. The enzyme dipeptidyl peptidase DPP4 (CD26), a surface protein involved in the regulation of inflammatory and metabolic processes, is also upregulated in senescent cells [29]. Similarly, the expression of transmembrane signaling proteins Notch-1 and NOTCH3, which are linked to cell cycle regulation, is altered [30]. In addition, researchers have reported increased expression of surface markers including vimentin, type 2

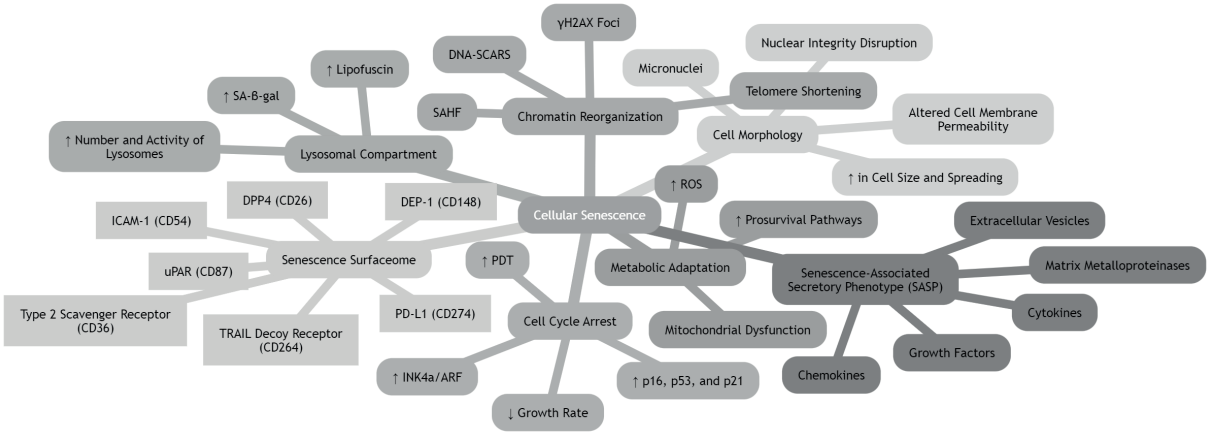

Fig. 1. Manifestations of cellular senescence. Details are provided in the text.
Notes: SAHF – senescence-associated heterochromatin foci; DNA-SCARS – DNA segments with chromatin alterations reinforcing senescence; SA-β-Gal – senescence-associated β-galactosidase; ROS – reactive oxygen species; DPP4 – dipeptidyl peptidase 4; DEP-1 – density enhanced protein tyrosine phosphatase-1; ICAM-1 – intercellular adhesion molecule 1; uPAR – urokinase plasminogen activator receptor; PDT – population doubling time; PD-L1 – programmed death-ligand 1; INK4a/ARF – inhibitor of kinase 4a/alternate reading frame

scavenger receptor (CD36), density-enhanced protein tyrosine phosphatase-1 – DEP-1 (CD148), the decoy TRAIL receptor (CD264), integrin associated protein (CD47), molecules of the major histocompatibility complex (MHC) class I, along with other markers [31–34].

Alterations in the lysosomal compartment serve as critical markers of cellular senescence and can aid in diagnosing aging-associated conditions, such as chronic inflammation in cardiovascular diseases. Senescent cells exhibit an accumulation of lysosomes and heightened lysosomal activity, driven by the need to process damaged organelles and macromolecules via autophagy [35]. Lysosomal hyperactivity is a characteristic of cells that have lost their ability to divide. The most recognized lysosomal marker of cellular senescence is senescence-associated β-galactosidase (SA-β-gal), used for identifying senescent cells both *in vitro* and *in vivo* [36]. Its activity increases due to alterations in lysosomal metabolism and the accumulation of metabolic byproducts [37]. Another lysosomal enzyme that has been identified as a marker of senescence is α-L-fucosidase [38]. Additionally, senescent cells' lysosomes accumulate lipofuscin, commonly referred to as the "aging pigment." This insoluble material results from oxidative processes and indicates reduced efficiency in lysosomal catabolic functions [39].

Nuclear alterations in senescent cells are linked to DNA damage and chromatin reorganization, manifesting through various phenomena. DNA damage in nuclei leads to the formation of micronuclei, nucleoplasmic bridges and nuclear buds [24]. Senescence-associated heterochromatin foci (SAHF) are distinct domains of facultative heterochromatin that form in the nuclei of senescent cells. These foci suppress the expression of E2F-dependent genes, which are critical for cell proliferation. SAHF represent a hallmark of significant epigenetic remodeling in senescent cells [40]. DNA segments with chromatin alterations reinforcing senescence (DNA-SCARS) are stable nuclear domains containing proteins of the DNA damage response (DDR) complex, such as 53BP1 and γH2AX. These long-lived structures reflect persistent DNA damage that remains unrepaired and help maintain the senescent state [41]. Histone H2AX phosphorylation at serine-139 marks DNA double-strand breaks and is a key early indicator of DNA damage. This marker plays a central role in initiating DDR and is widely used to signify active damage response processes [42]. Telomere shortening, which triggers DDR activation, is one of the most extensively studied markers of senescence. It serves as a predictive biomarker for assessing the biological age of cells and the risk of developing age-related diseases [43].

DNA damage activates signaling pathways that block the cell cycle to prevent the transmission of accumulated damage to daughter cells. One such pathway is the INK4a/ARF network, which involves the expression of tumor suppressor proteins $p16^{INK4a}$, p53, and p21 [21]. $p16^{INK4a}$ inhibits the activity of cyclin-dependent kinases CDK4/6, leading to hypophosphorylation of the retinoblastoma protein and suppression of E2F-dependent transcription of cell proliferation genes [44]. p53 is activated in response to DNA damage and regulates the expression of p21, a key inhibitor of the cell cycle. p21, in turn, inhibits CDK2, blocking cell cycle progression at the G1/S checkpoint [45]. Together, these proteins promote a prolonged exit from the cell cycle, leading to a stable senescent phenotype. The persistent cell cycle arrest in senescent cells results in a significant increase in population doubling time and a reduced specific growth rate in *in vitro* cultures, which likely mirrors similar changes in tissues *in vivo*.

Cellular metabolic adaptation to senescence is characterized by an increased production of reactive oxygen species (ROS), mitochondrial dysfunction, and the activation of prosurvival pathways. Senescent cells exhibit excessive ROS production, which arises from an imbalance between antioxidant systems and oxidative processes [46]. ROS play a dual role: on one hand, they act as inducers of cellular senescence by causing damage to DNA, proteins, and lipids;

on the other hand, they contribute to the maintenance of the senescent state by activating the DNA damage response [47]. Senescent mitochondria in endotheliocytes show decreased efficiency in oxidative phosphorylation, abnormal ROS accumulation, and structural alterations in the form of fragmentation or fusion [48]. In senescent cells, survival signaling pathways such as PI3K/AKT/mTORC1 and NF-κB are activated, which support cellular metabolism, reduce autophagy, regulate inflammatory processes, and help senescent cells resist metabolic stress and apoptosis [49, 50]. These processes facilitate cellular adaptation to the altered conditions and ensure the survival of senescent cells, despite their inability to divide.

As a result of the cellular disturbances described above, senescent cells begin to produce a wide range of bioactive molecules that form the senescence-associated secretory phenotype (SASP). This phenotype significantly impacts the microenvironment of senescent cells and plays a key role in tissue and organ dysfunction, as well as the progression of aging processes throughout the body. The components of SASP include pro-inflammatory cytokines (such as IL-6, IL-8, IL-1β) that contribute to chronic inflammation and attract immune cells; chemokines (CCL2, CCL5, CXCL10) that affect the recruitment of immune cells to aging tissues; growth factors (VEGF, TGF-β) that modulate angiogenesis; matrix metalloproteinases (MMP-1, MMP-3, MMP-9) that degrade the extracellular matrix and promote tissue remodeling; and extracellular vesicles containing signaling proteins, RNAs, microRNAs, and non-coding nucleotides, which influence the surrounding cells [14].

SASP exerts a paracrine effect, promoting senescence in neighboring healthy cells (phenotype transmission). Additionally, by stimulating chronic inflammation and degrading the extracellular matrix, it leads to alterations in tissue architecture. Functionally, this results in impaired local regeneration and tissue remodeling, organ dysfunction, and the progression of age-related diseases, including cardiovascular conditions [51, 52]. Therefore, SASP can be considered a promising diagnostic and prognostic marker in the development of novel approaches to modulating aging, with the goal of improving health and extending lifespan.

Cellular senescence and endothelial dysfunction

Modern medicine is rapidly advancing and increasingly integrating scientific achievements from molecular biology, genetics, and physiology. New biomarkers of disease development and progression are enhancing our understanding of disease pathogenesis and serve as the foundation for the development of new diagnostic and therapeutic approaches.

In the past, when evaluating the long-term prognosis after a patient was discharged following a myocardial infarction, doctors primarily focused on indicators such as heart pump function, comorbidities, and laboratory test results (e.g., hemoglobin, lipid profile, creatinine). However, in the context of the COVID-19 pandemic and the onset of large-scale wars, additional markers are gaining importance. These include indicators that reflect the activation of systemic inflammation and the ratio of cellular components of the immune system [53, 54].

As an integrated indicator of global cardiovascular risk, endothelial function is increasingly being used in clinical practice. Endothelial dysfunction is also a manifestation of endothelial cell senescence, which can accelerate the development of atherothrombotic complications, such as myocardial infarction, stroke, and sudden death [55]. In these cases, there is an observed increase in vascular tone, hypertension, and imbalance between nitric oxide production and the generation of ROS, which are the basis for endothelial dysfunction [56]. Several studies have shown that the accumulation of senescent endothelial cells and the specific phenotypic and functional changes associated with endothelial cell senescence can play a significant role in the development and

progression of cardiovascular diseases [57]. In smokers, dysfunction of senescent endothelial progenitor cells has been identified, leading to a reduction in their angiogenic potential [58]. At the same time, the pathophysiological mechanisms linking endothelial senescence and myocardial infarction remain insufficiently explored.

Diagnostic and prognostic significance of senescence markers in clinical practice

Cellular senescence plays a crucial role in the pathogenesis of cardiovascular diseases, contributing to the development of conditions such as atherosclerosis, heart failure, hypertension, and myocardial infarction. Senescence of cells, particularly endothelial cells and cardiomyocytes, leads to changes in the microenvironment of the heart and blood vessels, disrupting their structure and functions [59–61]. Specifically, in cardiovascular cells, telomere shortening is associated with an increased risk of atherosclerosis and heart failure. Telomere shortening reduces the ability of cells to replicate, thereby impairing the regenerative potential of cardiac progenitors following ischemic or hypoxic injuries [62].

In patients with aortic valve calcification, increased expression of $p16^{INK4a}$ has been observed. This protein inhibits CDK4/6, leading to cell cycle arrest in the G1 phase, thereby limiting tissue repair and promoting the senescence of endothelial cells and cardiomyocytes [63]. Therefore, $p16^{INK4a}$ may serve as a useful marker for studying the role of cellular senescence in cardiovascular diseases.

Elevated expression of p53 and p21 is observed in cells that undergo damage due to cardiovascular diseases, such as chronic ischemic heart disease or myocardial infarction. These proteins are activated in response to DNA damage and contribute to cell cycle arrest and the induction of senescence, which may result in a reduced ability of cells to regenerate and remodel heart tissue [64].

The detection of increased numbers of senescent cells in patients with cardiovascular diseases may indicate the extent of accelerated senescence in tissues and organs, as well as the risk of worsening disease progression [65, 66]. Particularly important is the monitoring of these processes in patients at high risk for future complications, such as acute coronary events, heart failure, or death. Therefore, understanding the processes that lead to accelerated cellular senescence, identifying patients at high risk for complications, and exploring potential interventions to correct this process will be crucial for developing new standards for assessing compensatory capabilities in patients with cardiovascular diseases and creating new approaches to personalized therapy.

The identification of cellular senescence markers in peripheral blood may become a promising strategy not only for diagnosing age-associated metabolic and immune disorders but also for assessing cardiovascular risk [67, 68]. Components of the SASP produced by senescent cells in the myocardium and vascular tissues, including IL-6, IL-8, TNF-α, and matrix metalloproteinases, induce chronic inflammation, which leads to endothelial dysfunction and disrupts the balance between angiogenesis and vascular remodeling [57, 69]. Consequently, the detection of these markers in blood plasma enables the evaluation of inflammatory processes that play a critical role in the development of atherosclerosis and other cardiovascular diseases.

In the case of systemic exposure to negative stress factors, hematopoietic stem cells from the bone marrow, compromised at the level of their niche and prone to accelerated aging, will transmit the pathological phenotype associated with senescence to all their progenitors and differentiated cells [70]. Accordingly, evaluating markers of cellular senescence in both circulating stem and mature blood cells could serve as a convenient method for assessing and predicting cardiovascular risk.

Researchers have demonstrated that senescent $CD4^+$ T cells are capable of infiltrating the

heart, promoting pro-inflammatory processes, and increasing the heart's response to stress, ultimately contributing to the development of heart failure [71]. On the other hand, the population of senescent T lymphocytes during acute myocardial infarction not only exhibits a high pro-inflammatory potential but also cytotoxic properties. Furthermore, an increased number of senescent $CD57^+CD8^+$ T cells in patients with myocardial infarction correlates with cardiovascular mortality after the disease. The authors suggest that the secretion of IL-17 may alter IL-23 levels, affecting T-cell subpopulations, thus contributing to myocardial dysfunction following a prior myocardial infarction [72]. Studies on acute heart failure have also confirmed the role of senescent immune cells ($CD4^+CD57^+$ T lymphocytes) in activating inflammatory processes and exacerbating disease progression over a 6-month observation period, with subsequent cardiovascular deaths, re-hospitalizations for heart failure, and heart transplants [73].

Severe concurrent infections, including COVID-19, in patients with cardiovascular diseases, particularly during acute emergency situations, can significantly worsen the hospital course of the underlying disease. In the context of COVID-19, evidence suggests that the SARS-CoV-2 virus may induce or accelerate cellular senescence [74]. It has been confirmed that the SARS-CoV-2 protein can induce cellular senescence (virus-induced senescence, VIS), promoting the release of pro-inflammatory factors and exacerbating inflammatory processes, which, in severe cases of COVID-19, can lead to a "cytokine storm" with a poor prognosis [75]. Moreover, such disruptions may affect tissue regeneration and repair processes following acute coronary syndrome, potentially amplifying the damage caused by the virus long after the infectious disease has resolved, increasing the risk of death and recurrent coronary events.

One of the pathogenic mechanisms underlying this phenomenon may be the persistence of a low-grade inflammatory process following COVID-19 in patients with acute coronary syndromes, this, in turn, creates conditions for accelerated senescence of immune system cells [76]. The negative impact of senescent immune cells manifests through myocardial dysfunction and an impaired immune response to cardiac injury, leading to chronic systemic inflammation and inadequate myocardial repair after a prior myocardial infarction [77].

Although the detection of SA-β-galactosidase, commonly used in cell culture studies, can also be identified in blood cells, its activity serves as a marker of cellular senescence and associated systemic inflammation in the context of atherosclerosis [78]. Epigenetic clocks based on DNA methylation allow for the assessment of biological age, which has been shown to be a better predictor of cardiovascular diseases than chronological age [10]. Telomere shortening in leukocytes may also serve as a marker of systemic cellular senescence at the organismal level, linked to an increased risk of cardiovascular diseases. Studies have demonstrated that telomere shortening in blood cells correlates with the development of atherosclerosis and other cardiovascular pathologies [79]. The combination of several senescence markers (such as SASP and telomere length) may potentially enhance the accuracy of predicting the risk of life-threatening cardiovascular events, such as myocardial infarction.

Overall, a comprehensive assessment and dynamic monitoring of cellular senescence markers can not only assist in identifying individuals with subclinical inflammation and early signs of cardiovascular diseases, but also help identify potential targets for therapeutic interventions aimed at slowing down cellular senescence and reducing its negative impact on the cardiovascular system. Particular attention should be given to unresolved questions regarding the impact of these disruptions on the subsequent risk of complications during and after exposure to significant external stress

factors, including past infections and wartime conditions.

Prospects for pharmacological correction of cellular senescence

The development of new therapeutic approaches targeting senescent cells and reducing significant clinical outcomes, such as myocardial infarction or stroke, will depend on a precise understanding of the biology of aging in each of the key cell types involved in the pathogenesis of cardiovascular diseases. Meanwhile, researchers are exploring the potential of "senolytic therapy" to target senescent cells in order to improve treatment outcomes for patients with COVID-19, especially among the elderly or those with chronic conditions [74, 80]. Promising therapeutic strategies include clearing tissues of senescent cells by blocking their survival pathways with senolytic drugs, or modulating their SASP phenotype using senomorphics to reduce cardiovascular risk [81, 82].

Among the most promising agents actively researched for their impact on cellular senescence in cardiovascular pathology, researchers are considering bioflavonoids and the tyrosine kinase inhibitor Dasatinib. Dasatinib opposes heart adiposity and cardiac fibrosis, improving an index of diastolic function [83]. Dasatinib also suppresses atherosclerotic lesions by suppressing cholesterol uptake [84]. Quercetin, a natural flavonoid with anti-inflammatory, antioxidant, and anti-apoptotic properties, may serve as a promising therapeutic tool for aging-related diseases by reducing oxidative stress, inflammation, and correcting mitochondrial dysfunction [85]. Quercetin interferes with networks containing the Bcl-2 family, p53/p21/Serpine, and PI3K/AKT, and targets senescent endothelial cells and mesenchymal stem cells [86].

Following the discovery of first-generation senolytics like Dasatinib and Quercetin, numerous additional agents for influencing cellular senescence have been identified, with several new promising molecular targets under investigation [87, 88]. Resveratrol improves telomerase activity and increases telomere length through a SIRT1-mediated mechanism, while reducing ROS, senescent products, and DNA damage [89]. Melatonin can reduce ROS accumulation and suppress inflammation, as well as increase telomere length [90]. Rapamycin inhibits the secretory phenotype of senescent cells via an Nrf2-independent mechanism [91]. Coenzyme Q10 and N-acetyl-L-cysteine are ROS inactivators [92].

Inhibition of pro-inflammatory cytokines such as TNF-α and IL-1β may also be beneficial for treating cardiovascular diseases associated with cellular senescence. For instance, TNF-α inhibitors (Etanercept, Adalimumab, Infliximab) and IL-1β inhibitors (Canakinumab) have shown promising results in clinical studies, reducing systemic inflammation and the risk of adverse cardiovascular events in atherosclerosis patients [93, 94]. The CANTOS study demonstrated that inhibition of IL-1β with Canakinumab lowers the risk of cardiovascular events in atherosclerotic patients, confirming the role of pro-inflammatory cytokines in the pathogenesis of cardiovascular diseases [95]. Tanezumab, a monoclonal antibody targeting nerve growth factor, can reduce inflammation and alleviate pain associated with osteoarthritis and other inflammatory conditions. Its use may also lower levels of pro-inflammatory cytokines like IL-6 and IL-1β, which contribute to the development of atherosclerosis and cardiovascular diseases [96, 97]. A new promising class of senolytic agents includes chimeric antigen receptor (CAR) T cells designed to target senescent cells. For instance, uPAR-specific CAR T cells have been shown to effectively eliminate senescent cells both in vitro and in vivo [98]. However, senolytic therapy is still in its early stages and requires thorough testing to ensure proper specificity, safety, and efficacy.

In conclusion, research aimed at identifying more specific biomarkers of cellular senescence, developing new optimized strategies, and improving existing detection methods is highly

relevant for both fundamental science and clinical medicine. Reliable identification of such cellular, molecular and genetic markers is crucial not only for a deeper understanding of the biology of aging but also for creating diagnostic and therapeutic approaches that allow for targeted interventions in the senescence of cells and tissues. The identification of biomarkers of cellular senescence could become a key aspect of a personalized approach in treating many age-associated socially significant diseases, which is one of the priorities in modern precision medicine.

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В.М. Кирик[1,2], О.М. Пархоменко[1]

ПОТЕНЦІЙНІ ПРОГНОСТИЧНІ МАРКЕРИ КЛІТИННОГО СТАРІННЯ ПРИ ВІКАСОЦІЙОВАНІЙ ПАТОЛОГІЇ СЕРЦЕВО-СУДИННОЇ СИСТЕМИ

[1]ДУ «ННЦ Інститут кардіології, клінічної та регенеративної медицини ім. акад. М.Д. Стражеска Національної академії медичних наук України», Київ;
[2]ДУ «Інститут геронтології ім. Д. Ф. Чеботарьова Національної академії медичних наук України», Київ;
e-mail: labcellculture@gmail.com

В огляді розглянуто проблему клітинного старіння та його вплив на розвиток вікасоційованих серцево-судинних захворювань в прогностичному аспекті. Розглянуто зв'язок клітинного старіння і старіння організму в цілому та з ендотеліальною дисфункцією, зокрема у пацієнтів кардіологічного профілю. Акцентується увага на проявах клітинного старіння та їх маркерах, які можуть бути використані для комплексної діагностики та прогнозування ризику гострих серцево-судинних подій. Визначено потенціал та обмеження сенолітичної терапії для елімінації старих клітин та зменшення системного запалення. Підкреслюється важливість розвитку нових методів для виявлення маркерів клітинного старіння та впровадження персоніфікованого підходу в лікуванні вікасоційованих серцево-судинних захворювань у контексті сучасної прецизійної медицини.

Ключові слова: клітинне старіння; старіння організму; серцево-судинні захворювання; ендотеліальна дисфункція; сенолітики.

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