Decoding Cardiac Aging: Integrative Genetic, Cellular, and Molecular Insights Through a Data-Driven Perspective

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Abstract

The occurrence of heart disease rises among older people because they experience cardiac ageing which represents an intricate biological process that modifies heart functions. Heart health protection methods must originate from understanding how genetic and cellular and molecular elements produce cardiac ageing. Pathological cardiovascular diseases like atherosclerosis along with heart failure during ageing demonstrate rapid dysfunctions and fibrosis with inflammatory components whereas normal ageing exhibits gradual cellular reduction. A better understanding of cardiac ageing at the molecular level can be achieved by studying genetic factors consisting of CISD1, CISD2, CISD3, SIRT1, SIRT3, TERT, and p53 genes together with epigenetic variations. A normal functioning heart depends on genetic elements to control cell ageing while maintaining oxidative stress control and sustaining mitochondrial output. Modern scientific knowledge of ageing hearts links the degradation of mitochondria along with oxidative stress and telomere shortening together with impaired cardiomyocyte regeneration capability. The heart speeds up its ageing process through Inflammaging which involves low-grade chronic inflammation together with extracellular matrix remodelling and fibrosis. Heart function and ageing regulation are controlled by seven signalling pathways that include mTOR AMPK and FOXO SIRT1/PGC-1α and Wnt/β-catenin and TGF-β and NF-κB. Age-related cardiovascular illnesses occur because of inflammation together with fibrosis mitochondrial failure and metabolic dysregulation and their deregulation exacerbates these conditions. The approach to delaying and stopping cardiac ageing involves therapeutic interventions on these genetic cellular and molecular pathways. Progressive age-related gene function effects may become possible with CRISPR-based gene therapy and other genetic and epigenetic modification methods. Scientific studies involving pharmacological compounds discovered their ability to enhance mitochondrial activity while counteracting oxidative stress which results in reduced ageing rates. Medical practitioners employ three types of drugs, senolytics other than flavonoids alongside mitochondrial-targeted medicines. The combination of exercise together with other lifestyle approaches helps mitochondria maintain health and reduces inflammation which enables the body to withstand the cellular effects of ageing. Scientists have significantly advanced their knowledge about the genetic and cellular sources together with molecular factors that contribute to heart ageing. The emerging innovations for heart ageing deceleration display promising results although medical implementation remains challenging. Leading future heart health studies should focus on developing better therapy protocols testing them on patients and

developing unique plans to boost cardiovascular wellness in senior citizens. Doing in-depth studies of cardiac ageing mechanics while obtaining solutions for its challenges will lead to prolonged lives for elderly individuals.

Keywords: Cardiac Aging, Mitochondrial Dysfunction, Telomere Shortening, Inflammaging, Genetic and Epigenetic Regulation, Senolytics and Flavonoids, Signaling Pathways.

1. Introduction

Age-related heart deterioration leads to more cardiovascular diseases and heart failure together with reduced cardiac output. This defines cardiac ageing as heart tissue ageing through time-dependent structural and functional degradation. Heart cells bear the biggest impact from ageing because they remain active and need high energy constantly even though various organs naturally deteriorate in old age. (Amaral et al., 2013). The heart sustains damage gradually because it undergoes minimal tissue regeneration in comparison to other tissues. Growing older causes the heart to develop major alterations through cardiomyocyte degeneration, fibrosis progression, mitochondrial dysfunction, telomere shortening and persistent low-grade inflammation. The ageing processes diminish heart muscle contraction while lowering signal conduction efficiency and reducing tolerance to exercise-related physical demands or injuries. Aging naturally initiates these changes but such natural progression increases susceptibility to illnesses like hypertension alongside atrial fibrillation which may result in heart failure. Understanding cardiac ageing is vital because it affects life span and quality of life. Public health institutions globally express increasing worry about cardiovascular illnesses that occur with age progression. The development of specific treatments which postpone or manage heart failure symptoms from ageing requires a clear distinction between natural heart ageing and disease-related cardiovascular conditions. Cardiac ageing research has become possible due to advances in genetics molecular biology and bioinformatics techniques. The advances in biological research have developed therapeutic approaches that include pharmaceutical medicines and changes to daily lifestyle patterns as well as genetic intervention methods. (Jeevaratnam et al., 2017). Physiological ageing overlaps with specific points of pathological cardiovascular diseases but these two processes remain distinct. The natural process of cardiovascular function deterioration during ageing constitutes physiological ageing because it is unavoidable with age. This condition leads to minute structural and functional changes in heart rhythms and myocardial performance alongside moderate wall stiffness in arteries. These changes in cardiovascular efficiency lead to overall performance reduction but usually do not result in immediate severe medical complications. People maintain a satisfactory quality of life after age-related cardiovascular system changes because their bodies adapt to daily requirements.

The deterioration of ageing effects leads to pathological cardiovascular disorders which result in disease alongside system malfunction. The combination of heart failure with atherosclerosis arrhythmias and myocardial infarction leads to severe heart and bloodstream damage. Three

main factors triggering pathological ageing include oxidative stress and inflammation together with genetic predispositions that accelerate natural physiological aging declines. The heart fails to distribute blood effectively because of long-term hypertension and myocardial infarction damage which leads to heart failure but atherosclerosis arises from artery plaque buildup which causes artery stiffness and narrowing. The extent of the damage along with the root causes distinguish pathological cardiovascular conditions from standard physiological ageing. Pathological cardiovascular conditions differ from physiological ageing due to their combined characteristics of severe dysfunction along with repair impairments and clear tissue destruction. Certain pathological disorders have stronger genetic and environmental factors because individuals might accelerate ageing through lifestyle risk exposures that lead to disease development such as unhealthy eating habits and smoking alongside inactivity. Treatment strategies aiming for both ageing consequences and pathological cardiovascular disease progression need clinicians to differentiate between these phenomena. Worsening heart function occurs progressively over time because genetic and cellular and molecular events occur in succession. Genes that control essential cellular processes including oxidative stress and mitochondrial function together with cellular senescence form among the most important genes involved in ageing. The function of cardiomyocytes depends on healthy mitochondria and redox balance regulation conducted by the genes CISD1, CISD2 and CISD3. The sirtuin protein family contains two members SIRT1 and SIRT3 which enhance mitochondrial development while reducing harmful oxidative responses to control metabolic state and life expectancy (Lian et al., 2023). Telomere maintenance depends on the telomerase gene (TERT) function which protects cardiomyocytes from reaching senescence. Aged cardiac tissue shows reduced regenerative abilities alongside cellular senescence mainly because of the p53 and p16 genes.

Among biological factors that lead to cardiac ageing the most significant elements include declining cardiomyocyte function while reducing regenerative capacity and causing endothelial dysfunction. After sustaining damage cardiomyocytes regenerate minimally since these cells stop dividing through the normal process and function as heart muscle cells. The reactions of cardiomyocytes to stress reduce with age because damage accumulates in their structure. The ageing process of endothelial cells that protect blood arteries leads to production reductions of nitric oxide and vascular stiffness which deteriorates cardiovascular health. The important cellular ageing process in the heart includes fibroblast activation because it leads to elevated collagen production and the development of cardiac fibrosis. Uneven heart muscle contraction occurs because fibrosis makes the organ stiff so it cannot perform regular contractions or rest normally. As our bodies age critical alterations occur in both mitochondrial performance and oxidative damage together with telomere shortening throughout the heart. With ageing our mitochondria develop issues which reduce our energy production abilities and increase the production of reactive oxygen species (ROS) (Liu et al., 2019). The ageing process accelerates because oxidative stress targets proteins as well as lipids and DNA molecules. The process of cellular senescence depends heavily on telomere shortening which protects the ends of chromosomes. Your heart loses its regenerative potential and faces elevated danger of

cardiovascular diseases like heart failure through the cell division-induced telomere shortening process. The ageing process of the heart begins when low-grade chronic inflammation persists throughout life to initiate inflammaging. Cytokines together with chemokines function as inflammatory chemicals that disrupt mitochondrial operations elevate oxidative damage and promote fibrosis formation. Degenerative cardiovascular diseases along with aging occur more rapidly due to this repetitive harmful mechanism. These cellular genetic and molecular elements interweave numerous relationships to form a basis that helps scientists investigate cardiac ageing. The knowledge about these characteristics will allow researchers to develop better treatments to handle cardiac ageing because these treatments could positively affect both cardiovascular health and the quality of life for elderly individuals.

Table 1: Summary of key genetic, epigenetic, cellular, and molecular mechanisms underlying cardiac ageing, along with associated signalling pathways and potential therapeutic strategies aimed at delaying age-related cardiovascular decline.

Category	Key Elements	Description
Genetic Factors	CISD1, CISD2, CISD3, TERT, SIRT1, p53	Regulate mitochondrial health, telomere length, and senescence
Epigenetics	DNA methylation, histone mods, ncRNAs	Alter gene expression and aging progression
Cellular Aging	Cardiomyocyte loss, fibrosis, inflammation	Reduced regeneration, increased ECM stiffness, inflammaging
Key Pathways	mTOR, AMPK, FOXO, SIRT1/PGC-1α, NF-κB	Control metabolism, stress response, and inflammation
Mitochondrial Dysfunction	ROS, telomere shortening, energy decline	This leads to cellular damage and aging
Therapeutic Strategies	CRISPR, flavonoids, senolytics, exercise	Target genes, reduce ROS, improve mitochondrial function

2. Genetic Mechanisms of Cardiac Aging

2.1 Key Genes Implicated in Cardiac Aging

Cardiac ageing depends on proteins CISD1, CISD2 and CISD3 to function because these membrane proteins maintain mitochondrial operations and establish cellular redox balance. Membrane-bound proteins regulate three fundamental heart operations including bioenergetic process and oxidative stress management along with calcium homeostasis during any stage of life. The protein CISD1 helps both stabilize mitochondria and regulate mitochondrial calcium which protects mitochondria from oxidative damage. Cisd1 protects mitochondrial efficiency while preventing energy generation decline that occurs during cardiovascular ageing at which stage substantial oxidative damage occurs in cardiac cells. The mitochondria rely on Reactive oxygen species (ROS) for normal operations and CISD2 acts as an essential factor for ROS production while simultaneously working to eliminate ROS. Mitochondrial function remains

proper in aging hearts because CISD2 functions as a protective mechanism against oxidative stress which preserves both DNA and proteins and lipids. MitoNEET which scientists refer to as CISD3 acts as a main controller of mitochondrial respiratory operations through assistance with iron-sulfur cluster assembly. Cardiac muscle protein CISD3 safeguards mitochondria against malfunctions and oxidative stress through its role in monitoring mitochondrial iron and sulphur levels (Munir, Baig, et al., 2025). A combination of CISD proteins works together to protect mitochondrial structures which ultimately prevents both myocardial age-related dysfunction as well as cardiac disorders.

The heart cell ageing process depends on SIRT1 and SIRT3 as two main NAD+-dependent deacetylases. The enzymes control the functions of mitochondria as well as cellular metabolic rates and life duration. The biological functions acting upon DNA repair and metabolism and gene expression receive regulation by SIRT1 located in the nucleus. Adult cardiomyocyte functions remain maintained through SIRT1 because this enzyme promotes mitochondrial growth while boosting heart-based oxidative metabolic processes. The enzyme achieves these health benefits by deacetylating transcription factors like FOXO and PGC-1α which enhances the function of mitochondria metabolic energy output and stress response activation. The pro-inflammatory pathways along with NF-κB are important for heart ageing yet SIRT1 decreases their activation to control inflammation. Activating SIRT1 enzyme and expression function decreases as people age while oxidative stress increases with age alongside inflammation and metabolic dysfunction which intensifies cardiovascular diseases. (Pasha et al.). The enzyme SIRT3 primarily located in mitochondria executes control over three fundamental cellular processes: oxidative phosphorylation and the tricarboxylic acid cycle as well as fatty acid oxidation. The antioxidant enzymes catalase and superoxide dismutase (SOD2) receive activation through SIRT3 that enables important reduction of oxidative damage. Researchers show that age-related heart benefits from activating SIRT3 since this leads to improved mitochondrial health and lowers ROS levels which helps the heart remain healthy. Further decline of heart function and mitochondrial dysfunction occurs as SIRT3 expression decreases throughout age-related years. A possible therapeutic intervention for heart health promotion in elderly patients while blocking cardiac ageing would activate both SIRT1 and SIRT3 systems. These genes function to stop cell and molecular breakdowns that trigger cardiac ageing processes. The ageing process affects mitochondrial operation genes such as CISD1 CISD2 CISD3 SIRT1 and SIRT3 the most. Cardiac function deterioration coincides with ageing because these genes function improperly after people reach a certain age level. (Roy et al., 2013). The development of treatment solutions for counteracting cardiac ageing and enhancing heart health among ageing populations would benefit incredibly from insights into the protective molecular mechanisms of these genes.

2.2 Epigenetic Modifications in Aging Hearts

Gene expression needs epigenetic modifications to avoid sequence alterations in the DNA. Age-related alterations become crucial in determining how quickly the heart ages because they modify both cellular functionality and stress response abilities of cardiomyocytes. DNA methylation represents an extensive field of inquiry in epigenetic research because scientists have identified it as the addition of methyl groups to DNA cytosine bases found in CpG islands. Genes experience both hypomethylation and hypermethylation following DNA methylation pattern changes that occur within the ageing heart. Genomic modifications in this process enable the expression of pro-inflammatory and pro-fibrotic genes and reduce the expression of genes that defend cells from oxidative stress and provide stress tolerance. The promotion of DNA hypermethylation in genes that control mitochondrial activity and cell cycle regulation becomes increasingly common with age and leads to heart dysfunction. (Shaikh, 2010). Heart muscle cell functions become compromised because of this change. Heart failure together with other cardiovascular diseases becomes more likely when methylation disappears from specific gene loci to activate their pro-inflammatory and pro-fibrotic components. The modifications of DNA methylation in ageing hearts significantly alter gene expression patterns that ultimately lead to dysfunctional heart pathologies.

Heart cell aging controls gene expression through three types of epigenetic modifications which include DNA methylation together with histone alterations and chromatin remodelling. DNA encloses itself within proteins which form chromatin. DNA accessibility changes under the influence of transcriptional apparatus activities through post-translational modifications like acetylation, methylation phosphorylation and ubiquitination modifications. The aging process of hearts occurs as histone modifications lead to chromatin changes which produce a compact DNA structure and deactivate genes important for cardiomyocyte maintenance and function. Histone methylation serves to activate or suppress gene expression based on conditions yet histone acetylation primarily causes active gene transcription. (Surgeon). The age-related decrease in histone acetylation throughout the entire cell causes suppression of mitochondrial biogenesis together with stress resistance and autophagy genes within an ageing heart. The health of cardiomyocytes requires functionality from these essential genes. Studies have reported expression modifications of chromatin remodelling complexes that perform chromatin structure maintenance work in ageing heart tissue. The changes disrupt the normal operations of these complexes thus reducing heart sensitivity towards cellular stress alongside DNA damage while accelerating ageing progression. The pathophysiology of age-related cardiovascular disorders depends on chromatin remodelling as well as histone modifications to control the gene expression patterns of the ageing heart.

The research indicates that non-coding RNAs specifically including miRNAs and lncRNAs function fundamentally in the control of heart aging processes. The human body uses microRNAs (miRNAs) as tiny single-stranded RNA molecules to control expressions of messenger RNAs (mRNAs) by either causing their complete breakdown or slowing down their translation process. Expert research has found several microRNAs (miRNAs) that demonstrate

changing expression patterns during heart ageing which influence cardiac disturbances in the elderly population (Zhang et al., 2016). The key events in heart ageing involve inflammation together with fibrosis and apoptosis while miR-1, miR-21 and miR-34a play a significant role in influencing these processes. The two characteristics of cardiac aging known as cellular senescence and myocardial fibrosis show evidence of development through miR-34a expression. When miRNAs focus on genes that control mitochondrial function cellular oxidative stress response and cell cycle progression they produce dramatic effects on cardiac ageing progression. The gene expression regulatory mechanism of long non-coding RNAs (lncRNAs) occurs through chromatin remodelling as well as transcription factor binding and RNA molecule interactions. These molecules are significantly longer than microRNAs. MALAT1 together with H19 functions as essential long non-coding RNAs to control inflammatory responses fibrosis formation and cardiomyocyte death during heart ageing. Therapeutic research has focused on the non-coding RNA elements as they form part of the critical control network governing heart ageing. The heart develops aged-related epigenetic regulation by both long non-coding RNAs (lncRNAs) and microRNAs (miRNAs) (Campisi et al., 2011). The processes of gene expression together with cell survival and tissue remodelling change because of these RNA modifications which subsequently determine aged cardiovascular disease development and progression.

3. Cellular Mechanisms of Cardiac Aging

3.1 Cardiomyocyte Aging and Senescence

Age-related heart failure progresses mainly from changes that occur in cardiomyocytes both through senescence and ageing processes. Adult cardiomyocytes lose their potential to regenerate themselves to the point where they drastically decline throughout the ageing process. The self-renewal capabilities of Cardiomyocytes stand inferior compared to most other tissue types during periods of stress or injury. The ageing heart must endure increased oxidative damage together with inflammation and mechanical stress as chronic pressures while the inability to regenerate heart tissue becomes most noticeable in these situations. The aging process makes cardiomyocytes vulnerable to death while causing fibrosis together with atrophy so heart function naturally diminishes. The main feature of ageing cardiomyocytes is senescence where cells stop dividing irreversibly. Cardiomyocytes in this state permanently stop functioning fail to repair damage and simultaneously accumulate DNA damage while releasing inflammatory substances that worsen tissue damage. The senescence-associated secretory phenotype (SASP) stands out as an essential process because it results in cardiomyocyte production of inflammatory cytokines along with growth factors and extracellular matrix proteins. Fibrosis and remodelling of the heart tissues occur due to these substances. Age-related heart failure appears because of cellular senescence accumulation and also due to normal cardiomyocyte death. Mitochondrial dysfunction causes most cardiomyocyte functional deterioration during cardiac ageing making this malfunction vital to cardiac ageing processes (Dai, Rabinovitch, et al., 2012). The cellular

energy production inside mitochondria delivers ATP using an oxidative phosphorylation process. Appropriate heart function in cardiomyocytes depends on healthy mitochondria since these cells need continuous energy output for sustained contractions. The condition of mitochondria worsens during the older stages of life. The evolution of this dysfunction emerges through reduced mitochondrial biogenesis together with decreased ATP generation in addition to accumulating mitochondrial DNA (mtDNA) damage. Age-related changes lead to reduced metabolic performance by making the heart produce energy less effectively because mitochondria decrease their energy output capabilities. The insufficient ATP supply affects heart muscle contractability leading to heart failure and reduced cardiac output.

The increased production of reactive oxygen species (ROS) represents a vital characteristic of damaged mitochondria within ageing cardiomyocytes. (Ibebunjo et al., 2013). Most cellular reactive oxygen species (ROS) arise from cellular mitochondria before they accumulate and start damaging DNA lipids and proteins through oxidation. A destructive cycle begins with oxidative stress which rapidly advances because of mitochondrial dysfunction that worsens harm to cells. Acceptable homeostasis of calcium and proper function of ion channels and intact mitochondrial systems are impaired by cardiomyocyte oxidative stress which consequently causes arrhythmias and diminished contractile capabilities. The ability of cardiomyocytes to perform autophagy and mitophagy functions becomes impaired which leads to lower mitochondrial function because these essential processes are responsible for waste mitochondrial removal to maintain cellular health. The heart ages along with the accumulation of damaged organelles since defective mitochondria fail to clear from cellular structures (Khavinson, 2013). The deterioration of energy metabolism becomes associated with mitochondrial failure when metabolic regulatory cellular signalling pathways experience modifications. As people age their hearts typically develop problems with the mTOR (mechanistic target of rapamycin) pathway that controls cell growth along with metabolism and protein synthesis. The reduction in this system's function impedes the biogenic process of mitochondria together with the maintenance of cellular energy balance. With age, the sensitivity of AMP-activated protein kinase (AMPK) decreases leading to worsened metabolic decline along with mitochondrial dysfunction. The natural aging process of cardiomyocytes together with age-related heart disorders develops mainly because of deteriorating mitochondrial activity and energy metabolism.

3.2 Endothelial Cell Dysfunction

The regulation of vascular tone and blood flow together with vessel integrity depends on endothelial cells that line blood vessels' interior surfaces for homeostasis to occur. Our blood vessels experience a deterioration of state because ageing causes endothelial cells to undergo both structural and functional transformations. Elderly individuals experience reduced NO production in their bodies and this marks the failure of endothelial cells. The vasodilator NO performs an important function in maintaining the health of blood vessels. Endothelial nitric

oxide synthase (eNOS) generates nitric oxide functional in two ways including vessel expansion and inflammatory response reduction and platelet clump prevention. The bioavailability of NO in the vasculature, however, declines with age due to a decline in eNOS activity. Low levels of NO block essential blood artery dilation thus creating stiff blood vessels which cut down blood flow. The inability of blood vessels to properly dilate stands as a principal reason behind hypertension development which thus increases the risk for cardiovascular conditions such as stroke and coronary artery disease. Endothelial dysfunction needs prevention through nitric oxide which serves as a vasodilator while showing protective anti-inflammatory behaviour (Munir, Wattoo, et al., 2025). Aging causes two main characteristics including oxidative stress and inflammation which drive endothelial cell dysfunction toward worse states. The quantity of reactive oxygen species (ROS) increases in older individuals which accelerates nitric oxide breakdown resulting in decreased availability of the substance. The continuous deterioration between oxidative stress and impaired endothelial function initiates a damaging cycle which drives cellular ageing to worse levels. As endothelial cells stop successfully managing vascular tone and decreasing inflammation they cause atherosclerosis and increased arterial stiffness while creating cardiovascular disorders which negatively affect blood vessel walls. The deterioration of cardiovascular health in aged people results mostly from endothelial dysfunction which serves as a fundamental component in age-related vascular diseases.

3.3 Fibroblast Activation and Cardiac Fibrosis

Heart tissue remodelling during ageing enables the activation of fibroblasts together with cardiac fibrosis development as its main characteristic. Foam structures of human heart tissue depend on extracellular matrix (ECM) support that fibroblasts create primarily. Old-age fibrosis mostly arises from cardiac fibroblast stimulation that produces excessive ECM components, especially collagen. The combination of reduced cardiac function with stiff heart muscle occurs in Heart failure with preserved ejection fraction (HFpEF) and other age-related heart diseases due to age-related fibrosis. As individuals grow older two essential and opposite changes occur: the ECM components, specifically collagen, transition in distinct directions and matrix metalloproteinase enzyme activity decreases. The activation of fibroblasts occurs due to three main factors which are mechanical stress and inflammation together with transforming growth factor-beta (TGF-β) signaling molecules. (Rattan, 2019). The activation of fibroblasts through TGF-β signaling promotes cell division and leads to myofibroblast development which demonstrates critical significance for scientific research. Specialised fibroblasts which go by the name myofibroblasts demonstrate contraction capabilities while generating high quantities of collagen with additional extracellular matrix ingredients. The myocardial tissue becomes rigid and thick when it accumulates myofibroblasts and exceeds normal extracellular matrix distribution which disrupts normal muscle contractions.

Heart electrical conduction problems originate from cardiac fibrosis thus disrupting normal electrical signals that control heart function. The structural modifications of fibrosis in myocardial tissue produce electrical dysfunction and delay conduction spread which results in increased arrhythmogenic conditions specifically including atrial fibrillation. (Rattan, 2019). During diastole, the heart expands poorly to fill with blood since fibrosis causes a reduction in myocardial compliance. The occurrence of heart failure among elderly individuals alongside diastolic dysfunction is primarily due to cardiac fibrosis. The aged extracellular matrix remodelling process negatively affects heart functional decline along with cardiovascular disease progression.

3.4 Inflammation and Immunosenescence

Age-related inflammation exists as "inflammaging" which denotes an enduring yet mild inflammatory condition. Age-related disorders such as cardiovascular issues like atherosclerosis, hypertension and heart failure receive influence from inflammatory mechanisms. The ageing body maintains continuous immune system activation even when the person faces no dangers from outside threats. The development and activation of inflammatory factors which include cell damage accumulation and changes to immune responses together with cytokine and inflammatory mediator release causes this persistent low-grade inflammatory condition. Endothelial dysfunction together with vascular stiffness and atherosclerotic plaque formation leads to cardiovascular illnesses in elderly patients since pro-inflammatory signals promote these conditions. (Rattan, 2008). Different immune cell populations become activated during inflammaging while the production of pro-inflammatory cytokines such as interleukin IL-1, IL-6, and TNF-α takes place simultaneously with increased activity of inflammatory pathway NF-κB (nuclear factor kappa B). The cardiac system represents one among many tissues which inflammatory mediators affect beyond solely the immune system (Volkova et al., 2005). The progression of vascular dysfunction becomes speeded up due to chronic inflammation as it causes the worsening of atherosclerosis along with fibrosis and vascular ageing. Senior citizens face heart hypertrophy along with arrhythmias and these problems worsen from the effects of inflammaging.

Cells in an ageing state produce secretions called Senescence-Associated Secretory Phenotype (SASP) which promotes tissue damage together with inflammation. Cells move into a senescent condition following stress exposure to DNA harm or telomere reduction while maintaining metabolic activity. Older adults face a higher risk of cardiovascular disorders because their tissues accumulate ageing cells, particularly in heart tissue. Different chemical secretions from senescent cells compose the SASP factors (Triposkiadis et al., 2019). The secreted chemicals consist of growth factors together with proteases and pro-inflammatory cytokines. Cardiac tissue remodelling as well as inflammatory deterioration are substantially affected by the released chemical factors. Research shows that the impact SASP produces on cardiac tissue contains

numerous overlapping effects. Arterial damage together with endothelial dysfunction and fibrosis appears in ageing hearts because SASP factors increase exposure to a persistent inflammatory environment. Cardiac fibroblasts together with endothelial cells illustrate this case (Rattan, 2024). The cells produce inflammatory cytokines IL-6 and TNF-α as they reach advanced age. The released cytokines promote both the activation of immune cells and increase the pace of fibrosis development. A heart filled with pro-inflammatory conditions hinders tissue regeneration while promoting fibrosis thus creating obstacles for natural tissue regenerative processes. The factors released from SASP cause heart muscle thickness and rigidity that interfere with cardiac contractility by deranging the normal composition of extracellular matrix components. The SASP generates injury to the heart's electrical functions while fostering tissue scarring at the same time. Aging cells release inflammatory cytokines with growth factors that initiate functional changes in ion channels while creating abnormal conducting areas in the heart. Heart failure symptoms triggered by age result in reduced cardiac output together with cardiomyocyte dysfunction and these problems become worse due to SASP. Cardiac ageing pathophysiology and the initiation of age-related cardiovascular diseases directly reflect the accumulation of senescent cells together with their released SASP elements (Song et al., 2020).

4. Molecular Pathways Driving Cardiac Aging

4.1 Molecular Pathways Driving Cardiac Aging

Mitochondrial dysfunction together with oxidative stress function as the primary aging factors that primarily affect the heart system. Production of adenosine triphosphate (ATP) as the cellular energy unit happens through oxidative phosphorylation in mitochondria. Chemical ageing brings deterioration in our mitochondria's performance thus we create fewer ATP molecules combined with more reactive oxygen species (ROS) that derive from oxygen metabolic processes. Hydroxyl radicals (OH) represent one group of free radicals within reactive oxygen species (ROS) together with hydrogen peroxide (H2O2) and superoxide (O2). The harmful radicals exhibit damaging properties to three fundamental biological structural forms: DNA, lipids and proteins. The accumulation of reactive oxygen species (ROS) increases with age due in part to the worsening of mitochondrial malfunction (Amorim et al., 2022). The electron transport chain produces reactive oxygen species (ROS) which cause damage to mtDNA because it lies in proximity to this chain thus making mtDNA more prone to mutations than nuclear DNA. The build-up of mitochondrial DNA mutations disrupts mitochondria processes which intensifies the effects of oxidative stress. The damage to cardiac cells increases as well as the production of energy declines when mitochondria become impaired (Bátkai et al., 2007). Heart failure alongside other cardiovascular conditions leads to irregular cellular relaxation and contraction processes which stem from ROS-induced disorders in cardiac muscle cell calcium management.

All types of cellular ageing occur through inflammation death and senescence and oxidative stress functions as the common trigger mechanism. Increased ROS levels activate nuclear factor

kappa-light-chain-enhancer of activated B cells (NF-κB) signaling molecules which then trigger inflammatory responses that intensify cardiac ageing pathophysiology. The CISD proteins CISD1, CISD2, and CISD3 are crucial for the preservation of mitochondrial function and the defence against oxidative stress in the hearts of elderly individuals. CISD proteins consisting of the CDGSH iron-sulfur domain-containing (CISD) family operate to regulate the mitochondrial membrane stability while handling biogenic reactions and oxidative stress responses that sustain mitochondrial homeostasis (Bátkai et al., 2007). The mitochondrial preservation function of CISD1, CISD2, and CISD3 occurs through their ability to sustain proper mitochondrial activity and control excessive ROS production. These proteins theoretically shape mitochondria correctly while simultaneously controlling metabolic processes within the mitochondria (Almeida et al., 2017). The mitochondrial redox status depends heavily on CISD3 since it controls the electron transport chain's activity while strengthening mitochondrial antioxidants to prevent reactive oxygen species accumulation. The optimal stability of mitochondrial membrane potential supports cellular survival through energy generation and CISD proteins contribute to this process.

CISD proteins act to prevent mitochondria from experiencing demise through their protective functions. When mitochondrial function deteriorates it releases cytochrome c together with pro-apoptotic substances creating a condition which results in cellular death. The stability features of mitochondrial membranes are protected by CISD proteins thus reducing the frequency of apoptosis through mitochondrial mechanisms (Khan et al., 2017). The impaired activity of aged cardiomyocyte mitochondria allows CISD proteins to delay both cellular ageing and apoptosis thus promoting heart function stability. Age-related deterioration of tissues produces higher mitochondrial dysfunction together with enhanced oxidative stress because of decreased CISD protein expression notably CISD2 and CISD3. The essential role of CISD proteins becomes evident because these proteins protect cells from mitochondrial damage to guarantee their survival most significantly in the heart. After all, it depends on mitochondria for both physical contractions and general functioning.

4.2 Telomere Attrition and Cellular Senescence

Telomeres serve as the repeating nucleotide sequences located at chromosome ends to protect DNA from breakdown and stop chromosomal linkages. In somatic cells, the error of DNA polymerases during chromosomal end replication leads to progressively shorter telomeres. Then cells go through apoptosis or senescence when telomeres reach their specific shortenable length. Sexual reproduction uses this important mechanism during ageing as well as for triggering age-related medical conditions that affect cardiac health. (Childs et al., 2018)The shortening of telomeres in cardiomyocytes leads to deteriorating cellular regeneration potential according to scientific studies. Heart cells or cardiomyocytes lack self-repair ability after damage occurs because they do not divide as other cell types can. The division and repairing capabilities of

ageing cardiomyocytes decrease steadily since their telomeres become shorter. The decreased tissue regeneration ability in the heart leads to additional complications with normal cardiac ageing decline. Cardiac stress adaptation abilities such as those seen under hypertension or after myocardial infarction or cardiovascular injuries become hindered because of senescent cardiomyocytes. The degradation of telomeres creates effects throughout different cardiac cell types. The telomeres of two different cardiac cell types including blood artery lining endothelial cells and heart-emphasized fibroblasts diminish through aging thus making cardiac cell aging more complex. The ageing process of blood vessels and endothelial cell function develops because telomere shortening suppresses the production of nitric oxide (Loffredo et al., 2013). Shortenings of telomeres within fibroblasts create heart vessel damage and trigger extracellular matrix fibrosis together with matrix remodeling that causes heart fibrosis and final heart failure development. The shelterin complex together with telomerase reverse transcriptase (TERT) maintains telomeres at length which prevents premature ageing of cells. Telomeres stay undiscovered as DNA is damaged by proteins that comprise the shelterin complex performing binding functions (Pearson et al., 2008). Cell cycle arrest with DNA damage occurs when this complex prevents response pathways from activation for telomere preservation. The shelterin complex ensures the correct operation of telomeres while they undergo cellular division.

The combination of proteins known as telomerase enables the enzyme complex to add repeated DNA sequences onto telomeres causing telomere length extension (Donato et al., 2018). The catalytic component of this complex belongs to TERT. Telomeres experience continuous shortening in most somatic cells following cell division because few or no TERT molecules exist to perform telomere-lengthening functions in these cells. Some cancer cells alongside germ cells and stem cells retain their telomere length and proliferative properties due to their elevated levels of the telomere-elongating enzyme TERT (Rahman et al., 2013). A reduction in heart TERT expression leads to telomere shortening in cardiomyocytes together with other cardiac cell types during ageing. The reduction in TERT activity leads to cellular senescence together with reduced cell regeneration potentials. When cardiac cells age they produce substances through the senescence-associated secretory phenotype (SASP) that intensify tissue fibrosis and cause degeneration as well as inflammatory reactions. Studies demonstrate that TERT restoration in ageing cardiomyocytes produces three benefits: longer lifespan without senescence onset and enhanced mitochondrial performance as well as tissue repair mechanisms (Tenchov et al., 2023). Heart functional outcomes together with cardiac fibrosis patterns caused by ageing show improvement in animal subjects receiving elevated TERT gene expression. Research indicates that gene therapy together with specific small chemicals has the potential to counteract heart telomere shortening. The major factors that lead to cardiac ageing include both telomere attrition and reduced TERT activity levels (Gude et al., 2018). Cardiomyocyte telomere shortening during ageing leads to three major consequences including heart function deterioration cellular ageing and reduced heart tissue maintenance ability. Science shows that age-related cardiac dysfunction could be treated by recovering TERT functionality that the shelterin complex helps to protect from damage.

4.3 Autophagy and Proteostasis Dysfunction

Cellular maintenance requires autophagy to break down unnecessary cellular elements such as organelles as well as lipids and proteins which helps preserve homeostasis. A proper operation of autophagy sustains healthy mitochondria alongside maintaining overall cardiac cellular functions. The efficiency of autophagic processes declines as we age so the heart develops dysfunctional proteins along with problems controlling mitochondrial quality. The breakdown in autophagy together with proteostasis functions as a primary factor that leads to heart ageing and age-related cardiovascular diseases (Walters & Cox, 2018). Autophagy has its subtype called mitophagy which specializes in eliminating damaged mitochondria from cells one at a time. Machine-like cellular energy production deteriorates as a major indicator of ageing alongside numerous age-related diseases. Minimal removal of defective mitochondria by the heart remains essential because of the persistent high-energy needs of heart muscle tissue. The decline in mitophagy occurs in older age thus dysfunctional mitochondria accumulate inside cardiomyocytes. Among various adverse effects of this condition stands cardiac function deterioration together with elevated oxidative stress and diminished ATP production as well as pro-apoptotic factor liberation. The process of both defective mitochondria accumulation and dysfunctional mitophagy results in elevated reactive oxygen species (ROS) production (Lakatta, 2015). The highly reactive ROS chemical family can cause oxidative damage to cellular proteins along with fatty acids and DNA substances (Yao et al., 2019). Mitochondrial DNA suffers damage from excessive reactive oxygen species production within the heart which subsequently reduces mitochondrial operations and accelerates the ageing process. Multiple heart diseases such as heart failure and arrhythmias arise because of mitochondrial dysfunction which happens naturally with age.

Cellular mechanisms that control protein production folding and transport together with destruction receive the definition of "protein homeostasis." Proper maintenance of cellular health depends on a strong proteostasis network because cardiomyocytes along with post-mitotic cells possess limited abilities in protein turnover (Csiszar et al., 2005). A shift happens during elderly cardiac cell protein synthesis to break down balance which results in higher abnormal protein accumulation. Aggregates from accumulating proteins cause both cellular damage and disruptions of normal cell operations. Cardiac dysfunction becomes a major concern when protein aggregates continue increasing inside the heart due to their multiple damaging effects. Protein aggregation functions impair heart contractions together with other vital functions by disrupting important metabolic and structural proteins in their regular function. Misfolded proteins create additional inflammation alongside mitochondrial dysfunction since they activate cellular stress mechanisms that include both unfolded protein response (UPR) and oxidative stress response. Cells experience additional proteostasis deterioration when accumulated proteins exceed the limit of their proteasomal and autophagic waste processing systems (Davalli et al., 2016). Misfolded proteins undergo breakdown through the dual proteostasis network of

cardiomyocytes that consists of autophagy and proteasome systems. Age diminishes the operational success of both protein clearance systems. The ageing process reduces the functionality of mitophagy alongside other autophagic pathways thus resulting in lowered proteostasis levels. Aggregates form inside cells because the body fails to break down or unfold damaged proteins which in turn cause delayed cell operations leading to premature age-related cardiac deterioration. Cardiac ageing occurs mainly because of proteostasis breakdown coupled with impaired mitophagy (Ermolaeva et al., 2018). The elderly heart develops diminished autophagic activities combined with increased damaged mitochondria and misfolded proteins which leads to oxidative stress mitochondrial dysfunction and heart cell dysfunction. Cardiac function deterioration and age-related diseases such as arrhythmias and heart failure occur mainly because of molecular events.

5. Pathways Involved in Cardiac Aging

Several critical signal paths control multiple cardiac operations while simultaneously being complex frameworks that regulate ageing in the heart. The mTOR pathway controls important aspects of cardiomyocyte growth and cell metabolism together with cellular division regulation. Organ dysfunction during ageing occurs from mTOR dysregulation leading to cardiac enlargement along with abnormal protein production that causes cell aging. (Kohanski et al., 2016). The inhibitor rapamycin works by promoting autophagy alongside reducing inflammation which pushes back cardiac ageing while extending life expectancy. Autophagy as well as fatty acid oxidation and mitochondrial biogenesis function under the control of the AMPK pathway which serves to monitor cellular energy levels. When AMPK safeguards deteriorate due to age-related reasons it leads to mitochondrial errors and increases oxidative pressure throughout the body. Heart ageing effects can be reduced through AMPK activation because it enhances mitochondrial functioning and decreases inflammatory response.

FOXO transcription factors control three vital processes: stress resistance mechanisms autophagy and lifespan regulation. These factors get triggered by stress to create protective mechanisms which support the survival of cells. The activation sequence between FOXO SIRT1 and AMPK enables these factors to manage autophagy and mitochondrial functions that defend against heart ageing effects. αραts dysfunction and cellular senescence because the reduced activity of SIRT1 or AMPK leads to improper FOXO signalling (Lakatta, 2002). The SIRT1/PGC-1α axis constitutes a vital mechanism through which heart ageing progresses. PGC-1α assists with mitochondria functioning while SIRT1 monitors mitochondrial formation and inflammation pathways and regulates oxidative stress reactions in addition to being a NAD+-consumptive deacetylase. The structural deterioration of mitochondria becomes more severe because the heart ages when SIRT1 and PGC-1α concentrations decrease. Research indicates mitochondrial health improvement alongside age-related cardiac decline reduction can be obtained by enhancing SIRT1 or PGC-1α activities.

An activation of Wnt/β-catenin signalling determines the control of myocardial remodelling alongside cardiac fibrosis. When Wnt/β-catenin pathway overactivation makes the heart fibrosis excessively it leads to a stiffened heart and reduced functional ability due to aging processes. The process of extracellular matrix component production including collagen ends in fibrosis that makes the heart unable to function properly through normal relaxation and contraction. During aging the TGF-β pathway plays a fundamental role in cardiac fibrosis because it determines the activity of fibroblast cells and their impact on remodelling of the extracellular matrix (Liberale et al., 2020). Persistent activation of TGF-β leads to excessive collagen deposition while making the myocardium stiff which eventually results in heart failure together with other age-related cardiovascular diseases. The blocking of TGF-β signalling pathways among elderly patients could help them fight fibrosis and protect their heart functions.

The NF-κB pathway serves to control cellular stress and inflammation pathways which become connected to cardiac aging processes toward the end of life. The heart during ageing produces "inflammaging" that results from sustained NF-κB activation leading to low-grade and extended inflammatory responses. (Ocorr et al., 2007). The heart experiences worsened damage and dysfunctional operation when inflammation occurs because it leads to increased oxidative stress while accelerating cellular ageing and creating fibrosis. Through NF-κB signaling the heart ages faster because cytokines such as TNF-α and IL-6 grow in number which results in inflammation production. Optimizing NF-κB inhibition represents a promising therapeutic mechanism for postponing cardiac ageing while improving heart conditions in elderly individuals.

Cardiac ageing regulation depends primarily on seven molecular pathways including mTOR and AMPK FOXO SIRT1/PGC-1α and Wnt/β-catenin and TGF-β and NF-κB. Heart ageing develops features like inflammation along with oxidative stress fibrosis and mitochondrial dysfunction from disturbed molecular pathways. (Li et al., 2020). Understanding these key pathways enables medical professionals to create innovative therapy strategies for elderly heart health that potentially have the ability to stop or reverse ageing effects on the heart.

6. Interventions and Potential Strategies to Delay Cardiac Aging

Worldwide interest in heart ageing interventions is rising since both the population is ageing and age-related cardiovascular conditions are becoming more widespread. Molecular and cellular processes leading to heart ageing can potentially be prevented through investigations of genetic and epigenetic regulatory approaches. The potential correlates between cardiac ageing genes such as CISD2 together with SIRT1 and TERT allow their expression to be treated through gene therapy including CRISPR technologies. The heart muscle cell requires CISD2 to preserve mitochondrial health and protect itself against oxidative stress. (Ovadya & Krizhanovsky, 2014). It is plausible that CISD2 gene therapy might enable better mitochondrial performance along with prolonged cardiac durability during normal ageing. Gene editing techniques might be used to target SIRT1 for protecting the ageing heart because this gene controls both cellular stress

response mechanisms and mitochondrial biogenesis and oxidative metabolism. TERT works as a possible target entity for telomere maintenance enzyme treatment. The restoration of telomere length in cardiomyocytes through CRISPR-based treatments emerges as a possible strategy to address cellular senescence along with heart ageing problems.

Two proven methods for heart ageing delay consist of dietary interventions and pharmaceutical therapeutic approaches. Scientific evidence shows that hesperetin and (-)-(2S)-7,4′-dihydroxyflavanone in plant-derived flavonoids demonstrate properties which protect mitochondria as well as fight inflammation and act as antioxidants. Cardiovascular diseases of ageing may be prevented by hesperetin found in citrus fruit because it enhances mitochondrial function while activating SIRT1 pathways. A different flavonoid substance (-)-(2S)-7,4′-dihydroxyflavanone demonstrates its ability to switch on CISD3 which controls both mitochondrial functions and redox stability (Roh et al., 2016). The mitochondrial activity and reduction of oxidative stress from specific biochemical pathways make these flavonoids beneficial for cardiovascular disease defence in older individuals.

The new field of pharmacological intervention has been expanded with the use of senolytics and senostatics combined with flavonoids. (Ribeiro et al., 2023). Senolytics act as targeted chemicals that specifically eliminate aged cells that create a build-up within old tissues leading to diseases related to cardiovascular ageing. The heart experiences accelerated ageing due to the joint effect of dysregulated tissue homeostasis and pro-inflammatory chemical releases from these cells. New tests on preclinical animals have shown that the medications quercetin and dasatinib successfully eliminated aged cells while simultaneously enhancing cardiac function thus potentially providing therapeutic potential. Senostatics function by protecting the toxic substances which ageing cells produce instead of eliminating such cells from existence. Heart failure initiation along with other cardiovascular complications could be delayed through these treatments which decrease inflammation and minimize tissue damage in age-related heart.(Vaughan et al., 2018). Research shows a variety of promising strategies exist to control cardiac ageing through nutrition-based interventions and pharmaceutical solutions and systems managing genetic and epigenetic elements. Scientists may postpone or reverse heart ageing manifestations through molecular targeting of CISD2, SIRT1, TERT and chemical usage of flavonoids, senolytics, and senostatics. More extensive research of safety parameters as well as effectiveness evaluation and long-term outcome assessment must occur before widespread clinical application becomes feasible for these interventions. (Anderson et al., 2018). The fundamental mechanisms that drive ageing process deterioration make mitochondrial and metabolic treatments the key players in delaying cardiac ageing. Mitochondrial biogenesis stands out as one of the most effective ways to activate proteins SIRT1 and SIRT3. The longevity gene SIRT1 triggers particular pathways that both enhance metabolic efficiency and promote new mitochondrial growth to manage oxidative stress while regulating mitochondrial function. Cells can experience reduced negative effects of ageing when SIRT1 becomes

activated thereby improving mitochondrial efficiency. SIRT3 functions inside the mitochondria as a protein to control antioxidant responses while also managing mitochondrial dynamics which leads to protecting mitochondrial health. Studies have proven that SIRT3 activation protects bodies from age-related cardiovascular disease and improves oxidative metabolism functions while enhancing mitochondrial performance. (Dai, Chen, et al., 2012). Cardiac ageing prevention depends on sirtuins-stimulating treatments because they help protect mitochondria function and reduce oxidative stress damage.

The focus of metabolic and mitochondrial pills is to reduce ROS accumulation since it acts as another vital aspect. The main cause of cellular ageing and mitochondrial dysfunction through oxidative stress originates from reactive oxygen species (ROS) metabolic byproducts. The protection of ROS damage requires the utilization of antioxidants. Numerous studies demonstrate that antioxidants found in foods such as resveratrol together with vitamins C and E plus others successfully defend mitochondria from damage and reduce oxidative stress levels. The antioxidants function by destroying harmful free radicals to create yet also protect the health of mitochondria which results in reduced stress on the complete body system (Donato et al., 2018). The heart function gets enhanced while the cardiovascular diseases related to ageing receive protection from this intervention. Research indicates that antioxidant supplementation within treatment plans helps protect mitochondria from failure and slows the ageing process of heart tissues. Physicians utilize exercise together with metabolic and mitochondrial treatment to delay the ageing processes that affect hearts alongside lifestyle modifications. The health of mitochondria improves through increased energy production efficiency and stimulated mitochondrial formation when people exercise regularly. Physical activity greatly activates signalling pathways that control mitochondrial and metabolic function through SIRT1 AMPK and PGC-1α activation. These pathways help decrease age-related heart diseases while improving cardiovascular function because they enhance the number and efficiency of cardiomyocyte mitochondria (Fajemiroye et al., 2018). Exercise helps decrease two age-related phenomena known as "inflammaging." It reduces low-grade chronic inflammation coupled with cell senescence accumulation. Physical exercise reduces cardiovascular disease risk alongside arterial stiffness and vascular dysfunction because it controls pro-inflammatory cytokines and boosts immune system performance.

Exercise and mitochondrial therapies gain more potency through lifestyle measures such as heart-healthy dietary patterns alongside sufficient rest and stress-management strategies and avoidance of harmful smoking and alcohol consumption. Heart health benefits appear when individuals combine these approaches which fight against aging-related cardiovascular deterioration. A combination of metabolic and mitochondrial treatments with exercise practice and lifestyle restructuring enables people to achieve longer and better heart health as they grow older. Conditions that drive cardiac ageing are being rapidly understood through modern studies on heart ageing genes and molecular pathways. The discovery of new genes and signalling pathways persists regardless of extensive study on mitochondrial dysfunction along with

inflammation and oxidative stress because these developments may yield both new therapeutic targets and discoveries. Research on Klotho genes provides a basis for potential treatment development since they show anti-ageing and heart-protective characteristics. (Greco et al., 2015). The study of DNA methylation and histone modifications along with autophagy pathways and the senescence-associated secretory phenotype (SASP) has experienced increased investigation in recent times. The discovery of new mechanisms provides prospects to develop targeted interventions which could either delay or reverse several age-related cardiovascular conditions such as heart failure along with arrhythmias and atherosclerosis.

A major challenge in cardiac ageing research emerges from converting results discovered in preclinical trials for their clinical application. The bodily processes of humans prove significantly complex when compared to in vitro research and animal studies which collectively explain aging mechanisms as well as therapeutic methods. The effectiveness of anti-ageing medicines in people remains a challenge due to human differences during therapeutic responses complex laboratory-to-human translation from animal models and delayed assessment times for therapeutic efficacy. (Shah et al., 2023). The deployment of gene editing particularly CRISPR-Cas9-based therapeutic strategies and changes in genes related to ageing requires extensive safety analysis before clinical adoption. Improved comprehension of treatment combinations for ageing alongside age-related disorders must be pursued while better methods of measuring ageing in clinical trials need to be developed. Modern studies actively search for customized anti-ageing treatments capable of improving heart disease health. Medical science is advancing personal healthcare strategies for cardiovascular systems because scientists continue to understand enhanced factors that create distinct ageing patterns. Personalised medicine functions as a therapeutic approach which develops exact and efficient treatments by creating individualized interventions based on genetic information life patterns and personal ageing markers. (Srivastava, 2017). Drugs that stimulate mitochondrial biogenesis operate best on patients with particular mitochondrial function variants and anti-inflammatory medications can benefit those with inflammatory gene sequences. Careful evaluation of drug responses and adverse reactions becomes feasible through pharmacogenomics since the method determines suitable medications for individual patients. Personalised anti-ageing medicinal approaches have great potential but multiple barriers exist which prevent their widespread use in medical practice. The discovery of proper biomarkers along with genetic ethics management and cost reduction plans stand as major obstacles before implementation.

Our journey toward enhancing cardiovascular health and postponing cardiac ageing remains extended because of the excellent excitement we currently feel about these possibilities. (Steenman & Lande, 2017). Modern medical approaches now yield positive results from personalised anti-ageing therapies together with growing genetic research into separate genetic pathways. The safe clinical application of these innovations requires researchers to overcome significant scientific as well as technological and regulatory obstacles. The successful

advancement of elderly cardiovascular health requires researchers to collaborate with doctors and policymakers to address the identified obstacles.

Conclusion

Research on cardiac ageing has provided extensive knowledge about all factors that accelerate heart cell deterioration including genetic elements cellular processes and molecular alterations. Research results showcase that specific genetic genes maintain homeostasis in cells and function as key elements for mitochondria and telomere preservation. These variables include CISD1, CISD2, CISD3, SIRT1, and TERT. Three main cardiovascular illness drivers during ageing such as mitochondrial failure cellular senescence and oxidative stress experience changes because of these gene dysregulations. The speed of cardiac ageing becomes faster because of cellular processes which damage endothelial systems and trigger fibroblast activation leading to fibrosis and making cardiomyocytes become old prematurely. Three factors that significantly contribute to reduced cardiac performance during ageing include impaired autophagy together with telomere reduction and excessive accumulation of reactive oxygen species. Different metabolic processes and the stress response together with mitochondrial cell creation operate through the mTOR pathway and AMPK signalling along with the SIRT1/PGC-1α axis. The mechanisms of cardiac ageing and age-related heart disorders show faster progression when their regulatory functions are dysregulated. The NF-κB signalling pathway together with inflammaging represents recognized inflammatory mechanisms that deeply impact the ageing of the heart. The relationship between persistent inflammation and heart tissue degradation has been proven from this evidence. Research developers work to build therapeutic methods which target these cellular genetic and molecular pathways for slowing down or stopping cardiac ageing progression. The development of CRISPR-based gene therapy with epigenetic modification shows promise to upgrade cardiac health among elderly patients who carry genes linked to ageing processes. Heart health and ageing can potentially be minimized by three therapeutic approaches: senolytics as well as flavonoids combined with metabolic and mitochondrial treatments. The heart function improves through both exercise and lifestyle modifications because these activities boost mitochondrial efficiency while reducing inflammation thus assisting patients to maintain their heart health and remain younger longer. Research achievements in this area remain promising yet actual medicines available to patients represent several years of development ahead. The field requires more research regarding human ageing pathways together with investigations of long-term utilization risks and individual population variations. Personalised medication proves to be an emerging therapeutic tool because it relies on distinctive genetic readouts alongside molecular characteristics to help customize treatment approaches for each patient. The examination of cardiac ageing is achieving breakthroughs which reveal important information about the molecular as well as cellular factors that control ageing in cardiac tissues. Additional research is necessary to understand both cardiac ageing problems and treatment solutions even though notable development has been achieved in this field. Future research will help improve

senior citizens ' quality by examining cardiovascular disease treatment through analysis of intricate interrelations between genetic environmental and epigenetic factors.

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