International Journal of Scientific Research and Engineering Development-– Volume 8 Issue 5, Sep-Oct 2025
Available at www.ijsred.com

RESEARCH ARTICLE OPEN ACCESS

Biological Mechanisms of Ageing and Emerging Methods to Delay Its Progression

Rajshree Chaturvedi
(Dhirubhai Ambani International School, Mumbai, India
Email: rjchat2009@gmail.com)

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Abstract:

Ageing is a process marked by a decline in bodily functions and increased susceptibility to diseases. The rapid increase in the global aging population, driven by decreasing birth rates, presents significant challenges including age-related diseases, diminished quality of life, and considerable social and economic pressures. Despite these challenges, a definitive solution to effectively slow the body's natural ageing process remains elusive. In this paper, we will examine the primary causes of ageing, such as telomere shortening, oxidative stress, and accumulation of altered proteins, to develop a clear understanding of the ageing process. This paper examines the primary causes of ageing, including telomere shortening, oxidative stress, and the accumulation of altered proteins, to foster a clearer understanding of the process. It also explores methods to mitigate ageing, such as targeting telomerase, increasing antioxidant concentrations via superoxide dismutase (SOD), and enhancing proteasome activity to clear damaged proteins.

Keywords **—Cellular ageing, telomerase, antioxidant concentrations, proteasome activity, oxidative stress.**

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I. INTRODUCTION

Globally, the percentage of people aged 65 years and above is rising at a faster rate than that of those who are younger [1-2]. Between 2015 and 2050, the proportion of adults above 60 years of age will nearly double from 1 billion to 2.1 billion [3]. Ageing refers to the gradual deterioration of internal molecular functions essential for survival and reproduction [4]. Due to ageing caused by cellular damage over a period of time, people are at a higher risk of diseases like osteoarthritis and will often see a progressive decline in mental abilities.

Therefore, studying ageing can not only help find effective methods to slow ageing, but also improve one's health and reduce healthcare costs, ultimately enhancing their overall quality of life. Understanding the biology of ageing is crucial to gain knowledge about what occurs in human bodies with ageing and to investigate the trends in the world population, to prevent age-related disorders. It can significantly help to develop strategies and methods to maintain healthy cellular functions, too. Ageing often hinders the physical and psychological well-being of individuals. Most importantly, due to ageing, individuals' mental abilities weaken, their social status is lowered, and they might face stress to adapt to new environments, eventually leading to a negative self-image [5]. More than 80% of people above the age of 55 years are severely affected by osteoarthritis, and it is the leading cause of hospital visits of older individuals [6]. Older individuals are also more prone to nutrient deficiencies, leading to these diseases and eventually, a poor quality of life. Thus, they make an individual unable to work and perform daily tasks, which leads the person to dependency, preventing normal autonomous functioning [7]. The number of people aged over 80 years is expected to increase: from 21.8 million in 2008 to 61.4 million in 2060 [8]. This can lead to a decline in the working-age population, creating a shortage of qualified workers, and causing the need for financial security [9]. Thus, with ageing being not just a physical problem, but also affecting the

mental and physiological well-being of the population, it is necessary to understand its causes and treatments.

II. CAUSES OF AGEING

A. Telomere Shortening

Telomere shortening is a fundamental cause of ageing. A telomere is the area of repeating DNA sequence, 'TTAGGG', at the end of a linear chromosome [10]. Telomeres protect chromosome ends from becoming unravelled or tangled; without this protection, unstable chromosomes can arise, leading to breaks and fusions during cell division. This impairment in cell division can damage DNA and alter gene expression, as the distortion of the DNA base sequence during RNA transcription leads to altered protein synthesis.

Telomeres shorten every time a cell divides, and eventually, they become so short that the cell can no longer divide [11]. DNA shortens due to the 'End-Replication Problem,' which posits that the ends of linear DNA cannot be fully duplicated during lagging-strand DNA synthesis [12]. The enzyme, DNA polymerase, uses an RNA primer- a short strand of RNA- to copy the DNA for cells to divide. However, DNA polymerase can only move in one direction to create new DNA. So, while the leading strand can be copied, the lagging strand is copied in irregular segments, resulting in a section where DNA never gets copied- the end of the telomeres (Figure 1) [13]. Hence, the telomeres shorten each time a cell divides.

This progressive shortening of telomeres ultimately leads to the Hayflick limit, where cells cease to divide after approximately 40-50 divisions [14]. Hence, after cells reach the Hayflick limit, they stop dividing but are still active, reaching a stage of cellular senescence [15]. Therefore, as a result of telomere shortening, the decreased ability of cells to multiply decreases cellular functions. As cells reach the non-dividing stage, they accumulate and release inflammatory toxic chemicals into the body, contributing to chronic inflammation and tissue degradation [16]. This decline in cell regeneration weakens the body's ability to repair and produce new tissues, causing age-related conditions such as weakened muscles, thinner skin, and increased susceptibility to diseases like arthritis and cardiovascular issues [17]. For example, a study published in the journal, Ageing, involving 1983 participants aged 65 and older, proved that individuals with shorter telomeres had an increased risk of age-related disorders [18]. Thus, the continuous loss of cell division capacity and the accumulation of senescent cells lead to the physiological decline associated with ageing.

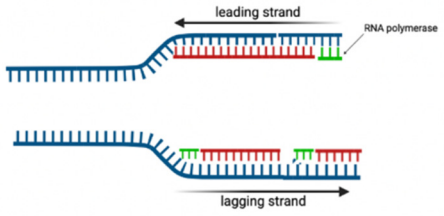

Fig. 1 Schematic of end of replication problem. A cartoon representing the end of replication problem where the lagging strand cannot be fully duplicated due to a shortened strand of RNA. Figure created with Biorender.com.

B. Oxidative Stress

Oxidative stress contributes to cell death and senescence, prompting living cells to undergo increased division as a compensatory mechanism, which ultimately accelerates telomere shortening [19]. It can be defined as the damage caused as a result of redox imbalances between reactive oxygen species (ROS) and antioxidant molecules [20]. ROS are primarily produced by the electron transport chain (ETC) in the inner membrane of mitochondria. ETC is a collection of proteins in the inner mitochondrial membrane, via which electrons travel through during redox reactions and release energy (Figure 2) [21]. It generates ATP by transferring electrons from NADH to oxygen, the final electron acceptor. As electrons move through the chain of protein complexes, energy is released and used to transfer protons across the membrane, creating a proton gradient, which leads to the formation of ATP from ADP in a process named oxidative phosphorylation [22]. The ETC is made up of 5 complexes. ROS are produced at complex I (NADH coenzyme Q reductase) and complex III (ubiquinol cytochrome c reductase) [23]. As electrons move through the ETC, some of them escape and react with oxygen species. This phenomenon is particularly prevalent at complexes I and III. When

an oxygen molecule undergoes reduction and gains an electron, it can form one of several unstable molecules that are highly reactive. These include superoxide anions (O2-), hydroxyl radicals (OH), and hydrogen peroxide (H2O2) [24]. These are also called free radicals. Our body has a natural defence system for these radicals called antioxidants. Antioxidants prevent cells from damage by suppressing oxidation and neutralising free radicals [25]. As ROS molecule production exceeds the capacity of antioxidant defence systems, it leads to the accumulation of free radicals, causing oxidative stress. Oxidative stress is caused because ROS can remove bases, or oxidise DNA strands, causing mutations. This can occur in the nucleus, where most DNA resides, or in the mitochondria, which also houses DNA. The mtDNA (mitochondrial DNA) is more susceptible to attack by these ROS molecules since it is located in the matrix (ETC), where ROS is produced. ROS can change the base sequence of mtDNA and oxidise it. This causes faulty proteins to be made and causes a malfunctioning ETC. A malfunctioning ETC induces leaky electron flow. These leaked electrons react with oxygen to form more superoxides, and the cycle repeats, causing cells to become senescent. ROS also attacks telomeric DNA. Since telomeres have high guanine content, they have the lowest redox potential and thus, ROS, specifically hydroxyl radicals (OH), oxidise guanine, producing 8-oxoguanine. This can cause base mispairing since it would then pair with adenine instead of cytosine. As telomeric regions have a low ability to repair damaged DNA, telomeres containing such DNA damage will not be fully replicated at the next cellular division [26]. Therefore, telomeres containing such DNA damage will shorten more following the next cellular division. They also lead to premature senescence. Senescent cells exhibit the senescence-associated secretory phenotype (SASP), releasing inflammatory cytokines that cause chronic inflammation and tissue remodelling. This damages nearby cells, which in turn release more SASP, leading to a further accumulation of senescent cells and contributing to ageing, as previously discussed.

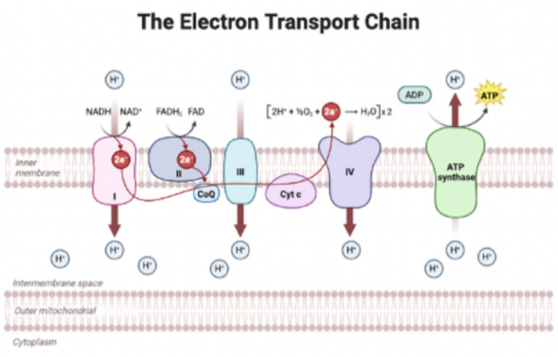

Fig. 2 Schematic of the electron transport chain. A cartoon representing the movement and transfer of electrons in the ETC. Figure created with Biorender.com.

C. Accumulation of Altered Proteins

I. Errors in Protein Synthesis: The accumulation of altered proteins is a prominent cause of ageing, stemming from errors in protein synthesis, damage caused by reactive oxygen species (ROS), and glycation. These alterations can consist of errors in protein synthesis, as explained in the telomere shortening paragraph, along with damage caused by ROS and glycation [27]. In terms of protein synthesis, errors can occur during translation, causing a change in the amino acid sequence. During translation and transcription, the mRNA copies the base sequence of the DNA and carries this copy to the ribosomes, which then assemble these base sequences into peptide chains and fold them into proteins. The secondary and tertiary structures play a major role in ensuring proper protein function. The secondary structure, involving connections between stretches of a polypeptide chain like α-helices and β-pleated sheets, acts as a scaffold (Figure 3). The tertiary structure refers to the three-dimensional folding resulting from interactions between R groups (Figure 3) [28]. These unique structures can alter the way in which a protein folds, and the protein may not be able to perform its function correctly. If these types of errors consistently recur, it could lead to loss of proteostasis, the cell's ability to maintain accurately folded and functional proteins [29]. Loss of proteostasis can lead to impaired cellular function, promoting protein aggregation and ultimately contributing to cellular senescence.

To counteract these issues, chaperone proteins (RAC and NAC- ribosome-associated complex and

nascent-chain associated complex, respectively) help proteins to fold correctly, to form a 3-D shape, the tertiary structure [30]. However, over time, these chaperone proteins become less efficient due to oxidative stress. As a result, cells accumulate misfolded proteins that chaperones would otherwise prevent. This contributes to the creation of toxic protein aggregates and disrupts normal cellular functions, leading to several age-related disorders that have altered protein accumulations, like Alzheimer's and Parkinson's. Hence, errors in proteins can play a significant role in aging. However, in addition to this, several pathways can become dysfunctional, leading to quicker ageing.

II. Ubiquitin-proteasome system (UPS) and Autophagy Pathways: The ubiquitin-proteasome system (UPS) is a pathway for destroying short-lived, misfolded, or damaged proteins [31]. The 26S proteasome recognizes and degrades these dysfunctional proteins into small peptides. However, oxidative stress and accumulation of damaged proteins can directly weaken the proteasome itself. ROS can oxidize and carbonylate the major proteasomal proteins. Concurrently, an overload of aggregated proteins can physically clog the proteasome, further reducing its efficiency. This causes altered proteins to accumulate, eventually leading the cell to become dysfunctional and senescent [32]. The autophagy-lysosome pathway is responsible for degrading long-lived proteins and weakened organelles. In this process, damaged cellular material is taken into a double-membrane vesicle (the autophagosome) and then delivered to the lysosome, where hydrolytic enzymes digest it (Figure 4) [33]. However, over time, the autophagic process weakens and naturally slows down, marked by minimized expression of major autophagy-related genes like ATG5 and LC3 [34]. The ATG5 gene is responsible for the formation of new autophagosomes, and the LC3 gene generally helps to recognise and target certain proteins for degradation [35]. Lysosomes become less efficient at degradation due to enzyme dysfunction and altered membrane configuration [36]. As a result, damaged mitochondria aren't cleared, leading to an increase in the production of excess ROS. As explained earlier, ROS accumulation is known to increase signs of ageing. This increase in ROS significantly contributes to chronic inflammation and neurodegeneration. When excess ROS is around, proteins are highly prone to oxidative damage due to the high reactivity of specific amino acid side chains, like cysteine, methionine, and tyrosine [37]. As mentioned above, ROS can cause structural changes. These changes can include inclusion of carbon monoxide into an organic compound, such as an alcohol or an alkene and side chain oxidation [38]. These specific alterations are what disrupt regular protein folding by weakening secondary and tertiary structures. As a result, oxidized proteins may misfold, exposing hydrophobic domains that are normally buried within the protein. This exposure increases the likelihood of non-specific aggregation, forming insoluble protein clumps. These clumps are toxic, interfering with organelle function and intracellular signalling. Hence, the pathways becoming dysfunctional can significantly contribute to the entire ageing process. A study published in Nature Communications demonstrated that 35% of the ubiquitylation changes observed in the aged mouse brain can be linked to reduced proteasome activity. This proves that a major portion of age-related changes is due to UPS dysfunction [39].

III. Glycation: Moreover, glycation plays a major role in protein degradation. Glycation is a spontaneous, non-enzymatic chemical reaction that occurs when reducing sugars, such as glucose, react with free amino groups of proteins [40]. The process starts with the formation of a Schiff base (a reversible imine linkage), which rearranges into a more stable structure known as an Amadori product [41]. Over time, and specifically due to oxidative conditions, these intermediates undergo further complex conformations and oxidations to create a group of irreversible compounds known as advanced glycation end products (AGEs) [42]. This process cannot be controlled and progresses with age. Glycation alters protein structure and function via the creation of covalent cross-links between amino acid residues on the same or different protein molecules, a process fuelled by reactive carbonyl groups present in AGEs [43]. Such cross-linking alters the original conformation of proteins, which is crucial for maintaining their biological function.

This disruption impairs the protein's ability to fold properly into its functional three-dimensional shape. Therefore, glycation too is a severe root of ageing, portraying that the accumulation of altered proteins acts as a triggering source of the ageing process.

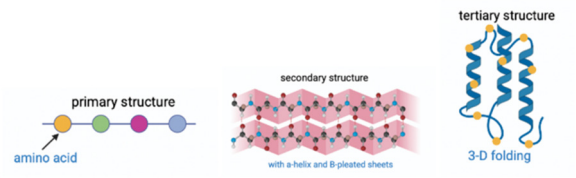

Fig. 3 Schematic of the primary, secondary and tertiary structures. A cartoon representing the unique structures involved in protein synthesis. Figure created with Biorender.com.

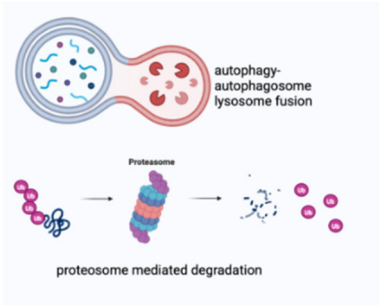

Fig. 4 Schematic of the autophagy-lysosome pathway. A cartoon representing the damaged cellular proteins taken into the autophagosome and then transferred to the lysosome, where it is broken down. Figure created with Biorender.com.

III. METHODS TO SLOW DOWN AGEING

Several treatments can slow down the ageing process. These include activating the enzyme telomerase, increasing the levels of antioxidants, and activating certain proteasome mechanisms. Telomerase, an enzyme discovered by Carol W. Grieder, extends telomere length and prevents shortening by adding G-rich bases over time [44]. Thus, telomerase helps restore telomere length and prevents their progressive shortening. Telomerase is a ribonucleoprotein complex consisting of telomerase reverse transcriptase (TERT) and telomerase RNA component (TERC), both of which are essential for extending telomere length [45]. The telomerase complex utilizes TERC and TERT to synthesize DNA, thereby extending telomeres through reverse transcription [46]. If the sequence of RNA is 'AAUCCC', telomerase can synthesize the complementary DNA sequence 'TTAGGG'. These add more of these sequences to restore the telomere length. Since telomerase prevents telomeres from shortening, cells continue to grow and divide, rather than dying, slowing down the ageing process. Upon reaching the Hayflick limit, cells either enter a state of senescence or, if reactivated, restore telomere length through telomerase. However, reactivating telomerase carries a significant risk of developing mutations, which can lead to uncontrolled cell growth and an increased risk of cancer [47]. Telomerase allows cells to bypass their stage of senescence, enabling them to divide uncontrollably, forming tumours. Even with this risk, a study by Stanford University researchers in 2015 showed that human cells with artificially extended telomeres showed reversed signs of ageing [48]. Furthermore, increased antioxidant consumption can significantly contribute to slowing ageing. Vitamins such as C, E, and selenium act as potent antioxidants, which are also associated with longer telomeres, thereby contributing to a slower ageing process [49]. Antioxidants protect proteins and nucleic acids from oxidation. They donate electrons to ROS, helping ROS to get stabilised, preventing them from damaging cells and conserving mitochondrial function. Via this, they also reduce inflammation, helping cells maintain their normal structure and function. Additionally, activating proteasome mechanisms clears the accumulation of damaged/misfolded proteins. Reinforcing UPS pathways through fasting, caloric restriction, or external compounds or drugs like rapamycin, metformin, and resveratrol can reinstate protein balance by activating autophagy systems and improving cellular cleanup [50]. Certain drugs can have side effects, too, which is why caloric restrictions are a safer means to enhance UPS pathways. They obstruct mTOR, a protein that generally represses autophagy, and activate energy sensors like AMPK and SIRT1, which enhance cellular cleanup [51]. This helps clean out misfolded proteins, decreases cellular stress levels, and therefore, slows ageing.

IV. CONCLUSIONS

Ageing results from fundamental processes like telomere shortening, oxidative stress, and altered protein accumulation. While these changes are

natural, interventions like telomerase activation, increased antioxidant intake, and strengthened protein clearance pathways through caloric restriction can mitigate their effects. Scientific work in the future should focus on these mechanisms to create effective anti-ageing therapies. Meanwhile, individuals can support healthy aging by having a diet rich in nutrients and antioxidants and leading an active lifestyle, bridging science and regular habits for an improved quality of life.

REFERENCES

[1] Tenchov, Rumiana , et al. "Aging Hallmarks and Progression and Age-Related Diseases: A Landscape View of Research Advancement." ACS Chemical Neuroscience, vol. 15, no. 1, 14 Dec. 2023, https://doi.org/10.1021/acschemneuro.3c00531

[2] World Health Organization. "Ageing and Health." World Health Organization, 1 Oct. 2024, www.who.int/news-room/fact-sheets/detail/ageing-and-health.

[3] World Health Organization. "Ageing and Health." World Health Organization, 1 Oct. 2024, www.who.int/news-room/fact-sheets/detail/ageing-and-health.

[4] Gilbert, Scott F. "Aging: The Biology of Senescence." Nih.gov, Sinauer Associates, 2000, www.ncbi.nlm.nih.gov/books/NBK10041/.

[5] Kaučič, Boris Miha, et al. Ageing - a Problem or a Challenge for Modern Society. 1 Nov. 2016, www.researchgate.net/publication/323882332_Ageing_-_a_problem_or_a_challenge_for_modern_society.

[6] Palo, Nishit, et al. "Effects of Osteoarthritis on Quality of Life in Elderly Population of Bhubaneswar, India." Geriatric Orthopaedic Surgery & Rehabilitation, vol. 6, no. 4, 24 Sept. 2015, pp. 269–275, https://doi.org/10.1177/2151458515604357.

[7] Kaučič, Boris Miha, et al. Ageing - a Problem or a Challenge for Modern Society. 1 Nov. 2016, www.researchgate.net/publication/323882332_Ageing_-_a_problem_or_a_challenge_for_modern_society.

[8] Banos, Oresti, et al. "Daily Living Activity Recognition Based on Statistical Feature Quality Group Selection." Expert Systems with Applications, vol. 39, no. 9, July 2012, pp. 8013–8021, https://doi.org/10.1016/j.eswa.2012.01.164. Accessed 13 Dec. 2019.

[9] Borji, H.S. "4 Global Economic Issues of an Aging Population." Investopedia, 11 Dec. 2023, www.investopedia.com/articles/investing/011216/4-global-economic-issues-aging-population.asp.

[10] "Telomeres: Definition, Structure, Shortening and Role in Ageing." BYJUS, byjus.com/neet/telomeres/.

[11] National Human Genome Research Institute. "Telomere." Genome.gov, 9 May 2024, www.genome.gov/genetics-glossary/Telomere.

[12] Ohki, R., et al. "In Vitro Reconstitution of the End Replication Problem." Molecular and Cellular Biology, vol. 21, no. 17, 1 Sept. 2001, pp. 5753–5766, www.ncbi.nlm.nih.gov/pmc/articles/PMC87295/, https://doi.org/10.1128/mcb.21.17.5753-5766.2001.

[13] Cooper, Geoffrey M. "DNA Replication." Nih.gov, Sinauer Associates, 2016, www.ncbi.nlm.nih.gov/books/NBK9940/.

[14] Watts, Geoff. "Leonard Hayflick and the Limits of Ageing." The Lancet, vol. 377, no. 9783, June 2011, p. 2075, https://doi.org/10.1016/s0140-6736(11)60908-2. Accessed 28 Dec. 2019.

[15] "Hayflick Limit." Drishti IAS, 2025, www.drishtiias.com/daily-updates/daily-news-analysis/hayflick-limit. Accessed 15 Apr. 2025.

[16] Orrenius, Sten, et al. "Cell Death Mechanisms and Their Implications in Toxicology." Toxicological Sciences, vol. 119, no. 1, 9 Sept. 2010, pp. 3–19, https://doi.org/10.1093/toxsci/kfq268.

[17] Dharmarajan, T. S. "Physiology of Aging." Geriatric Gastroenterology, 2021, pp. 101–153, https://doi.org/10.1007/978-3-030-30192-7_5.

[18] Huang, Xuanqi, et al. "The Relationship between Telomere Length and Aging-Related Diseases." Clinical and Experimental Medicine, vol. 25, no. 1, May 2025, p. 72, pubmed.ncbi.nlm.nih.gov/40044947/, https://doi.org/10.1007/s10238-025-01608-z.

[19] Barnes, Ryan P., et al. "The Impact of Oxidative DNA Damage and Stress on Telomere Homeostasis." Mechanisms of Ageing and Development, vol. 177, Jan. 2019, pp. 37–45, https://doi.org/10.1016/j.mad.2018.03.013.

[20] Birch-Machin, M.A., and A. Bowman. "Oxidative Stress and Ageing." British Journal of Dermatology, vol. 175, no. S2, 26 Sept. 2016, pp. 26–29, https://doi.org/10.1111/bjd.14906.

[21] Ahmad, Maria, et al. "Biochemistry, Electron Transport Chain." PubMed, StatPearls Publishing, 4 Sept. 2023, www.ncbi.nlm.nih.gov/books/NBK526105/.

[22] PMC, Europe. "Europe PMC." Europepmc.org, 26 Sept. 2018, europepmc.org/article/NBK/nbk526105.

[23] Lenaz, Giorgio. "Role of Mitochondria in Oxidative Stress and Ageing." Biochimica et Biophysica Acta (BBA) - Bioenergetics, vol. 1366, no. 1-2, Aug. 1998, pp. 53–67, https://doi.org/10.1016/s0005-2728(98)00120-0.

[24] National Cancer Institute. "NCI Dictionary of Cancer Terms." National Cancer Institute, Cancer.gov, www.cancer.gov/publications/dictionaries/cancer-terms/def/reactive-oxygen-species

[25] National Cancer Institute. "Https://Www.cancer.gov/Publications/Dictionaries/Cancer-Terms/Def/Antioxidant." Www.cancer.gov, 2 Feb. 2011, www.cancer.gov/publications/dictionaries/cancer-terms/def/antioxidant.

[26] Reichert, Sophie, and Antoine Stier. "Does Oxidative Stress Shorten Telomeres in Vivo ? A Review." Biology Letters, vol. 13, no. 12, Dec. 2017, p. 20170463, https://doi.org/10.1098/rsbl.2017.0463.

[27] HIPKISS, A. "Accumulation of Altered Proteins and Ageing: Causes and Effects☆." Experimental Gerontology, vol. 41, no. 5, May 2006, pp. 464 – 473, https://doi.org/10.1016/j.exger.2006.03.004. Accessed 30 Aug. 2020.

[28] "23.4C: Protein Structure." Medicine LibreTexts, 23 July 2018, med.libretexts.org/Bookshelves/Anatomy_and_Physiology/Anatomy_and_Physiology_(Boundless)/23%3A_Nutrition_and_Metabolism/23.4%3A_Proteins/23.4C%3A_Protein_Structure. Accessed 2 June 2025.

[29] Höhn, Annika, et al. "Proteostasis Failure in Neurodegenerative Diseases: Focus on Oxidative Stress." Oxidative Medicine and Cellular Longevity, vol. 2020, 27 Mar. 2020, pp. 1–21, https://doi.org/10.1155/2020/5497046.

[30] Deuerling, Elke, et al. "Chaperone Interactions at the Ribosome." Cold Spring Harbor Perspectives in Biology, vol. 11, no. 11, 1 Nov. 2019, pp. a033977–a033977, https://doi.org/10.1101/cshperspect.a033977.

[31] Wojcik, Cezary, and Mario Di Napoli. "Ubiquitin-Proteasome System and Proteasome Inhibition: New Strategies in Stroke Therapy." Stroke, vol. 35, no. 6, June 2004, pp. 1506–1518, https://doi.org/10.1161/01.str.0000126891.93919.4e.

[32] Wang, Shoubi, et al. "Autophagy Dysfunction, Cellular Senescence, and Abnormal Immune-Inflammatory Responses in AMD: From Mechanisms to Therapeutic Potential." Oxidative Medicine and Cellular Longevity, vol. 2019, 22 May 2019, pp. 1–13, https://doi.org/10.1155/2019/3632169. Accessed 9 Feb. 2022.

[33] Tanida, Isei, et al. "LC3 Conjugation System in Mammalian Autophagy." The International Journal of Biochemistry & Cell Biology, vol. 36, no. 12, Dec. 2004, pp. 2503–2518, https://doi.org/10.1016/j.biocel.2004.05.009.

[34] Wang, Mei, et al. "Bach2 Regulates Autophagy to Modulate UVA-Induced Photoaging in Skin Fibroblasts." Free Radical Biology & Medicine, vol. 169, 1 June 2021, pp. 304–316, https://doi.org/10.1016/j.freeradbiomed.2021.04.003. Accessed 23 Apr. 2024.

[35] Tanida, Isei, et al. "LC3 Conjugation System in Mammalian Autophagy." The International Journal of Biochemistry & Cell Biology, vol. 36, no. 12, Dec. 2004, pp. 2503–2518, https://doi.org/10.1016/j.biocel.2004.05.009.

[36] Trivedi, Purvi C., et al. "Lysosomal Biology and Function: Modern View of Cellular Debris Bin." Cells, vol. 9, no. 5, 4 May 2020, https://doi.org/10.3390/cells9051131.

[37] Davies, Michael J. "Methionine Oxidation Products as Biomarkers of Oxidative Damage to Proteins and Modulators of Cellular Metabolism and Toxicity." Redox Biochemistry and Chemistry, vol. 12, 5 May 2025,

p. 100052, www.sciencedirect.com/science/article/pii/S2773176625000057, https://doi.org/10.1016/j.rbc.2025.100052.
[38] Caito, S, et al. Toxicology of Metals. 15 Dec. 2014, https://doi.org/10.1016/b978-0-12-801238-3.00209-9.
[39] Marino, Antonio, et al. "Aging and Diet Alter the Protein Ubiquitylation Landscape in the Mouse Brain." Nature Communications, vol. 16, no. 1, 6 June 2025, www.nature.com/articles/s41467-025-60542-6, https://doi.org/10.1038/s41467-025-60542-6. Accessed 14 Sept. 2025.
[40] "Glycation - an Overview | ScienceDirect Topics." Www.sciencedirect.com, www.sciencedirect.com/topics/biochemistry-genetics-and-molecular-biology/glycation.
[41] "Amadori Rearrangement - an Overview | ScienceDirect Topics." www.sciencedirect.com,www.sciencedirect.com/topics/chemistry/amadori-rearrangement.
[42] Twarda-Clapa, Aleksandra, et al. "Advanced Glycation End-Products (AGEs): Formation, Chemistry, Classification, Receptors, and Diseases Related to AGEs." Cells, vol. 11, no. 8, 1 Jan. 2022, p. 1312, https://doi.org/10.3390/cells11081312.
[43] "Overview of Crosslinking and Protein Modification | Thermo Fisher Scientific - US." Thermofisher.com, 2025, www.thermofisher.com/in/en/home/life-science/protein-biology/protein-biology-learning-center/protein-biology-resource-library/pierce-protein-methods/overview-crosslinking-protein-modification.html. Accessed 2 June 2025.
[44] The Nobel Prize. "The Nobel Prize in Physiology or Medicine 2009." NobelPrize.org, 2009, www.nobelprize.org/prizes/medicine/2009/press-release/.
[45] Cong, Y.-S., et al. "Human Telomerase and Its Regulation." Microbiology and Molecular Biology Reviews, vol. 66, no. 3, 1 Sept. 2002, pp. 407–425, https://doi.org/10.1128/mmbr.66.3.407-425.2002.
[46] Autexier, Chantal, and Neal F. Lue. "The Structure and Function of Telomerase Reverse Transcriptase." Annual Review of Biochemistry, vol. 75, no. 1, June 2006, pp. 493–517, https://doi.org/10.1146/annurev.biochem.75.103004.142412.
[47] Boccardi, Virginia, and Luigi Marano. "Aging, Cancer, and Inflammation: The Telomerase Connection." International Journal of Molecular Sciences, vol. 25, no. 15, 5 Aug. 2024, pp. 8542–8542, www.mdpi.com/1422-0067/25/15/8542#:~:text=The%20relationship%20between%20inflammation%20and, https://doi.org/10.3390/ijms25158542.
[48] Conger, Krista. "Telomere Extension Turns Back Aging Clock in Cultured Human Cells, Study Finds." News Center, 22 Jan. 2015, med.stanford.edu/news/all-news/2015/01/telomere-extension-turns-back-aging-clock-in-cultured-cells.html
[49] Wright, W E, et al. "Normal Human Chromosomes Have Long G-Rich Telomeric Overhangs at One End." Genes & Development, vol. 11, no. 21, 1997, pp. 2801–9, www.ncbi.nlm.nih.gov/pmc/articles/PMC316649/, https://doi.org/10.1101/gad.11.21.2801.
[50] de Cabo, Rafael, et al. "The Search for Antiaging Interventions: From Elixirs to Fasting Regimens." Cell, vol. 157, no. 7, 19 June 2014, pp. 1515–1526, www.cell.com/cell/fulltext/S0092-8674(14)00679-5?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS0092867414006795%3Fshowall%3Dtrue,https://doi.org/10.1016/j.cell.2014.05.031.
[51] Sadria, Mehrshad, and Anita T. Layton. "Interactions among MTORC, AMPK and SIRT: A Computational Model for Cell Energy Balance and Metabolism." Cell Communication and Signaling, vol. 19, no. 1, 20 May 2021, https://doi.org/10.1186/s12964-021-00706-1. Accessed 8 Aug. 2022.

