Jurnal Eduhealth
Volume 16, Number 04 2025 DOI 10.54209/eduhealth.v16i04
ESSN 2808-4608 (Online)
https://ejournal.seaninstitute.or.id/index.php/healt

The Role of Mitochondria in Aging and Modern Anti-Aging Therapeutic Approaches

Teguh Tanuwidjaja
Master's Program in Skin Aging and Aesthetics, Faculty of Medicine, General Achmad Yani University

Article Info
Keywords:
Mitochondria,
Aging,
Oxidative
Stress,
Mitochondrial Biogenesis,
Anti-Aging Therapy

ABSTRACT
Aging is a complex biological process characterized by a progressive decline in cellular and tissue function, ultimately affecting homeostasis and the overall health of the organism. One of the main mechanisms involved in the aging process is mitochondrial dysfunction, the energy-producing organelles that also play a crucial role in regulating oxidative stress, apoptosis, and cellular metabolism. This study aims to analyze the role of mitochondria in the aging mechanism and review various modern anti-aging therapeutic approaches that focus on restoring mitochondrial function. The research method used was a literature review, reviewing the latest scientific literature on mitochondrial biology, cellular aging processes, and potential therapies such as the use of mitochondrial antioxidants. The results indicate that mitochondria play a crucial role in the aging process through oxidative stress and mitochondrial DNA (mtDNA) damage, which leads to decreased energy production and cellular dysfunction. When the number of free radicals increases and mitochondrial repair capacity decreases, cells become vulnerable to damage that triggers aging and degenerative diseases such as Alzheimer's and Parkinson's. Various modern therapeutic efforts have been shown to improve this condition, including the use of mitochondria-targeted antioxidants (MitoQ), mitochondrial biogenesis-stimulating compounds (methylene blue), and SIRT1 activation to enhance cell defense. Lifestyle approaches such as regular exercise and a healthy diet also support mitochondrial function, while mitochondrial transplantation in animal studies has shown promising results in improving energy and slowing aging.

Corresponding Author:
Teguh Tanuwidjaja
Master's Program in Skin Aging and Aesthetics, Faculty of Medicine, General Achmad Yani University
Teguh.tanuwidjaja@lecture.unjani.ac.id

INTRODUCTION

Aging is a natural biological process experienced by all living things, characterized by a gradual decline in physiological and cellular function over time, ultimately leading to death. This process is degenerative and unavoidable, with various internal and external factors contributing to accelerated tissue damage (Zalukhu et al., 2016). One of the main theories explaining the mechanism of aging is the free radical theory, which states that the accumulation of free radicals and oxidative stress in cells can cause damage to critical components such as DNA, proteins, and membrane lipids. This oxidative damage disrupts

Jurnal Eduhealth
Volume 16, Number 04 2025 DOI 10.54209/eduhealth.v16i04
ESSN 2808-4608 (Online)
https://ejournal.seaninstitute.or.id/index.php/healt

normal cell function and accelerates cell death, thus triggering the systemic aging process (Yuslianti, 2018).

Oxidative damage to mitochondria is considered a major factor determining the aging process, as mitochondria play a central role in maintaining energy balance and cellular stability (Layal, 2016). Mitochondria not only function as centers for energy production in the form of ATP, but also as important regulators of apoptosis, metabolism, and the response to oxidative stress. When mitochondria are damaged due to the accumulation of free radicals, their production efficiency decreases, producing more reactive oxygen species (ROS), which exacerbate cellular damage. This condition creates a vicious cycle that accelerates the degradation of cells and body tissues (Utami, 2009).

The view that mitochondria act as a "biological clock" that regulates longevity is further strengthened by various scientific findings demonstrating a close relationship between mitochondrial health and the body's resistance to aging (Situmorang & Zulham, 2020). Optimally functioning mitochondria maintain the efficiency of cellular energy production through oxidative phosphorylation, while suppressing the formation of excess free radicals that can damage cellular structures. Furthermore, mitochondria play a role in regulating calcium homeostasis, apoptosis signaling, and new cell biogenesis, all of which contribute to tissue rejuvenation (Isrul et al., 2025). Conversely, mitochondrial dysfunction leads to decreased cellular energy capacity, increased oxidative stress, and the accumulation of mitochondrial DNA mutations, which accelerate the aging process. This condition not only reduces cell vitality but is also a major trigger for the development of various age-related degenerative diseases, such as Alzheimer's, Parkinson's, type 2 diabetes, and other metabolic disorders (Fijri et al., 2022).

In the context of modern research on anti-aging therapies, various scientific approaches now focus on restoring and enhancing mitochondrial function as a primary strategy to slow the aging process (Sari et al., 2019). One widely studied approach is the use of mitochondria-specific antioxidants, such as MitoQ and SkQ1, which can penetrate the mitochondrial membrane and directly neutralize free radicals at their source of formation. Furthermore, activation of the mitochondrial biogenesis pathway, particularly through increased expression of PGC-1α (Peroxisome Proliferator-Activated Receptor Gamma Coactivator 1-alpha), is a key focus because it plays a role in the formation of new, more efficient mitochondria (Sayuti & Yenrina, 2019). NAD^+ (Nicotinamide Adenine Dinucleotide)-based therapies also show great potential, given that this molecule functions as a crucial cofactor in redox reactions and the activation of sirtuins, enzymes that play a role in extending cell lifespan and protecting DNA from oxidative damage (Irianti & Pramono, 2022).

In addition to pharmacological interventions, non-pharmacological approaches such as calorie restriction, regular exercise, and the consumption of natural compounds like resveratrol and coenzyme Q10 have also been shown to increase mitochondrial efficiency and reduce oxidative stress (Saras, 2023). These approaches emphasize the importance of maintaining a balance between energy production and free radical control to maintain optimal cell function. With the growing understanding of the role of mitochondria in aging, research in

Jurnal Eduhealth
Volume 16, Number 04 2025 DOI 10.54209/eduhealth.v16i04
ESSN 2808-4608 (Online)
https://ejournal.seaninstitute.or.id/index.php/healt

modern anti-aging therapies aims not only to extend lifespan but also to improve quality of life by extending healthspan (Kaeberlein, 2018).

Several previous studies have shown that mitochondrial dysfunction plays a significant role in the aging process. Balaban, Nemoto, and Finkel (2005) explained that decreased efficiency of the electron transport chain in mitochondria increases the production of reactive oxygen species (ROS), which accelerates cell and tissue damage. This research is supported by Lopez-Otín et al. (2013), who identified mitochondrial dysfunction as one of the primary biological hallmarks of aging, confirming that decreased mitochondrial function directly contributes to the body's degenerative processes. Furthermore, Gomes et al. (2013) found that decreased NAD^+ levels during aging disrupt communication between the nucleus and mitochondria, thus accelerating cellular damage. Based on these findings, it is clear that mitochondrial function is closely linked to the mechanisms of aging, making further research into modern therapeutic strategies targeting the restoration and enhancement of mitochondrial function highly relevant.

Although various previous studies have confirmed the crucial role of mitochondria in the aging process, most studies have focused on mechanistic or biochemical aspects without integrating these findings with more applicable modern anti-aging therapeutic approaches. Therefore, there remains a research gap regarding the integration of understanding mitochondrial biology with the application of modern anti-aging therapies such as mitochondrial antioxidants, mitochondrial biogenesis activators, and NAD^+-based therapies that can support longevity and optimal cellular health.

This study aims to comprehensively analyze the role of mitochondria in the aging process and examine various modern anti-aging therapeutic approaches that focus on restoring and enhancing mitochondrial function. Furthermore, this study aims to identify the potential and challenges of implementing mitochondria-based therapies in slowing the aging process and preventing age-related degenerative diseases. Theoretically, this research is expected to enrich the scientific literature on the relationship between mitochondrial function and aging and provide a scientific basis for the development of more effective and sustainable anti-aging therapies. Practically, the results of this study can serve as a reference for researchers, medical professionals, and the healthcare industry in designing intervention strategies that target mitochondria to slow aging and improve human quality of life. Furthermore, this research can provide insight to the public regarding the importance of maintaining mitochondrial health through lifestyle and therapies that support energy balance and cellular protection.

METHOD

This study employed a library research method with a descriptive qualitative approach (Sugiyono, 2012). The data used were derived from secondary sources, including scientific journals, books, research reports, and academic articles discussing the role of mitochondria in the aging process and the development of modern anti-aging therapies. Literature selection was conducted purposively, selecting sources that were relevant, up-to-date (over the last five to ten years), and possessed high scientific credibility. The collected data were analyzed

Jurnal Eduhealth
Volume 16, Number 04 2025 DOI 10.54209/eduhealth.v16i04
ESSN 2808-4608 (Online)
https://ejournal.seaninstitute.or.id/index.php/healt

in depth to identify patterns, relationships, and conceptual developments regarding mitochondrial function and therapeutic interventions targeting them.

Data analysis was conducted using content analysis techniques, which aim to systematically interpret scientific information to gain a comprehensive understanding of the biological mechanisms of aging involving mitochondria. Each finding was compared across sources to assess its consistency and validity, then synthesized into thematic conclusions regarding the contribution of mitochondria to aging and the potential of modern anti-aging therapies. This approach enabled researchers to formulate an integrative conceptual framework, illustrating the interrelationships between theory, empirical results, and future research directions.

RESULT AND DISCUSSION

The Role of Mitochondria in the Human Aging Process

Mitochondria, known as the "powerhouses of the cell," generate most of the cellular energy in the form of ATP through oxidative phosphorylation. Their role in aging is complex:

1. Mitochondrial Free Radical Theory

The mitochondrial free radical theory is one of the most influential theories in explaining the biological mechanisms of aging. This theory was first proposed by Denham Harman in 1956, stating that free radicals—specifically reactive oxygen species (ROS)—play a critical role in accelerating the aging process through oxidative damage to cellular components (Astuti et al., 2023). Mitochondria, as the primary energy-producing organelles in cells, are the primary source of ROS formation during oxidative phosphorylation in the electron transport chain. Under normal physiological conditions, the body possesses endogenous antioxidant defense systems such as superoxide dismutase (SOD), glutathione peroxidase (GPx), and catalase, which function to neutralize these free radicals. However, with age, the ability of this system declines, while ROS production increases, leading to an imbalance between the formation and elimination of free radicals, known as oxidative stress.

Oxidative damage resulting from ROS accumulation can affect various important macromolecules in cells, such as lipids, proteins, and nucleic acids, including mitochondrial DNA (mtDNA). Unlike nuclear DNA, mtDNA has less protection because it lacks protective histones and is located very close to the site of ROS formation in the inner mitochondrial membrane. As a result, mtDNA is more susceptible to mutations and oxidative damage. Mutations in mtDNA can disrupt the synthesis of proteins necessary for the electron transport chain, ultimately reducing the efficiency of ATP production. This condition not only accelerates cellular decline but also creates a vicious cycle, as damaged mitochondria produce more ROS, further exacerbating cellular damage.

In the context of aging, this theory explains that the accumulation of oxidative damage in mitochondria is a key factor determining longevity and the quality of tissue function. Numerous modern studies support this theory by showing that increased oxidative stress is correlated with accelerated aging and the onset of degenerative diseases such as Alzheimer's, Parkinson's, and cardiovascular disease. Therefore, modern anti-aging therapeutic strategies now focus heavily on controlling oxidative stress by increasing

Jurnal Eduhealth
Volume 16, Number 04 2025 DOI 10.54209/eduhealth.v16i04
ESSN 2808-4608 (Online)
https://ejournal.seaninstitute.or.id/index.php/healt

antioxidant activity, protecting mtDNA, and stimulating mitochondrial biogenesis. These efforts are expected to maintain optimal mitochondrial function, slow the aging process, and increase an individual's healthspan.

2. Accumulation of mtDNA Damage

The accumulation of damage to mitochondrial DNA (mtDNA) is a key mechanism contributing to the aging process and the decline in cellular function. Mitochondria have their own relatively small genome, yet they are vital because they encode some of the proteins essential for the electron transport chain, the primary process for generating energy in the form of adenosine triphosphate (ATP). Unlike nuclear DNA, mtDNA is not protected by histones and is located very close to the site of reactive oxygen species (ROS) formation in the inner mitochondrial membrane. This condition makes mtDNA highly susceptible to oxidative damage, including point mutations, deletions, and structural changes that can disrupt the stability of the mitochondrial genome.

Damage or mutations in mtDNA can directly impact the function of the electron transport chain, ultimately reducing the efficiency of energy production in cells. This decreased efficiency not only reduces the cell's capacity to maintain normal physiological functions but also increases electron leakage in mitochondria, which generates more ROS. This phenomenon creates a vicious cycle of mitochondrial dysfunction, where mtDNA damage leads to increased ROS production, and increased ROS further exacerbates mtDNA damage. As a result, cells experience chronic oxidative stress, metabolic disorders, and ultimately decreased viability, leading to cellular senescence or apoptosis.

3. Regulation of Apoptosis (Programmed Cell Death)

Mitochondria play a crucial role as the primary regulators of apoptosis, or programmed cell death, the body's natural mechanism for eliminating damaged or no longer functioning optimally. Under normal conditions, mitochondria maintain a balance between pro-apoptotic and anti-apoptotic signals to maintain tissue homeostasis. However, when mitochondrial dysfunction occurs due to oxidative stress, DNA damage, or metabolic disorders, mitochondrial membrane permeability can increase, leading to the release of pro-apoptotic proteins such as cytochrome c, Smac/DIABLO, and AIF (Apoptosis-Inducing Factor) into the cytoplasm. The released cytochrome c then interacts with the proteins Apaf-1 and procaspase-9 to form the apoptosome complex, which then activates the caspase enzyme cascade, triggering the programmed degradation of cellular components. This process is a natural defense mechanism to prevent the proliferation of damaged cells, but if excessive, it can accelerate the loss of functional cells in the tissue.

In the context of aging, unbalanced apoptosis regulation is one factor accelerating tissue degeneration. Accumulated oxidative stress and decreased mitochondrial capacity lead to excessive activation of the apoptosis pathway, particularly in tissues with high metabolic rates such as muscle, heart, and the nervous system. Consequently, the number of healthy cells capable of maintaining normal physiological functions decreases, accelerating the aging process and leading to the development of various degenerative diseases such as Alzheimer's, Parkinson's, and cardiomyopathy. Therefore, maintaining stable mitochondrial function and properly regulating apoptosis is a key focus of modern anti-aging therapy

Jurnal Eduhealth
Volume 16, Number 04 2025 DOI 10.54209/eduhealth.v16i04
ESSN 2808-4608 (Online)
https://ejournal.seaninstitute.or.id/index.php/healt

research. Therapeutic approaches such as the use of mitochondrial antioxidant compounds, increasing the expression of anti-apoptotic proteins (such as Bcl-2), and stimulating mitochondrial biogenesis are potential strategies to prevent excessive cell death and extend healthy lifespan at both the cellular and systemic levels.

4. Signaling Pathway Disruption

Mitochondrial dysfunction not only impacts energy production but also disrupts various intracellular signaling pathways that play a crucial role in regulating metabolism, growth, and cell repair. Mitochondria serve as the integration center for metabolic signals, communicating with the nucleus and other organelles to maintain energy balance and cellular homeostasis. When mitochondrial function is impaired, various signaling pathways such as AMPK (AMP-activated protein kinase), mTOR (mechanistic target of rapamycin), and SIRT (sirtuins) become imbalanced. The AMPK pathway, which detects the cell's energy status, loses its optimal ability to stimulate mitochondrial biogenesis and maintain energy balance. Meanwhile, hyperactivation of the mTOR pathway due to oxidative stress can accelerate aging by inhibiting autophagy, which is essential for the removal of damaged cell components.

Furthermore, impaired communication between mitochondria and the nucleus leads to changes in the expression of genes that regulate protein synthesis, DNA repair, and stress responses. Decreased activity of sirtuins, particularly SIRT1 and SIRT3, which are dependent on NAD^+ levels, further exacerbates this condition by reducing the cell's ability to adapt to metabolic and oxidative stress. As a result, cells lose efficiency in carrying out vital functions such as damage repair, tissue regeneration, and controlling inflammation. In the context of aging, disruption of these signaling pathways accelerates physiological decline and increases the risk of age-related chronic diseases. Therefore, modern anti-aging strategies are largely directed at restoring cellular signal balance through enhancing mitochondrial function, activating AMPK and sirtuin, and inhibiting mTOR so that the aging process can be slowed down and cellular function remains optimal.

Modern Anti-Aging Therapy Approaches to Slow the Aging Process

Modern anti-aging therapies target mitochondria to increase efficiency and reduce age-related damage.

Pharmacological Interventions

1. Mitochondrial-Targeted Antioxidants

Mitochondrial-targeted antioxidants are a key innovation in modern anti-aging therapies designed to neutralize free radicals directly at their source of formation, within the mitochondria. One of the best-known examples is MitoQ, a derivative of ubiquinone (coenzyme Q10) modified to more efficiently penetrate mitochondrial membranes by adding a lipophilic cationic triphenylphosphonium (TPP^+) group. This design allows MitoQ to selectively accumulate within mitochondria and effectively reduce reactive oxygen species (ROS) generated during oxidative phosphorylation. By neutralizing ROS at the mitochondrial level, MitoQ helps protect mitochondrial membrane lipids, proteins, and DNA from oxidative damage that can accelerate cellular aging. Furthermore, research shows that the use of mitochondria-targeted antioxidants can enhance cellular respiratory function, reduce

Jurnal Eduhealth
Volume 16, Number 04 2025 DOI 10.54209/eduhealth.v16i04
ESSN 2808-4608 (Online)
https://ejournal.seaninstitute.or.id/index.php/healt

inflammation, and improve energy efficiency, potentially slowing the aging process and reducing the risk of age-related degenerative diseases.

2. Enhancing Mitochondrial Biogenesis

Enhancing mitochondrial biogenesis is an important strategy in anti-aging therapy, aiming to renew and replace damaged mitochondria with new, healthier, and more efficient ones. This process involves activating a molecular pathway controlled by PGC-1α (Peroxisome Proliferator-Activated Receptor Gamma Coactivator 1-alpha), a key regulator of mitochondrial formation and function. One compound known to stimulate this process is methylene blue, which works by increasing the activity of enzymes in the electron transport chain and reducing free radical production, thus supporting a cellular environment conducive to mitochondrial regeneration. By increasing mitochondrial biogenesis, cells can maintain optimal energy production, improve redox balance, and increase resistance to oxidative stress. This approach not only helps slow cellular aging but also strengthens the function of age-related degeneration of tissues and organs, making it a key focus in the development of mitochondria-based anti-aging therapies.

3. Signaling Pathway Modulation

Modifying cellular signaling pathways is an important therapeutic approach to slowing aging, particularly by targeting proteins involved in metabolic regulation and cellular protection, such as sirtuin 1 (SIRT1). SIRT1 is an NAD^+-dependent deacetylase enzyme that regulates the expression of genes involved in DNA repair, energy metabolism, and the response to oxidative stress. SIRT1 activation has been shown to increase cellular resistance to oxidative damage by strengthening endogenous antioxidant defense mechanisms and suppressing excessive inflammatory pathways. In the context of age-related neurodegeneration, SIRT1 modulation can protect neurons from oxidative stress and apoptosis by stabilizing mitochondrial function and reducing the accumulation of toxic proteins characteristic of diseases such as Alzheimer's and Parkinson's. Natural compounds such as resveratrol and Nicotinamide Riboside (NR) are known to activate SIRT1, making them potential targets in modern anti-aging therapies that focus not only on extending lifespan, but also on maintaining optimal brain and nervous system function in old age.

Non-Pharmacological Interventions

1. Regular Exercise

Regular exercise is a natural and effective way to improve mitochondrial health and function. Consistent physical activity, particularly aerobic exercise such as running, cycling, or swimming, can stimulate mitochondrial biogenesis, the process by which new mitochondria are formed within cells. This increase in mitochondrial number and efficiency occurs through the activation of the AMPK (AMP-activated protein kinase) and PGC-1α pathways, which play a critical role in regulating energy metabolism and cellular adaptation to increased energy demands. Furthermore, exercise helps reduce oxidative stress by increasing endogenous antioxidant capacity, maintaining redox balance, and enhancing cells' ability to utilize oxygen efficiently. Thus, exercise not only contributes to increased stamina and fitness but also plays a significant role in slowing the cellular aging process and reducing the risk of age-related degenerative diseases.

Jurnal Eduhealth
Volume 16, Number 04 2025 DOI 10.54209/eduhealth.v16i04
ESSN 2808-4608 (Online)
https://ejournal.seaninstitute.or.id/index.php/healt

2. Dietary Interventions

Dietary interventions also play a crucial role in maintaining and improving mitochondrial function. A balanced diet rich in antioxidants, omega-3 fatty acids, and bioactive compounds like polyphenols (e.g., from green tea, berries, or red wine) can help protect mitochondria from oxidative damage. Furthermore, dietary strategies such as caloric restriction and intermittent fasting have been shown to activate molecular pathways such as SIRT1 and AMPK, which play a role in increasing the efficiency of energy metabolism, stimulating mitochondrial biogenesis, and reducing the accumulation of free radicals. This approach not only helps extend cell lifespan but also improves overall metabolic health, making it an integral part of mitochondria-based anti-aging strategies in modern lifestyles.

Innovative Therapy

Mitochondrial transplantation is one of the most promising breakthroughs in modern regenerative and anti-aging therapies. This approach is based on the concept of transferring healthy, optimally functioning mitochondria from young tissues or cells to tissues that have experienced aging or damage due to oxidative stress. This procedure aims to restore the cell's bioenergetic function by replacing damaged mitochondria, thereby increasing ATP production, reducing free radical levels, and stabilizing cellular homeostasis. Experimental studies in animals, particularly in aging mice, have shown very positive results—transplantation of young mitochondria can improve muscle function, enhance cognitive activity, and slow the physiological signs of aging. Furthermore, significant improvements in mitochondrial function are accompanied by reduced inflammation and increased tissue regenerative capacity. While this research is still in its early stages and requires further clinical trials to confirm its safety and effectiveness in humans, the concept of mitochondrial transplantation opens up new prospects for the development of cell-based anti-aging therapies that have the potential to revolutionize the way we treat aging and age-related degenerative diseases.

CONCLUSION

Aging is a natural process that occurs over time and involves a gradual decline in cellular function. One key factor in this process is the mitochondria, which play a crucial role in energy production and maintaining the body's metabolic balance. When mitochondria are damaged by oxidative stress and the accumulation of mitochondrial DNA (mtDNA) mutations, energy production declines and the number of free radicals increases, creating a cycle that accelerates cellular aging and triggers various degenerative diseases such as Alzheimer's, Parkinson's, and metabolic disorders. Therefore, mitochondrial health is a key determinant of longevity and quality of life. Various modern therapeutic approaches have been developed to maintain and restore mitochondrial function. Mitochondria-targeted antioxidants such as MitoQ can neutralize free radicals directly at the source, while compounds like methylene blue can stimulate the formation of new, healthier mitochondria. Furthermore, activation of the SIRT1 protein has been shown to protect cells from oxidative stress and improve neuronal function, while regular exercise and a healthy diet play a significant role in increasing energy efficiency and slowing the natural aging process. Recent innovations such as mitochondrial

transplantation have also shown great potential in repairing aging tissues by transferring healthy mitochondria from younger tissues. Animal studies have demonstrated improved energy function and improved age-related behaviors following this intervention. Overall, maintaining mitochondrial function through a combination of molecular therapy, a healthy lifestyle, and biotechnology innovation is an important step towards healthy aging and improving the quality of life in old age.

REFERENCES

Astuti, R., Umboh, M. J., Pradana, A. A., Silaswati, S., Susanti, F., Resna, R. W., ... & Rekawati, E. (2023). *Keperawatan Gerontik*. PT. Sonpedia Publishing Indonesia.

Balaban, R. S., Nemoto, S., & Finkel, T. (2005). Mitochondria, oxidants, and aging. *cell*, *120*(4), 483-495.

Fijri, S., Gustia, E., Dewi, O. T., & Marianti, L. (2022). Indonesia Penyakit Degeneratif Pada Lansia: Pencegahan Dan Penanganannya: Degenerative Diseases in the Elderly: Prevention and Treatment. *CONS-IEDU*, *2*(2), 99-117.

Gomes, A. P., Price, N. L., Ling, A. J., Moslehi, J. J., Montgomery, M. K., Rajman, L., ... & Sinclair, D. A. (2013). Declining NAD+ induces a pseudohypoxic state disrupting nuclear-mitochondrial communication during aging. *Cell*, *155*(7), 1624-1638.

Irianti, T. T., & Pramono, S. (2022). *Penuaan dan pencegahannya: Proses faali biokimiawi dan molekuler*. Ugm Press.

Isrul, M., Adnan, A., & Islamia, M. N. (2025). Eksplorasi Berbagai Fungsi Mitokondria Melalui Pendekatan Meta-Analisis dalam Biologi Seluler. *Spizaetus: Jurnal Biologi dan Pendidikan Biologi*, *6*(2), 301-311.

Kaeberlein, M. (2018). How healthy is the healthspan concept?. *Geroscience*, *40*(4), 361-364.

Layal, K. (2016). Peran Nrf2 dalam patogenesis stres oksidatif dan inflamasi pada penyakit ginjal kronik. *Syifa'MEDIKA: Jurnal Kedokteran dan Kesehatan*, *7*(1), 16-24.

López-Otín, C., Blasco, M. A., Partridge, L., Serrano, M., & Kroemer, G. (2013). The hallmarks of aging. *Cell*, *153*(6), 1194-1217.

Maretha, D. E. (2019, August). Biogenesis Mitokondria. In *Conferences of Medical Sciences Dies Natalis Faculty of Medicine Universitas Sriwijaya* (Vol. 1, No. 1, pp. 292-302).

Saras, T. (2023). *Antioksidan: keajaiban molekul pelindung tubuh*. Tiram Media.

Sari, W. P., Gaya, M. L., Irianto, G., & Karima, N. (2019). Managemen Topikal Anti-Aging pada Kulit. *Medical Profession Journal of Lampung*, *9*(2), 228-234.

Sayuti, I. K., & Yenrina, I. R. (2015). Antioksidan. *APPTI, Padang*.

Situmorang, N., & Zulham, Z. (2020). Malondialdehyde (mda)(zat oksidan yang mempercepat proses penuaan). *Jurnal Keperawatan Dan Fisioterapi (JKF)*, *2*(2), 117-123.

Sugiyono, P. D. (2012). Metode Penelitian Tindakan (Pendekatan Kuantitatif, Kualitatif, dan R&D). *Bandung: Remaja Rosdakarya*.

Utami, S. (2009). Etiologi infertilitas pada pria akibat dari mutasi DNA mitokondria (mtDNA). *Maranatha Journal of Medicine and Health*, *9*(1), 150489.

Yuslianti, E. R. (2018). *Pengantar radikal bebas dan antioksidan*. Deepublish.