Acta Scientific Biotechnology

Volume 4 Issue 3 April 2023

Review Article

Recent Developmental Strategies Targeting Aging: An Integrative Approach Towards Aging Disorders and its Treatment

Ayushi Poddar[1,2], Surya Kumar Ekka[1,2], Annie Jessica Toppo[1], Anupriya[1,2], Apeksha Sharma[1,2], Nisha Rani Soreng[2], Aditi Kumari[1,4], Priyangulta Beck[1], Dinesh Kumar[1], Rupa Verma[3] and Mukesh Nitin[1]*

[1]Department of Tech. Biosciences, Digianalix, Tharpakhna, Ranchi, Jharkhand, India

[2]Department of Biotechnology, Gossner College, Ranchi, Jharkhand, India

[3]Department of Botany, Ranchi University, Ranchi, Jharkhand, India

[4]Department of Biotechnology, Marwari College, Ranchi, Jharkhand, India

***Corresponding Author:** Mukesh Nitin, Department of Tech. Biosciences, Digianalix, Tharpakhna, Ranchi, Jharkhand, India.

Received: February 28, 2023

Published: March 14, 2023

Abstract

In the process of ageing numerous genes and their related metabolic pithy are involved in deterioration of cells, tissues and organs. The ageing process of plants are different from animals but they develop various counter actions against ageing and its consequences. In this review, we try to highlight those mechanism which has ability to combat symptoms of ageing. Through these mechanisms or genes we could use them for human ageing process. For the re-evaluation of ageing process in cells and organs various complementary advanced techniques has various loop holes which is needed to rectify to get more precision for detection ageing process. Herein, through this review we can say that implementation of mechanism correlated with plant. So, in ageing of human this mechanisms could be employed as one of the remedy to slow down the process, along with cure the worst form of ageing caused due to glitch in gene regulation.

Keywords: Ageing; DNA Methylation; Senescence; Biosensors; Telomere

Abbreviations

HvS40: *Hordeum vugare* S40; AtS40: *Arabidopsis thaliana* S40; OsS40: *Oryza sativa* S40; SAG: Senescence Associated Genes; SEN: Senescence Enhanced Genes; RCCRC: Red Chlorophyll Catabolite Reductase; AtNAP: *Arabidopsis thaliana* apetala3/pistillata; TPL1: Terminal Flower 1; ROS: Reactive Oxygen Species; SA: Salicylic Acid; PRRs: Pattern Recognition Receptors; PAMPs: Pathogen Associated Molecular Patterns; MAMPs: Microbes Associated Molecular Patterns; PTI: Pattern Triggered Immunity; ETI: Effected Triggered Immunity; DNAm: DNA Methylation; CpGs: Cytosine Guanine Dinucleotides; DNMTs - DNA Methyltransferrases; GATA6: GATA Binding 6 Protein; daf-16: FOXO Famili Transcription Factor; TFs: Transcription Factors; RCS: Reactive Species Scavengers; HSP: Heat Shock Protein; p66shc: Splice Variant of p53 sch/p46 sch; IGF1: Insulin Like Growth Factor 2; ATP: Adenosine Triphosphate; AXP: An Acronym for ATP, ADP, AMP; NAD^{+}: Nicotinamine Adenine Dinucleotide; QTL: Quantitative Trait Locus; AtMGL: *A. thaliana* Methionine Gamma Lyase; AtRALFL8: *A. thaliana* Alkalization Factor Like 8; AZI1: Azelaic Acid Induced 1

Introduction

Ageing can be a boon and curse to society. It can be a threat or miracle in today's era. According to macro-trends, the life expectancy of humans in 2023 has been increased by 0.24% from 2022 and it goes upto 73.16years. There has been a gradual increase of 0.24% in longevity of the population since 2019 per year due to better medical facilities, results in decrease in the mortality rate. Humans can live for up to 100 years, however the nematode *Caenorhabditis elegans* ages and passes away in a matter of weeks indicating that over the course of evolution, mutations have expanded lifespan more than 2,000-fold, assuming that the ancestor we share with worms aged slowly. We are now seeing some wistful poetry and imaginative fiction after ages [1].

Ageing a biological process that develops as a result of the gathering of a wide range of molecular and cellular damage over time. The victims of a steady decline in their physical and mental abilities and rises the chance of contracting diseases and results dying [2]. The senescence of leaves is the most evident sign of ageing in plants [3]. A form of apoptosis that develops in plants is senescence, which is the final stage of leaf development [4]. Animal ageing is characterized by a deterioration in physiological activities across a range of tissues and organs, which increases the chances of mortality. Most human diseases, including cancer and heart ailments, are mostly caused by ageing [5].

There are several genes responsible for ageing in plants which are directly or indirectly affecting senescence. The HvS40 gene, found in barley species, represents the marker for senescence. It helps in expression during age-dependent and dark-induced senescence. Another gene found in *Arabidopsis*, AtS40-3 gene plays a similar role is natural senescence. The OsS40 gene, present in rice leaves, also showed identical activities in senescence [6]. Cell senescence is caused by gene LSC54, present in *Arabidopsis* cells, which was found to be associated with the oxidative stress levels in the cell. Genes that play a role in senescence of cells come under senescence associated genes (SAG) or senescence enhanced genes (SEN). Ageing caused by organ senescence includes genes that have the involvement in the plant cell senescence found to regulate a role in organ senescence. *Arabidopsis* RCCRC (Red chlorophyll Catabolite Reductase), functions in chlorophyll degradation, *Arabidopsis* AtNAP, functions in cell and tissue specialization, *Zea Bronze* 1, plays a role in vacuole function, TPL1 (terminal flower 1) regulates juvenile period in perennials [7]. Aging in animals is partly the same as the internal regulatory signaling of aging in plants. In plants and animals life span can be expanded on treatment with NAD^+. NAD^+ can help in enhancing defense mechanisms for virulent pathogens in the model plant *Arabidopsis* by increasing the production of reactive oxygen species (ROS). It can also boost mitochondrial and stem cell functions in mice model [8]. Salicylic acid (SA) is a very important hormone that helps in regulating various aspects of growth and development in plants as well as thermogenesis and disease resistance. Moreover SA and its derivative, Aspirin are widely known as pharmacological agents for humans. SA helps in treating warts, acne and psoriasis, while aspirin involves in treating fever, pain, swelling, inflammation and also reduces the risk of heart attack, stock and some cancers [9].

Plants and animals depend on biotic factors like pathogens and insects as well as some abiotic factors. Growth of pathogens and rapid risk of diseases are the main causes of aging [8].

Inspite of the fact that plants do not possess immune cells that are found in invertebrates, they contain an innate immune system that spots and restricts the growth of pathogens. One element of this system searches for molecules with distinctive patterns that are special and widely conserved in microbes using pattern recognition receptor (PRRs) on the plant cell surface. Detection of these pathogen associated molecular patterns (PAMPs) and microbes associated molecular patterns (MAMPs), leads to stimulation of pattern triggered immunity (PTI). In most of the cases PTI further restricts the growth of new pathogen colonies yet, a part of pathogen has evolved effected triggered immunity (ETI) which contains other elements of the innate immune system [9,10].

There are various detection techniques used in ageing. Predicting seed deteriorations in gene banks often involves estimation of seed viability, germination, vigor and integrity. Various techniques are available to access seed aging, the method involves direct visual inspections of seed, standard germination test and biochemical test and non destructive or non-invasive approaches [11]. Current methods for crop diseases are direct detection method and indirect detection method. Direct detection methods include polymerase chain reaction method, fluorescence in-situ hybridization, enzyme linked immunosorbent assay, immunofluorescence, flow cytometry. Indirect methods involves thermography, fluorescence Imaging, hyperspectral techniques, gas chromatography [12].

The most well-known epigenetic alteration, DNA methylation (DNAm) at cytosine guanine dinucleotides (CpGs), has the ability to suppress gene expression when linked to gene promoters. DNA methyltransferases (DNMTs) control the methylation of CpG in animals. DNMTs are necessary for the initial creation of DNA methylation patterns during early development and for maintaining established DNA methylation patterns throughout the animal's lifespan. Epigenetic drift and clock-type DNAm are the two types of age-associated DNA seen in vertebrates [13] (Figure 1).

Figure 1: Analytical Tools and Techniques Applied for the Analysis of Ageing and Its Impacts A) Microfluidics B) Biosensors C) Quantitative Trait Loci (QTL) D) DNA Methylation (DNAm) E) Bioinformatic Tools F) Genomic Tools.

In this article we will mainly discuss the ageing in plants and animals. The genes which cause ageing and the problems associated with ageing and how ageing can be slowed down in genetic level and longevity can be increased by different factors. We also highlighted few tools and techniques through which various ageing changes in the cellular and gene level can be detected, along with their shortcomings. By cross referring those loopholes we can develop the pathway to cure various age related disorders and ailments (Figure 2).

Figure 2: Pathway to study the genes combating ageing process in plants and implementing those genes through docking studies against age-related disorders.

Ageing in plants and animals

Ageing is an undeniable prospect of life and no one can escape it. It leads us under enormous area of research and brings intriguing subject to scientists. This leads us to the question about ageing and the factors that are responsible for ageing. Ageing affects all of the organisms and their efficiency to do work over a period of time. The ageing rate is increased by environmental factors and numerous diseases that change the body function and tissue structure of the body.

The process of ageing can differ from one organism to another. As different organisms have different lifespans. These are some factors that make the study of ageing difficult as the process of ageing in different organisms [14].

Ageing in plants is functionally different from animals. Ageing in plants can be induced by two factors either stress induced or age related that cause ageing [15]. Yellowing of leaves is the first step that plants experience in leaf senescence which starts at the margins of leaves and goes to the interior of the leaf [3].

Effects of ageing in plants and animals

Ageing is an inevitable process in both plants and animals and we cannot escape it. Therefore many problems can be associated with old age. Common problems that occur due to old age in animals, especially humans, can be different types of diseases such as breathing problems, diabetes, Alzheimer's and coronary diseases, other problems are loss of hearing, muscle pain and weak bones, poor eyesight and bowel movements [16]. Common problems that occur due to old age in plants cause loss of tissue repair that occur because of the cell cycle arrest in progenitor cells and other factors [17] such as oxidative stress, telomere damage, DNA damage etc. [18].

Ageing is the overall decreased efficiency of the body and its root cause is genes and other factors such as eating habits, environmental factors etc. Ageing in animals is mainly controlled by the gene daf-2. Metabolism, stress resistance and development are also other factors that can be controlled by this gene. This gene also shows its effects on another gene called daf-16 which encodes for different factors [19]. Ageing in humans is controlled by gene GATA 6 (GATA binding protein 6) [20]. Ageing in plants or genes that control senescence in leaves are NAC (an acronym for NAN, ATAF and CUC, TFs) important for leaf senescence [21].

Biotic and abiotic stresses responsible for ageing in plants

Plants have to cope up with a wide range of intricate complications including various environmental elements. They have developed distinct adaptations and survival strategies in the course of evolution [22-25].

Stress can be interpreted as an extrinsic and intrinsic restrictions that lowers a plant capacity to convert energy into biomass and slows down photosynthetic rate [26].

There are two different types of stresses that plant face are biotic and abiotic stresses. Abiotic stresses refers to a factor in the environment that affects plant as a result of physical and chemical stress variations. On the other hand biotic stress is a biological unit that includes diseases, insects and other pests that are exposed to crop plants [27]. Some stresses can harm plants. a number of metabolic processes affect these plants [28]. Salinity, drought, floods, temperature extremes, heavy metal radiations etc are examples of abiotic stresses. It plays a significant role in the loss of important crop plants across the globe. Pathogens including nematodes, oomycetes, fungi, bacteria, and herbivores can all assault an organism during biotic stress. Major yield loss worldwide is attributed to diseases brought on by these infections. Sessile plants cannot ignore these environmental cues since they are unable to move away from them. For the lifecycle to be effectively finished, one must be skilled at handling these stresses. Plants have therefore created a number of adaptation mechanisms to cope with these dangers and survive in these environments. The genetic coding of the plants regulate how it reacts to these challenges. It is necessary to combat disease resistant crop variants to ensure food safety and security in succeeding growing season. It should also be taken in account to trying seed with growing and routing hormones [28].

Abiotic stresses

Plants go through a variety of abiotic stresses which directly have an influence on crop yet across the world the various categories of abiotic stress that falls on this section include drought, salt, cold, heat and toxins.

Drought

Water scarcity is a major environmental constraint on plant growth and yield. The amount and distribution of rainfall, evaporative needs, and soil moisture storing capacity, all variables that are unpredictable, determine severity of drought [29]. Due to rising temperatures and CO_2 levels in the atmosphere, the climate has changed in all parts of the world today. Due to the uneven distribution of rainfall brought on by climate change, which manifests as drought, a significant stressor is created. Plants are dying off early because of the terrible drought conditions that are creating a steady decrease in the amount of soil water that is available to plants [30].

Salt

Salt stress is one of the most important components that stops crop development and yield because soil salinity lowers crop productivity which poses global menaces to the agriculture world. It is a situation that develops when salt builds up over time in the soil or groundwater [31].

Cold

It has been visualized that one of the most important abiotic factors that decreases agricultural crop productivity by affecting crop quality and post-harvest life. The growth of several crop plant species has been found to be significantly impeded by chilling, with rice showing sterility when subjected to chilling temperatures during anthesis [32].

Heat

The global rise in temperature has become a important issue, affecting not only plant growth but also plant yield, specially in agricultural products. The main factor affecting crop growth and food security is heat stress [33]. Heat stress negatively affects plants' photosynthetic productivity, seed germination rate, and yield. An anther becomes dysplastic when a petal cell experiences heat stress during the reproductive growth stage. Whenever plants are exposed to temperatures above about 29–30°C, for instance, maize yields drop off significantly [34].

Toxins

Due to growing reliance on chemical fertilizers, sewage wastewater irrigation, and rising industrialisation, toxic metals have been added to agricultural soils, having negatively effected the soil-plant environment system [35]. Over time, these metals travel into the food chain and bioaccumulate in the air, water, and slowly make their way into plant's life cycle [36].

Plants defence against biotic and abiotic stresses

In biotic stress cases, PTI further restricts the growth of new pathogen colonies yet, a part of pathogen has evolved affected triggered immunity (ETI) which contains other elements of the innate immune system [9]. There are five general stresses against abiotic stresses. These involve cuticle, unsaturated fatty acids, reactive species scavengers, molecular chaperones, and compatible solute.

Cuticle is the transparent external lipid membrane that seals the aerial surface of the organs on terrestrial plants. As the main point of contact between a plant and its surroundings, the cuticle is vital for controlling liquid and gas fluxes, fending off disease and insect attacks, and enduring a variety of abiotic stresses. The use of an outermost shield made of basic molecules, which is a clever invention of land plants and essential to their success in colonizing the planet [37].

The main constituents of the membrane and the primary sources for the cuticle are unsaturated fatty acids with 16 or 18 carbon atoms. Unsaturated fatty acids are a key factor in determining membrane fluidity [38]. Protein deactivation and ion leakage in the biomembrane are brought on by cold-driven rigidification and heat-driven fluidization, which makes membrane fluidity vulnerable to numerous abiotic stresses, particularly at high temperatures [39].

Reactive carbonyl species (ROS) and reactive oxygen species are among the reactive species scavengers (RCS) because RCS results from ROS-induced lipid peroxidation and ROS increased by RCS activities in the other direction, these two substances got intertwined. Abiotic stressors have the ability to cause both ROS and RCS to spike, transforming the two scavengers into general defences. The highly evolved ROS scavenging mechanism employed by plants are both enzymatic and non-enzymatic methods [38].

In order to speed up protein folding, assembly, transport, and destruction, molecular chaperones are activated. All living things use heat shock protein (HSP), which is a good example of a molecular chaperon, to protect against all harmful conditions that can cause protein damage. HSPs prevent the aggregation of denatured proteins, aid in their refolding, or present them to lysosomes or proteasomes for proteolysis, results in restoring cellular homeostasis [40].

Compatible solutes are tiny, organic molecules that are electrically neutral and have a high solubility and low toxicity. Sugar, amino acids, and their derivatives are among the compounds [38]. These metabolites may assemble in an abiotic environment to function as osmoprotectants against dehydration, RCS scavengers, and stabilizers of proteins and membranes [41].

Effect of environmental stress on plant survival

In seasonal rains, ephemeral plants develop blossom and germinate very quickly. Thus, they finish their life cycle during a time of sufficient moisture and produce dormant seeds before the start of the dry season. Ephemeral plants avoid stress to withstand environmental stress, therefore they never fully suffer the strain of drought or cold temperatures. These plants sustain the environmental stress by stress avoidance. Many plants have the capacity to withstand a specific stress and are therefore regarded as stress-resistant [41].

Genes responsible for longevity

Though ageing is an undeniable process, it can be slowed by certain genes and physical activity that improve longevity.

Telomere plays an important role in age related problems in humans. Therefore, its shortening in length can affect humans. Studies have shown that people doing regular exercise can improve telomere length. The gene p66shc in mice helps in longevity of life and different diseases. Classes of genes that increase longevity in worms, flies and mice are insulin/IGF-1 signalling, such as daf-2 and ge-1 mutants [42]. Leaf senescence also occurs due to age but can be reduced by various factors such as external and internal factors. External factors can induce heat, light, pest attack and drought and internal factors can include hormones such as abscisic acid, salicylic acid, auxin, ethylene can increase leaf senescence and hormones like cytosine and polyamines can decrease leaf senescence [6].

Tools and techniques employed for analysing ageing and its effects

Microfluidics for single cell analysis

To investigate the ongoing complexities of cellular system, microfluidics has been emerged as one of the powerful technology. As compared to the size of single cell, microfluidic channels have capacity tens to hundreds of microns (~10 µm in size and roughly ~1pL in volume). In this growing era of discoveries related to human body microfluidics could play vital role to understand whole genome haplotyping of single human cells. Through single cell "omics", issues related to metabolomics, transcriptomics, proteomics can be studied. For understanding the profession of disease or changes in cellular level information can be effectively revealed by implementing this technology [43-45].

FiNAD biosensors

In various metabolic mechanisms like glycolysis, the tricarboxylic acid and fatty acid β oxidation are employed to convert the molecules to generate ATP through anaerobic glycolysis and mitochondrial phosphorylation [12]. The milimolar of ATP has capability to hinder the activity of NAD^+ or AXP and its related enzymes like STR1, PARP, CD38. Eventually, AXP had tendency to compete the binding with NAD^+ to the NAD+/NADH transcriptional factors like Rex of NaDR [46]. Thus, on the basis of previous reports we can say that activities of crucial enzymes ad transcriptional factors depend on the NAD^+/AXP ratio. This crucial ration can be detected by FiNAD sensor, which provides relevancy towards, physiological key as metabolic indicator of energy metabolism for diseased or ageing related conditions [47,48].

DNA methylation

Till date, epigenetic alteration and suppression of gene expression when associated with gene promoters are studied thoroughly in cytosine guanine dinucleotides (CpGs) based DNA methylation (DNAm). For the inception of methylation pattern in early development phase and its maintenance throughout life span DNA methyltransferasee are required (DNMTs). These DNMTs also regulate CpG methylation mechanism in animals. "Epigenetic drift" and "clock type" are two different forms of the age associated DNAm in vertebrates [49]. The previous studies reports DNMT1 is one of the eminent factor accountable for CpG methylation maintenance and with declination of age of an individual, its activity declines results in decrement of global methylation of "drift" in ages cell and cellular system [49]. Increment or decrement of methylation proportion at specific sites of CpG is directly associated with "clock type" DNAm. This can be related to functional changes of gene expression with gradual decline in age [50]. There are numerous reports on the age related transfigurations occurrence due to DNAm in human and mice model tissues. These reports identified the set of CpG sites pretentious by chronological age [51]. Another report studied on 34 identical twins (21-55 years old) in which DNAm levels were found on 88 CpG sites significantly associated with chronological age (27K Bead Chip) [52,53].

Quantitative trait loci

In general, cognitive factor is influences through genes, in which 50% of the variation is accountable. From the age of 11 till 80, almost 50% of phenotype variance are arises during age influenced through gene level. This effect contributes to the life long trains of intelligence. Age related cognitive variation is known as continuous trait, if it is influenced through genes. These genetic variations are caused due to polygenic or oligogenic effects which referred as quantitative trait locus (QTL). These loci are helpful to analyse the variation amongst the aged and non aged cells [54-56].

Genomic tools

Methionine homeostasis gene, methionine gamma lyase (AtMGL), rapid alkalinization factor-like 8 (AtRALFL8) involved in cell wall remodeling, and azelaic acid induced 1 (AZI1) functioning in systemic plant immunity are some of the significant candidate genes discovered for improvement of plant tolerance to combined stresses [57,58]. Genes implicated in crosstalk between the signalling pathways linked to pathogen infection and coupled drought stress lead to tolerance to both stresses. Some studies have also suggested that *A. thaliana* and *V. vinifera* are able to tolerate both pathogen and drought stress by using proline and polyamine metabolism [59-61].

Limitation of Tools and techniques employed for analysing ageing and its effects

There's always a two side of coins, similarly every research has its pros and cons in every term of research, here's are some cons of techniques and tools which are used in analysis of effects on aging.

Utilizing microfluidic techniques, microfluidic devices can be utilised to investigate and create microstructures as small as a micrometre and smaller. These devices have various advantages over traditionally sized systems, such as the capacity to combine processes that often require a whole laboratory into a straightforward micro-sized system. Microfluidic approaches, however, are not without their drawbacks [62].

Polydimethylsiloxane (PDMS), for instance, is frequently used to fabricate microfluidic chips, although it has a number of disadvantages. When water vapour or hydrophobic molecules are unintentionally released during an experiment, PDMS can capture them. Additionally, the material's deterioration over time may limit the chip's performance. Additionally, PDMS cannot be used to fabricate chips that need to withstand high pressure or temperature [63]. Other materials used to make microfluidic chips include silicon and glass [64], although each has its own drawbacks. Glass chips are delicate and likely to breaking, but silicon chips are costly to create and challenging to change once fabricated [65]. Another drawback of microfluidics is channel clogging, which can prevent conduction in a device [64]. Moreover, because of elements like tensile force or chemical cytotoxicity from fabrication materials [11] cell viability in a chip may be unstable. A microfluidic system's usefulness and lifespan may be hindered as a result.

Since in vitro imaging enables better understand in changes in cell morphology and size, it is a helpful method for assessing ageing in cell cultures [66]. However, when it comes to researching ageing in the context of neurodegenerative disorders, it has a number of drawbacks. For instance, the endosome and cell structure in the central nervous system are not replicated by in vitro models [67]. They are also unable to appropriately detect DNA methylation alterations linked to senescence or measure the cell product [66]. They also have a weak understanding of age-sensitive injuries [68]. Moreover, they are unable to accurately represent the uncertainty of in vivo immunosurveillance [68].

DNA methylation is a phenomenon that has been linked to ageing and disorders that are related to getting older. Age-related disorders and ageing are both associated with changes in DNA methylation across the genome, according to studies [69]. Biomarkers of DNA methylation may be used to estimate the time till death [69,70]. The use of DNA methylation in the study of ageing does have some restrictions, though. For instance, the causes of DNA methylation and the relationship between DNA methylation and ageing are unclear. Moreover, there is a lack of information regarding the intra-individual changes in gene-specific DNA methylation over period in a dataset drawn from the community [71]. Also, although some evidence suggests that age-dependent DNA methylation alterations may be restored by certain interventions, including dietary restriction or exercise [70], extensive study is required to clarify the function of DNA methylation in ageing and longevity [72].

Caloric restriction has been discovered to slow down the progression in mice, worms, and flies.Research have demonstrated that calorie restriction can affect predictors of lifespan and health by altering molecular processes such DNAm [73]. The survey of calorie restriction on ageing does have some restrictions, though. For instance, research has shown that environmental or genetic factors may reduce the effects of calorie restriction [74]. Furthermore, it might be challenging to distinguish between the effects of caloric restriction on ageing caused by a decrease in calories and those caused by other food factors like vitamins and minerals. Last but not least, the results of long-term studies on humans make it challenging to make generalisations regarding the consequences of calorie restriction on human aging [75].

The drawback of microneedling technology in the study of ageing is that not all skin types may benefit from it, and if performed improperly, it can have negative effects [76,77]. Typically, 0.5 mm or 1.0 mm needles are applied in microneedling strategies to handle wrinkles and ageing skin, that may not be appropriate for deeper wrinkles or more severe age indications [76]. Moreover, a number of variables, including age, skin type, and needle geometry, can affect effective microneedling treatments [78,79]. Thus, it's crucial to speak with a doctor before beginning any microneedling treatments to make sure they're secure and suitable for the patient's particular requirements.

Conclusion

In this venture of understanding an unfolding the chapters of longevity of human life span, the knowledge of genetic loss transforming the cellular lifespan provide us significant hints on modulating life style to attain healthy life span. In this review, we try to highlight various genes from various organisms which provide the valuable clues on the basis of human ageing. In this article various genes and mechanism has been discussed through which we can get better understanding about the plants defence mechanism against ageing. This knowledge could help us to develop new methodologies which proves to be beneficial for human ageing and its consequences.

Along with, genes responsible for ageing, we also focused on the new tools and techniques which enables the detection or modulation of gene responsible for ageing. Though in these techniques there are numerous loop holes which need to be rectified through advanced strategies to prevent the coarse consequences of ageing.

Conflict of Interest

Declare if any financial interest or any conflict of interest exists.

Bibliography

1. Kenyon Cynthia J. "The Genetics of Ageing". *Nature* 464.7288 (2010): 504-512.
2. World Health Organization. "World report on ageing and health". World Health Organization (2015).
3. Jing HC., *et al*. "Ageing in Plants: Conserved Strategies and Novel Pathways". *Plant Biology* 5.05 (2003): 455-464.
4. Quirino Betania F., *et al*. "Molecular Aspects of Leaf Senescence". *Trends in Plant Science* 5.7 (2000): 278-282.
5. Wheeler Heather E and Stuart K Kim. "Genetics and Genomics of Human Ageing". *Philosophical Transactions of the Royal Society B: Biological Sciences* 366.1561 (2011): 43-50.
6. Jehanzeb Muhammad., *et al*. "The Role of the S40 Gene Family in Leaf Senescence". *International Journal of Molecular Sciences* 18.10 (2017): 2152.
7. Pujol Benoit. "Genes and Quantitative Genetic Variation Involved with Senescence in Cells, Organs, and the Whole Plant". *Frontiers in Genetics* 6 (2015): 57.
8. Wang Hongning., *et al*. "Cell-Autonomous and Non-Autonomous Roles of Daf-16 in Muscle Function and Mitochondrial Capacity in Aging C. Elegans". *Aging (Albany NY)* 11.8 (2019): 2295.
9. Klessig Daniel F., *et al*. "Systemic Acquired Resistance and Salicylic Acid: Past, Present, and Future". *Molecular Plant-Microbe Interactions* 31.9 (2018): 871-888.
10. Chakraborty Nilanjan. "Salicylic Acid and Nitric Oxide Cross-Talks to Improve Innate Immunity and Plant Vigor in Tomato against Fusarium Oxysporum Stress". *Plant Cell Reports* 40.8 (2021): 1415-1427.
11. Fu Yong-Bi., *et al*. "Towards a Better Monitoring of Seed Ageing under Ex Situ Seed Conservation". *Conservation Physiology* 3.1 (2015).
12. Fang Evandro F., *et al*. "Nad+ in Aging: Molecular Mechanisms and Translational Implications". *Trends in Molecular Medicine* 23.10 (2017): 899-916.
13. Jung Sang-Eun., *et al*. "Dna Methylation-Based Age Prediction from Various Tissues and Body Fluids". *BMB Reports* 50.11 (2017): 546.
14. Short Kevin R., *et al*. "Age and Aerobic Exercise Training Effects on Whole Body and Muscle Protein Metabolism". *American Journal of Physiology-Endocrinology and Metabolism* 286.1 (2004): E92-E101.
15. Schippers Jos HM., *et al*. "Living to Die and Dying to Live: The Survival Strategy Behind Leaf Senescence". *Plant Physiology* 169.2 (2015): 914-930.
16. Knewtson Kelsey E., *et al*. "Estrogen Signaling Dictates Musculoskeletal Stem Cell Behavior: Sex Differences in Tissue Repair". *Tissue Engineering Part B: Reviews* 28.4 (2022): 789-812.
17. Russo Giulia and Andrea Genre. "Divide and Be Conquered—Cell Cycle Reactivation in Arbuscular Mycorrhizal Symbiosis". *Frontiers in Plant Science* 12 (2021): 753265.

18. Gahtyari Navin Chander., *et al*. "Genetic Analysis and Marker Association of Physiological Traits under Rainfed and Heat Stress Conditions in Spring Wheat (Triticum Aestivum L.)". *Genetika* 54.3 (2022): 1049-1068.

19. Gems David and Linda Partridge. "Insulin/Igf Signalling and Ageing: Seeing the Bigger Picture". *Current Opinion in Genetics and Development* 11.3 (2001): 287-292.

20. Jiao Hongli., *et al*. "Gata6 Regulates Aging of Human Mesenchymal Stem/Stromal Cells". *Stem Cells* 39.1 (2021): 62-77.

21. Fraga Otto Teixeira., *et al*. "Senescence-Associated Glycine Max (Gm) Nac Genes: Integration of Natural and Stress-Induced Leaf Senescence". *International Journal of Molecular Sciences* 22.15 (2021): 8287.

22. Heil Martin and Richard M Bostock. "Induced Systemic Resistance (Isr) against Pathogens in the Context of Induced Plant Defences". *Annals of Botany* 89.5 (2002): 503-512.

23. Swarbrick Philip J., *et al*. "Metabolic Consequences of Susceptibility and Resistance (Race-Specific and Broad-Spectrum) in Barley Leaves Challenged with Powdery Mildew". *Plant, Cell and Environment* 29.6 (2006): 1061-1076.

24. Bolton Melvin D. "Primary Metabolism and Plant Defense—Fuel for the Fire". *Molecular Plant-Microbe Interactions* 22.5 (2009): 487-497.

25. Massad Tara Joy., *et al*. "Costs of Defense and a Test of the Carbon-Nutrient Balance and Growth-Differentiation Balance Hypotheses for Two Co-Occurring Classes of Plant Defense". *PLoS One* 7.10 (2012): e47554.

26. Atafar Zahra., *et al*. "Effect of Fertilizer Application on Soil Heavy Metal Concentration". *Environmental Monitoring and Assessment* 160 (2010): 83-89.

27. Gimenez Estela., *et al*. "Worldwide Research on Plant Defense against Biotic Stresses as Improvement for Sustainable Agriculture". *Sustainability* 10.2 (2018): 391.

28. Umar Olayinka Bolaji., *et al*. "Stresses in Plants: Biotic and Abiotic". *Current Trends in Wheat Research* (2021).

29. Hazel Jeffrey R. "Thermal Adaptation in Biological Membranes: Is Homeoviscous Adaptation the Explanation?". *Annual Review of Physiology* 57.1 (1995): 19-42.

30. Grime J Philip. "Evidence for the Existence of Three Primary Strategies in Plants and Its Relevance to Ecological and Evolutionary Theory". *The American Naturalist* 111.982, 1977): 1169-1194.

31. He Mei., *et al*. "Abiotic Stresses: General Defenses of Land Plants and Chances for Engineering Multistress Tolerance". *Frontiers in Plant Science* 9 (2018): 1771.

32. Jiang Wenzhu., *et al*. "Genotype× Environment Interactions for Chilling Tolerance of Rice Recombinant Inbred Lines under Different Low Temperature Environments". *Field Crops Research* 117.2-3 (2010): 226-236.

33. Liliane Tandzi Ngoune and Mutengwa Shelton Charles. "Factors Affecting Yield of Crops". *Agronomy-Climate Change and Food Security* (2020): 9.

34. Liu Xiaomin., *et al*. "Effects of Chilling on the Structure, Function and Development of Chloroplasts". *Frontiers in Plant Science* 9 (2018): 1715.

35. Nievola Catarina C., *et al*. "Rapid Responses of Plants to Temperature Changes". *Temperature* 4.4 (2017): 371-405.

36. Rauwane Molemi and Khayalethu Ntushelo. "Understanding Biotic Stress and Hormone Signalling in Cassava (Manihot Esculenta): Potential for Using Hyphenated Analytical Techniques". *Applied Sciences* 10.22 (2020): 8152.

37. Srivastava Vaibhav., *et al*. "Agroecological Responses of Heavy Metal Pollution with Special Emphasis on Soil Health and Plant Performances". *Frontiers in Environmental Science* 5 (2017): 64.

38. Slama Inès., *et al*. "Diversity, Distribution and Roles of Osmoprotective Compounds Accumulated in Halophytes under Abiotic Stress". *Annals of Botany* 115.3 (2015): 433-447.

39. Wang Wangxia., *et al*. "Role of Plant Heat-Shock Proteins and Molecular Chaperones in the Abiotic Stress Response". *Trends in Plant Science* 9.5 (2004): 244-252.

40. Zaid Hilal., *et al*. "Diabetes and Metabolism Disorders Medicinal Plants: A Glance at the Past and a Look to the Future 2018". *Evidence-based Complementary and Alternative Medicine: eCAM* 2018 (2018).

41. Zhang Ji-Yi., *et al*. "Heterologous Expression of Two Medicago Truncatula Putative Erf Transcription Factor Genes, Wxp1 and Wxp2, in Arabidopsis Led to Increased Leaf Wax Accumulation and Improved Drought Tolerance, but Differential Response in Freezing Tolerance". *Plant Molecular Biology* 64 (2007): 265-278.

42. Rodríguez-Rodero Sandra., *et al*. "Aging Genetics and Aging". *Aging and disease* 2.3 (2011): 186. PMID: 22396873

43. Yin, Huabing and Damian Marshall. "Microfluidics for Single Cell Analysis". *Current Opinion in Biotechnology* 23.1 (2012): 110-119.

44. Whitesides George M. "The Origins and the Future of Microfluidics". *Nature* 442.7101 (2006): 368-373.

45. Fan H Christina., *et al*. "Whole-Genome Molecular Haplotyping of Single Cells". *Nature Biotechnology* 29.1 (2011): 51-57.

46. Grose Julianne H., *et al*. "Regulation of Nad Synthesis by the Trifunctional Nadr Protein of Salmonella Enterica". *Journal of Bacteriology* 187.8 (2005): 2774-2782.

47. Toledano Elie., *et al*. "3′-5′ Phosphoadenosine Phosphate Is an Inhibitor of Parp-1 and a Potential Mediator of the Lithium-Dependent Inhibition of Parp-1 *in Vivo*". *Biochemical Journal* 443.2 (2012): 485-490.

48. Zou Yejun., *et al*. "Illuminating Nad+ Metabolism in Live Cells and *in Vivo* Using a Genetically Encoded Fluorescent Sensor". *Developmental cell* 53.2 (2020): 240-252. e7.

49. Jones Meaghan J., *et al*. "Dna Methylation and Healthy Human Aging". *Aging Cell* 14.6 (2015): 924-932.

50. Steegenga Wilma T., *et al*. "Genome-Wide Age-Related Changes in Dna Methylation and Gene Expression in Human Pbmcs". *Age* 36 (2014): 1523-1540.

51. Grönniger Elke., *et al*. "Aging and Chronic Sun Exposure Cause Distinct Epigenetic Changes in Human Skin". *PLoS Genetics* 6.5 (2010): e1000971.

52. Bocklandt Sven., *et al*. "Epigenetic Predictor of Age". *PloS One* 6.6 (2011): e14821.

53. Paoli-Iseppi De., *et al*. "Measuring Animal Age with Dna Methylation: From Humans to Wild Animals". *Frontiers in Genetics* (2017): 106.

54. Wright Alan., *et al*. "A polygenic basis for late-onset disease". *TRENDS in Genetics* 19.2 (2003): 97-106.

55. Deary Ian J., *et al*. "The stability of individual differences in mental ability from childhood to old age: Follow-up of the 1932 Scottish Mental Survey". *Intelligence* 28.1 (2000): 49-55.

56. Deary Ian J., *et al*. "Searching for genetic influences on normal cognitive ageing". *Trends in Cognitive Sciences* 8.4 (2004): 178-184.

57. Pandey Prachi and Muthappa Senthil-Kumar. "Plant Responses to Combined Drought and Pathogen Infection: Current Understanding on the Role of Phytohormones". *Plant Tolerance to Individual and Concurrent Stresses* (2017): 133-149.

58. Atkinson Nicky J., *et al*. "Identification of Genes Involved in the Response of Arabidopsis to Simultaneous Biotic and Abiotic Stresses". *Plant physiology* 162.4 (2013): 2028-2041.

59. Ahmad Bilal., *et al*. "Impact of Biotic and Abiotic Stresses on Plants, and Their Responses". *Disease Resistance in Crop Plants: Molecular, Genetic and Genomic Perspectives* (2019): 1-19.

60. Hatmi Saloua., *et al*. "Drought Stress Tolerance in Grapevine Involves Activation of Polyamine Oxidation Contributing to Improved Immune Response and Low Susceptibility to Botrytis Cinerea". *Journal of experimental botany* 66.3 (2015): 775-787.

61. Gupta Aarti., *et al*. "Drought Stress Predominantly Endures Arabidopsis Thaliana to Pseudomonas Syringae Infection". *Frontiers in Plant Science* 7 (2016): 808.

62. Anonymous, Elvefow Manual.

63. Christelle ANGELY. Chip materials in microfluidics: a review. 03 Nov (2020), Darwin Microfluidics.

64. Anonymous. Advantages And Disadvantages Of Microfluidics. Bartleby Research. 1-11.

65. Lee Chang-Soo. "Grand Challenges in Microfluidics: A Call for Biological and Engineering Action". *Frontiers Media SA* 1 (2020): 583035.

66. Oja S., *et al*. "Automated Image Analysis Detects Aging in Clinical-Grade Mesenchymal Stromal Cell Cultures". *Stem Cell Research and Therapy* 9 (2018): 1-13.

67. Slanzi Anna., *et al*. "*In Vitro* Models of Neurodegenerative Diseases". *Frontiers in Cell and Developmental Biology* 8 (2020): 328.

68. Dickerson Michelle., *et al*. "Age-Relevant *in Vitro* Models May Lead to Improved Translational Research for Traumatic Brain Injury". *Current Opinion in Biomedical Engineering* (2022): 100391.

69. Salameh Yasmeen., *et al*. "Dna Methylation Biomarkers in Aging and Age-Related Diseases". *Frontiers in Genetics* 11 (2020): 171.

70. Xiao Fu-Hui., *et al*. "Progress on the Role of Dna Methylation in Aging and Longevity". *Briefings in Functional Genomics* (2016): Elw009.

71. Madrigano Jaime., *et al*. "Aging and Epigenetics: Longitudinal Changes in Gene-Specific Dna Methylation". *Epigenetics* 7.1 (2012): 63-70.

72. Wilkinson Gerald S., *et al*. "Dna Methylation Predicts Age and Provides Insight into Exceptional Longevity of Bats". *Nature Communications* 12.1 (2021): 1615.

73. Waziry R., *et al*. "Effect of Long-Term Caloric Restriction on Dna Methylation Measures of Biological Aging in Healthy Adults from the Calerie Trial". *Nature Aging* (2023): 1-10.

74. Vaughan Kelli L., *et al*. "Caloric Restriction Study Design Limitations in Rodent and Nonhuman Primate Studies". *The Journals of Gerontology: Series A* 73.1 (2018): 48-53.

75. Sohal Rajindar S and Michael J Forster. "Caloric Restriction and the Aging Process: A Critique". *Free Radical Biology and Medicine* 73 (2014): 366-382.

76. Singh Aashim and Savita Yadav. "Microneedling: Advances and Widening Horizons". *Indian Dermatology Online Journal* 7.4 (2016): 244.

77. Amore Roberto., *et al*. "Facial Anti-Aging Treatments with Soft Peeling and Microneedling Technique". *Applied Sciences* 11.13 (2021): 6068.

78. Sasaki Gordon H. "Micro-Needling Depth Penetration, Presence of Pigment Particles, and Fluorescein-Stained Platelets: Clinical Usage for Aesthetic Concerns". *Aesthetic Surgery Journal* 37.1 (2016): 71-83.

79. Makvandi Pooyan., *et al*. "Engineering Microneedle Patches for Improved Penetration: Analysis, Skin Models and Factors Affecting Needle Insertion". *Nano-Micro Letters* 13 (2021): 1-41.