MERIT RESEARCH JOURNALS
www.meritresearchjournals.org

Merit Research Journal of Medicine and Medical Sciences (ISSN: 2354-323X) Vol. 5(12) pp. 604-610, December, 2017
Available online http://www.meritresearchjournals.org/mms/index.htm

Review

Oxidative Stress Causes Aging: Genetics and Epigenetics

[1,2]Kiran Shahbaz

[1]Center for Health Technology, Faculty of Science, University of Technology Sydney, Australia

[2]Director: Department of Neuroscience, Perfect Health Pvt. Ltd, Islamabad, Pakistan.

E-mail : Kiran.Shahbaz@uts.edu.au

Abstract

Reactive Oxygen Species (ROS) if increase abnormally cause oxidative stress (OS) resulting in aging ultimately involve genetic and epigenetic factors. Oxidative stress (OS) depicts a disparity among the systemic manifestation of reactive oxygen species and a living system's ability to knowingly detoxify the reactive intermediates or otherwise to repair the ultimate loss. Turbulence in the normal redox state of the cells may cause toxic effects through the production of peroxides and free radicals that damage all gears of the cell, mainly DNA, proteins and lipids. Oxidative stress (OS) in aging brain has shown remarkable damage with memory decays causing Alzheimer's disease. Oxidative stress (OS) occurs when any of the molecules in the body get in touch with reactive oxygen species. These molecules become oxidized or "burned" and lose an electron and become excited. They wander around and cause damage to cells at organelle (mitochondria 'mt' and endoplasmic reticulum 'ER') and genetic level (transcriptional changes, genome instability), if they aren't "cleaned up" neutralized or balanced. The effect is accelerated aging, finally leading to death. Progeria is accelerated aging due to a genetic disorder. If we posit the agents responsible for oxidative stress, for example, glutathione; aging may be delayed. Present study will strongly focus to revolutionize the management plan for oxidative stress (OS) and longevity. This review emphasizes on oxidative stress, reasons for oxidative stress, what ROS does with genes and main impact of those effects on aging.

Keywords: Oxidative Stress, Aging, Genetics, Epigenetics, Senescence

INTRODUCTION

Normally "the non-specific response of the body to any command for change" is called stress (Figure 1).

STRESS A Dilemma

When unbalanced, stress is a dilemma.

Psychological stress concerns the position of "normal" tension, preoccupation, and agitation as surveyed from people. Sometimes extreme and sometimes an energy inoculation, its statistical allocation is normal, and in developmental of various physical and mental disorders it is considered a precipitating factor. So, it's different from distress and psychopathology, which are dysfunctional and melancholic. Similarly, chronic stress propels disease by activating the hypothalamic-pituitary-adrenocortical (HPA) axis has been a concept in many researches (Millar *et al*., 2007) is a valid reason of aging.

Aging

Aging increases defenselessness to age linked diseases, while genetics determines openness or resistance between species and individuals within species. Oxidative anxiety equivalents to maturing. Some age-related changes (like turning gray hair) are said to be random to an expansion in mortality. Some biogerontologists consider that the similar fundamental changes that grounds graying hair also increase mortality in other organ. As an individual approaches age, that

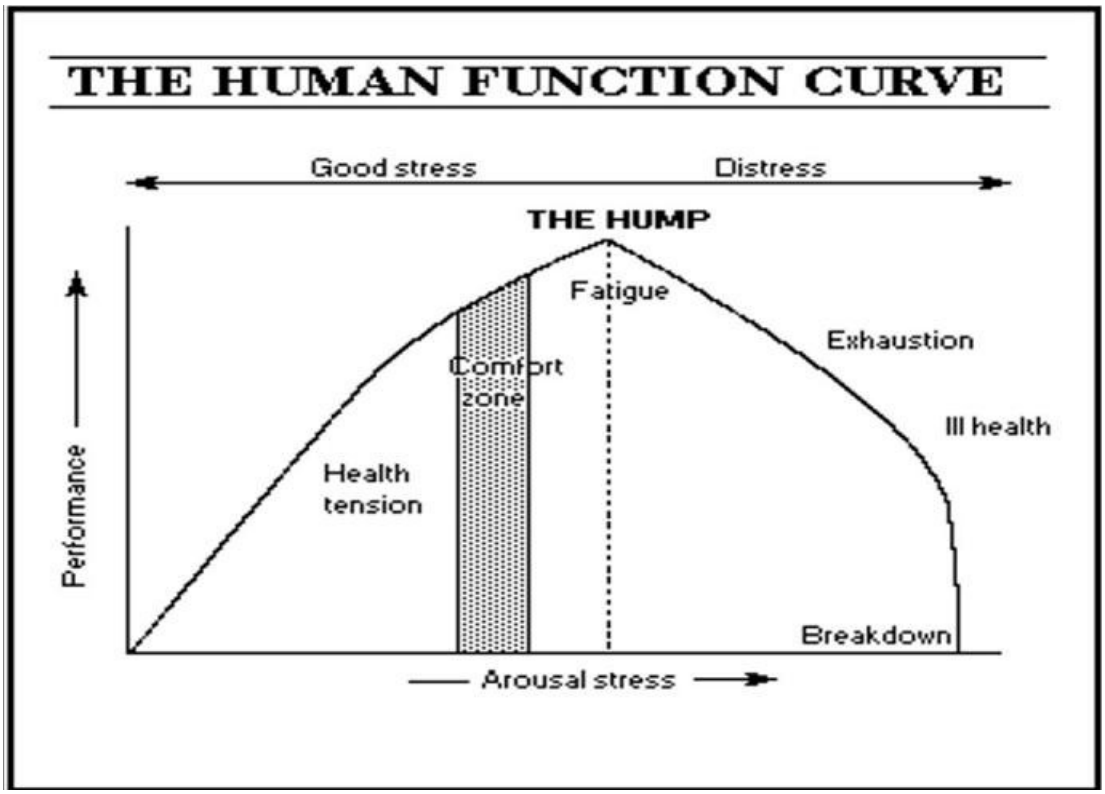

Figure 1. The human function curve adapted from Nixon, P 1976. It shows a marked line between good stress and distress ultimately showing distress starts after fatigue however best out is obtained in comfort zone.

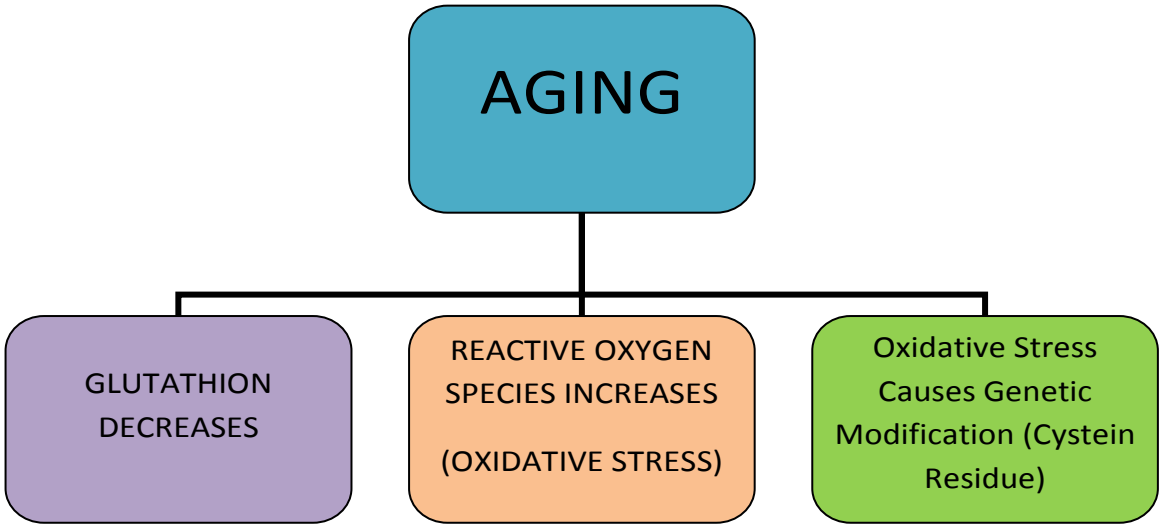

Figure 2. Schematic diagram showing factors involved in human aging where most important is ROS regulation by oxidation of cysteine residues on gene (Apel et al.,2004) suggesting oxidative stress responsible for genetic modification reducing age.

individual will start facing the exaggerated amounts of diseases. Biological aging is thought to occur ideally during the period of survival beyond the natural or essential lifespan (ELS) in Darwinian terms and organisms survive to gain ELS by help of genetically known longevity maintaining maintenance and repair systems (MRS) (Rattan., 2006). (Figure 2)

Table 1. Radicals and Species that may undergo reduction or oxidation to give rise to oxidation stress within the cellular environment

Radicals	Non-radicals
Superoxide: O_2^-	Hydrogen peroxide: H_2O_2
Hydroxyl: OH^-	Hypochlorus acid: HOCL
Peroxyl: RO_2^-	Hypobrromus acid: HOBr
Alkoxyl: RO^-	Ozone: O_3
Hydroperoxyl: HO_2^-	Singlet oxygen: Δg

Genes and aging

Several efforts are being made to identify the genes which are involved in the long ages from the humans enjoying longest period of age on earth but still these genes are unknown (Murabito *et al.,* 2012). Finding aging and longevity genes is a challenge for scientist in future.

Oxidative stress

Oxidative stress is distinct as a pandemonium in the balance between the manufacture of reactive oxygen species (free radicals) and antioxidant defenses. It is read in relation to its probable role in the production of tissue damage in diabetes mellitus. The amount of oxidative damage increases as an organism ages and is postulated to be a major causal factor of senescence. Reactive oxygen species (ROS) are powerful redox messenger causing oxidation of lipids, proteins and DNA and resides in the mitochondria of cell (Marchi *et al.,* 2011) when increased, decreases cell life if not life, quality of cell's life.

Glutathione (GSH) – *Master of Long Race*

GSH an antioxidant molecule in the brain when decreases cause an increase in oxidative stress and aging. It is a redox modulator and its decreases upgrades the excitotoxic molecules in the body. Hence it causes oxidative stress in the cell when depletes (Samiec *et al.,* 1998; Bains *et al*., 1997).

Epignetics

If microevolution (genetic) is slow the epigenetic (Shahbaz *et al.,* 2016) factors have faster effect on aging through oxygen free radicals. It includes histone modification and DNA methylation (D'Aquila *et al*., 2013; Tollefsbol, 2010; Rando, 2010).

Oxidative Stress and Related Species

Oxygen Species

Radicals of oxygen (superoxide anion, hydroxyl radical, and peroxy radicals), receptive non-radical oxygen species, for example, hydrogen peroxide and singlet oxygen, and carbon, nitrogen, and sulfur radicals incorporate the differing qualities of responsive particles that can incorporate an oxidative stress to cells. It has been unsurprising that a biggest of 5 % of the aggregate oxygen digestion system of liver tissue results in the formation of in part reduced oxygen species, for example, those appeared. This speaks to a critical stress under standard conditions, and verification is accessible about some cell harm that happens under these circumstances. (Table 1)

Atmospheric Oxygen

Air oxygen is not to a great extent receptive with biological molecules in light of the fact that the two orbital electrons partaking in oxidation responses have the comparable spin condition. Thusly electrons that are supplementary to these orbital amid lessening of oxygen must be included separately than as a couple of electrons all through paired spin. One superoxide anion is molded by one electron diminishment of oxygen. A second appearance of oxygen, i.e., singlet oxygen, is a substantially more reactive structure with paired electrons. Reduction of this appearance of oxygen does

not have the taking after spin state impediment.

Hydrogen peroxide (H_2O_2)

Hydrogen peroxide is a non-radical molecule (paired electrons) created by the same sources that deliver superoxide anion since two atoms of superoxide anion dismute to hydrogen peroxide and oxygen eagerly. There are likewise various other particular chemicals and enzymes that deliver hydrogen peroxide straight. Hydrogen peroxide can circle over significant separations and might pass cellular layers deliberately in this procedure. Consequently, pools of hydrogen peroxide equilibrate rapidly. Hydrogen peroxide and superoxide anion can be found both inside and outside cells. In the vicinity of a transition cation, for example, iron or copper, superoxide anion can offer ascent to the exceptionally reactive hydroxyl radical species (HO) by the Haber-Weiss response.

HABER-WEISS REACTION

$$O_2^- + H_2O_2 \longrightarrow O_2 + HO^- + HO$$

Here, Iron catalyzes the reaction by the following mechanism. Summing up of 2 reactions together gives the reaction above.

$$Fe^{III} + O_2^- \longrightarrow Fe^{II} + O_2$$
$$Fe^{II} + H_2O_2 \longrightarrow Fe^{III} + HO^- + HO$$

Peroxyl radicals

According to Weindruch 2001, Peroxyl radicals take place through the oxidation of lipids or other organic molecules in oxidative stress. They are shaped by addition of oxygen to alkyl radicals. The peroxyl radical species, which are not extremely reactive, might diffuse an impressive separation. They have been appeared to counter devotedly with sulfhydryl bunches (thiols) to create the thiyl radical.

Singlet oxygen

Singlet oxygen is made by oxidation of other mostly diminished oxygen species, bringing about oxygen with matched races in the responsive orbital. The differing qualities of oxygen species depicted above show the many-sided quality of the responses that can come about because of an oxidative anxiety. Components, for example, the site of creation, the accessibility of move metals, and the activity of catalysts choose the destiny of every radical species and its accessibility for response with cell particles. The H_2O_2 fixation under stable state conditions in liver has been unsurprising to be 10-7 - 10-9 M, while superoxide anion is 10-11 M. (Zhang *et al*., 2013)

Oxidative Stress in the Aging Brain

Mitochondrial Changes

According to Gemma 2002 antioxidant enzymes SOD, catalase, glutathione peroxidase and glutathione reductase, for instance, show decreased exercises in the brains of patients with Alzheimer's infection It is gathered that free radicals of mitochondrial source are among the essential drivers of mitochondrial DNA (mtDNA) harm. Different studies have demonstrated that the age-related expansion in oxidative harm to mitochondrial DNA is more noteworthy than the oxidative harm that jumps out at atomic DNA in rodents For instance, oxidative DNA harm has been recognized in human cerebrum mitochondrial DNA and in rodent liver at levels more than 10 times higher than in atomic DNA from the same tissue. This higher vulnerability of mtDNA to oxidative harm might be because of an absence of mtDNA repair systems, an absence of security by histone proteins, and the way that mtDNA is found near the inward mitochondrial layer where responsive oxygen species are created. A few studies have discovered expanded levels of 8-hydroxy-2′-deoxyguanosine (8-OHdG), a biomarker of oxidative DNA harm, in mtDNA in the matured mind High levels of 8-OHdG have been found in both atomic DNA (nDNA) and in mtDNA of the after death brains of matured subjects In harmony with the mitochondrial free radical hypothesis of maturing, a reverse relationship has been appeared between the levels of oxidative harm to mtDNA and most extreme life span in both the heart and the cerebrum: gradually maturing warm blooded animals show lower mtDNA harm than the individuals who are quicker. In distinction, this relationship is not connected with atomic DNA. Mitochondrial DNA has a high change rate; and when a transformation happens, cells at first contain a blend of wild-sort and mutant mtDNAs. Over numerous eras, the mtDNA genotype of a cell genealogy can move toward dominatingly mutant or wild-sort mtDNAs. As the rate of mutant mtDNA builds, the cell vitality ability diminishes in suspicion of it falls underneath the bioenergetic edge — the base vitality yield essential for a cell or tissue to work regularly. Expanding verification in demonstrates that assembling of oxidation of DNA, lipid, and protein by free radicals is responsible for the practical decline in the matured cerebrum. In the maturing mind, and in the packaging of a few neurodegenerative sicknesses, there is a turn down in the ordinary antioxidants protection components, which expands the defenselessness of the cerebrum to the destructive impacts of oxidative harm. Elevated levels of cortical mtDNA erasures have been found in patients with Alzheimer's ailment.

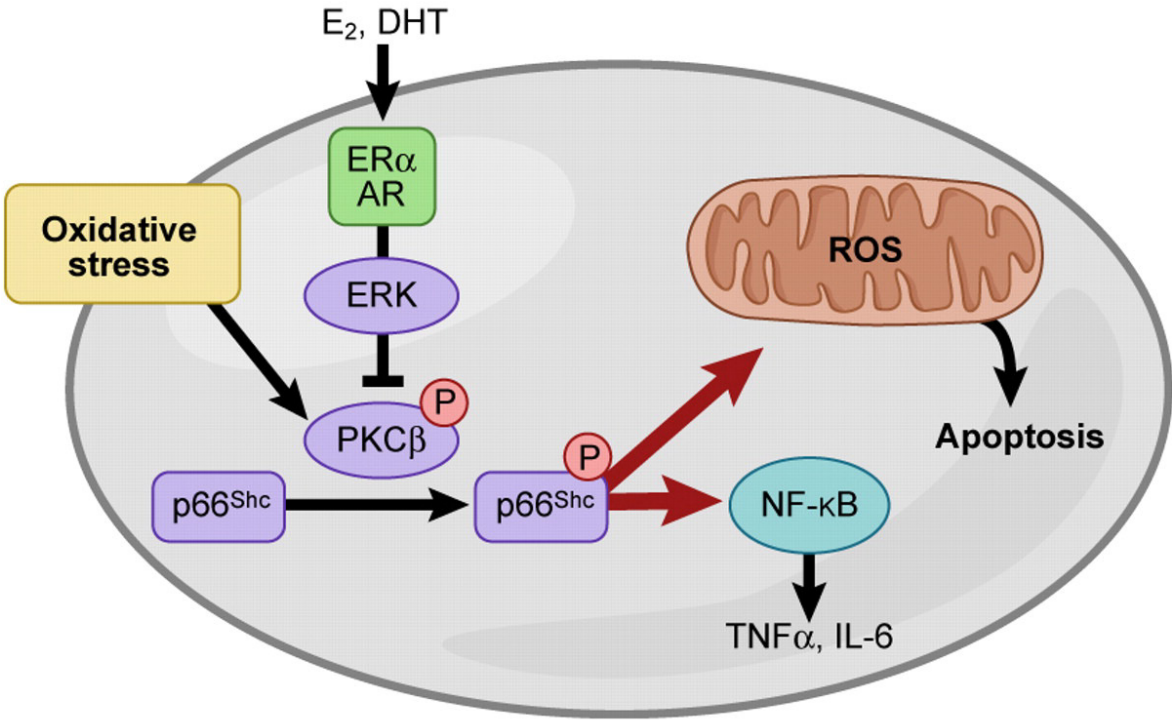

Figure 3. Mechanism of oxidative stress and aging (Almeida, 2010).

Mechanism of damage

Proteins are adjusted in structure and capacity by radical responses. Metal-catalyzed protein oxidation result moreover of carbonyl gatherings or cross-connecting or discontinuity of proteins. Lipid (peroxidation) aldehydes can respond with sulfhydryl (cysteine) or essential amino acids (histidine, lysine). Similarly, change of substance nucleotide bases, single-strand breaks and cross-connecting are the regular impacts of responsive oxygen species on nucleic acids.

Antioxidant Defense mechanisms

Antioxidant defense mechanisms safeguard mechanisms have advanced to shield cell parts from the assault of oxidative stress and related oxidative harm. The enzymes catalase and SOD are the boss safeguards against ROS. Grass changes over superoxide anions into H_2O_2, and catalase changes over H_2O_2 to sub-atomic oxygen and water. These mechanisms might incorporate antioxidant enzymes, for example, SOD, super-oxide reductases, catalase, glutathione peroxidases (Gpx), and a great deal of warmth stun proteins. Grass exists in two structures: MnSOD is in participation essentially in the mitochondria while Cu/ZnSOD is in participation mainly in the cytoplasm (Beckman *et al*., 1998).

Mammalian cells hold complicated defense mechanisms to detoxify (metabolize) radicals. SOD catalyzes the dismutation of O_2^{-}• to $H_2O_2 + O_2$. H_2O_2 is converted to $O_2 + H_2O$ by catalase or by glutathione peroxidase (GPx), which uses glutathione (GSH) as the reducing agent. Redox-active metals, such as iron, bind to storage and transport proteins (e.g., ferritin, transferrin, lactoferrin) to diminish configuration, and radical-scavenging antioxidants (e.g., vitamin E) break off the chain reactions (Figure 3).

Management Plan

Oxidative stress can cause the following problems tiredness, obesity, sick, and old, lines at the corner of your eyes and the ache in your knees after hard training. It affects you all the time. It can increase the speed of aging and also may lead to death (Poliquin *et al.,* 2013).

Real-Life Guidelines to Fight Oxidative Stress

Stay conscious that chronic patience exercise causes a lot of oxidative stress and can considerably compromise health at the long run. It starts compromising the performance it has to be taken under control. Ploiquin highly recommend four activities to fight oxidative stress.

Practice a martial art to raise glutathione and decrease markers of stress. A series of studies have shown that practices including judo, tai chi, tae kwon do,

jiu jitsu, soo bahk do, and aikido all diminish oxidative stress. Researchers do agree that martial art uniquely sets apart from other physical activities in enabling the body to better counter stress, and noted the benefits to be healthy. These are the mind-body activities that have the capacity to change energy flow in the body.

Strength training has been shown to elevate glutathione and decrease oxidative stress. It's the perfect way to direct stress because it lets you get rid of your aggressions, whereas enhancing the body's antioxidant system. For example, one recent study found both a hypertrophy-type and a strength-type training protocol done for six weeks increased resting levels of glutathione by the end of the study. Markers of oxidative stress were lower as healthy.

Laughing can increase glutathione and clash oxidative stress. Research shows that inducing authentic laughter can put off cellular and genetic damage from oxidative stress. The effect is a healthier immune system, and down the road, a longer life.

Meditation can raise glutathione and contradict oxidative stress. For example, research shows that IL-6, a stress biomarker, is lower in people who have an effective meditation practice. Yoga can also struggle oxidative stress, though, research shows meditation may be more effectual than yoga for raising glutathione.

Three Level Models for Reducing Oxidative Stress

The reduction of oxidative stress could be achieved in three levels:
By lowering the generation of oxidative stress
By stabilizing mitochondrial energy production and efficiency or By increasing levels of endogenous and exogenous antioxidants
By lowering exposure to environmental pollutants with oxidizing properties.

CONCLUSION

Aging is the process during which structural and functional changes accumulate in a body as a result of the flow of time. The changes manifest as a collapse from the body's peak fertility and physiological functions until death. Oxidative stress (OS) is a cause of free radicals, oxides and superoxides that occur as a result of redox reactions within the cells also at a genetic level. All the oxidized molecules need to be cleaned up otherwise they will bounce around neighboring cells altering the physiological environment. They increase the rate of aging, causing age related diseases such as cancers, cardiac atrophy, stroke, diabetes, parkinson's disease (PD), multiple sclerosis (MS) and Alzheimer's disease (AD). If etiological factor in a disease is known, its cure is possible by ameliorating that factor or delaying its action (Shahbaz *et al.,* 2014). It is found that oxidative stress (OS) can be managed with the help of improved diet and daily life best practices. It will reduce the probability of the molecules to get oxidized/burnt up. Chief important guideline is affective laughter and meditation. Three way model is a pivotal approach. Researchers have shown the impact of oxidative stress (OS) but the real mechanism remained equivocal. They have given the guidelines for dealing with oxidative stress and delaying aging. The current review is important from clinical point of view. It will help the researchers and other clinicians to design the management plans according to individuals effectively.

Funding

The Australian President's Award (APA) equivalent, The UTS President's Scholarship (UTSP) and The UTS International Research Scholarship (UTS IRS)

REFERENCES

Almeida M (2010). Aging and oxidative stress: a new look at old bone. IBMS BoneKEy, 7(10), 340-352.
Apel K, Hirt H (2004). Reactive oxygen species: metabolism, oxidative stress, and signal transduction. *Annu. Rev. Plant Biol.*, *55*, 373-399
Bains JS, Shaw CA (1997). Neurodegenerative disorders in humans: the role of glutathione in oxidative stress-mediated neuronal death. *Brain Research Reviews*, *25*(3), 335-358.
Beckman KB, Ames BN (1998). The free radical theory of aging matures. *Physiological reviews*, *78*(2), 547-581.
D'Aquila P, Rose G, Bellizzi D, Passarino G (2013). Epigenetics and aging. *Maturitas*, *74*(2), 130-136.
Gemma C, Mesches MH, Sepesi B, Choo K, Holmes DB, Bickford PC (2002). Diets enriched in foods with high antioxidant activity reverse age-induced decreases in cerebellar β-adrenergic function and increases in proinflammatory cytokines. *The J. Neurosci.*,*22*(14), 6114-6120.
Marchi S, Giorgi C, Suski JM, Agnoletto C, Bononi A, Bonora M, Rimessi A (2011). Mitochondria-ros crosstalk in the control of cell death and aging. *J. Signal transduction*, *2012*.
Miller GE, Chen E, Zhou ES (2007). If it goes up, must it come down? Chronic stress and the hypothalamic-pituitary-adrenocortical axis in humans. *Psychological bulletin*, *133*(1), 25
Murabito JM, Yuan R, Lunetta KL (2012). The search for longevity and healthy aging genes: insights from epidemiological studies and samples of long-lived individuals. *The J. Gerontol. Series A: Biological Sciences and Medical Sciences*, *67*(5), 470-479.
Nixon PG (1976). The human function curve. With special reference to cardiovascular disorders: part I. *The Practitioner*, *217*(1301), 765.
Poliquin PO, Chen J, Cloutier M, Trudeau LÉ, Jolicoeur M (2013). Metabolomics and in-silico analysis reveal critical energy deregulations in animal models of Parkinson's disease. PLoS One, 8(7), e69146.
Rando TA (2010). Epigenetics and aging. *Experimental gerontology*, *45*(4), 253.
Rattan SI (2006). Theories of biological aging: genes, proteins, and free radicals. *Free radical research*, *40*(12), 1230-1238.
Samiec PS, Drews-Botsch C, Flagg EW, Kurtz JC, Sternberg P, Reed RL, Jones DP (1998). Glutathione in human plasma: decline in association with aging, age-related macular degeneration, and diabetes. *Free Radical Biology and Medicine*, *24*(5), 699-704.

Shahbaz K, Mehfooz A, Khadam W (2014). Breast Cancer Vaccination-An Envisioned Future. *Indo Ame. J. Pharma. Res. 4*(3), 1580-1585.
Shahbaz K (2016). Pharmenzymonetics And Pharmgeonetics: A New Door In Pharmacology. J. PP. Sci, 6(2).
Tollefsbol TO (Ed.). (2010). *Epigenetics of aging*. Springer.
Weindruch R, Kayo T, Lee CK, Prolla TA (2001). Microarray profiling of gene expression in aging and its alteration by caloric restriction in mice. *The J. Nutr. 131*(3), 918S-923S.
Zhang SM, Hernan MA, Chen H, Spiegelman D, Willett WC, Ascherio A (2002). Intakes of vitamins E and C, carotenoids, vitamin supplements, and PD risk. *Neurology*, *59*(8), 1161-1169.