

How Butterfly Effect or Deterministic Chaos Theory in Theoretical Physics Explains the Main Cause of Cancer

(Introducing the Chaos Theory in Cancer Biology)

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Abstract

In animal cells, mitochondria are unique organelles in that they contain a genome of their own. There are small circular chromosomes in each mitochondrion that have genes for some of the mitochondrial proteins. But the mitochondrial chromosomes do not have genes for all the proteins found in mitochondria. The genes for the remaining proteins are found in the cellular genome which is found in the nucleus. So to get some functional mitochondria requires gene expression of both nuclear and mitochondrial genes. By the Evolutionary Metabolic Hypothesis of Cancer (EMHC), the main reason behind the cause of cancer, is increasing the amounts of Reactive Oxygen Species and intracellular inflammation which cause damage to the mitochondria. Increasing the inflammation will cause chaos in normal cells and causes the nucleus to send wrong messages instead of apoptosis, that means turning the oxidative phosphorylation into fermentation in cytosol. Therefore, by three-year study over cancer and normal cells, we have come to the conclusion that the real reason behind the cause of cancer is the increasing of ROS above the normal limits that causes butterfly effect inside the normal cells.

Keywords: *Butterfly Effect; Chaos Theory; Cancer Biology; Mitochondrion; Emhc Hypothesis; Reactive Oxygen Species; Intracellular Inflammation*

Introduction

Butterfly Effect

Chaos theory is a branch of mathematics which is focused on the behavior of dynamic systems that are highly sensitive to initial conditions. Chaos is an inter-disciplinary theory stating that within the apparent randomness of chaotic complex systems, there are underlying patterns, constant feedback loops, self-similarity, repetition, fractals, self-organization, and reliance on programming at the initial point known as sensitive dependence on initial conditions. The butterfly effect (BE) describes how a small change in one state of a deterministic non-linear system can result in large differences in a later state, that means a butterfly flapping its wings in Italy can cause a hurricane in Texas [1].

Small differences in initial conditions such as those due to rounding errors in numerical computation yield widely diverging outcomes for such dynamical systems, a response popularly referred to as the butterfly effect rendering long-term prediction of their behavior impossible in general [2,3]. This happens even though these systems are deterministic, e.g. their future behavior is fully determined by their initial conditions, with no random elements involved [4]. In other words, the deterministic nature of these systems does not make them foreseeable [5,6]. This behavior is known as deterministic chaos, or simply chaos. The theory was summarized by Edward Lorenz

as [7]: Chaotic behavior exists in many natural systems, such as weather and climate [8,9]. It also occurs spontaneously in some systems with artificial components, such as road traffic [10]. This behavior can be studied through analysis of a chaotic mathematical model, or through analytical techniques such as recurrence plots and Poincare maps. Chaos theory has applications in several disciplines, including meteorology, anthropology [11,12], sociology, physics [13], environmental science, computer science, engineering, economics, biology, ecology, and philosophy. The theory formed the basis for such fields of study as complex dynamical systems, edge of chaos theory, and self-assembly processes [13].

Nearly for over a hundred years, biologists have been keeping the track of populations of different species with population models. Most models are continuous, but recently scientists have been able to implement chaotic models in certain populations [14]. For instance, a study on models of Canadian lynx showed that there was chaotic behaviors in the population growth [15]. Chaos can also be found in ecological systems, such as hydrology. While a chaotic model for hydrology has its shortcomings, there is still much to learn from looking at the data through the lens of chaos theory [16]. Another biological application is found in cardio-tocography. Fetal surveillance is a delicate balance of obtaining accurate information while being as non-invasive as possible. Better models of warning signs of fetal hypoxia can be reached through chaotic modeling [17,52].

Evolutionary Metabolic Hypothesis of Cancer (EMHC)

The first living cells on Earth are thought to have arisen more than 3.5×10^9 years ago, when the Earth was not more than about 109 years old. The environment lacked oxygen but was presumably rich in geochemically produced organic molecules, and some of the earliest metabolic pathways for producing ATP may have resembled present-day forms of fermentation. In the process of fermentation, ATP is made by a phosphorylation event that harnesses the energy released when a hydrogen-rich organic molecule, such as glucose, is partly oxidized. The electrons lost from the oxidized organic molecules are transferred via NADH or NADPH to a different organic molecule or to a different part of the same molecule, which thereby becomes more reduced. At the end of the fermentation process, one or more of the organic molecules produced are excreted into the medium as metabolic waste products. Others, such as pyruvate, are retained by the cell for biosynthesis. The excreted end-products are different in different organisms, but they tend to be organic acids. Among the most important of such products in bacterial cells are lactic acid which also accumulates in anaerobic mammalian glycolysis, and formic, acetic, propionic, butyric, and succinic acids [64].

The first cell on the earth before the entrance of the bacteria did contain nucleus and used the fermentation process to produce ATP for its energy. Then an aerobic proteo-bacterium enters the eukaryote either as a prey or a parasite and manages to avoid digestion. It then became an endosymbiont. As we observe, the fermentation process used the glucose or even glutamine to produce ATP, but the aerobic process used the glucose, fat and protein to produce more ATP than the previous one. The symbio-genesis of the mitochondria is based on the natural selection of Charles Darwin. Based on Otto Warburg Hypothesis, in nearly all cancer cells, the mitochondrion is shut down or are defected and the cancer cell do not use its mitochondrion to produce ATP [65]. This process of adaptation is based on Lamarckian Hypothesis of Evolution and the normal cells goes back to the most primitive time of evolution to protect itself from apoptosis and uses the fermentation process like the first living cells 1.5 billion years ago. Therefore, cancer is an evolutionary metabolic disease which uses glucose as the main food to produce ATP and Lactic Acid. The prime cause of cancer is the abundance of Reactive Oxygen Species produced by mitochondria that is a threat to the living normal cell and causes mitochondrial damage mainly in its cristae [66].

Nucleus and Mitochondria Connection

Voltage dependent anion channel (VDAC) was discovered in 1976 and since that time, has been thoroughly studied [53]. It is well known that VDAC transports metabolites across the outer mitochondrial membrane. The simple transport function is indispensable for correct mitochondria functions and, consequently for cell activity, and makes VDAC crucial for a range of cellular processes including ATP rationing, Ca^{2+} homeostasis and apoptosis [54]. Recent data obtained for *Saccharomyces cerevisiae* cells used as a model system concern-

ing the putative role of VDAC in communication between mitochondria and the nucleus. The *S. cerevisiae* VDAC isoform known as VDAC1 which is termed YVDAC, mediates the cytosol reduction-oxidation state that contributes to regulation of expression and activity of cellular proteins including proteins that participate in protein import into mitochondria and antioxidant enzymes. At the same time, copper and zinc-containing superoxide dismutase (CuZnSOD) plays an important role in controlling YVDAC activity and expression levels [55]. Therefore; it is proposed that VDAC constitutes an important component of a regulatory mechanism based on the cytosol redox state [63].

Reactive oxygen species

Reactive oxygen species (ROS) are chemically reactive chemicals containing oxygen. Examples include: peroxides, superoxide, hydroxyl radical, and singlet oxygen [19].

In biology, ROS are formed as a natural by-product of the normal metabolism of oxygen, and have important roles in cell signaling and homeostasis [20]. However; during times of environmental stress that means, UV or heat exposure, ROS levels can increase highly [21]. This may result in significant damage to cell structures. Cumulatively, this is known as oxidative stress. ROS are also generated by exogenous sources such as ionizing radiation [22].

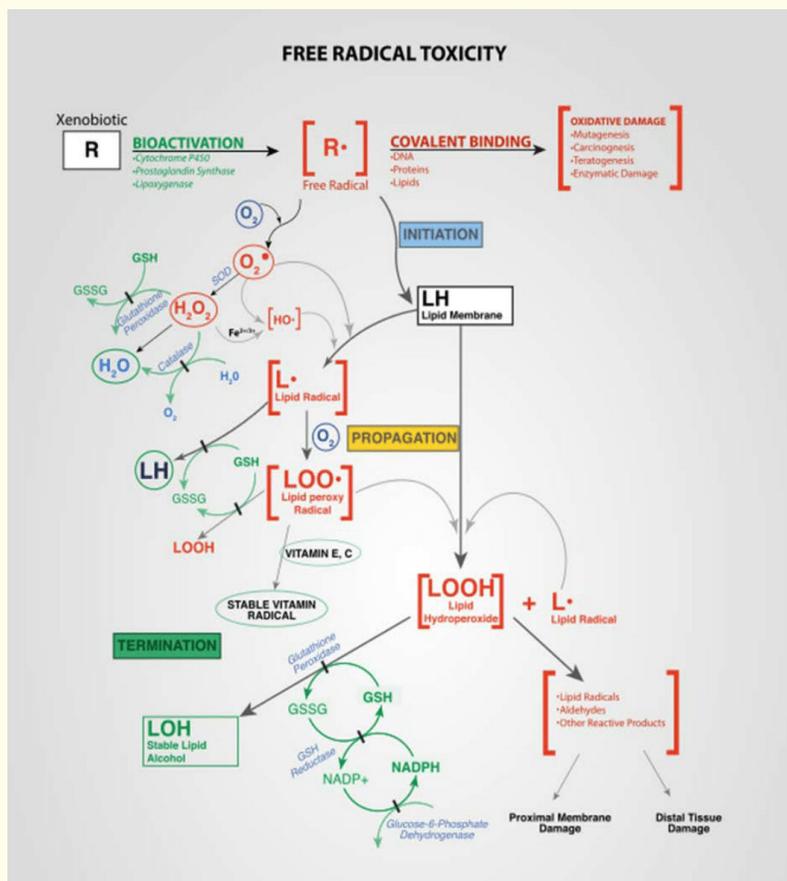


Figure 1: Free Radical Mechanisms in Tissue Injury. Free radical toxicity induced by xeno-biotics and the subsequent detoxification by cellular enzymes [56].

Endogenous ROS

ROS are produced intracellularly through several mechanisms and depending on the cell and tissue types, the major sources being the professional producers of ROS: NADPH oxidase (NOX) complexes in cell membranes, mitochondria, peroxisomes, and endoplasmic reticulum [23]. Mitochondria convert energy into a usable form for the cell, adenosine triphosphate (ATP) [57]. The process in which ATP is produced, called oxidative phosphorylation, includes the transport of protons across the inner mitochondrial membrane by the means of the electron transport chain. In the electron transport chain, electrons are passed through a series of proteins by means of oxidation/reduction reactions, with each acceptor protein along the chain having a greater reduction potential than the previous. The last destination for an electron through this chain is an oxygen molecule. In normal conditions, the oxygen is reduced to produce water, however; in around 0.1% to 2% of electrons passing through the chain, this number derives from studies in isolated mitochondria, though the exact rate in live organisms is yet to be fully agreed on, oxygen is instead prematurely and incompletely reduced to give the superoxide radical, most well documented for Complex I and Complex III [24]. Superoxide is not particularly reactive by itself, but can inactivate specific enzymes or initiate lipid peroxidation in its protonated form, hydro-peroxyl $\text{HO}\cdot$. The pK_a of hydro-peroxyl is 4.8. Therefore; at physiological pH, the majority will exist as superoxide anion [58].

If too much damage is present in mitochondria, a cell goes into apoptosis state or programmed cell death. Bcl-2 proteins are layered on the surface of the mitochondria, detect damage, and activate a class of proteins called Bax, which punch holes in the mitochondrial membrane, causing cytochrome C to leak out [59]. This cytochrome C binds into Apaf-1, or apoptotic protease activating factor-1, which is free-floating in the cell cytoplasm. Using energy from the ATPs in the mitochondrion, the Apaf-1 and cytochrome C bind together to form apoptosomes. The apoptosomes bind into and activate caspase-9, another free-floating protein. The caspase-9 then cleaves the proteins of the mitochondrial membrane, causing it to break down and start a chain reaction of protein denaturation and at last, phagocytosis of the cell [60].

Another type of reactive oxygen species is singlet oxygen, which is produced as a byproduct of photosynthesis in plants for instance. In the presence light and oxygen, photosensitizers like chlorophyll, may convert triplet oxygen to singlet oxygen [25]:

Singlet oxygen is highly reactive, specifically with organic compounds that contain double bonds. The resulting damage caused by singlet oxygen reduces the photosynthetic efficiency of chloroplasts. In plants exposed to excess light, the increased production of singlet oxygen can result in cell death [26]. Several substances like carotenoids and tocopherols, contained in chloroplasts quench singlet oxygen and protect against its toxic behaviors. In addition to direct toxicity, singlet oxygen acts as a signaling molecule [27]. Oxidized products of beta-carotene arising from the presence of singlet oxygen act as second messengers that can either protect against singlet oxygen induced toxicity or cause programmed cell death. Levels of Jasmonate play a key role in the decision between cell acclimation or cell death in response to elevated levels of this reactive oxygen species [28].

Materials and Methods

Effects of Reactive Oxygen Species on cell metabolism are highly documented in a various species. These contain not only roles in apoptosis, but also positive effects such as the induction of host defense genes and mobilization of ion transport systems [29]. This implicates them in control of cellular function. Particularly, platelets involve in wound repair and blood homeostasis release ROS to recruit additional platelets to sites of injuries. These also provide a link to the adaptive immune system by means of the recruitment of leukocytes [30].

Reactive oxygen species are implicated in cellular activity to a variety of inflammatory responses including cardiovascular disease. They may also be involved in hearing impairment by means of cochlear damage induced by elevated sound levels, in ototoxicity of drugs such as cisplatin, and in congenital deafness in both animals and humans. ROS are also implicated in mediation of apoptosis or programmed cell death and ischemic injury. Specific examples include stroke and heart attack [31].

In general, harmful effects of ROS on the cell are most often: damage of DNA or RNA, oxidations of polyunsaturated fatty acids in lipids, oxidations of amino acids in proteins, and oxidative deactivation of specific enzymes by oxidation of co-factors [32,40].

Oxidative damage

In aerobic organisms, the energy needed to fuel the biological functions is produced in the mitochondria by means of the electron transport chain. In addition to energy, reactive oxygen species with the potential to cause cellular damage are produced. ROS can damage lipid, DNA, RNA, and proteins, which theoretically, contributes to the physiology of aging. ROS are produced as a normal byproduct of cellular metabolism. particularly, one main contributor to oxidative damage is hydrogen peroxide (H_2O_2), which is converted from superoxide that leaks from the mitochondria. Catalase and superoxide dismutase ameliorate the damaging effects of hydrogen peroxide and superoxide, by converting these compounds into oxygen and hydrogen peroxide which is later converted to water, resulting in the production of benign molecules. However, this conversion is not 100 percent efficient, and residual peroxides persist in the cell. While ROS are produced as a byproduct of normal cellular functioning, excessive amounts can cause deleterious effects [32].

Memory capabilities decline with age, evident in human degenerative diseases such as Alzheimer's disease, which is accompanied by an accumulation of oxidative damage. Current research studies show that the accumulation of ROS can decrease an organism fitness, since oxidative damage is a contributor to senescence. particularly, the accumulation of oxidative damage may lead to cognitive dysfunction, as concluded in a study, in which, old rats were given mitochondrial metabolites and then given cognitive tests. Outcomes demonstrated that the rats performed better after receiving the metabolites, suggesting that the metabolites reduced oxidative damage and improved mitochondrial functioning [33].

Accumulating oxidative damage can then affect the efficiency of mitochondria and further increase the rate of ROS production [34]. The accumulation of oxidative damage and its implications for aging, depends on the special tissue type where the damage is happening. Additional experimental outcomes suggest that oxidative damage is responsible for age-related decrease in brain functioning. Older gerbils were found to have higher levels of oxidized protein in comparison to younger gerbils [40]. Treatment of old and young mice with a spin trapping compound caused a decline in the level of oxidized proteins in older gerbils, but did not have an effect on younger gerbils. Additionally, older gerbils performed cognitive tasks better during treatment, but ceased functional capacity when treatment was discontinued, caused oxidized protein levels to incline. This led researchers to conclude that oxidation of cellular proteins is mainly important for brain functioning [35].

Cancer and ROS

ROS are constantly generated and eliminated in the biological system and are required to drive regulatory pathways. Under normal physiological circumstances, cells control ROS levels by balancing the production of ROS with their elimination by scavenging systems. But under oxidative stress conditions, excessive ROS can damage cellular proteins, lipids and DNA, leading to fatal holes in cells that contribute to carcinogenesis [36].

Cancer cells exhibit greater ROS stress than normal cells, due to oncogenic stimulation, increased metabolic activity and mitochondrial malfunction. ROS is a double-edged sword. On one hand, at low levels, ROS facilitates cancer cell survival since cell-cycle progression driven by growth factors and receptor tyrosine kinases (RTK) require ROS for activation and chronic inflammation, a major mediator of cancer, is regulated by ROS [23]. On the other hand, a high level of ROS can suppress tumor growth through the sustained activation of cell-cycle inhibitor [24,25] and induction of cell death as well as senescence by damaging macromolecules. In fact, most of the chemotherapeutic and radio-therapeutic agents kill cancer cells by augmenting ROS stress [26].

The ability of cancer cells to distinguish between ROS as a survival or apoptotic signal is controlled by the dosage, duration, type, and site of ROS production. Modest levels of ROS are required for cancer cells to survive, whereas excessive levels kill them [27].

Metabolic adaptation in tumors, balances the cells' need for energy with equally important need for macro-molecular building blocks and tighter control of redox balance. Therefore, production of NADPH is greatly enhanced, which functions as a co-factor to provide reducing power in many enzymatic reactions for macromolecular biosynthesis and at the same time rescuing the cells from excessive ROS produced during rapid proliferation. Cells counterbalance the detrimental effects of ROS by producing antioxidant molecules, such as reduced glutathione (GSH) and Thioredoxin (TRX), which depend on the reducing power of NADPH to maintain their activities [28].

Most risk factors associated with cancer interact with cells through the generation of ROS. Reactive Oxygen Species then activate several and various transcription factors such as nuclear factor kappa-light-chain-enhancer of activated B cells, activator protein-1 (AP-1), hypoxia-inducible factor-1 α and signal transducer and activator of transcription 3, leading to the expression of proteins that control inflammations, cellular transformation, tumor cell survival, tumor cell proliferation and invasion, angiogenesis and metastasis as well. ROS also control the expression of various tumor suppressor genes like p53, retinoblastoma gene (Rb), and phosphatase and tensin homolog [36].

Carcinogenesis and ROS

ROS-related oxidation of DNA is one of the prime causes of mutations, which can produce several types of DNA damage, including non-bulky (8-oxoguanine and formamido-pyrimidine) and bulky base modifications, abased sites, nonconventional single strand breaks, protein-DNA adducts, and intra-interstrand DNA crosslinks [37]. It has been estimated that endogenous ROS produced by means of the normal cell metabolism, modify approximately 20000 bases of DNA in one day in a single cell. 8-oxoguanine is the most abundant among various oxidized nitrogenous bases observed. During DNA replication, DNA polymerase impairs 8-oxoguanine with adenine, leading to a G \rightarrow T trans-version mutation. The resulting genomic instability directly contributes to carcinogenesis. Cellular transformation leads to cancer and interaction of atypical PKC- ζ isoform with p47phox controls ROS production and transformation from apoptotic cancer stem cells through blebbishield emergency program [38,39].

Cell proliferation

Uncontrolled proliferation, is a hallmark of cancer cells. Both exogenous and endogenous ROS have been shown to enhance proliferation of cancer cells. The role of ROS in promoting tumor proliferation is as well supported by the observation that agents with potential to inhibit ROS generation can also inhibit cancer cell proliferation [40]. Although ROS can promote tumor cell proliferation, a great increase in ROS has been associated with reduced cancer cell proliferation by induction of G2/M cell cycle arrest, increased phosphorylation of ataxia telangiectasia mutated, checkpoint kinase 1 and 2 (Chk-1, Chk-2), and reduced cell division cycle 25 homolog c (CDC25) [41].

Cell death and ROS

A cancer cell can be terminated in three ways. Apoptosis, necrosis and autophagy. Excessive ROS can induce apoptosis through both the extrinsic and intrinsic pathways [42]. In the extrinsic pathway of apoptosis, ROS are generated by Fas ligand as an up-stream event for Fas activation by means of phosphorylation, that is necessary for subsequent recruitment of Fas-associated protein with death domain and caspase 8 and apoptosis induction as well [29]. In the intrinsic pathway, ROS acts to facilitate cytochrome c release by activating pore stabilizing proteins Bcl-2 and Bcl-xL and inhibiting pore-destabilizing proteins Bcl-2-associated X protein, Bcl-2 homologous antagonist-killer as well [35].

The intrinsic pathway is also known as the caspase cascade and is induced through mitochondrial damage which triggers the release of cytochrome c. DNA damage, oxidative stress, and loss of mitochondrial membrane potential lead to the release of the pro-apoptotic proteins mentioned above stimulating apoptosis [36]. Mitochondrial damage is closely linked to apoptosis and since mitochondria are easily targeted there is potential for cancer therapy [37].

The cytotoxic nature of ROS is a driving force behind apoptosis, however; in higher amounts, ROS can result in apoptosis and necrosis which is a form of uncontrolled cell death in cancer cells [43]. Many research studies have shown the associations between ROS levels and

apoptosis, but a newer line of researches outcomes has connected ROS levels and autophagy [44]. ROS can also induce apoptosis through autophagy, that is a self-catabolic process involving sequestration of cytoplasmic contents for degradation in lysosomes [40]. Therefore, autophagy can also regulate the cell's health in times of oxidative stress. Autophagy can be induced by ROS levels through many different pathways in the cell in an attempt to dispose of harmful organelles and prevent damage, such as carcinogens, without inducing apoptosis [45]. Autophagic cell death can be forced by the over-expression of autophagy where the cell digests too much of itself in an attempt to minimize the damage and can no longer survive. When this type of cell death occurs, an increase or loss of control of autophagy regulating genes is commonly co-observed [46].

Therefore; more complete understanding of autophagic cell death is attained and its relation to ROS, this form of programmed cell death may serve as a future cancer therapy. Autophagy and apoptosis are two different cell death mechanisms brought on by high levels of ROS in the cells, thus, autophagy and apoptosis poorly act through strictly independent pathways. There is a clear connection between ROS and autophagy and a co-relation seen between excessive amounts of ROS leading to apoptosis [47].

The depolarization of the mitochondrial membrane is also characteristic of the initiation of autophagy. When mitochondria are damaged and begin to release ROS, autophagy is initiated to dispose of the damaging organelle. If a drug targets mitochondria and creates ROS, autophagy may dispose of so many mitochondria and other damaged organelles that the cell is no longer viable. The extensive amount of ROS and mitochondrial damage may also signal for apoptosis. The balance of autophagy within the cell and the crosstalk between autophagy and apoptosis mediated by ROS is crucial for a cell's survival. This crosstalk and connection between autophagy and apoptosis could be a mechanism targeted by cancer therapies or used in combination therapies for highly resistant cancers [61].

Chronic inflammation and cancer

Experimental and epidemiologic research over the past several years has indicated close associations among ROS, chronic inflammation, and cancer [48]. ROS induces chronic inflammation by the induction of COX-2, inflammatory cytokines (TNF α , interleukin 1 (IL-1), IL-6), chemokines (IL-8, CXCR4) and pro-inflammatory transcription factors (NF- κ B). These chemokines and chemokine receptors, in turn, promote invasion and metastasis of various tumor types [49].

Both ROS-elevating and ROS-eliminating strategies have been developed with the former being predominantly used. Cancer cells with elevated ROS levels depend heavily on the antioxidant defense system. ROS-elevating drugs further increase cellular ROS stress level, either by direct ROS-generation (e.g. motexafin gadolinium, elesclomol) or by agents that abrogate the inherent antioxidant system such as SOD inhibitor (e.g. ATN-224, 2-methoxyestradiol) and GSH inhibitor (e.g. PEITC, buthionine sulfoximine (BSO)). The result is an overall increase in endogenous ROS, which when above a cellular tolerability threshold, may induce cell death [44,45]. On the other hand, normal cells appear to have, under lower basal stress and reserve, a higher capacity to cope with additional ROS-generating insults than cancer cells do. Therefore, the elevation of ROS in all cells can be used to achieve the selective killing of cancer cells [46].

Radiotherapy also relies on ROS toxicity to eradicate tumor cells. Radiotherapy uses X-rays, γ -rays as well as heavy particle radiation such as protons and neutrons to induce ROS-mediated cell death and mitotic failure [29].

Due to the dual role of ROS, both pro-oxidant and antioxidant-based anticancer agents have been developed. However, modulation of ROS signaling alone seems not to be an ideal approach due to adaptation of cancer cells to ROS stress, redundant pathways for supporting cancer growth and toxicity from ROS-generating anticancer drugs. Combinations of ROS-generating drugs with pharmaceuticals that can break the redox adaptation could be a better strategy for enhancing cancer cell cytotoxicity [50].

James Watson and others have proposed that lack of intracellular ROS due to a lack of physical exercise may contribute to the malignant progression of cancer, because spikes of ROS are needed to correctly fold proteins in the endoplasmic reticulum and low ROS levels may thus specifically hamper the formation of tumor suppressor proteins [53]. Since physical exercise induces temporary spikes of ROS,

this may explain why physical exercise is beneficial for cancer patient prognosis [52]. Moreover, high inducers of ROS such as 2-deoxy-D-glucose and carbohydrate-based inducers of cellular stress induce cancer cell death more potently because they exploit cancer cell high avidity for sugars [51].

Relation Between Cancer and Chaos Theory

In animal cells, mitochondria are unique organelles in that they contain a genome of their own. There are small circular chromosomes in each mitochondrion that have genes for some of the mitochondrial proteins. But the mitochondrial chromosomes do not have genes for all the proteins found in mitochondria. The genes for the remaining proteins are found in the cellular genome which is found in the nucleus. So to get some functional mitochondria requires gene expression of both nuclear and mitochondrial genes. The human mitochondrial genome is a small circular DNA molecule 16,568 bp in length containing 37 genes [56].

Twenty-four of the genes specify RNA molecules involved in protein synthesis while the remaining 13 encode proteins required for the biochemical reactions that make up respiration. The remaining mitochondrial OXPHOS proteins, the metabolic enzymes, the DNA and RNA polymerases, the ribosomal proteins and the mtDNA regulatory factors are all encoded by nuclear genes, synthesized in the cytosol and then imported into the organelle. There is coordination of both nuclear and mitochondrial genes during mitochondrial function and biogenesis [62].

The main cause of cancer is the damage to the mitochondria in normal cells. Nearly all cancer cells contain damaged mitochondria and the real reason behind this is increasing inflammation or Reactive Oxygen Species produced by each mitochondrion. Increasing the ROS in a cell can cause damage to the mitochondrion DNA and also Nucleus DNA, but another reason behind turning the normal cell into cancer cell is the chaos caused by the increasing of ROS. These chaos causes some abnormal messaging between the DNA of the nucleus to stop the apoptosis and turning the oxidative phosphorylation to the fermentation in cytosol. Normally by damaging to the mitochondria, the cell should go to apoptosis estate, however; the nucleus sends wrong messages to stop the apoptosis and do fermentation process to survive the cell. Even some normal left mitochondria would be shut down and stop the oxidative phosphorylation. This is the main and the real reason why increasing intracellular inflammation can cause cancer [Somayeh Zaminpira, Soroush Niknamian, ECRONICON, 2017].

Conclusion

The prime cause of cancer is the damage to the mitochondria in normal cells. Nearly all cancer cells contain damaged mitochondria and the basic reason behind this, is increasing the intracellular inflammation or basically the incline in Reactive Oxygen Species (ROS) produced by each mitochondrion in oxidative phosphorylation. Increasing the ROS in a cell can cause damage to the DNA of the mitochondrion and also Nucleus DNA, but another reason behind turning the normal cell into cancer cell is the chaos caused by the increasing of inflammation inside each cell and increasing the intracellular ROS. These chaos causes some abnormal messaging between the DNA of the nucleus to stop the apoptosis and turning the oxidative phosphorylation to the fermentation in cytosol. Normally by damaging to the mitochondria, the cell should apoptosis. however; the nucleus sends wrong messages to stop the apoptosis and do fermentation process in cytosol to survive the cell. Even some normal left mitochondria would be shut down and stop the oxidative phosphorylation. This is the main and the real reason how increasing intracellular inflammation can cause cancer. This research introduces the butterfly effect inside the normal cells is the basic reason behind the cause of cancer.

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