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Relationships between Oxidative Stress, Cancer Development and Therapeutic Interventions

Ahmed OM*

Department of Zoology, Beni-Suef University, Egypt

***Corresponding author:** Osama M Ahmed, Department of Zoology, Beni-Suef University, Egypt, Tel: + 01001084893; E-mail: osamamoha@yahoo.com

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Editorial

Oxidative stress is defined as an imbalance between the generation and elimination of reactive oxygen species (ROS) [1]. Low or moderate amounts of ROS have beneficial effects on several physiological processes including wound healing, killing of invading pathogens and tissue repair processes [2]. However, excessive production of ROS can lead to damage of deoxyribonucleic acid (DNA), lipids and proteins that in turn may result in oxidative tissue damage and cancer [3].

Recent studies have reported the important roles of oxidative stress in development of cancer [4] at its various steps including initiation, promotion and progression [5]. Initiation results when a normal cell sustains a DNA mutation that, when preceded by one or more rounds of cell division, results in fixation of the mutation, producing an initiated cell [4]. Thus, initiation is irreversible despite the initiated cell may eventually die during the development of the neoplasm. On the other hand, promotion is an epigenetic event which exhibits a change in gene expression without change in DNA thereby it is reversible [6]. Progression like initiation is an irreversible process that requires further mutations from genetic instability [7].

Oxidative damage to cellular DNA can lead to mutations and may, therefore, play an important role in the initiation [7]. Moreover, oxidative stress may also participate in the progression stage of the cancer process by adding further DNA alterations to the initiated cell population [7]. Following additional oxidative stress, multiple cell divisions and acquisitions of further mutations in the preneoplastic focal lesions, the formation of benign and/or malignant neoplasms can occur during the progression stage [4]. ROS-induced DNA damage can result in single- or double-strand breakage, base modifications, DNA cross-linking and deoxyribose modification [8,9]. If the oxidative DNA damage is not repaired prior to DNA replication, DNA mutation, replication errors, and genomic instability can occur [8,9].

The majority of mutations induced by ROS appear to involve modification of guanine, causing G→T transversions [10]. 8-Hydroxydeoxy guanosine (8-OHdG) and 8-oxoguanine (8-oxoG) are considered by many publications as the most common lesions produced by ROS during carcinogenesis; hydroxydeoxy guanosine (8-OHdG) is more common than 8-oxoguanine (8-oxoG) [4,11]. 8-OHdG in its stable syn conformation can pair with both cytosine and adenine [4]. If the A:G mismatch is not repaired, a G:C to T:A transversion will occur, commonly found in mutated oncogenes and tumor suppressor gene which are important regulatory genes for cell proliferation and apoptosis [4,10,12].

As the excessive production of ROS is involved in and associated with the process of carcinogenesis, the use of antioxidants during the cancer development may have protective and preventive potentials against DNA alterations during initiation and further DNA mutation during progression. Thus, scavenging of reactive oxygen species by antioxidants may be beneficial for prevention of carcinogenesis. Based on this elucidation, many natural antioxidants were tested by previous publications which reported their efficiencies in protection against and prevention of cancer development [13,14]. In another way, a number of natural compounds have also been demonstrated by different publications to provide promising cancer treatment as they selectively kills cancer cells by induction of ROS generation while it is less toxic to normal cells [15-17]. This is due to the fact that cancer cells are sensitive to oxidative stress. Thus, the mechanism of action for many cancer chemotherapeutic drugs involves ROS-mediated apoptosis of cancer cells [4].

In conclusion, [1] the exacerbated production of ROS plays a crucial role in the development of cancer [2] the supplementation of antioxidants may mitigate carcinogenesis by scavenging ROS that cause mutations in oncogenes and tumor suppressor genes and [3] finally the developed cancer cells that are more sensitive to ROS can be combated by chemotherapeutic agents via induction of oxidative stress.

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