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ARE MICROBIAL INFECTIONS AND SOME ANTIBIOTICS CAUSES CANCER?

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Abstract. Nowadays, it seems that all branches of science and phenomenons including microbiology, cancer, apoptosis, and hematology are closely related together. In this brief review, the aim was to show those mitochondria and the mechanisms including apoptosis induced by antigens released in microbial infections or applied therapeutic antibiotics can play an important role in the development of many diseases including cancer and other mitochondrial related disorders in humans. In this review, selected articles were studied using keywords such as mitochondria, apoptosis, infection, and antibiotics in various scientific search engines. Studies show that the methods of dealing with microbial infections can in many cases lead to poor fates related to mitochondrial related immune system involvement or recovery. Therefore, mitochondrial involvement with microbial antigens and or therapeutic antibiotics, and in turn the effects on the immune system can drive the balance to good or bad, which needs to be challenged in future research. The effect of some antibiotics and microbial antigens on the oxidative pathways of mitochondria suggests that the use of antimicrobials must be controlled in terms of the severity of the adverse effects on oxidative stress. In particular, this effect is very important in terms of the disorders including carcinogenicity and could be one of the new scientific topics in future studies.

Keywords: *Mitochondria, infection, antibiotics, cancer.*

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1. Introduction

Mitochondria play a key role in inducing apoptosis by internal or external factors (Peña-Blanco & García-Sáez, 2018). Apoptosis also called programmed cell death (PCD), is an important physiological mechanism by which the immune system maintains homeostasis and responds to various cellular damages, including damage caused by microbial infections, and application of therapeutic antibiotic (Lesnefsky et *al.*, 2016; Husnik *et al.*, 2018; Goldfield *et al.*, 1978). According to the explanations given, in this review study, the role of infections, and antigens released by microbes in the infectious processes and the effect of therapeutic antibiotic applications have been discussed on the mitochondrial induced apoptosis and some related complications such as cancer incidence.

2. Antibiotics, microbial antigens, and mitochondrial related disorders

In mitochondria, due to their structural similarity to bacteria, different antibiotics affect oxidative stress in eukaryotic cells by affecting the electron transfer chain and ultimately the production of reactive oxygen radicals (Lesnefsky *et al.,* 2016; Peña-Blanco *et al.,* 2018; Khalilov *et al.,* 1993). Previous research showed that different antibiotics have a detrimental effect on eukaryotic mitochondrial activity and oxidative pathway, which as we know oxidative pathway is one of the main antimicrobial defense systems in eukaryotes (Kalghatgi *et al.,* 2013; Akbarzadeh *et al.,* 2018b). Concentrations of antibiotics used in the treatment of bacterial infections, regardless of their therapeutic concentrations, can cause various disturbances due to disruption of mitochondrial activity other than such as drug resistance in humans by affecting mitochondria (Kalghatgi *et al*., 2013). It was realized from studies that almost three major groups of antibiotics, including aminoglycosides, quinolones, and beta-lactams, have a devastating effect on mitochondria ribosomes, topoisomerases, and carnitine / L-carnitine transporters, respectively (Foster II & Tekin 2016; Cuypers *et al*., 2018; Fan *et al.* 2018; Jiang, *et al*., 2018). Besides, a study has shown that each of the so-called antibiotics cause damage to the DNA, protein, and intracellular lipid molecules by producing reactive oxygen radicals from the mitochondria, and even these damage occur at therapeutic doses (Rasouly *et al.,* 2019; Eftekhari *et al*., 2019). The lack of induction of oxidative stress radicals by bacteriostatic drugs such as tetracycline suggests that these drugs are better substitutive for use in certain clinical infectious cases (Lesnefsky *et al*., 2016; Asadi *et al.,* 2018).

In addition to the antibiotics mentioned, various antigens released from pathogenic bacteria also affect mitochondria and oxidative stress, followed by intracellular destruction of mammals. An example of these antigens is PorB porin of *Neisseria gonorrhea*, which is an ATP-binding protein and by an unknown mechanism breakdown the mitochondrial membrane potential and starting apoptosis in host cells (Deo *et al.,* 2018; Akbarzadeh *et al*., 2018). Besides, the role of various Gram-negative and positive bacteria including Shigella, Mycobacterium, Bacillus, and Listeria have been demonstrated in inducing apoptosis and suicide of leukocyte cell lines. Various molecules of the mentioned bacteria such as lipopolysaccharide, lipoteichoic acid, exotoxins such as lethal factor (*Bacillus anthracis*), listeriolysin and bacterial hemolysins are involved in this phenomenon (Bewley *et al*., 2016; Pitt *et al*., 2016; Anders *et al*., 2017; Ha *et al*., 2017; Ciancarella *et al.,* 2018; Feng *et al*., 2020; Wang *et al.,* 2020).

Whether or not the phenomenon of apoptosis is bad or good against infections or antigens released from microbes as well as after application of the so-called antibiotics discussed earlier, the main purpose of this article is to have a survey on the association of these situations with cancer, which at first glance, maybe a bit unscientific or illogic. The essential role of mitochondrial-mediated reactive oxygen species (ROS) in tumorigenesis has been proven for years. This includes the regulation of signal networks, proliferation, and growth of malignancies and the survival of tumor cells. ROS intermediates after induction by various factors such as microbes, can cause damage to the DNA of host cells, and activate oncogenes and blocking intracellular tumor suppressors (Idelchik *et al*., 2017; Pecorini *et al*., 2020; Youssef *et al*., 2013). Although one of the consequences of apoptosis following infections is the elimination of the causative agent, its consequences may be of spreading of the disease or

suppression of the immune system. However, intracellular microorganisms also have mechanisms to counteract apoptosis and intracellular survival of bacteria, which predisposes hosts to chronic emerging diseases including cancer and other disorders (Naderer & Fulcher, 2018).

3. Conclusion

The effect of some antibiotics on the oxidative pathway of mitochondria suggests that the use of antimicrobials must be controlled in terms of the severity of the adverse effects on oxidative stress. In particular, this effect is very important in terms of the disorders including carcinogenicity and is one of the new scientific topics under study.

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