LUPINE PUBLISHERS

Journal of Clinical & Community Medicine

DOI: 10.32474/JCCM.2020.01.000113

ISSN: 2690-5760

Letter to Editor

Antibiotic Induced Changes to Mitochondria, a Potential Mechanism for Antibiotic Induced Carcinogenesis

Jorma Jyrkkanen*

UBC Zoology Grad and SFU Education, Kelowna, Canada

***Corresponding author:** Jorma Jyrkkanen, UBC Zoology Grad and SFU Education, Kelowna, Canada

Received: January 16, 2020 **Published:** February 03, 2020

Letter to the Editor

Sameer Calghatgi (2013) demonstrated that mitochondria, a primitive endosymbiotic bacteria, related to extant SARII marine bacteria and Rickettsias, in eukaryotes is responsible for oxidative phosphorylation (OP) and ATP and NAD production, when exposed to clinically equivalent doses of antibiotics that target bacteria (cipromycin, ampicillin, kanamycin), exhibited a decline in glutathione titre, an increase in reactive oxygen (ROS) and an increase in lipid peroxide. The antibiotics tested were from 3 categories; quinolonesorganofluorine compounds such as ofloxacin, norfloxacin (noroxin), ciprofloxacin (Cipro), moxifloxacin (Avelox); aminoglycosides-Gentamicin, amikacin which create holes in the outer cell wall of bacteria suggesting mitochondria might be at risk of similar damage[1] β-lactams or penicillin derivatives such as cephalosporins, monobactams, carbapenems, carbapenems that inhibit cell wall synthesis in bacteria and by inference mitochondrial reproduction. Glutathione is an antioxidant that soaks up ROS and is essential for many neurological and other body functions. Glutathione is capable of preventing damage to important cellular components caused by reactive oxygen species such as free radicals, peroxides, lipid peroxides, and heavy metals. ROS has been linked to mutation of the cell's DNA protector, the P53 gene and lipid peroxide [2] has been linked to carcinogenesis in the molecular basis of alcoholism and red meat and treated meat carcinogenesis [3]. Lipid peroxide is a mutagen. Calghatgi also found damage to DNA. This is another finding often associated with carcinogenesis. It has also been found that antibiotics can render the immune system less effective in infection and inflammation control.

Researchers reporting in Frontiers in Microbiology found that short chain fatty acids (SCFA) from resident bacteria were important in protecting the immune system, and inflammation control. Both of these side effects have important ramifications for prevention of cancer initiation. Antibiotics diminished resident bacteria carrying out this role and supplemental SCFA were not effective in ameliorating the effect. Dysbiosis of resident microbes is unequivocally associated with immune-related disorders and opportunistic and pathogenic infections which can themselves set the stage for cancer [4]. If Helicobacter pylori, Streptococcus bovis, Salmonella typhae, Fusobacterium, Chlamydophyla, Bartonella or caries bacteria proliferate as a consequence this can lead to increased risk of cancers particularly in epithelial tissue. Seeing that these changes were consistent with steps found in carcinogenesis [5] I asked the question, what is the clinical and epidemiological evidence that antibiotics increase the risk of cancer? It appears others have also addressed this question [6-8]. In addition, one of the antibiotics classes tested was linked to a decline in pyruvate, the feed stock for the citric acid cycle and ATP and NAD production or OP, thus relegating the cell to a low oxygen environment. This is called the Warburg Effect which cancer cells have been shown to prefer in which they employ glycolysis instead of oxidative phosphorylation for their energy. It can be expected that this ideal environment for glycolysis favoring cancer cells will be the norm whenever and wherever mitochondria are damaged as they are with these antibiotics tested and with common pesticides. Clearly regulatory agencies need to pay more attention to these findings. Since 50% of cancers have a mutated P53 gene from prior studies and lipid peroxide is linked to mutagenesis and carcinogenesis in at least two cancers. I propose the hypothesis that these findings point to a DNA+P53 damaging ROS increasing-Lipid Peroxide increasing-mutagenic-(possible decreased pyruvate)+glutathione deficiency immune compromise syndrome underlying the mechanism for antibiotic carcinogenesis.

Further research suggested by these studies includes testing all antibiotics for their mitochondrial impacts. These findings also raise the question are there pesticides with similar consequences and there are intriguing findings in China. 9/12 common pesticides tested fragmented mitochondria at normal application doses [9]. These results in turn raise the obvious question, are the consequences similar in terms of potential long-term carcinogenicity? Another interesting question [10]. The heart muscle is full of mitochondria [11]. Do antibiotics and pesticides affect the hearts mitochondria and if so in what way and for how long? I would expect this heart loss of OP combined with ROS and

increased peroxides to lead to a condition [12] like chronic fatigue and possibly compromised coronary function. These findings in normal mitochondria of their stress response to antibiotic biocides is consistent with their evolutionary origin from bacteria and are linked to biochemical pathways already shown linked to carcinogenesis and confirmed in the literature [13].

References

1. Louis Gonzalez III, Jianne P Spencer (1998) Aminoglycosides A practical Review. Am Fam Physician 58(8):1811-1820.
2. Siraj I Mufti, Vasanthi Nachiappan, Cleamond D Eskelson (1997) Ethanol-Mediated Promotion of Esophageal Carcinogenesis: Association with Lipid Peroxidation And Changesin Phospholipid Fatty Acid Profile Of The Target Tissue. Alcohol and Alcoholism 32(3): 221-231.
3. Marten OCB, Naud N, Taché S, Debrauwer L (2018) Targeting Colon Luminal Lipid Peroxidation Limits Colon Carcinogenesis Associated with Red Meat Consumption. Cancer Prev Res (Phila) 11(9): 569-580.
4. Natarajan Bhaskaran, Cheriese Quigley, ClarissaPaw, Shivani Butala, Elizabeth Schneider (2018) Role of Short Chain Fatty Acids in Controlling Tregs and Immunopathology During Mucosal Infection. Front Microbiol 24(9): 1995.
5. Kohanski MA, Tharakan A, Lane AP, Ramanathan M Jr (2016) Bactericidal antibiotics promote reactive oxygen species formation and inflammation in human sinonasal epithelial cells. Int Forum Allergy Rhinol 6(2): 191-200.
6. Boursi Ben, MD Eur J (2015) Cancer Antibiotics increased risk of cancer. 51(17): 2655-2664.
7. Annamaria Keskinen, Harri Rissanen, Timo Klauck, Eero Pukkala, Markku Heliövaara, et al. (2008) Antibiotic use predicts and increased risk of cancer. 123(9): 2152-2155.
8. Newman Tim (2017) Antibiotics may increase the risk of bowel cancer. Medical News.
9. Chen T (2017) (My comment) Pesticides induced mitochondrial fragmentation at low levels. Int J Mol Sci 18(12).
10. IARC (1990) Ampicillin was tested for carcinogenicity byoral administration in mice and rats It increased the incidences of mononuclear-cell leukemia and of pheochromocytomas of the adrenal medulla in male rats. A slight increase in the incidence of benign lung tumors was observed in female mice. P: 50.
11. Calghatgi Sameer (2013) Bactericidal antibiotics induce mitochondrial dysfunction and oxidative damage in mammalian cells. Sci Trans Med 5(192): 192ra85.
12. Millipore Sigma. Penicillin/Streptomycin/Amphotericin B Solution (100X), Tissue Culture Grade. Calbiochem-harmful and teratogenic and carcinogenic pp: 516104.
13. Steinberg Pablo (2019) Red meat derived Nitroso Compounds, Lipid Peroxidation Products and Colorectal Cancer. Foods 8(7): 252.

DOI: 10.32474/JCCM.2020.01.000113