



## The Role of Antioxidant Substances in the Enhancement of the Immune System against Cancer Cells

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The big advantage of the exploration of the molecular and cellular mechanisms of the immune system especially the last two decades opened the door to many innovating and new promising cancer therapies that can save lives and even prevent cancer of any cause. For instance, a variety of cell-based immunotherapies using T cells, NK cells, and dendritic cells have been established and contributed majorly in very useful clinical laboratorial results preventing or even curing cancer [1].

For many decades, there was a conflict on the scientific community on the use of antioxidants for the treatment against human cancers [2]. However, a yellow colored substance called curcumin has been proven that has antioxidant and anticancer activities [3]. In addition, this herbal supplement has been shown to modulate immune system and especially to help eradicate cancer cells via different immunological mechanisms [4]. Moreover, the antioxidant ascorbic acid (vitamin C) has been demonstrated to play an important role in stimulating the immune system by the natural killer cells (NKC), which directly kill the cancer cell line k562 [5]. Furthermore, Chang, *et al.* have shown that administration of resveratrol, a dietary polyphenol compound possessing antioxidant properties at low doses that are nontoxic to immune cells, inhibits lung metastasis of breast cancer tumor [6]. In addition, Toliopoulos, *et al.* showed the immunomodulating properties of resveratrol on NK cells by a series of experiments, which demonstrated the right concentration of this antioxidant with the maximum capacity of killing of the NK cells against tumor cells [7].

Despite the recent advances medicine, chemotherapy, radiation therapy and immuno-therapy are widely considered either alone or in combinations for a variety of cancers. On the other hand, one of the consequences of chemotherapy and radiation therapy is the generation of reactive oxygen species (ROS), which via its direct and indirect effects on tumor cells, induces DNA damage, which is lethal for humans [8]. Therefore, several nutritional cancer chemo-

preventive compounds (genistein, daidzein, and glycitein) having antioxidant properties have been documented to potentiate radiation therapy-induced cytotoxic effects on cancer cells while reducing its toxicity on normal surrounding tissues [9]. Survival of cancer patients was reported in many trials, where administration of a series of antioxidants took place such as glutathione, melatonin, vitamin A and E, NAC, selenium, L-carnitine, Co-Q10, ellagic acid, an antioxidant mixture such as vitamin C and E with beta-carotene or selenium supplementation [10].

A large percentage of cancer patients undergoing active treatments uses antioxidants and not all antioxidants are likely to be beneficial; as well, their mode of action on cellular systems and interaction with anticancer drugs remained largely unexplored. However, there is scientific proof with a diagnostic test called NK cytotoxicity assay, which proves the efficiency of the antioxidant's administration *in vivo* and *in vitro*. Toliopoulos, *et al.* used k562 cancer cell line and human NK cells with encouraging results. This testing assay can be used with any cancer cell line that can even be extracted from solid tumors being under surgery and they can be tested either alone with antioxidants or with combination with NK cells [11].

The major issue to be visualized in the immune system is that the number of the NK and NKT cells is a complete different marker from the cytotoxicity of the NK cells. This difference had been demonstrated with different kinds of individuals *in vivo* and the conclusion that was drawn is that there may be circumstances that the number of NK and NKT was high but the NK cytotoxic activity was low and vice versa. Another encouraging note in this study is the methodology of quantification of NK cytotoxicity assay. This technique can be used to investigate modified NK function found in various disorders and to evaluate the effects of drugs on NK activity. Moreover, the NK cell cytotoxicity can be used as a prognostic value for the probability of developing metastasis in patients

with primary tumors. Therefore, stability of the immune system will be remained and attacks will be prevented of foreign invaders [11].

Conclusively, the antioxidant application on cancer immunotherapy should be tested with further preclinical and clinical studies because they are needed to establish the clinical implications of doses and timings based on treatment regiments, disease stage, and especially immune suppression status. All these require very well specialized medical equipment and expert scientific staff, which will also has high morale and ethical deontology in order to reveal realistic results that will help in the fight against cancer.

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