Selective Pro-Oxidant Therapy for the Treatment of Malignancies

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Introduction

Selective Pro-Oxidant Therapy (SPT) represents a powerful new method of killing cancer cells while causing no harm to normal cells. SPT is a natural and nontoxic approach to cancer therapy that leverages a key vulnerability of cancer cells that does not exist in normal cells. Selectively killing cancer cells has been a major challenge in oncology since the introduction of chemotherapy and radiotherapy. Presented here is a practical, safe and effective method for selectively killing cancer cells without toxicity, side effects or the risk of inducing secondary cancers.

All chemotherapy agents and targeted drugs trigger cancer cell death by causing an excess level of oxidative stress. These agents are limited by off-target toxicity and buildup of resistance. Response to chemotherapy can be significantly improved by limiting antioxidant defense systems. The same principle applies to radiotherapy which is an oxidative assault on cancer cells. Antioxidant defense systems protect cancer cells from internal oxidative stress overload and from externally induced oxidative stress.

Weakening antioxidant defense systems opens the door to utilizing nontoxic and selective natural agents instead of chemotherapy and radiation. These agents are largely phytochemical or can be common vitamins. By targeting antioxidant defense systems, cancer can potentially be cured without causing harm to the cancer patient or increasing the risk of second cancers. This approach is applicable to all forms and stages of cancer.

All forms of cancer exhibit abnormal mitochondria and energy metabolism which results in a strong dependence in antioxidant defense systems. Dysfunctional mitochondria produce high levels of free radicals from the process of producing energy for the cell (ATP). Observed in all cancers is an elevated oxidative stress (ROS) level compared to normal cells.

Implementation of SPT is done in conjunction with Targeted Amino Acid Deprivation Therapy (TAADT) which together weakens the two major antioxidant defense systems of cancer cells. Why is it so important to target the cancer cell's antioxidant defense systems? The reason is that one of the main differences between normal cells and cancer cells is the level of oxidative stress (ROS) which is much greater in cancer cells.

SPT can be implemented with inexpensive orally administered agents within a home-based program. Cost is an issue since SPT is not a therapy that would be covered by medical insurance. SPT and TAADT are both very affordable treatment options that have been demonstrating excellent safety and effectiveness across a wide array of cancers.

Antioxidant Defense Systems

There are two main antioxidant defense systems within all of our cells. The purpose of these antioxidant systems is to protect the cell from oxidative (or free radical) damage caused from internal oxidative stress or to detoxify external oxidative or toxic threats. Cancer cells strongly rely upon antioxidant defense systems to neutralize free radicals generated by their abnormal metabolism.

Oxidants include hydrogen peroxide, superoxide, which are reactive oxygen species. Cancer cells operate at a much higher level of ROS than normal cells which creates a very significant vulnerability for cancer cells. This vulnerability can be exploited therapeutically to selectively kill cancer cells.

Weakening antioxidant defense systems is the basis for triggering cancer cell death by induction of apoptosis, ferroptosis, necrosis or other forms of programmed or regulated cell death. Effective treatment of cancer must incorporate some form of selective induction of cell death that eradicates cancer stem cells and tumor cells.

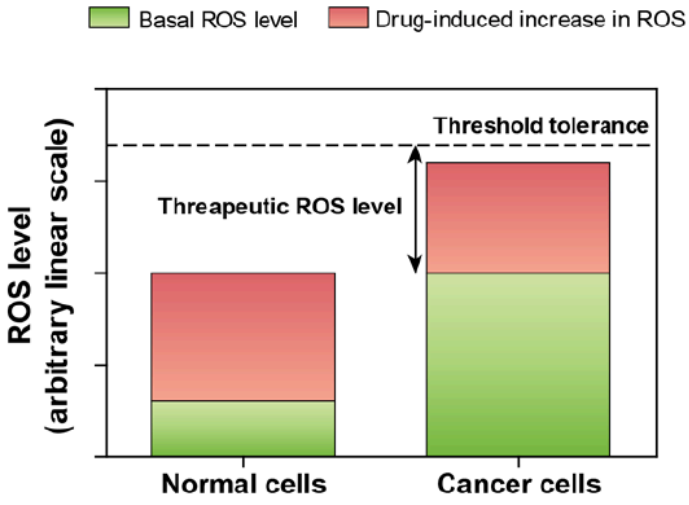

Figure 1. Comparison between ROS level in normal and cancer cells.

Glutathione Antioxidant System

Glutathione is the primary antioxidant defense system in all cells. Glutathione is observed to be upregulated in cancer cells. There are multiple ways in which the glutathione antioxidant defense system can be targeted and rendered incapable to regulate ROS within cancer cells. TAADT is a natural and safe means to deplete glutathione by limiting dietary cysteine intake.

Thioredoxin Antioxidant System

Thioredoxin is a secondary antioxidant defense system which is upregulated in cancer cells. There are multiple natural agents that have been discovered that inhibit the thioredoxin antioxidant system. Dual knockout of the glutathione and thioredoxin antioxidant system is lethal to cancer cells and harmless to normal cells.

Natural Pro-Oxidants

Natural pro-oxidants can be agents that either directly induce oxidative stress or inhibit antioxidant systems. Some pro-oxidants are actually antioxidants but behave as a pro-oxidant at high concentration. Vitamin C is a prime example of this dual nature of antioxidants.

Sodium Selenite

Sodium selenite is an inorganic form of selenium found in nutritional supplements. Being water soluble, sodium selenite is highly bioavailable and is an excellent agent for treating all forms of cancer. Sodium selenite exerts selective anticancer activity mainly as a thioredoxin antioxidant inhibitor. There are other ways in which sodium selenite selectively kills cancer cells. It has been observed that there is a high uptake of sodium selenite into tumor tissue.

Piperlongumine

Piperlongumine is a compound derived from Long Pepper, an ayervedic herb common in India as a spice and medicine. Piperlongumine is a thioredoxin reductase (TRXR1) inhibitor. The oral bioavailability of piperlongumine is suitable for acheiving a therapeutic threshold for cancer therapy.

Other Pro-oxidants

There is a multitude of potentially therapeutic natural pro-oxidants but the vast majority exhibit low bioavailability. Ideally, pro-oxidants should be able to be administered orally.

The following is a list of natural pro-oxidants that have good bioavailability and strong evidence for their anticancer effects.

Vitamin E Delta Tocotrienol, High Dose Zinc Picolinate, High Dose Copper, Cnidium Monnieri (Osthole), Vitamin K3 (Menadione Sodium Bisultite)

High ozonide ozonated oils are a very promising means to induce oxidative stress. There are capsules available which essentially provides a means to implement continuous ozone therapy.

The scope of this paper is not inclusive of off-label drugs. There are many off-label drugs that can be powerful pro-oxidants or interfere with antioxidant systems. One prescription drug of great interest is Auronifin which happens to be very costly. Celecoxib is another example.

Some over-the-counter medications may prove to be useful as pro-oxidants. NSAIDs have been shown to induce apoptosis through an oxidative mechanism. Adult 325 mg aspirin may have some pro-oxidant potential but is limited by stomach wall irritation.

Conclusion

SPT is an innovative new approach to treating cancer by a combination of inhibiting the thioredoxin antioxidant defense system and inducing oxidative stress with natural agents. SPT works best when combined with TAADT since this is a nontoxic means to deplete glutathione. Dual knockout of the glutathione and thioredoxin antioxidant defense systems by itself triggers apoptosis selectively in cancer cells. Adding additional oxidative stress and ferroptosis inducers represents a powerful and efficient method to kill both tumor cells and cancer stem cells.

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