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Winning the War on Cancer - Part II

Article by Dr Nyjon Eccles, 04/02/2013

In the last article "Losing the War on Cancer" I discussed the current failure of chemotherapy to turn the tide of increasing incidence of cancer. I looked at the reasons why this was the case. I discussed the clues from Nature that suggest that the cancer prevention actions of the phyto-nutrients in fruit and vegetables are likely to be due to a range of nutrient-gene interactions and not just an anti-oxidant effect. Specific phyto-nutrients decrease DNA damage, improve cell communication, improve cell detoxification, are anti-inflammatory, boost Immunity and improve circulation and there may be other as yet undefined actions of phyto-nutrients that are relevant to their cancerostatic effect.

The key to unravelling the cancer mystery I believe lies in correctly identifying the mechanisms by which a normal regulated cell becomes an "unruly" unregulated one.

The cell is an exceedingly complicated and subtle machinery in which all functions are carefully regulated. A normal cell divides only when division is needed. A cancer cell divides also when no division is needed. This means that the cell regulators are out of order. Many efforts to show the difference between the chemical makeup of a normal and a cancer cell have hitherto failed. The cellular structures are identical, only the regulators are disturbed. Something has gone wrong that has to be repaired.

How does a normal cell become unregulated?

In recent years there has been a great deal of focus on the possible assaults on a cell that may cause it to mutate and become abnormal. Does a virus or a toxin or free radical cause damage to DNA and lead to an alteration in the cells regulatory genes, for example those involved in normal programmed cell death. Interesting though this is in theory, it has not led to any major solution to the cancer problem.

There have been some historical clues to suggest that a fundamental flaw that occurs in all cancers is a disturbance in cell metabolism, that makes the cell prefer a fermentation of glucose (using glycolysis) for energy production rather than the more efficient oxidative metabolism (which requires oxygen and generates much more energy). (Warburg,1930; Szent-Gyorgyi et al, 1963). It seems that this switch to fermentation may be a mechanism for allowing cell division and therefore growth to occur and may be the process that normally happens when the cell needs to divide. After this normal cell division the process then reverts back to oxidative metabolism, with its associated electron flow, and which requires a more organised cell structure. Therefore, it may be that the uncontrolled growth of cancer cells is associated with them being stuck in a fermentation process. We must then ask the question – What keeps them stuck in this process? Or what turns off the ability of the cell to revert back to a normal oxidative cell metabolism - which seems to be associated with cell regulation?

These arguments are not new and have been presented before by Albert Szent- Gyorgyi, the Hungarian-born Nobel prizewinner, in the 1950s and 60s. (Dr. Albert Szent-Gyorgyi was the Nobel Laureate in Medicine in 1937 for the isolation and discovery of Vitamin C. Known as the "Father of Nutritional Science", he also discovered iso-flavones and vitamin P. In his last 40 years, he researched the regulatory processes of cell growth, and thereby the regulation of cancer itself).

Otto Warburg in 1930, has championed the fact that anoxia is the cause of cancer for decades. The first notable experimental induction of cancer by oxygen deficiency was described by Goldblatt and Cameron (1953), who exposed heart fibroblasts in tissue culture to intermittent oxygen deficiency for long periods and finally obtained transplantable cancer cells, whereas in control cultures that were maintained without oxygen deficiency, no cancer cells resulted. Warburg emphasizes, "but there is only one common cause into which all other causes of cancer merge, *the irreversible injuring of respiration.*" I will present evidence later that this change in cell respiration may not be irreversible after all.

One of the many mysteries about muscles is the fact that they rarely develop cancer. This may be because they are so dependent on oxygen and oxidative metabolism or so rich in mitochondria, the power centres of the cell, that there is too much oxidative reserve for cancer to develop.

It is now well accepted that most cancers are more glycolysis-dependent than normal cells. Cancer cells have lost their capacity to conduct oxidations, and also the mechanisms that use the energy of oxidation for useful work. Instead a low-grade process, wasteful fermentation, is used to produce energy. As stated above, this may be the norm for the cell when it wants to divide. Positron emission tomography (PET) imaging has now confirmed that most malignant tumours have increased glucose uptake and metabolism. Warburg suggested, but did not prove, that this was due to ''abnormal mitochondria'' (Warburg, 1930); that is, cancer cells are forced to use inefficient, non-mitochondrial means of generating ATP (the energy unit of cells). Szent-Gyorgyi was also of the opinion that *this apparent mitochondrial ''dysfunction'' is in fact reversible*. It was his research that suggested that this fermentation energy is transferred to the mitotic mechanism, where it forces cell division. In other words as stated earlier, efficient oxidative energy production is associated with organised cell structure, whereas fermentation is associated with lack of structure and the inclination to cell division. When cancer cells multiply they are merely performing an innate function.

It has been reported that human cancer cell lines have a more negative membrane potential compared to several non-cancerous cell lines, suggesting that this might be a hallmark of malignancy (Bonnet et al, 2007). Since a significant proportion of cell energy production (70% or more) is channelled towards maintaining electrical integrity by supporting the ion pumps at the cell membrane, it becomes clear that this abnormal membrane potential of cancer cells is likely to be secondary to the cell being "metabolically" compromised.

Mitochondrial Function and cancer

Mitochondria are the seat of energy production in the cell producing 80% of the energy needs of the cell. Several differences have been observed between the mitochondria of cancer cells and those of normal cells. It has been suggested that mutations in mitochondria might cause cancer

(Woods & DuBuy, 1945). More recently it has been shown that mitochondria are integrally involved in apoptosis or programmed cell death (Petit & Kroemer,1998; Zamzami et al, 1996). The mitochondria contain their own DNA (less then 1% of nuclear DNA), which seems to be more susceptible to damage and mutations than nuclear DNA. The accumulation of mutations in mitochondrial DNA has also been suggested to play a causative role in ageing. Various tumour cell lines exhibit differences in the number size and shape of mitochondria relative to normal controls. The mitochondria of rapidly-growing tumours tend to be fewer in number, smaller and have fewer internal folds than mitochondria of slowly growing tumours. Alterations in the inner membrane composition of tumour mitochondria have also been noted (Modica-Napolitano & Singh, 2002). The mitochondrial membrane potential of cancer cells is approximately 60mV higher than that of control epithelial cells (Modica-Napolitano & Aprille, 1987). *Mitochondrial dysfunction is one of the most profound features of cancer cells*.

Cancer progression and its resistance to treatment depend, at least in part, on suppression of apoptosis (programmed cell death). As stated above, mitochondria are recognized as regulators of apoptosis.

We have already established that cancer seems to be associated with a glycolytic phenotype. Furthermore, it appears that glycolytic phenotype is indeed associated with a state of apoptosis resistance (Plas and Thompson, 2002). Many glycolytic enzymes have been recognized to also regulate apoptosis, and several oncoproteins induce the expression of glycolytic enzymes (Kim and Dang, 2005).

All the available evidence suggests that if we want to understand cancer better and find a remedy then we have to turn our attention specifically to mitochondria, for it is here that the energy malfunctions that occur in cancer are to be found.

Mitochondrial changes have multiple downstream effects, beyond energy production, because mitochondria regulate several critical functions including calcium concentration and free radical (Reactive Oxygen Species, ROS)-redox control. Mitochondria have an important role in apoptosis that may explain the apoptosis resistance that occurs in many human cancers.

Cancer cells have been shown to have more hyperpolarized mitochondria and were relatively deficient in potassium channels. If this metabolic-electrical remodelling is an adaptive response, then its reversal might increase apoptosis and inhibit cancer growth. The Michelakis research group showed that dichloroacetate (DCA), a small, orally available small molecule and a well-characterized inhibitor of the key enzyme in the glycolytic chain, pyruvate dehydrogenase, was able to change the metabolism of cancer cells from the cytoplasm-based glycolysis to the mitochondria-based glucose oxidation. DCA also reversed the inhibition of potassium channels in all cancer, but not normal cells. The net effect was a reversal of resistance to apoptosis (Bonnet et al, 2007). DCA treatment significantly increases glucose oxidation (which only occurs in functional mitochondria), *indicating that the metabolic cancer signature (aerobic glycolysis) is reversible*, rather than a consequence of permanent mitochondrial damage. Szent-Gyorgyi concluded this but this was also the conclusion of Koch (1958, see below) whose work strongly suggested that the metabolic/mitochondrial abnormality in cancers could be reversed. DCA was shown to significantly decrease tumour growth in rats without toxic effects. At this time, though approved as a drug treatment for mitochondrial diseases in humans, and apart from anecdotal reports, there are no formal clinical trials in patients with cancer.

Dr. William Koch's research (1958) focused on the means to restore the body's oxidation mechanism back to its original vitality, thereby re-equipping the body with its innate ability to restore and maintain health, not only in cancers but also in a host of other diseases.

Organized Medicine launched a fifty-year assault aimed at discrediting Dr. Koch's reputation, medical practice and research, along with those of any physician who dared to validate his Theories or use his Reagents. Dr Koch's theories emphasized the relationship between environmental toxins, dietary deficiencies and a depleted oxidation mechanism, as primary initiators of the disease process.

In his work he discovered that removal of the parathyroid gland of animals led to accumulation of toxic substances in the body. He also observed that the urine of the animals without parathyroid glands carried large amounts of lactic acid, which meant that the oxidation process was badly handicapped by the substances that were produced in the parathyroidectomized animals. These substances had blocked the normal tissue oxidation process. This turned out to be a momentous discovery, which paved the way for his original cancer research. By studying the tissues that survived the longest, he found out that the common feature was the presence of the di-carbonyl groups. He postulated that the toxic amines of various metabolic, bacterial, viral or of fungal agents (present day antibiotics included) are able to cripple these important carbonyls by condensing with them. These functional carbonyls were crucial to the preservation of electron transport and metabolic function of the cell but when they were complexed by toxins this could lead to an irreversible compromise of metabolic function. Unfortunately Dr. Koch was never given the research facilities and cooperation by the medical profession he had asked for and wanted.

Despite several cases of advanced cancers being treated successfully by Koch (by the injection of carbonyl compounds) in 1919 under the auspices of the Wayne County Medical Society branch of the American Medical Association (AMA), the Journal of the A.M.A. published over 20 negative editorials and articles about Dr. Koch and his treatment dating back to February 12, 1921.

In 1968, Dr. Szent-Gyorgyi also wrote about the cancerostatic action of carbonyl compounds (Szent-Gyorgyi et al, 1967) and how they are able to arrest cell division. He described these substances in urine and also in tissue extracts from several body organs. His research suggested that these substances when present are not only able to inhibit cell proliferation but also to maintain cells in a normal oxidative metabolism. The suggestion is that the body can lose its ability or become compromised in its ability to produce these substances thereby encouraging the development of cancer.

Further evidence that compromised mitochondrial function is a fundamental cause of the development of cancer is also suggested by the reported efficacy of the Kucera cancer support regime. Dr Michael Kucera, a Czech physician, has spent 20 years or more researching mitochondrial medicine and has developed a nutritional combinations for mitochondrial support (Personal communication, 2009). A combination of these nutrients with specific immune support nutrients has led to remarkable success in cancer remissions. *Over 700 cancer patients have been treated with this regime during the last 10 years. These have been patients with variable cancers, most of them non-localised i.e. they have already spread (including breast, prostate, colon and gastric cancers). Overall a 70% remission at 5 years is reported and an 80-90% remission when the formulas are combined with chemotherapy. No side effects were observed. Compare this to the efficacy of chemotherapy of 2-3% and with significant side effects.* To my knowledge this may be the most effective treatment regime available and is the regime of choice used in my own clinic. It is even more remarkable that the regime is a purely oral-based regime. The fundamental basis for this high level of efficacy must be due to the core benefit to the mitochondria.

Coenzyme Q10 will be more familiar to many of you. This fat-soluble substance is present in most eukaryotic cells, primarily in the mitochondria. It is a component of the electron transport chain and participates in aerobic cellular respiration, generating energy in the form of ATP. Ninety-five percent of the human body's energy is generated this way (Ernster & Dallner, 1995; Dutton et al, 2000) Therefore, those organs with the highest energy requirements—such as the heart and the liver—have the highest CoQ10 concentrations (Okamato et al, 1989; Aberg et al, 1992; Shindo et al, 1994).

Interest in coenzyme Q10 as a potential therapeutic agent in cancer was stimulated by an observational study that found that individuals with lung, pancreas, and especially breast cancer were more likely to have low plasma coenzyme Q10 levels than healthy controls (Folkers et al, 1997). There are a few case reports and an uncontrolled trial (see below) suggesting that coenzyme Q10 supplementation may be beneficial as an adjunct to conventional therapy for breast cancer (Hodges et al, 1999).

Although CoQ10 is best documented in the treatment of heart failure, two medical journal articles suggest tremendous promise in the treatment of cancer. Folkers (1997) described 10 cancer patients given CoQ10 for heart failure. One of the patients, a 48-year-old man diagnosed with inoperable lung cancer, had no signs of either cancer and heart failure symptoms while taking CoQ10 for 17 years.

Knud Lockwood, M.D (1994), a cancer specialist in Copenhagen, Denmark, described his treatment of 32 "high-risk" breast cancer patients with antioxidant vitamins, essential fatty acids, and CoQ10. "No patient died and all expressed a feeling of well-being," he wrote "These clinical results are remarkable …..After 24 months, all still survived; about 6 deaths would have been expected." Six of the 32 patients showed partial tumour remission, and two benefited from very high doses of CoQ10. One, a 59-year-old woman with a family history of breast cancer, had a tumour recurrence 1.5-2 centimetres in diameter but one month after increasing the CoQ10 intake to 390 mg. daily, the tumour had disappeared. Mammography confirmed its absence. Another patient, age 74, had a small tumour removed from her right breast. She refused a second operation to remove additional growths and began taking 300 mg of CoQ10 daily. Three months later, an examination and mammography revealed no evidence of the tumour or metastases. Lockwood, who has apparently treated some 7,000 cases of breast cancer over 35 years, wrote that until using CoQ10, he had "never seen a spontaneous complete regression of a 1.5-2.0 centimetre breast tumour, and has never seen a comparable regression on any conventional anti-tumour therapy."

Although none of the above are controlled studies they provide circumstantial evidence for my hypothesis that mitochondrial metabolic malfunction are critical to cancer development and should be the primary target in the war against cancer. Indeed, I have presented evidence from several pioneering doctors/researchers to show that when the mitochondria are supported and/or their metabolic defect is corrected that this is associated with cancer remissions. I am not the first to suggest this but I cannot ignore the evidence before me. I am convinced that this is the key to unravelling the cancer mystery. History has given us the clues…..it is time to stop ignoring them!

It was not the purpose of this article to focus on anything but the physical side of treatment but it would be an omission in the context of the title of this article "Winning the war on cancer" not to at least comment on the role of belief and positive thought to influence positive outcome in the war. This important component has been discussed elsewhere (Byrne, 2006; Chopra, 1989).

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