BACK

A NEW THEORY OF THE CELL AND CANCER

A commentary on the theory of Perth biophysicist Eleni Papadoulos-Eleopulos

Introduction

Although there have been significant improvements in outcome for some of the less common cancers (testicular, lymphomas, childhood leukaemias), the common epithelial cancers remain problematic. These are in men (lung, prostate, bowel) and in women (lung, bowel, ovarian, breast). For example, breast cancer is the major cause of cancer death in Australian women accounting for 10,000 new cases and 2,600 deaths each year. That amounts to approximately one new case every hour and one death every 3 hours. To date cancer treatments are surgery (although often impossible to remove completely), irradiation and chemotherapy (chemical toxins). All treatment modalities are non-selective, that is, they produce deleterious effects on normal tissues. This is much more of a problem with irradiation and chemotherapy which may result in significant, unwanted effects and frank toxicities. Experts agree that the *National Cancer Act of 1971*, signed into US law by President Richard Nixon (the "War on Cancer"), has been lost.[1, 2]

How can matters be improved?

A deeper understanding of the mechanism controlling cellular growth is required. Such knowledge could lead to treatments that address the root cause. Such a theory was developed in the mid-1970s and published in its final form in 1982 in the *Journal of Theoretical Biology* under the title *A mitotic theory.*[3-6]

A mitotic theory hypothesises the redox (reduction/oxidation) theory of cellular functioning. An oxidising agent is one which removes electrons from another substance. A reducing agent (also called an antioxidant) is one which donates electrons to another substance. This theory takes a step back from the minutiae of "genes", DNA, RNA, proteins and considers the cell acting as a whole within its particular environment. The theory is based on the facts that:

1. For a cell (or organ) to perform its various functions it requires a source of energy.

2. The cell (organ) must be able to transform energy into work.

3. All cellular (organ) functions are cyclical. For example, in performing its work the heart and intestine periodically contracts and relaxes; we breathe in and out.

According to the redox theory normal cells are energised by their relative abundance of reducing substances, that is, electron-rich substances (reducing agents, antioxidants). The electrons are "stored" in many cellular constituents, especially in an ubiquitous cellular protein called myosin, present in all cells and in all parts of all cells. The energised myosin constitutes the cellular potential energy store, that is, the energy available to do work. The cell (organs) transform this energy into work in order to perform its (their) various and different functions. In its energised state the functional sulphydryl groups of myosin (SH1 and SH2), magnesium and ATP are bound together in the form of a ring. Energy is liberated when the ring is broken, the ATP is hydrolysed and electrons flow from myosin to oxygen and another ubiquitous cellular protein called actin. The charge transfer leads to interaction between the two proteins, that is, contraction of the actin/myosin system. During this process the concentration of

reducing substances decreases, that is, the cell becomes progressively oxidised and the cellular potential energy store depleted. The store is replenished by reducing substances in food whereupon the cell is ready to resume doing work. This ebb and flow (oscillation) of oxidation/reduction continues as long as the cell functions. Because of their ubiquity, actin and myosin can be considered the "wiring" of the cell; and because biological tissue is a good conductor, redox changes in one part of the cell (organ) may be communicated to other parts of the cell (organ). In this manner the redox and the oscillating charge transfers in the actin/myosin redox couple play their pivotal role in determining cellular structure and function.

According to the redox theory, at a given instant every cell is characterised by a particular redox state and each function by a cycle during which the alternating oxidation/reduction takes place. In other words the redox state and its oscillation lie at the root of cellular differentiation, that is, for example, whether the cell is a brain, kidney or cancer cell. It is often stated cancer is caused by changes in the DNA (mutations) or by cancer causing genes (oncogenes). However, in experiments conducted in the 1960s (upon which present day animal cloning is based) the exchange of cell nuclei proved that the character of a cell is determined by factors outside the nucleus.[7-11] That is, factors within the cytoplasm determine what the DNA does – not *vice versa*. At present there is much evidence that the DNA function is regulated by the cellular redox state and its oscillations.[12]

How can the redox theory help patients with cancer?
The redox theory postulates that cellular division is under the control of and is determined by the cellular redox state. At present evidence exists which shows that all agents which initiate cellular division are oxidising. All known cancer causing chemicals (carcinogens), including cigarette smoke and asbestos, are oxidising agents. Radiation, which also causes cancer, does so by oxidising cellular constituents. The agents presently used to treat cancer, that is chemotherapy and radiation are also oxidising. These agents may destroy cancer but leave the body oxidised and thus prone to future development of the disease. This is well documented in clinical practice.

According to the redox theory of cancer:
Cancer can be prevented by the intake of antioxidants. These should preferably be obtained by a proper diet. Intake of supplements should always be based on measurements of the redox.

Cancer can be treated by antioxidants. These are readily available and cheap. However, their administration must be based on measurements of cellular redox.

Admittedly at present there is a plethora of books, diets and antioxidant advice and treatments available. However they are based on *ad hoc* observations without a basic understanding of the critical role of redox in cellular function. Because of this, their proponents are unaware that the incorrect dose and timing may cause more harm than good. In addition, in most cases, the "antioxidants" recommended are vitamins A, C E and selenium. There are many problems connected with these particular supplements, including the fact that they may act as oxidants.[13]

Is there evidence to support the redox theory?
A theory is only as good as its predictions. Two (non-cancer related) predictions of the redox theory have been confirmed by experiments.

Any attempt to explain cardiovascular diseases must involve an understanding of the contraction/relaxation of muscle. The theory predicted that muscle contraction is

caused by oxidation (oxidants) and relaxation by reduction (antioxidants). Also, the stronger the oxidant the more forceful contraction it will induce. This hypothesis tested in 1985 in experiments where graded amounts of oxidants were added to rat aorta suspended in a water bath. The results were as predicted. It is significant that before this experiment it was thought that muscle function (contraction/relaxation) was regulated by ionised calcium (Ca^{++}). On this basis several colleagues predicted the redox experiment would fail. In fact the redox experiment proved a direct and linear relationship between the oxidising potential of the oxidant and the force of contraction. The oxidants included a number of chemicals not normally present in the body (non-physiological) thereby validating the general applicability of the theory. The calcium theory does not predict or explain these observations. Also as predicted, several antioxidants produced relaxation.[14, 15]

Similar experiments have proven that muscle contraction induced by physiological substances such as serotonin and adrenaline can be reversed by reducing agents. This is also as the theory predicts, was unexpected and not accounted for by the calcium hypothesis and has the potential for widespread application in clinical practice.[15]

Generalised cerebral (brain) arterial spasm is a serious and often fatal consequence of subarachnoid haemorrhage (a variety of stroke). For many years the cause of this condition was a mystery and was extensively researched in attempts to define the responsible agent in shed, intracranial blood. The redox theory hypothesised not one particular substance but rather the oxidising potential of altered blood *en masse* as the cause. This has been experimentally verified in published[16] and unpublished experiments involving dog basilar artery, human blood several weeks old and cerebrospinal fluid obtained from patients with cerebral ischaemia and subarachnoid haemorrhage.

The future of the redox theory

While the experimental proof in regard to muscle contraction is significant, application of the theory to cancer suffers from the lack of carefully conducted experimental verification. This would involve experiments documenting the effects of different doses and timings of doses of various oxidising and reducing substances on both normal and cancerous cells. Critical to these experiments is measurement of the cellular redox state. Unfortunately, the political reality is that treatments based on the redox theory attract little interest or favour. The redox theory is badly in need of champions.

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References and Notes

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2. The parlous state of the *War against Cancer* is illustrated by the National Cancer Institute's recruitment of cosmologist Professor Paul Davis in 2011 to head twelve new institutions to look at the cancer problem afresh. "As best he can remember, says Paul Davies, the telephone call that changed his professional life came some time in November 2007, as he was sitting in the small suite of offices that comprise his Beyond Center at Arizona State University (ASU) in Tempe...The caller — Anna Barker, then the deputy director of the US National Cancer Institute (NCI) in Bethesda, Maryland — explained that she needed his help in the 'War on cancer'. Forty years into the government's multibillion-dollar fight, said Barker, cancer survival rates had barely budged. The hope now was that physicists could bring some radical new ideas to the table, and she wanted Davies to give a keynote address at an NCI workshop explaining how. Ummm, sure, said Davies, who until that minute had been only vaguely aware that the NCI existed. "But I don't know anything about cancer." "That's okay," Barker replied. "We're after fresh insights". And in yet another battle of the *War*, in his January 20th 2015 State of the Union address President Obama said "Tonight, I'm launching a new Precision Medicine Initiative to bring us closer to curing diseases like cancer and diabetes".
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