Medical Hypotheses (2007) **69**, 262–272

medical
hypotheses

ELSEVIER

http://intl.elsevierhealth.com/journals/mehy

Restoration of cellular energetic balance with L-carnitine in the neuro-bioenergetic approach for cancer prevention and treatment

Ba X. Hoang [a,*], D. Graeme Shaw [b], Phuong Pham [c], Stephen Levine [d]

[a] *Allergy Research Group, 4010 Moorpark Ave, Ste 119, San Jose, CA 95117, USA*
[b] *Advanced Integrative Medicine, 5050 El Camino Real, Suite 110 Los Altos, CA 94022, USA*
[c] *Department of Molecular Biology, University of Southern California, Los Angeles, California 90089, USA*
[d] *Allergy Research Group, 2300 North Loop Rd, Alameda, CA 94502, USA*

Received 26 October 2006; accepted 17 November 2006

Summary Mitochondrial research has contributed to two paradigm shifts in oncology — Warburg's glycolytic metabolism and the relationship between mitochondrial function and mutagenesis. Mitochondrial dysfunction is a common phenotype in aging and cancer. Decline in mitochondrial function is due to the accumulation of mutations in mitochondrial DNA.

We have hypothesized a neuro-bioenergetic concept in cancer prevention and treatment to constructively restore three physiological imbalances of cancer patients: membrane hyper-excitability, energy depletion and the build up of extra-cellular adenosine molecules. We have proposed the use of membrane-calming substances to reduce energy consumption and to restore the normal cellular energy metabolism. Based on our theory, L-carnitine's dual effect of enhanced energy production and excitatory neurotransmitter modulation should make it an ideal nutrient for cancer prevention and treatment. L-carnitine, its derivatives and other mitochondrial protectors/enhancers improve metabolic function, energy and detoxification. In combination with other membrane calming agents, L-carnitine could help reverse the membrane hyper-excitability to overcome a neuro-bioenergetic imbalance and can be used as a relevant and effective approach for cancer prevention and treatment.

Introduction

The so-called ''War Against Cancer'' proposed and directed by the cancer research community has focused heavily on destructive, inhibitive strategies toward cancer cells, their receptors, growth factors, energy metabolism, glycolysis, angiogenesis, fatty acids synthesis and many other identified pathways of carcinogenesis in order to prevent and treat cancers. There has been limited attention to constructive (pro-health, pro-body), non-toxic approaches in understanding and managing

* Corresponding author. Tel.: +1 408 2609714; fax: +1 408 2609724.
E-mail address: niscba@aol.com (B.X. Hoang).

0306-9877/$ - see front matter
doi:10.1016/j.mehy.2006.11.049

cancers as degenerative and aged-related human disorders.

In general, the improvement in cancer prevention and treatment has been linked to preventive intervention, early diagnosis and treatment, and changes in lifestyle. However, pharmaceutical treatments are responsible for only a small fraction of cancer cures [1]. Moreover, objective clinical responses to conventional treatment may not translate into substantial improvement in overall survival [2].

Nobel prize-winner Carlo Rubbia maintains that only a billionth of the world is actually made of matter and the rest is made of energy. In our previous publications, we have proposed and substantiated cancer as a pathology of disruption, cessation or distortion in the cellular information and energy fields. The major causes of these events are environmental and endogenous toxins (mainly in sub-toxic concentrations), chronic infection and ionizing radiation that induce membrane hyper-excitability leading to depletion of cellular energy and excess extra-cellular adenosine [3].

Cancer cells have similar properties to neuronal progenitor cells that are stimulated by glutamate. The hyperexcitability leads to a disparity between energy consumption and supply. These changes are triggered by such hypoxia-induced stimulants as an increase in cytoplasmic free calcium, a decrease in adenosine triphosphate (ATP) and extracellular accumulation of adenosine produced by ATP breakdown [4].

The cells try to survive in this hostile environment with compensatory and adaptive mechanisms leading to transformation, proliferation and migration similar to organo-morphogenesis in embryogenesis, the wound-healing process or the restorative reaction in neurotrauma and/or excitotoxic neurological injuries [5].

Energy balance, defined as the integrated effects of diet, physical activity, environment and genetics on growth, function, adaptation and body weight over the life course, has been a recent focus for understanding the chronology of many chronic diseases. Research from many sources supports the positive influence of physical activity, low toxin environment, green tea, polyunsaturated fatty acids (PUFA) and other dietary patterns on cancer risk and prognosis. However, the concepts of energy enhancement, dietary improvement and detoxification remain of little interest to the conventional cancer research community.

Adverse changes in energy balance are considered to be a major factor underlying many of the pathways involved in cancer initiation and progression. In this article, we will provide evidence for using an energy metabolism restorative approach in cancer prevention and treatment.

Mitochondrial dysfunction and cancer

The mitochondria are widely recognized as the main source of cellular ATP, producing 90% of the cell's energy. This energy organelle is also intimately involved in the life and death of the cell, capable of integrating pro- and anti-apoptotic signals and committing the cell to apoptosis. It is a critical integrating center for control of carbon, nitrogen and oxygen metabolism and in Ca^{2+}, Fe^{2+} and Cu^{2+} storage.

Mitochondrial research has contributed to two paradigm shifts in oncology. The first one was the pioneering research done 80 years ago by Warburg showing that cancer cells often rely heavily on glycolytic metabolism, even in the presence of an adequate oxygen supply [6]. The molecular genetic basis of this phenomenon remains an intriguing subject for current research [7,8]. Tumors have significantly higher energy demands than normal cells. Because of this, they often employ alternative energy production including glycolysis, the anaerobic breakdown of glucose into ATP.

The second paradigm shift in oncology is the greater understanding of the relationship between mitochondrial function and mutagenesis. The mitochondria provide the energy to sustain life, but also the signals of their own demise. Apoptosis is a requisite for the physiological or therapeutic elimination of cancer cells. Researchers believe that cancer cells require mitochondrial energy to avoid apoptosis, which contributes to their replicative potential and limits the efficacy of cancer chemotherapy [9].

Mitochondrial dysfunction is a common phenotype in aging and cancer. An interesting clue to the molecular mechanisms underlying age-associated cancers is the apparent defect in mitochondrial function. Studies have established that the decline in mitochondrial function is due to the accumulation of mutations in mitochondrial DNA. These observations suggest that the mitochondrial dysfunction that accompanies aging may exert a major influence on carcinogenesis [10].

Mitochondria are involved in a strikingly diverse range of disease processes. Primary genetic disorders fall into two broad classes involving deficiencies in either nuclear or mitochondrial genes. As early as 1988, Scholte reported over 60 human diseases with defects in nuclear genes encoding mitochondrial functions [11]. There are currently 129