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D.I.Y. Treatment of Cancer

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Abstract

The cancer cells are different from normal human body cells. The scientists advocating the Somatic Mutation Theory speculated that cancer is caused when mutations have caused the Human Genome of the human body-cells to be changed into the Cancer Genomes of the cancer cells. There is, however, no good reason to assume that mutations of the Human Genome would cause the cancer cells to grow and replicate out of control. There is, in fact, no good evidence indicating that there has ever been such mutations, or that cancer cells had been human body cells before they are changed by mutations into cancer cells. Perhaps cancer cells have always been cancer cells, but some cancer cells have not been inherited by the offsprings from their ancestors.

Some of us believe that the difference between Human and cancer cells have resulted from the difference of their inherently different genomes, and have not resulted from changes, or mutations. The evolution of the eukaryote genomes and the evolution of the Cancer Genomes during the course of Earth's history have followed parallel paths of evolution that indicate adaptations of the metabolic modes in response to the ever-increasing oxygenation of the Earth's atmosphere during the past few billion years. Compared to that of the Human Genome of the human body cells, the cancer cells have genomes that indicate a retarded development in the evolution of the metabolisms. When the Human genome encodes a progressive mode of OXPHOS, the cancer genomes may still encode the anammox mode of metabolism.

We cannot deny an assumption that cancer cells have inherited evolving cancer genomes that encode different metabolic modes, while their hallmark is the uncontrolled cell-growth and replications. |We have good evidence that cancer genomes have also evolved to encode progressively different metabolic modes. Chinese medical scientists have found, for example, a wealth of evidence that some forms of cancer may have been caused by the nitrite pollution of the public water supply. China's Deep Standardized Well Water (DSWW) Program of substituting nitrite-free deep ground waters as the source of public water supply was partially successful. Local cancer-mortality rates were reduced by half at places where there had been such substitutions. Nitrite, as a reducing agent, could be the indispensable chemical in our food or drink intakes that could render the interior of cancer cells anaerobic. Nitrite,

as an oxidation agent, could then be the substrate of the metabolic reaction anaerobic ammonium oxidation (anammox). The source of oxygen would then be mineral-oxygen from the nitrite. PET scan studies have indicated an advanced stage of metabolism, when cancer cells have evolved to encode aerobic glycolysis under hypoxic conditions. We can postulate a hypothesis that predicts the starvation of cancer cells if there is no supply of nitrite in the food-take to the cancer cells as a substrate of anammox metabolism, or if there is no sufficient supply of glucose for glycolysis. We recommend thus to the UK's National Health Services to look into this matter that nitrite in public water is a health hazard. Such an investigation serves as a clinical trial on the efficacy of diet-treatments to cure cancer.

Keywords

cancer, cells, mutation, genome, metabolism, nitrite, anammox, glycolysis, starch, diet treatment

1. Introduction

Cancer has been an enemy to the mankind ever since the antique time. With the ever-increasing environmental devastations, the cancer incidence- and mortality-rates have been increasing rapidly during the 20th Century. In 2015 about 1/3 of the population of UK are afflicted with cancer. The current death rates are indeed alarming, when some 9.5 million persons died of cancer each year Worldwide. The annual financial costs of fighting cancer are estimated to be more than 1 trillion US dollars.

Cancer is a group of diseases involving abnormal cell-growth with the potential to invade or spread to other parts of the body. Many of us have lost our loved ones through the incompetent conduct of the War on Cancer. With the recent completion of The Cancer Genomic Atlas (TCGA) studies, many are beginning to realize that the big mistake has been our blind faith in the Somatic Mutation Theory (Ledford, 2015). Meanwhile, we noted a wealth of statistical evidence linking the origin of cancer to environmental degradation, such as the nitrite pollution of the public water supply (Xu, 2003). The hypothesis was first proposed during the first post-war years, when the cancer-mortality rate of Japan deceased rapidly with the use of refrigeration, instead of nitrite, as the meat-preservatives. The wealth of statistical data of uncertain scientific significance has led to an academic controversy. The SMT scientists won, when the US Environmental Agency ended the debates, rather arbitrarily, with their judgment that "nitrite is not carcinogenic." Nevertheless the statistics linking cancer-mortality rates to the nitrite-concentrations of drinking waters have continued to be impressive (Paik, Saborio, Oropeza, & Freeman, 2001; Kitamura et al., 2006; Tsuda & Hasegawa, 1990). Chinese scientists, working under conditions different from that of their colleagues in the West, carried out a large-scale clinical trial, namely the Standardized Deep Well-Water (SDWW) Program (Hsu, Huangfu, & Qin, 2011). Surface waters, from streams, lakes, in reservoirs, etc., are the normal sources of the public water supply. The SDWW comes from deeper groundwater reservoirs, which are not polluted, as the depth of appreciable groundwater-pollution is commonly less than 300 m. deep. The substitution of normal sources of water supply by SDWW has been a success. Where the substitution had been made, cancer-mortality rates

were reduced by half. The causes of the reduction are not certain. Scientists may continue to debate in their search for scientific explanations, but one fact remains, expressed in plain English, that the SDWW has saved life.

The editors of all reputed science journals of the West had rejected Hsu's manuscript reporting the Chinese victories in the War On Cancer, before it was published by a new journal searching for publishable manscripts (Hsu, Huangfu, & Qin, 2011). The article is being ignored, while Hsu continues, as a gentleman scientist, to search for a scientific explanation of the link between cancer and nitrite. He has come up with a surprise: Cancer could be, in many cases at least, considered an illness of chronic-poisoning by nitrite in public water supply. Rejected again by editors of reputed journals, Hsu's paper, co-authored with a geneticist R. Eckhardt, was published in the *Chinese Journal of Geology* (Hsu & Eckhardt, 2016). If cancer is not caused by spontaneous mutations, we need to see the 4th, the temporal dimension to understand the evolution of Cancer Genomes. Cancer is a geological problem.

Yes, there are *differences* between cancer cells and human body cells. The advocators of the SMT have assumed that the differences are manifestations of *changes*, and that the alleged changes have to be genetic mutations of the Human Genome of the human body cells. The experts do not consider other alternative explanations. Yes, cancer cells are obviously different in their mode of growth: a single cancer cell would produce cells that start uncontrolled proliferation and replication. The SMT scientists have simply assumed this hallmark is that the cancer cells are the *changed* body-cells whose genomes have been damaged by mutations. The SMT scientists have assumed that mutated genes have encoded the uncontrolled growth of cancer cells, when normal body cells were *changed* into cancer cells. The SMT scientists have further assumed that such cancer cells have been *changed* to become the fittest, because they are those that have survived. The SMT scientists have, however, not identified the "mutations" that should have caused the growth of tumors. They have not told us how did the "mutations" have come about, or why should the "mutated cells" have grown out of control, and multiplied to form tumors. They have not identified the retroviruses that are supposedly to have caused the "mutations." The word "mutations" hides our ignorance.

Great hopes were once placed on TCGA Project, which began in 2005 and ended a decade later. It was expected that a comparison of the sequence of normal DNA to those in different types of cancer cells could determine the exact "mutations" responsible for their origin. It was further hoped that a cataloguing of all such "mutations" that should have caused cancer would lead to an invention of the drugs that targets those "driver mutations" to cure cancer. TCGA has turned out to be an "expensive disappointment" to the followers of the SMT. TCGA scientists did find random collections, but not orderly sequences of mutations. Furthermore the genomes of cancer cells, or the cancer genomes, are so different from the Human Genome that cancer cells are not likely to have originated from small "transcription errors" that are supposedly the mutations of the Human Genome of human body cells. The SMT scientists cannot explain the genetics of cancer cells. They only speculated. We now suggest an alternative hypothesis that the cancer cells have never been Human body cells. Perhaps the cancer is

now considered incurable because the current mainstream-opinions have relied upon a fundamentally wrong theory.

The SMT scientists may have incorrectly assumed that the alleged *changes*, or mutations, are caused by retroviruses. No mutations, no retroviruses can be assigned as definitely causative of cancer! The SMT scientists may have made a fundamental mistake when they took for granted that cancer cells were once human body-cells with the Human Genome. The Theory has little theoretical basis for that speculation. TCGA studies have indicated that the cancer cells are descendents of cancerous stem cells. In essence, the SMT scientists may have been wrong when they simply assumed that the *differences* are *mutations,* i.e., they are *changes,* from of the Human Genome. The Theory has nevertheless become a paradigm, and the mainstream opinion has been adopted as the scientific basis to fight the War On Cancer. It is thus not surprising that the War has been a dismal failure.

Hsu and Eckhardt came to their interpretation because they recognized that *differences* are not necessarily manifestations of *changes*. We believe that the Cancer Cells have always been different from the Human body-cells. Cancer Cells have the Cancer Genomes, whereas the body-cells have the Human Genome. The two different types of genomes are inherently different. There is evidence that cancer cells have **inherited** the Cancer Genomes from the cancerous stem-cells; Cancer Genomes are **not mutations** of the Human Genome. A hallmark of the Cancer Genomes of Cancer cells is their uncontrollable growth and replications. This hallmark is not caused by mutations, or changes from the Human Genome. The growth of tumors is encoded by the inherited Cancer Genomes of Cancer cells. The “changes” from a bacterial genome into a cancer genome are not minor “transcription errors” that happened during a brief span of a patient’s lifetime. The parallel paths of the evolutionary changes of the metabolic modes of the eukaryote genomes and of the cancer genomes suggest that the process may have taken place, during the last 2 billion years or so, when the genomes evolved in response to the ever increasing oxygenation of the Earth’s atmosphere.

With their wrong postulate of random mutations, the SMT scientists could offer no prescription to stop the uncontrolled growth of tumors, except by killing off the tumor cells by chemo- or radiation therapies, or by removing the tumors with surgeries. At a more advanced stage, when metastasis has taken place, cancer cells spread through blood-circulation from one part to another part of the body. Tumors start to appear at unexpected sites, and are often discovered too late to be exterminated or removed. Terminal cancer is thus considered by the SMT scientists to be incurable. Those patients are sent to hospices, where treatment focuses on the patients’ comforts rather on a cure, and the medication includes mainly drugs for pain management. That was a mistake. We believe that terminal patients could be cured, if we have correctly understood the origin of cancer.

2. New Strategy and New Tactics to Fight the War on Cancer

The essence of the Cancerous Stem Cell Theory of Hsu and Eckhardt is the postulate that the inherited Cancer Genomes, not mutations, have made the cancer cells *different* (Hsu & Eckhardt, 2016). The

Cancer Genomes encode the uncontrolled growth and replications. The Cancer Genomes also encode the metabolic reactions that are different from those encoded by the Human Genome.

Metabolism is the set of life-sustaining chemical transformations within the cells of living organisms. The three main purposes of metabolism are the conversion of food/fuel to energy to run cellular processes, the conversion of food/fuel to building blocks for proteins, lipids, nucleic acids, & carbohydrates needed for the building of cells, and the elimination of nitrogenous wastes. The word *metabolism* refer to the sum of all chemical reactions that occur in living organisms, including digestion and the transport of substances into and between different cells. Those enzyme-catalyzed reactions allow organisms to grow and reproduce while maintaining their structures, and to change in response to their environments.

Metabolism is usually divided into two categories: catabolism, the *breaking-down* of organic matter for example, the breaking down of glucose to pyruvate, by cellular respiration, and anabolism, the *building-up* of components of cells such as proteins and nucleic acids. Usually, breaking-down releases energy and building-up consumes energy. The chemical reactions of metabolism are organized into metabolic pathways, in which one chemical is transformed through a series of steps into another chemical, by a sequence of enzymes. The metabolic system of a particular organism determines which substances are "nutritious" and which are "poisonous." For example, some prokaryotes use sulfide as a nutrient, yet this gas is poisonous to animals. The metabolic rate influences how much food an organism will require, and also affects how it is able to obtain that food. A striking feature of metabolism is the similarity of the basic metabolic pathways and components between vastly different species.

The metabolism of eukaryotes includes glycolysis, citric-acid cycle, and oxidative phosphorilation (OXPHOS). Glycolysis, a most primitive form of metabolism by the prokaryotes, takes place in cytoplasm. The citric-acid cycle occurs in the mitochondrial matrix, and the OXPHOS metabolism occurs at the internal folded mitochondrial membranes. The different modes of metabolism of cancer cells give the evidence of an evolutionary history of the metabolism from the prokaryotes to the eukaryotes, in response to a change of the increasingly oxygenated atmosphere.

Cancer was first suspected as a metabolic disease when Warburg postulated that the origin of cancer could be related to oxidative metabolic reactions under reducing conditions (Warburg, 1956). Hsu and others recognized a possible double role of nitrite (Hsu & Eckhardt, 2016). Nitrite as a reducing agent could render the interior of a cell oxygen-deficient. Nitrite, as an oxidizing agent, could be the substrate of oxidizing metabolic reactions such ammonium-oxidation metabolism by nitrite (anammox). They postulated that the ancestral Cancer Genomes may have evolved from a bacterial Anammox Genome so that they encode uncontrolled growth and replications, and also anammox metabolism (Hsu & Eckhardt, 2016)!

As a geologist studying biologic evolution in response to the changing atmospheric environment of the Earth, Hsu applied the Lynn Margulis theory (Margulis, 1967)! on the origin of eukaryotes to explain

the origin of cancer. He postulate that

(1) The Cancer Genomes have evolved from the Annamox Genome of a Precambrian anammox bacterium.

(2) The Anammox Genome was acquired by a Precambrian cyanobacterium. The cyanobacteria had first invented photosynthesis more than 1 billion years ago.

(3) Anaerobic bacteria seeking refuge in anaerobic environments when the Earth's atmosphere became increasingly oxygenated, because the release of oxygen to the atmosphere by the photosynthetic bacteria.

(4) An anammox bacterium found refuge in the anaerobic interior of a photosynthetic cyanobacterium.

(5) The symbiogenesis of the two formed the first eukaryote some 1 billion years ago.

(6) The body of evolving eukaryotes always had two genomes in parallel evolution at different rates.

(7) The Cyanobacterium Genome rapidly evolved into that of single-celled eukaryote, into fungi, plants and animals, while the Anammox Genome evolved, at a relatively slow rate, into the Cancer Genomes of the Cancer cells now found in the body of various eukaryotes such as *H. sapiens*. The Cancer Genomes are responsible for the two hallmarks of cancer cells: the uncontrolled growth and replication of cells and a metabolism mode different from the oxidative phosphorilation (OXPHOS), which is common to all eukaryotes.

(8) Cancerous stem cells "hibernate" when the condition of the cell interior does not permit anoxic or hypoxic metabolism, or when there is no supply of a substrate to sustain such metabolic reactions.

(9) The presence of nitrite in drinking water, which is diffused into cancer cells, could create a condition suitable for aerobic glycolysis under hypoxic or for anammox under anoxic conditions.

(10) Nitrite plays a double role, as a reducing agent to render the cell interior hypoxic or anoxic, as an oxidizing agent for metabolic reactions, such as in anammox, by cancer cells.

(11) Therefore, cancer cells which cannot survive when they are deprived of oxygen may be considered to have been "choked," or "starved," to death.

(12) Use of nitrite-free waters, such as the Sulan Water, as an anti-cancer substance in chemotherapy can "starve" the cancel cells to death, and they do not harm normal body cells.

3. Random Experiments

With a new understanding of the Origin of Cancer, we have a new insight into the functions of tumor suppressors. The SMT scientists postulated that alterations of the protein p53 are involved in nearly half of all cancer cells, and its nuclear role is to regulatory the shift from OXPHOS to the glycolytic pathway of metabolism. The SMT further postulated that transcription factors that are activated by cellular stresses or "DNA damages by somatic mutations" that trigger enzymes and pathways leading to the activation of tumor-suppression genes. They would thus arrest the growth of tumour cells. With our new understanding of the role metabolism in carcinogenesis, we may offer a different interpretation of the important p53 protein. In our experiments culturing cancer cells with nitrite-rich solutions, we

found a remarkable abundance of p53 in the solution. The abundance is consistent with our postulate that the metabolic mode of metabolism had been shifted by the p53 to suppress the growth of human body cells by OXPHOS. Therefore, a suppression of the p53, which promotes glycolysis metabolism of cancer cells, should lead to a suppression of tumor-growth.

Our CSC hypothesis on the origin of cancer is to be further tested by experiments. All living organisms depend upon metabolism to digest food and to store vital energy in the ATP. The metabolic processes are oxidation processes carried out under oxidative, hypoxic, or anoxic environment. Without metabolism to produce and to store the vital energy, a living organism cannot grow. When cancer cells cannot grow, tumors shrink in size. The change in tumor size could be observed and monitored, when cancer cells are being "starved" to death. The hypothesis thus predicts that the presence of nitrite in solutions culturing cancer cells favour the growth of tumors, and they should increase their size. The hypothesis also predicts that the absence of nitrite should favour the growth of body cells and suppress the growth of tumors, and their size should shrink. The predictions depend upon a recognition that the mode of metabolism of growing cancer cells is anammox by nitrite.

Hsu's pilot studies have only searched for an explanation of the statistical link between cancer and nitrite. PET scans may yet prove that some cancer cells may have the metabolic mode of anammox. Meanwhile, our friends sympathetic to our Human Genome. The growth of tumors is encoded by the inherited Cancer Genomes of Cancer cells. The "changes" from a bacterial genome into a cancer genome are not minor "transcription errors" that happened during a brief span of a patient's lifetime. The parallel paths of the evolutionary changes of the metabolisms of the eukaryote genomes and of the cancer genomes suggest that the process may have taken place the during, the last 2 billion years or so when the genomes evolved in response to the ever increasing oxygenation of the Earth's atmosphere.

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