OMMEGA Publishers
Answering Intelligence

International Journal of Cancer and Oncology

Int J Cancer Oncol Vol 6:2
ISSN:2377-0902

OPEN ACCESS

Research Article

DOI: 10.15436/2377-0902.19.2565

A Newer Method Cancer Treatment Which is Based on Link Rearrangement Operations of T Cells

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Abstract

There were appeared outcomes of experimental discoveries for immunotherapy of cancer treatment which can be used as supplemental possibilities to chemotherapy. The discovery of influences in the rearrangement of interactions between proteins like CTLA-4, PD-1 and CD-28, CD-80 (B-7-1), CD-86 (B-7-2) on processes for regulation of T cells functions showed suppression in cancer development. This discovery impelled us to study immune processes in patients with cancer treatment by Prolonged medical Starvation 42 to 45 days and supplementing with extracts of plants with giving very small quantity of cytotoxic substances, all of which influence on cancer metabolic processes. Also we studied above described discovery of influences immune mechanisms on regulatory processes in maintenance stability of Internal Energy in able-bodied organism causing Stationary State of an organism in norm as well as rearrangement of interactions between proteins CTLA-4, PD-1 and CD-28, CD-80 (B-7-1), CD-86 (B-7-2) due to cancer transmutation metabolism via influencing on regulation of immune processes changing maintenance stability Internal Energy of an organism causing Quasistationary pathologic State of cancer disease. Hence to conclude, the described mechanism of newer method in cancer treatment via "Prolonged medical Starvation (during 42-45 days)" with herbal extracts supplementing as well as with in additional very small dosage weak cytotoxic substances influencing on cancer processes, which induce cancer depression causing normal rearrangement operation of T cells as the link of healing mechanism, in proving best treatment of cancer patients.

Keywords: Warburg effect; T cells; Stem cells; Cancer cellular cycle; Mitosis; Meiosis

Introduction

Excessive increased anabolic processes due to intrusion viral genome into nuclear DNA genome induce viral haploid accelerating cellular cycle and cause transmutation affected cells. As the result of v-oncogenes operation using organism cells' electron transport chain for viral cellular oxidative processes, it increases enormous anabolic processes in cancer tissue leading to the enormous consumption of energy and Acetyl–CoA for anabolic processes. Insufficient energy and Acetyl-CoA in cancer tissue results in the overload of "nodal point of bifurcation anabolic and catabolic processes" [NPBac] because of the remained lack of Acetyl–CoA for catabolic oxidative processes. Excessive increase of lactic acids production is the necessary endergonic mechanism accumulation of energy for huge anabolic processes in condition glycolysis metabolism and enormous consumption of energy for anabolic processes in cancer tissue[1] (Figure 1). We studied the interactions between proteins CTLA-4, PD-1 and CD-28, CD-80 (B-7-1), CD-86 (B-7-2) on processes regulation in maintenance stability Internal Energy in norm and cancer pathology. It was discovered the influences of the rearrangement interactions between proteins CTLA-4, PD-1 and CD-28, CD-80 (B-7-1), CD-86 (B-7-2) on processes regulation T cells functions showing suppression cancer development[2-11]. Viral affected nuclear DNA of cells induce suppression of reticulo-endothelial system (RES), thereby it causes the suppression of T cells activity due to suppression in producing immunoglobulins like CTLA-4 and PD-1, which result in production supplementary quantity of immunoglobulins like CD-28, CD-80 (B-7-1), CD-86 (B-7-2), in fewer

Received date: July 23, 2019
Accepted date: October 28, 2019
Published date: November 4, 2019

Citation: Ponizovskiy, M.R. A Newer Method Cancer Treatment Which is Based on Link Rearrangement Operations of T Cells. (2019) Int J Cancer Oncol 6(2): 42-51.

quantities[12,13]. Considering mechanisms of the newer method cancer treatment via "Prolonged medical Starvation (during 42-45 days)" with herbal extracts supporting and very small dosage weak cytotoxic substances influences, it displays mechanism rearrangement operation of T cells as the link of healing mechanism in Immunotherapy as newer method for cancer treatment.

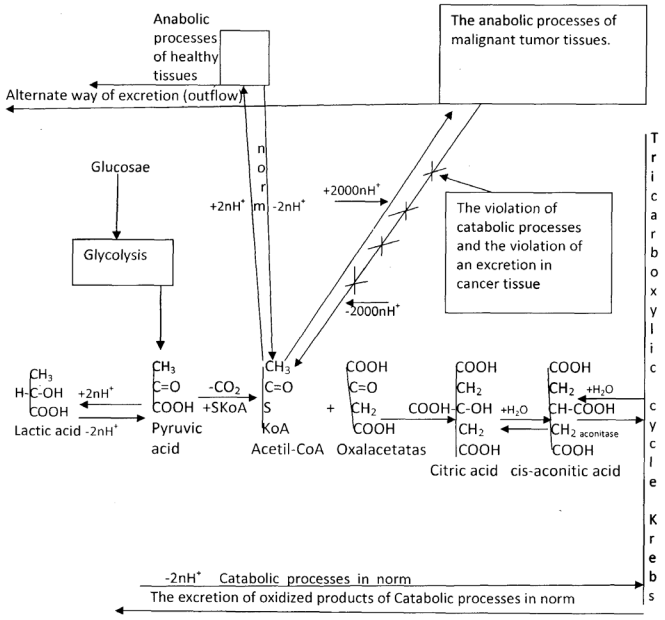

Figure1: The metabolism of a malignant tumor tissue and of a normal tissue

Materials and Methods

Borrowing by folk healer Rudolf Breus[14,15] the method cancer treatment and being familiarized himself with similar method cancer treatment making by folk healer Omelchenko, the author has substantiated scientific mechanism of this method cancer treatment in some published articles. The aim of this work is the study of mechanisms of cancer depression as consequence of prolonged medical starvation 42 – 45 days which is main link of newer method cancer treatment described in some published articles. This mechanism causes cancer depression via prolonged medical starvation thereby it results in autoimmune mechanism as the link of mechanism leading to cancer depression. Thus materials of this work are followings: published articles of Breus R[14,15], medical cards of cancer cured men been healed by Omelchenko, own experience of treatment patient Ch.described in some published works. Methods were used following: Explanation from point of views of thermodynamics, biophisics and biochemistry the outcomes as experimental works of mechanism oncogenesis as well as of mechanism of submitted new method cancer treatment.

The mechanism maintenance stability Internal Energy from the point of view of thermodynamics causing stable Stationary State of an organism in norm and Quasistationary State of an organism in pathology.

Considering mechanism maintenance stability Internal Energy from point of view of thermodynamics, it must show regulative mechanism of an organism which promote stability Internal Energy of Stationary State thermodynamic system of an orgnism in norm. The first law of thermodynamics shows following equation: $E = U + W_{int} + W_{ext}$ [E – Common Energy, U – Internal Energy, W_{int} – Internal Work, W_{ext} – External Work][16]. Just Internal Work (W_{int}) of mechanism maintenance stability Internal Energy (U) of an organism both in norm and pathology occurs via biochemical mechanism of three levels regulation of mechanism stability Internal Energy [highest level regulation [CENTRAL NERVOUS SYSTEM], high level regulation ["Equilibrium Constant of ionic metabolism", "Equilibrium Constant of acid –- alkaline metabolism", "Equilibrium Constant of oxidative – reduction Potentials of metabolism" and "Equilibrium Constant of coagulating system of blood"], low level regulation ["Equilibrium Constant of energy exchanges" and "Equilibrium Constant of metabolism"][17,18] (Figure 2). Stationary State of open non-equilibrium non-linear thermodynamic system of an able-bodied organism is characterized by stability of Internal Energy [the temperature 36,0°C – 36,9°C by which all enzymes operate, stable index pH=7,35 in blood and in neurolymph etc.] and Internal Medium [stable concentrations of substances in blood and neurolymph] according the first law of thermodynamics[16]. Stationary State of open thermodynamic system of an able-bodied organism displays balance catabolic exergonic processes & anabolic endergonic processes corresponding to low level maintenance stability Internal Energy of an organism. Quasi-stationary States of an open thermodynamic system of an organism in inflammatory processes are characterized by shift of balance catabolic processes & anabolic processes into excessive catabolic exergonic processes[19]. Quasi-stationary States of an open non-equilibrium non-linear thermodynamic system of an organism in cancer diseases are characterized by shift of balance catabolic processes & anabolic processes into excessive anabolic endergonic processes displaying Warburg effect mechanism[17,19]. Also interdependence related cellular chemical potentials (μ) of an organism's cells exert related cellular resonance waves of an organism's cells due to cellular capacitors operations[20] which induce biophysical mechanism maintenance stability Internal Energy (U) of an organism both in norm and pathology[20-22] (Figure 3). Besides biochemical mechanisms maintenance stability Internal Energy (U) of an organism in norm and pathology and biophysical mechanisms maintenance stability Internal Energy (U) of an organism in norm and pathology are subjected to regulative mechanisms of hormonal systems as well as defensive role of both humoral immune system and cellular immune mechanism via phagocytosis against environmental influences which are supplemented with autoimmune reactions and cleaning functions of reticuloendothelial system how autophagy[23]. These mechanisms of maintenance stability Internal Energy (U) of an organism in norm and in cancer pathology are considered as salient feature of newer method of cancer treatment by "Prolong medical Starvation 45 days" via using very small doses weak cytotoxic substance (see below).

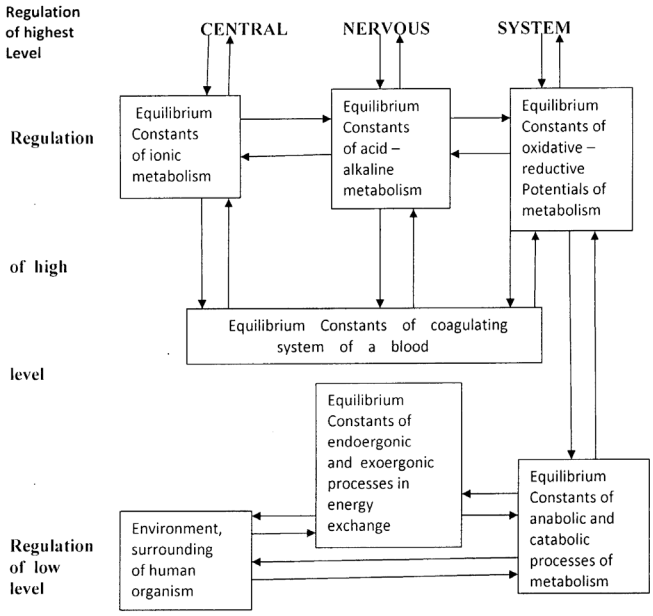

Figure 2: The mechanism of maintenance stability of internal energy and internal medium an organism.

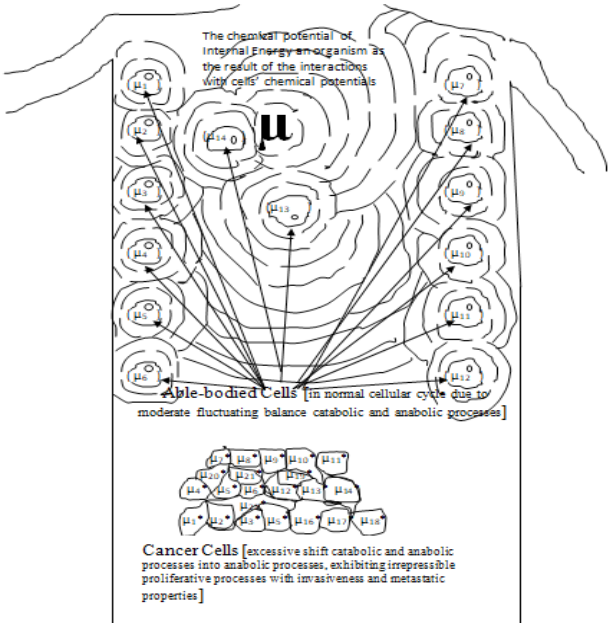

Figure 3: Balance Internal Energy both cells and an organism due to their chemical potentials (μ) promoting operation resonance waves of cellular capacitors and disbalance of chemical potentials (μ*) cancer cells.

The immune mechanisms, autoimmune mechanisms and autophagy promoting maintenance stability Internal Energy from the point of view of thermodynamics causing stable Stationary State of an organism in norm.

Autophagy, autoimmune mechanism and humoral immune mechanisms with cellular immune mechanisms generating by reticulo-endothelial system (RES) are supplementary mechanisms maintenance stability Stationary State of an organism[23,24]. All cells of an organism are advanced through aging processes which leads to cell death due to increased apoptotic processes via expending Basic Internal Energy (Ebas) through sequence Basic stem cells (neurons) → Totipotent stem cells → Pluripotent stem cells → Multipotent stem cells → Oligopotent stem cells → Unipotent stem cells → and then type cells[22,25].

Autophagy is the process causing the bulk degradation cytoplasmic components of dead cells which are enclosed by double-membrane structures known as autophagosomes which are subjected delivery them to lysosomes due to operation resonance waves of macrophages' capacitors with lysosomes' capacitors on autophagosome substances corresponding to the Schroedinger equation of the method of the molecular orbitals – a linear combination of atomic orbitals (MO LCAO)[20]. Thus Lisosomes' enzymes lyse the autophagosomes of dead cells and release a lot of decomposing proteins named autophagy-defective mutants (apg)[23,26-30]. Decomposed substances were subjected to metabolic processes forming Products of metabolism H_2O, CO2 and the other waste products which should be excreted from autophagy cells (macrophages, monocytes) into blood of an organism and then excreted into Environment[23] (Figure 4). But the some proteins named autophagy-defective mutants (apg) remain in cells-macrophages and in blood as the Products of Autophagy. These proteins are conjugated one anothers in processes degradations due to Lysosome enzyme operation causing Apg5/Apg12 conjugations[23]. Then Apg16 protein is added forming Apg12p–Apg5p–Apg16p conjugations[23,26-30]. Also these cytoplasmic components react with waste products of autophagy including into Apg12p–Apg5p–Apg16p conjugations of 350-KDa complex[23]. Apg7 is a ubiquitin-E1-like enzyme which takes part in Autophagy[23,26-30]. Besides Apg12p-Apg5p conjugation reaction is mediated by Apg7p, a ubiquitin activating ubiquitin-E1-like enzyme, and Apg10p, suggesting that it is a ubiquitination-like system[23,26-30]. Ubiquitination is the well known modification system, which is involved in selective protein degradation, endocytosis, etc[23]. Considering termination of each cell's life via Apoptosis and Autophagy, clearance from degradation components, are indispensable processes for maintenance stability Internal Energy and Internal Medium of an organism. Just insufficient processes of autophagy leads to heavy diseases due to violation local mechanism or whole mechanism maintenance stability Internal Energy and Internal Medium tissue or an organism[31,32]. Therefore there are suggested to exert Autophagy in treating some diseases[32]. Besides there were appeared some microRNAs as fragments of dead cells' nuclear genomes[33-37] which can contain as nuclear fragments of normal dead cells as well as dead cells' nuclear fragments affected with pathologic genome, e.g. microRNAs with v-oncogene strands. Also decomposed dead cells release a lot of microRNAs, thereby creating DNA-MicroRNA Complex which should be excreted into the Environment[23] (Figure 4). All of these microRNAs regulate the function of target genes at the post-transcriptional phase due to reaction resonance waves of autophagy cells' cellular capacitors on waves function of these microRNAs molecules corresponding to the Schroedinger equation of the method of the molecular orbitals – a linear combination of atomic orbitals (MO LCAO)[20]. Besides forming DNA-MicroRNA Complex create cell reprogramming of the generation induced pluripotent stem cell (iPSC)[23,33–37]. Just the lives of able-bodied cells and pathologic cells lead to Apoptosis both normal dead cells and pathologic dead cells. All dead cells should be destroyed and eliminated from tissues by cells of autophagy operation. Therefore there are arisen the autophagy as links which make clearance Internal

Energy (temperature 36,4°C – 36,9°C by which all enzymes operate etc.) and Internal Medium (stable concentration substances in blood and neurolymph) of an organism from dead cells and their waste substances. The balance forming autophagy products & clearance autophagy products causes balance pro-apoptotic factors [BCL-2 family proteins] & anti-apoptotic factors [BH3, BAX, BAK, BOK][32,33], which are the links of supplement mechanism maintenance stability Internal Energy (U) of an organism as Internal Works (W_{int}) according first law of thermodynamics[16]. Also there are occurred reverse reactions: DNA-MicroRNA Complices → induced pluripotent stem cells (iPSCs) [23,38-43]. These reverse reactions transit into normal right regulative developments inducing pluripotent stem cells [iPSC] which substitute Unipotent stem cells: Basic stem cells (neurons) → Totipotent stem cells → Pluripotent stem cells → Multipatent stem cells → Oligopotent stem cells → induced pluripotent stem cells (iPSCs)[DNA-MicroRNA Complex] → type cells. Then the conjugations DNA-MicroRNA Complices are broken up into DNA and MicroRNAs. Both DNA and MicroRNAs are subjected to metabolic disintegrations[23]. Further type cells in wound are developed by delivering energy through sequence of stem cells via Basic stem cells → Totipotent stem cells → Pluripotent stem cells → Multipotent stem cells → Oligopotent stem cells → Unipotent stem cells → type cells exerting proliferative processes via cellular cycle. On the other hand, an organism resists environmental influences causing maintenance stability Internal Energy (U) of an organism via External Works (W_{ext}) of an organism[17,19]. Penetration of strange high-molecular substance from Environment into an organism creates local change of chemical potential (μ) which exert the stimulation, via resonance waves of T cells capacitors, biosynthesis immunoglobulins in G1 phase cellular cycle of B leucocytes [B cells] producing immune antibodies. Humoral immune complements are proteins, which are synthesized in considerable quantity by hepatocytes and are produced also in fewer quantities by blood macrophages, blood monocytes, some epithelial cells. Complements activate as humoral immune reactions of antibodies creating esterase property with also proteolytic properties as well as exerting cellular immune reactions of phagocytosis. Thus antibodies bind antigens, and complements' both esterase and protease enzymes lyse antigens in humoral immune processes. Also an organism's local change of chemical potential (μ) promotes remote reactions across distance of phagocytes' [macrophages, monocytes etc.] cellular capacitors via resonance cellular waves on common molecular wave of strange high-molecular substance, due to the wave function of any molecule which is determined as the total wave functions of the nuclear orbitals, according to Schroedinger equation of linear combination of atomic orbitals (MO LCAO)[19,20,24]. The forming resonance waves cause attraction the immune cells to strange high-molecular substance and create the contact reaction of decomposing the high-molecular substance of the strange objects, ruining bacteria and other strange cells. Just biophysical mechanism of immune cells remote reactions transit into contact biochemical immune reactions for decomposition of the strange oblect[24]. These defensive mechanisms of humoral immune reactions and cellular immune reactions are defensive links of Internal Works (W_{int}) of an organism which are realized by biochemical and biophysical mechanisms maintenance stability Internal Energy (U) of an organism. The environmental influences on an organism's processes fluctuate from positive influences via inducing in production some Vitamins [Vitamin D etc.] to negative influences causing by some allergens. Just development of both an organism and cells of an organism through aging processes occurs under the permanent influences of various environmental allergens. The negative influences, causing by some allergens, damage the respiratory link of electron transport chain [one from five Complexes] of local tissue's cells causing either violation local tissue's respiratory function or general violation respiratory function of an organism. Violation of organism's general respiratory function causes violation of lung tissue's cells respiratory function inducing violation common catabolic aerobic oxidative processes of an organism[43,44]. Violation of local tissue's respiratory function causes allergic reactions via weak local inflammations because of forming local tissue imbalance of catabolic aerobic processes & catabolic anaerobic processes due to excessive catabolic aerobic processes that causes rhinitis, pharyngitis etc. The violation of lung tissue's cells respiratory function with violation of common catabolic aerobic oxidative processes of an organism causes common pathologic processes, e.g. bronchial asthma[10]. The environmental allergens react with some respiratory link of electron transport chain of local tissue's cells forming strange autoantigens of IgE. The cells of reticulo-endothelial system (RES), both T cells and B cells take part in humoral immune processes due to production immune antibodies by B cells and immune cellular reactions by T cells. The activation immune cellular reactions by T cells occur by immunoglobulins CTLA-4 and PD-1 exerting processes nuclear DNAs transcription and translation of biosynthesis immunoglobulins in G1 phase cellular cycle due to cellular capacitors' resonance waves reactions on autoantigen IgE substances' strange molecular waves, according to Schroedinger equation of linear combination of atomic orbitals (MO LCAO)[20]. Thus autoantigen IgE substances' strange molecular waves are subjected to influences by resonance waves of T cells' cellular capacitors, which realize autoimmune defensive reactions[19,20,24]. Just the mechanism of autoimmune reactions are realized by T lymphocytes [T cells] which are regulated by productions opposed mechanisms either producing immunoglobulins CTLA-4 and PD-1 for activation T cells operation or producing immunoglobulins CD-28, CD-80 (B-7-1), CD-86 (B-7-2) for desactivation T cells operation[2-11]. T cells are formed by thymocytes of RES in thymus and carry out various immune functions like: T helper cells stimulate autoimmune reactions of some immune cells [T lymphocytes and B lymphocytes] influencing by resonance waves of variable cellular capacitors in their walls and of their receptors. T killer cells, being exerted by T helper via their resonance waves of cellular capacitors[16], destroy some autoantigens of IgE (including some viral antigens coupled with autoantigens) via producing proteases and esterase enzymes[34-36]. T memory cells learn and remember to encounter antigens and via their resonance waves of cellular capacitors exerting T helper cells through interactions between relative resonance waves of T memory cells and resonance waves of T helper cells[16]. So, defensive autoimmune reactions caused by alarm exerting T cells and B cells promote production the immunoglobulins CTLA-4 and PD-1. The production the immunoglobulins CD-28, CD-80 (B-7-1), CD-86 (B-7-2) by RES cause suppression function all T cells in norm.

Thus fluctuating balance of these immunoglobulins maintains stablity Stationary State of an organism in norm.

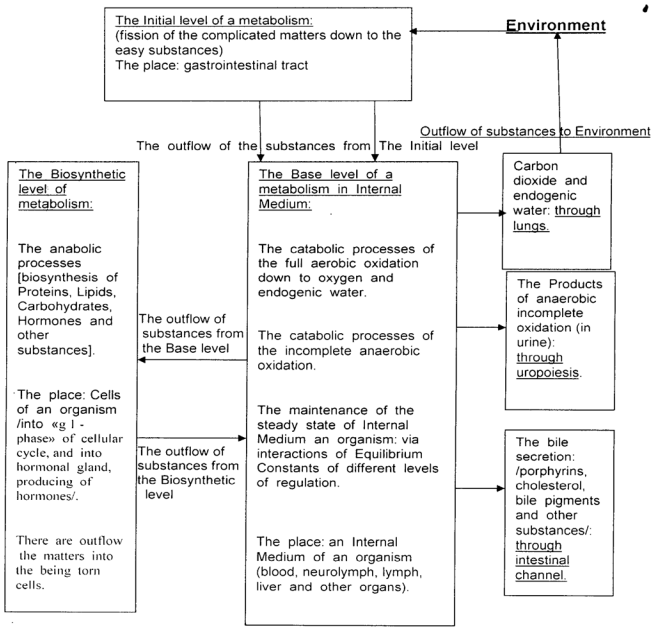

Figure 4: Three levels of metabolism causing excretion waste substance into environment.

Thermodynamic mechanisms maintenance stability Internal Energy during cellular cycle of able-bodied cells in norm and cancer cells in cancer disease considering affecting cells by cancer viruses and genomic mechanisms transmutations.

Basophilic chemical potential of cytoplasm (μ_{cytopl}) determines stability Internal Energy of an open thermodynamic system of cell[21-23]. The G0, G1, S, G2, M phases of cellular cycle show maintenance stable basophilic chemical potentials of cytoplasms (μ_{cytopl}) in each phase cellulyr cycle being subjected to mechanism stability Internal Energy of an open thermodynamic systems of all cells and an organism. Thus the famous Glansdorff and Prigogine theory must use for consideration mechanisms maintenace stability Internal Energy during cellular cycle. Taking into account minimization of gain entropy according Prigogine theorem as mechanism maintenance stability an open thermodynamic system of an organism, Glansdorff and Prigogine expand minimum production entropy into non linear field considering minimization of gain entropy for stability Stationary State of an open non linear non equilibrium thermodynamic system of an organism[20-22]. They divided local production Entropy into two data corresponding such formula:

$d_k\beta / dt = d_k/dt (\sum J_k X_k) = \sum J_k dX_k/dt + \sum X_k dJ_k/dt$ [β– Entropy, t– time, X– Force, J- Stream]

The stability system shows following formula: $dJ_k/dt = 0$; Hence $d\beta/dt = dx\beta/dt$, i.e. stability thermodynamic system defines Force (X).

However the minimization gain entropy shows: $d\beta/dt \leq 0$, i.e. negative fluctuation entropy. It is meant that it is far away from equilibrium of open thermodynamic system although the sign of equality defines Stationary State thermodynamic system. Just stability Stationary State is described so: 1) $d_x\beta = \sum dJ_k dX_k > 0$. It corresponds to positive fluctuations entropy ($d_x\beta > 0$) which exhibits stability Internal Energy (U) an open thermodynamic system reflecting balance catabolic exergonic processes & anabolic endergonic processes of low level regulation thermodynamic system.

However the positive fluctuations entropy ($d_x\beta > 0$) is recurring changed in situation of development thermodynamic system in Stationary State. Therefore thermodynamic system must return to initial state. But there arise possible negative fluctuations entropy which transits thermodynamic system into new Stationary State with decreased entropy ($\Delta S_x < 0$) (Figure 5). Just the permanent changed G0, G1, S, G2, M phases of cellular cycle in life of an open thermodynamic system of cell characterize permanent oscillations as positive fluctuations entropy (+dβ/dt) in each phase of cellular cycle exhibiting stability Internal Energy of cell as well as negative fluctuations entropy (-dβ/dt) exhibiting transitions from cellular phase into another cellular phase and also within phase from one state into another state, e.g. Mitosis (M) phase shares into Prophase, Prometaphase, Metaphase, Anaphase, Telophase. Each amplitude of positive fluctuations entropy ($+d_x\beta$) shows oscillations moderate shifts balance catabolic exergonic processes & anabolic endergonic processes into anabolic endergonic processes, i.e. biosynthetic fusion processes in norm. Each amplitude of negative fluctuations entropy ($-d_x\beta$) shows oscillations moderate shifts balance catabolic exergonic processes & anabolic endergonic processes into catabolic exergonic processes, i.e. oxidative fission processes in norm[20,22]. Versus Mitosis phase of normal cellular cycle, in cancer cells it occurs combined Mitosis-Meiosis phase cellular cycle due to combination normal diploid eukaryotic cellular cycle with viral haploid prokaryotic cellular cycle causing due to affected human nuclear DNA by oncologic viral DNA[23,45]. All viruses use human electron transport chain for its cellular oxidative processes to build new cells via proliferative processes of viruses' cells. However these consumptions energy are different by different viruses because different viruses obtain Basic Internal Energy [molecular bonds energy] in different levels of an organism. For example, influenza viruses obtain Basic Internal Energy [molecular bonds energy] from type cells being light separated by an organism, but v-oncogenes intrude in deep level Basic Internal Energy [molecular bonds energy] of cellular genome, maybe on levels either Oligopotent stem cells or even Multipotent stem cells using also mitochondrial oxidative processes of an organism's cells that give cancer cell possibility firm binding in genome and to develop itself in autonomic mode from some regulatory functions of an organism causing obstacles for treatment with moderate dosage cytotoxic drugs, compelling treatment with great dosage cytotoxic drugs. Just the viral oncogenes, which intrude in Oligopotent stem cells, replace Oligopotent stem cells into Cancer stem cells causing following sequence of cancerous genetic link Basic stem cells → Totipotent stem cells → Pluripotent stem cells → Multipotent stem cells → Cancer stem cells → Cancer cells. Cancer cells obtain energy through this link from Basic Internal energy. It is meant that several v-oncogenes genome bind affected human cells' genome with covalent bonds causing couple cancer cells' genomes which contain mixed genome containing from 49 till 56 chromosomes exhibiting aneuploidy, versus 46 chromosomes in normal eukaryotic cells. As concerning to HeLa independent

from an organism cancer cells, HeLa cells absorb whole mitochondrial oxidative system in their bodies creating independent metabolisms how in bacteria. Just, exerted by oncologic viral DNA, combined Mitosis-Meiosis phase of cellular cycle in cancer cells induces shift balance catabolic exergonic processes & anabolic endergonic processes into excessive anabolic endergonic processes causing disbalance catabolic exergonic processes & anabolic endergonic processes[23]. Besides Mitosis-Meiosis phase of cancer cellular cycle is subjected to accelerating cellular cycle which is induced by viral cellular cycle and is supported by excessive Free Radicals and produced by excessive quantity ROS/H_2O_2/Free Radicals in mitochondria of cancer cells[23,46,47]. Just cancer cells' mitochondria produce enormous superoxide O* which induce huge quantity Free Radicals (H*, OH*) via complex ROS/H_2O_2/Free Radicals causing 2nDNAs reaction with inducing irrepressible cancer proliferative processes of cancer cells' nuclei[23,46,47]. Therefore viral haploid Meiosis prevails over Mitosis exerting acceleration of cancer cellular cycle. Also Mitosis-Meiosis phase of cancer cellular cycle is shared into as Prophase → Prometaphase → Metaphase → Anaphase → Telophase in Mitosis phase as well as Prophase I → Metaphase I → Anaphase I → Telophase I in Meiosis I phase and Prophase II → Metaphase II → Anaphase II → Telophase II in Meiosis II phase[20,22,23,25]. Considering prevalence Meiosis over Mitosis in cancer cellular cycle is determined by prevalence [Prophase I → Metaphase I → Anaphase I → Telophase I with Prophase II → Metaphase II → Anaphase II → Telophase II] over [Prophase → Prometaphase → Metaphase → Anaphase → Telophase] expressing double prevalence approximately in cancer cellular cycle, i.e. ratio Meiosis particles : Mitosis particles = 2 : 1 approximately in Mitosis-Meiosis phase of cancer cellular cycle as compared to Mitisis phase of an organism's cells. It is meant, that maintenance stability Internal Energy of cancer Quasi-stationary State [$d_x\beta = \sum dJ_k dX_k$] for huge quantity particles of cancer cellular cycles are required considerably more energy from Basic Internal Energy (E_{bas}) via sequence Basic stem cells (neurons) → Totipotent stem cells → Pluripotent stem cells → Multipotent stem cells → Oligopotent stem cells → Unipotent stem cells → and then cancer cells which are expending more energy than for double less particles of an organism's cells' cellular cycles. Such prevalence cancer cells over organism's cells can lead to exhaustion of an organism activity causing suppression T cells immune mechanisms of an organism with releasing immunoglobulins CD-28, CD-80 (B-7-1), CD-86 (B-7-2) causing suppression activity T cells, and an organism is plunged into cancerous cachexia[12,13,22,23,25].

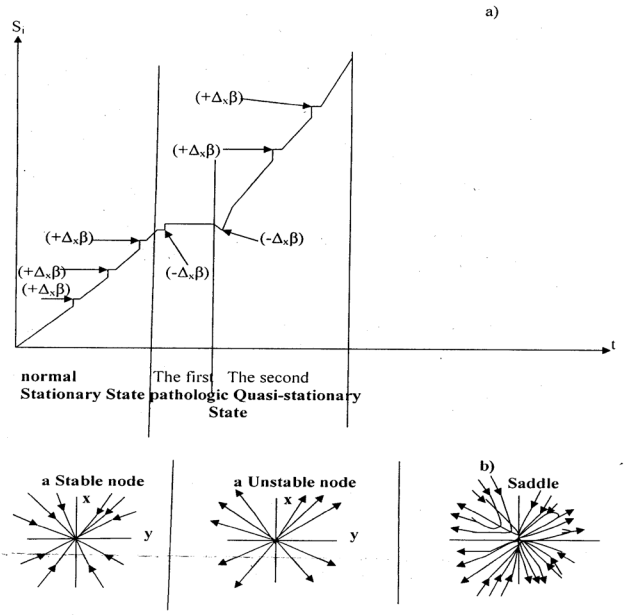

Figure 5: Change fluctuations of an entropy at transition from normal Stationary state into pathologic Quasi stationary state

The healing mechanism of "Prolonged medical Starvaticon 42 – 45 days with very small dosage and weak cytotoxic substances" in new method of cancer treatment.

Cancer cells' proliferations form cancer tumor which situates itself inside the human organism using the organism as Environment, and obtains the substances from depot of an organism for its metabolism (fat depots, carbohydrate depots etc.). Also an organism obtains substances from depots of an organism for its metabolism in condition of treatment by "Prolonged medical Starvation (during 42-45 days)"[48-51]. The treatment by "Prolonged medical Starvation (during 42-45 days)" causes considerable decrease in almost all depots of an organism, thereby exhausting organism's fat and hydrocarbonic depots, which leads to competition between cancer tissue and an organism for the use of remained decreased depot needing for metabolism of cancer cells and for maintenance stability Internal Energy of an organism (U_{org}) (normal temperature 36,0ºC-37,0°C by which all enzymes operate and other indices). Thus this competition between the organism and the cancer must lead to the win for most strong one. But the protective forces of the organism become stronger due to support with herbal extracts, delivering vitamins and microelements into the organism[48]. Besides increase expenditure energy of fat metabolism from fat depot leads to augmentation glutathione peroxide (GPX) and phospholipid hydroperoxide glutathione peroxidise (PHGPX) in all cells of an organism which neutralize redundant superoxide [O*] and ROS/H_2O_2/free radicals in G1/S phases cellular cycle of cancer cells cycle suppressing supplemental mechanisms of excessive proliferative processes of cancer cells[46,47]. Thus cancer cells' metabolism is plunged into depression: Suppression accelerating cancer cellular cycle leads to decrease anabolic processes in condition of "Prolonged medical Starvation (during 42-45 days)" exerting normal nuclear DNA [nDNA] replication via prevailing Mitosis over Meiosis in complex Mitosis-Meiosis phase[20-22]. Eliminating partial suppression of Anaerobic processes of oxidative phosphorilation by "Prolonged medical Starvation (during 42-45

days)" restores normal balance Aerobic oxidative processes & Anaerobic processes of oxidative phosphorilation in cancer cells decreasing Reactive Oxygen Species (ROS) in cancer cells[46,47] causing suppression of excessive nucleus DNA replication with normalization of cellular cycle of cancer cells and elimination irrepressible proliferative processes of cancer growth. Also complex Mitosis-Meiosis phase of cancer cellular cycle is broken into separate Mitosis and Meiosis where haploid Meiosis phase of viral cellular cycle is deprived of prevailing state over diploid Mitosis phase normal cellular cycle. Besides broken covalent bonds between Mitosis and Meiosis deprive barriering defence of viral pluripotent stem cells function causing normal cellular cycle with activity of diploid Mitosis phase in cancer cells[23]. Expression Mitosis in normal cellular cycles of all cells stimulates T cells [T lymphocytes] via appearance produced immunoglobulins CTLA-4 and PD-1 due to resonance waves of cellular capacitors T memory cells learn and remember waves function of viral substances containing in separated haploid Meiosis phase. Then T memory cells exert T helper cells, and T helper cells stimulate T killer cells and B cells for production antibodies against cancer viral substances of haploid Meiosis phase which is deprived barriering defence of covalent bonds between Mitosis and Meiosis causing loss viral pluripotent stem cells function and that exert phagocytosis of T killer cells.

Thus such basic phenomena of the cancer metabolism are inhibited[1,48- 51]:

a) Mechanism of "Warburg effect".
b) Biochemical and biophysical mechanisms of metastases and non-healing tumor ulcers formation.
Besides inhibition of Warburg effect by "Prolonged medical Starvation (during 42-45 days)" leads to cancer cells' depressions which are determined by following changes:
a) Expression normal cellular cycle and inhibition accelerated cancer cellular cycle.
b) Activated diploid Mitosis phase cellular cycle and suppression haploid Meiosis phase of viral cellular cycle.
c) Stimulated T killer cells and B cells produce antibodies against the autoantigen IgE substances causing suppression haploid Meiosis phase of viral cellular cycle and expression phagocytosis of T killer cells.
d) Simultaneously the very small dosage and weak cytotoxic substances destroy only the depressed cancer cells but it don't influence on an organism's able-bodied cells especially T cells. Thus influences of these very small dosage and weak cytotoxic substances on depressed cancer cells promote penetration through cellular walls of cancer cells the anticancer antibodies against viral substances for suppression haploid Meiosis phase which ruin haploid Meiosis phase as well as cancer cells by the phagocytes of T killer cells resulting in a cured organism.

Results

"Prolonged medical starvation" contributes to depression of cancer tumor metabolism that helps for efficient anticancer therapy with considerably decrease in dosage of cytotoxic drugs. Such approach to anticancer chemotherapy prevents damage to Internal Energy and Internal Medium of both an organism and cells of an organism, hence preventing damage of immune and hormonal systems as the links of defensive mechanism in regulative system of an organism. Immune and hormonal systems as the links of system stability Internal Energy and Internal Medium of an organism prevents both recurrence of cancer disease after longer duration anticancer chemotherapy and resistance to anticancer drugs which occur due to intensive anticancer chemotherapy with great dosage of cytotoxic drugs due to intrusion into Internal Energy and Internal Medium of an organism. Thus Warburg effect as therapeutic target of new method cancer treatment using prolonged medical starvation and combination immunotherapy with small dosage weak cytotoxic substances is more efficient method in treatment of cancer than modern methods cancer treatments with great dosage of cytotoxic drugs[52].

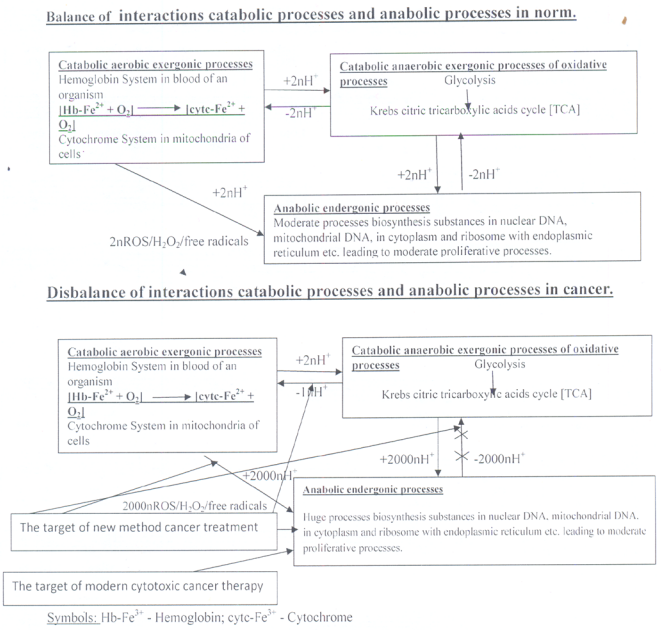

Figure 6: The targets of both the new cancer treatment and modern method of cancer treatment.

Discussion

There are two queries for discussion. Why does not prolonged medical starvation complete cure but only cause depression of cancer disease which is needed very weak small quantity cytotoxic substance for final cure? What of mechanism exerting expression autoimmune processes in depressed cancer process as result of prolonged medical starvation?

Just both able-bodied cells and pathologic cells use energy as for its metabolism via exchange substances and energy with Environment as well as use energy from parents inherited Basic Internal Energy (E_{bas}), located in Basic stem cells (neurons), for their development. "Prolonged medical starvation 42 – 45 day" suppresses metabolic processes of an organism due to blocking inflow substances and energy from Environment. Therefore both an organism and cancer tissue obtain substances for their metabolism from depots of an organism (fat depots, carbohydrate depots etc.). When depots are almost exhausted, able-bodied cells and cancer calls are compelled to use some Basic Internal Energy (E_{bas}) in metabolic processes for main-

tenance stability their Internal Energy for their survival. Thus when depots of an organism are almost exhausted, it leads to competition as between cancer tissue and an organism for the use of remained decreased depot as well as between able-bodied cells and cancer calls for use some Basic Internal Energy (E_{bas}) in metabolic processes needing for metabolism of both cancer cells and healthy cells and for maintenance stability Internal Energy of an organism (U_{org}) (normal temperature 36,0ºC-37,0°C by which all enzymes operate and other indices). Thus this competition must lead to the win for most strong one. But an organism and healthy cells are stronger than cancer cells as due to strength by supplementation extracts of herbs containing vitamins and microelements as well as due to relative chemical potentials ($\mu_{healthy}$) of an organism and healthy cells but non relative chemical potentials (μ_{cancer}) of cancer cells to chemical potentials of both an organism and healthy cells ($\mu_{healthy}$) (Figure 3). Therefore cancer cells are plunged into depression in which are occurred broken Meiosis -Mitosis phase of cancer cellular cycle with prevailing Mitosis phase of normal cellular cycles. Also expression of an organism's cells exerts expression autoimmune activity of T lymphocytes causing loss viral pluripotent stem cells function and break Warburg effect mechanism (see above). However depressed cancer cells are not died yet because they can be recovered after finished prolonged medical starvation but weak short dosage cytotoxic substance ruin depressed cancer cell easily without harm to immune and hormonal systems.

Conclusions

1. The stability Internal Energy and Internal Medium of Stationary State is the characteristic feature of a healthy organism.
2. The stability Internal Energy of Quasi-stationary pathologic State is characteristic of sick organism.
3. The stability Internal Energy of an organism is supported by immune processes and Autophagy.
4. The exertions of mechanisms transitions through G0 /G1 /S /G2 /M phases of cellular cycle are explained by Glansdorff-Prigogine theory.
5. Versus of influenza viruses, cancer viruses affect Stem cells forming Cancer stem cells and causing obstacle for treatment with mild dosage to small dosage of cytotoxic drugs.
6. Prolonged medical starvation 42 – 45 day with supporting by herbs' extracts delivering vitamins and microelements exert competitions between able-bodied cells and cancer cells for receiving energy and substances that cause maintenance stability their Internal Energy of Stationary State and Quasi-stationary pathologic State.
7. The supporting with vitamins and microelements in condition of prolonged medical Starvation and more relative chemical potentials of healthy cells and organism than cancer cells lead to plunge cancer cells to depression due to win of able-bodied cells.
8. Prolonged medical starvation 42 – 45 day impels expression autoimmune processes of T cells activity causing damage Warburg effect as the target of cancer metabolism that increase depression of cancer cells.
9. The small dosage weak cytotoxic substances ruin cancer cells in their depression state without suppression immune and hormonal systems, as compared to great dosage cytotoxic drugs.

Acknowledgment: This article is dedicated to the memory of my daughter T.M. Ponizovska.

Disclosure: The offered newer method in cancer treatment via "Prolonged medical Starvation supporting with herbal extracts and synergizing by small dosage weak cytotoxic substances" should be provided with detail in Clinical Trials for introducing This newer concept of cancer management officially in medical clinical practice, is the need of the hour.

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