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Review Article

The Benefit for Clinical Trial of the new Method Cancer Treatment as Opposed for Modern Chemotherapy of Cancer Therapy

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Abstract

The new method Cancer Therapy via combination "Prolonged medical starvation" with considerably decreased dosage of cytotoxic drugs was borrowed by folk healer Breuss R. Just the mechanism of the new method of cancer therapy operates via targeting of Warburg effect that exerts anticancer internal immunotherapy of an organism. Therefore, benefit of new method for cancer treatment of cancer disease ill man is occurred through using "Prolonged medical starvation" by an organism with the cancer disease leading to depression of oncoviral metabolism with exerting mechanism of immunotherapy. The considerably decreased dosage of cytotoxic drugs exerts cellular immune activity of immune phagocytes T cells and humoral immune antibodies from B cells which destruct of the depressed cancer oncoviral metabolism creating efficient Cancer Therapy. Just the modern methods of Cancer Chemotherapy with large dosage of cytotoxic drugs suppress as cancer oncoviral metabolism as well as immune and hormonal defending systems of a human organism that leads to majority of the occurred complete destructions of cancer oncoviral mechanism causing recovery of an organism. However often the large dosage of cytotoxic drugs cannot suppress complete destructions of all cancer oncoviral mechanisms which are occurred as in the cancer neglected organisms as well as leading to either relapse cancer disease or immune resistance to cytotoxic drugs after large dosage of cytotoxic drugs of modern methods Cancer Chemotherapy. There were described the biochemical and biophysical mechanisms of new method cancer treatment that leads to the benefits for cancer treatment of neglected cancer disease of ill man to use the method "Prolonged medical starvation" with very decreased dosage of cytotoxic drugs of new method cancer treatment with immunotherapy. Also, it was described the biochemical and biophysical mechanisms' state of some cancer disease after modern chemotherapy with large dose of cytotoxic drugs causing through formations resistance to some cytotoxic drugs and relapse cancer disease after some cancer disease remission. This work is substantiated the mechanism operation of the new method cancer treatment, which leads to prevention recurrence cancer disease and resistance to anticancer cytotoxic drugs in comparison with intensive anticancer chemotherapy with large dosages of cytotoxic drugs. Therefore, the assessing of advantage the new method of cancer therapy over the modern method of cancer therapy is substantiated in the article via opportunity to exert mechanism destruction oncoviral mechanism of cancer disease without expression of viral oncogenes (v-oncogenes) of cancer disease. As the conclusion, the offered method Cancer Therapy should be put into practical medicine after detail Clinical Trials.

Keywords: warburg effect; oncologic viruses (v-oncogenes); prolonged medical starvation; cytotoxic substaces; relapse cancer disease; resistance cytotoxic drug; neglected cancer disease

1. Introduction

The mechanism of new method cancer treatment operates via targeting Warburg effect of cancer metabolism. The mechanism of new method cancer treatment creates combination "Prolonged medical starvation" with considerably decreased dosage of cytotoxic drugs. This combination leads to destroy "aerobic oxidation in Glycolysis" of mechanism Warburg effect. There were substantiated the viewpoint of thermodynamic biophysical and biochemical descriptions of the mechanism Warburg effect causing oncogenesis mechanism which mechanism is destructed by the new method cancer treatment creating transiting from quasi-stationary pathologic state of an organism into normal stationary state of an organism and cells of an organism via mechanism maintenance

stability Internal Energy and Internal Medium according to first law of thermodynamics, i.e. stability of Internal Energy (ΔU) (stable temperature 36,0°C-36,9°C, stability of pH = 7,35 etc.) by which all enzymes operate (1, 2). There are as the positive influence Environment on a human organism as well as negative influences Environment on a human organism which can be as inorganic substances influences as well as organic substances influence even by living organisms how bacteria and viruses. The defensive mechanism of immune and hormonal systems of an organism resists the negative influences of pathologic substances and organisms how bacteria and viruses. Considering mechanisms of oncogenesis in different states of an organism, there were described mechanisms of oncogenesis with Cancer Tumor Metastases in neglected state of an organism either mechanism of resistance to anticancer cytotoxic drugs or mechanism of relapsed cancer disease causing by survival virusal oncogenes of suppressed immune systems and hormonal systems causing by large dosage cytotoxic drugs of modern methods cancer therapy. Firstly, neglected cancer disease cannot be complete treated by modern methods chemotherapy with large dosage of cytotoxic drugs because large doses of cytotoxic drugs create suppression defensive mechanisms of immune and hormonal systems. Secondly, The prevalence etiologic factors over organism's defensive immune and hormonal systems stimulates driving mechanisms of transmutation normal cells into cancer cells which lead to development of cancer disease. The prokaryotic organisms of oncologic viruses (v-oncogenes) have no the electron transport chain via five Complexes of respiratory system as opposed of the other prokaryotic organisms of different bacteria. All eukaryotic organisms including human organism have electron transport chain via five Complexes of respiratory system. Therefore oncologic viruses (v-oncogenes) live in cancer cells of the human organisms. Oncologic viruses (v-oncogenes) affect cells' nuclei of weak place of extracellular tissue which is supplied with lack of Basic Internal Energy (E_{bas}) causing by lack of hormonal support. Lack of cellular walls' of hormonal support results in disbalance intercellular cellular chemical potential ($\mu_{inter.cell}$) & extracellular chemical potential ($\mu_{outer.cell}$). Thus oncologic viruses (v-oncogenes) affect deep level of stem cells maybe Unipotent stem cells or even Oligopotent stem cells due to lack of energy from Basic Internal Energy (E_{bas}) in deep level of these stem cells which lead to find other cells of an organism with enough deep level energy from Basic Internal Energy. Thus these mechanisms create Metastases.

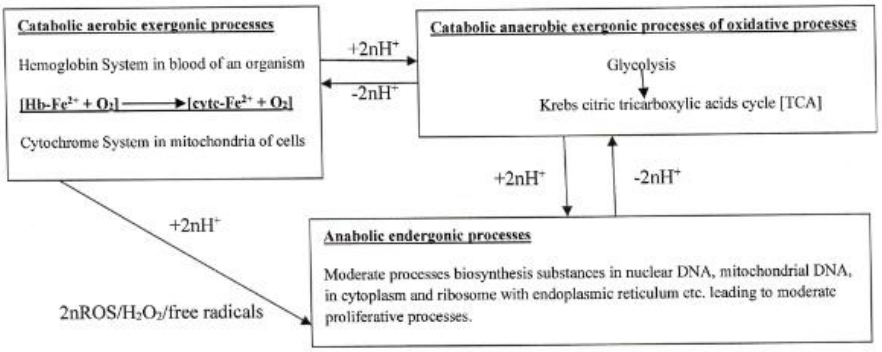
2. The mechanism of Warburg effect in cancer oncogenesis of metaboism.

An open non equilibrium nonlinear thermodynamic system of a human organism is subjected to thermodynamic laws where the thermodynamic first law is the following formula:

H = U + W(int) + W(ext) [H-Enthalpy (Common Energy), U-Internal Energy, W(int)-Internal Work, W(ext)-External Work].

The mechanism maintenance stability Internal Energy (U) (stable temperature 36,0ºC -36,9ºC, stable PH = 7,35 in blood etc.) is depended on interactions between Internal Work (W_{int}) of an organism and External Work (W_{ext}) of an organism which creates maintenance stability of organism's Internal Medium (stable concentration substances in blood and neurolymph). The stability Internal Energy (U) support stable balance anabolic endergonic processes & catabolic exergonic processes of an organism (Figure 1). It contains three level regulation: 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"] and low level regulation ["Equilibrium Constant of endergonic and exergonic processes of energy exchanges" and "Equilibrium Constant of anabolic and catabolic processes of metabolism"] (1. 2) (Figure 2). The mechanism maintenance stability Internal Energy (U) (temperature 36,0ºC-36,9ºC, by which all enzymes operate etc.) and Internal Medium (constant concentrations of substances in blood and in neurolymph) of an organism are also formed under the influences of interactions between mechanism maintenance stability Internal Energy (U) of both an organism and all cells of an organism. Just mechanism maintenance stability Internal Energy (U) of an organism determines stability Stationary State of an organism (1, 2). The affection of cells by v-oncogenes results in shift balance anabolic endergonic processes & catabolic exergonic processes into excessive anabolic endergonic processes. Excessive anabolic endergonic processes of cancer disease lead to excessive consumption energy via Acetyl–CoA for anabolic biosynthetic endergonic processes in cancer tissue which cause the overload of "nodal point of bifurcation anabolic and catabolic processes" [NPBac] because of the remained lack Acetyl–CoA for oxidative phosphorilation in catabolic exergonic anaerobic processes of Krebs tricarbonic acids cycle (TCA) (3. 4. 5. 6) (Figure 3). Also such shift into excessive anabolic endergonic processes and lack Acetyl-CoA cause partial suppression of catabolic anaerobic exergonic processes of oxidative phosphorilation (TCA) in cancer tissue, but some catabolic anaerobic processes remain for cancer cells survival (3. 4. 5. 6) (Figure 3). The increase of lactic acids production is the necessary mechanism of accumulation energy for huge anabolic endergonic processes in condition glycolysis metabolism which cause enormous consumption energy for anabolic processes in cancer tissue (3, 4, 5, 6) (Figure 1 and Figure 3). Thus, Warburg effect mechanism is formed oncogenesis of the metabolism of cancer tissue (3, 4). The partial suppression of catabolic anaerobic processes causes shift balance catabolic aerobic exergonic processes & catabolic anaerobic exergonic processes into prevailing catabolic aerobic exergonic oxidative processes (3, 4, 5, 6) (Figure 1 and Figure 3). The considerably increased Lactic Acids, as the marker of Glycolysis, and prevailing Aerobic catabolic exergonic oxidative processes determine "Aerobic Glycolysis" of Warburg effect in cancer metabolism (3, 4, 5, 6) (Figure 3).

Balance of interactions catabolic processes and anabolic processes in norm.



Disbalance of interactions catabolic processes and anabolic processes in cancer.

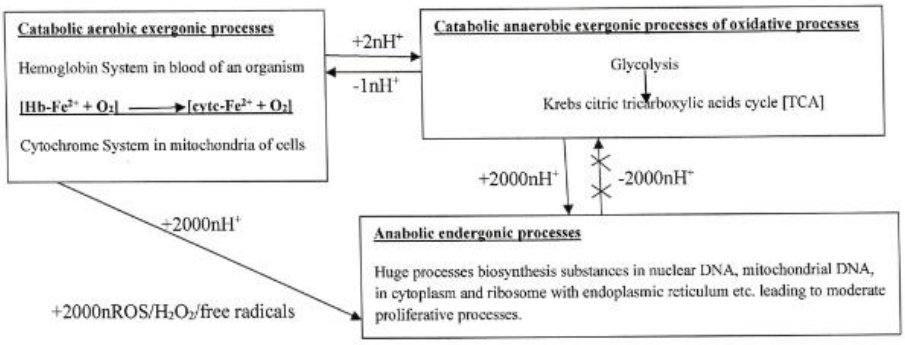
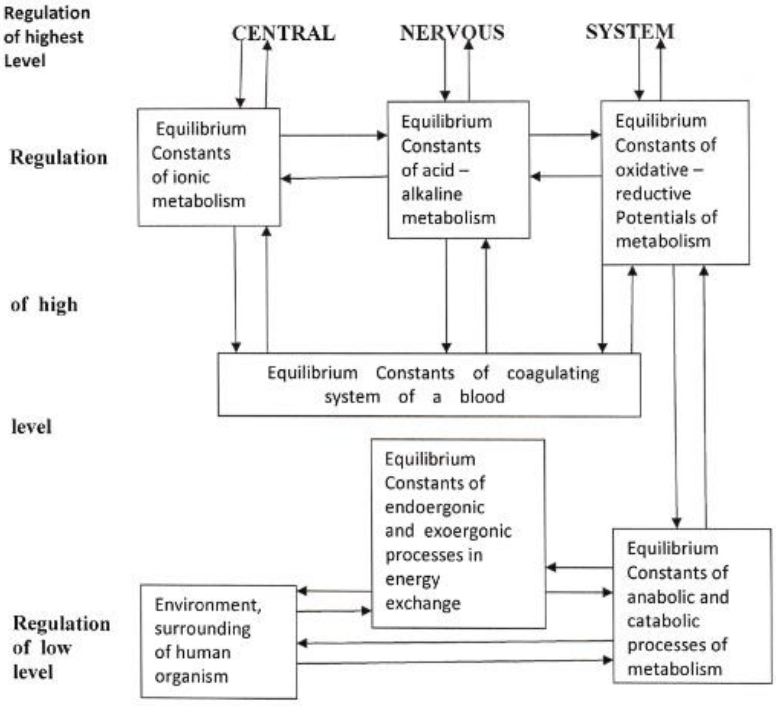


Figure 1: Influences of energy flow on interactions catabolic process and anabolic processes in noem and in cancer pathology



Footnotes: Metabolic and Energy "Equilibrium Constants" regulate interactions of intracellular and extracellular chemical potentials ($\mu_{int.} \leftrightarrow \mu_{ext.}$) for maintenance stability of Internal Energy and Internal Medium an organism. The intracellular and extracellular chemical potentials ($\mu_{int.}$ and $\mu_{ext.}$) cause the formations of the positive/negative charges on internal and external membranes of cellular wall, promoting operation of remote cellular reactions via cellular capacitors operation.

Figure 2: The mechanisum of maitenance stability of internal energy and internal medium an organism

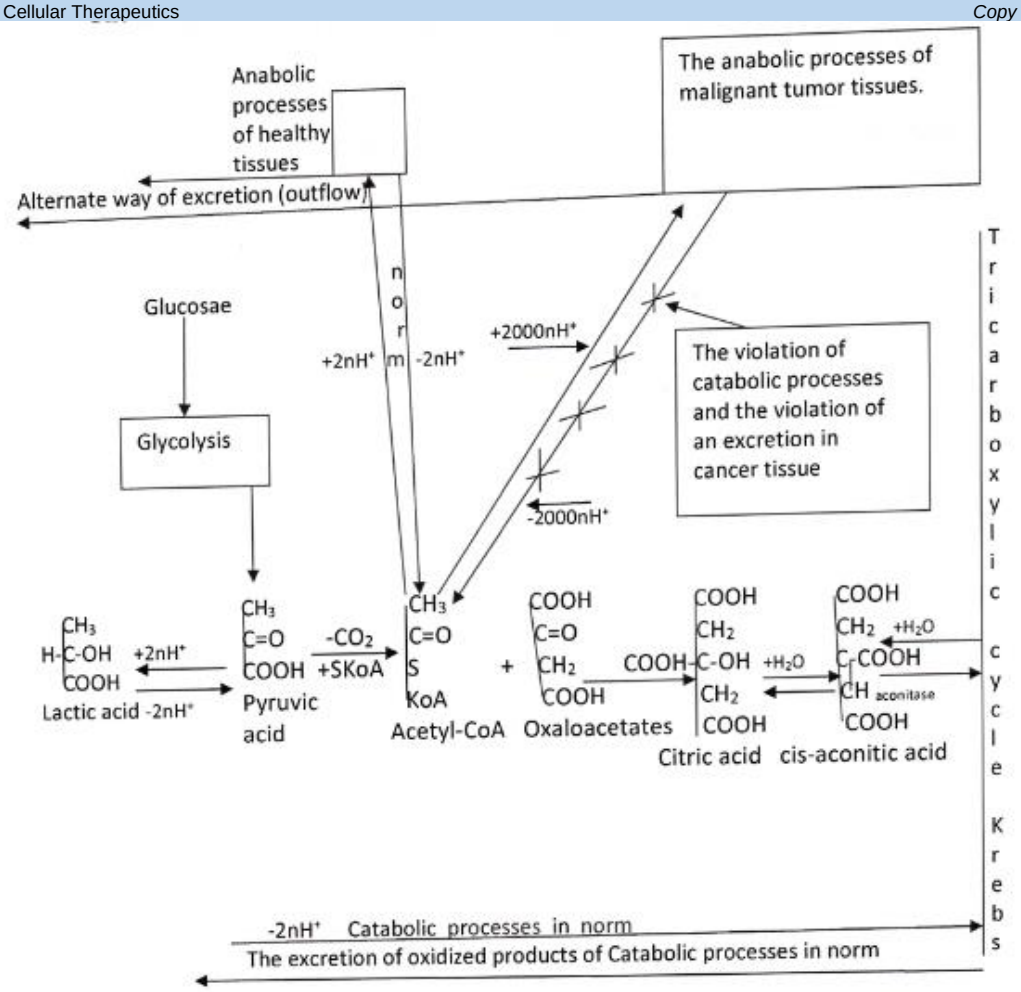


Figure 3: The metabolism of a malignant tumor tissue and of a normal tissue

The unlike Pasteur effect exhibiting "Incompatibility Glycolysis with Aerobic Oxidation" in normal tissue, Warburg effect exhibits Aerobic Glycolysis in cancer tissue metabolism, i.e. combination Aerobic Oxidation with Glycolysis which is defined by increase Lactic acids as crucial marker of Glycolysis. Hence there are Targets of cancer stem cells which use much energy for their development in cancer cellular cycle with increasing anabolic processes in disbalance anabolic processes & catabolic processes (Figure 4). The partial suppression catabolic anaerobic exergonic processes of oxidative phosphorilation in Krebs tricarbonic acids cycle [TCA] and considerably expression catabolic aerobic exergonic oxidative processes induce also expression oxidative processes in cancer cells (6) (Figure 5). Just mitochondria aerobic oxidative function in norm due to operation electron transport chain through Five Complexes includes cytochrome system [cytochrom C, cytochrom-c-oxidase, cytochrom P450 etc.] in cancer cells that receives stabile quantity Oxygen (O_2) being delivered by Hemoglobin system corresponding to stabile constant Respiratory Index [CO_2/O_2 = 0,8-1,0] of an organism (Figure 5). The shift balance Aerobic oxidative processes & Anaerobic processes of oxidative phosphorilation into expression Aerobic oxidative processes, owing to partial suppression of Anaerobic processes of oxidative phosphorilation, in mitochondria of cancer cells induces forming of excessive quantity of mitochondrial superoxide [O_2^{*}] because partial suppressed catabolic anaerobic processes of Krebs tricarbonic acid cycle (TCA) does not supply sufficient quantity ions of Hydrogen (H^+) for production H_2O via oxidation of Hydrogen ions, and Oxygen (O_2) adds electrons (e^-) forming Superoxide (O_2^{*}): $O_2 + e^- = O_2^{*}$(5, 6). The superoxide [O_2^{*-}] reduces Ferric iron [Fe^{3+}] into Ferrous iron [Fe^{2+}] with oxygen: $O_2^{*-} + Fe^{3+} \rightarrow Fe^{2+} + O_2$ (Figure 3 and Figure 5). Then superoxide anion is subjected to dismutation by manganese superoxide dismutase (MnSOD) and copper, zinc superoxide dismutase (Cu, ZnSOD) converting into hydrogen peroxide: $2O_2^{*-} + 2H^+ = H_2O_2 + O_2$. Thus Krebs tricarbonic acid cycle (TCA) reaction leads to forming increased quantity of Reactive Oxygen Species (ROS) (5, 6) (Figure 6). The excessive quantity of mitochondrial superoxide [O_2^{*}] does not support processes of anaerobic oxidative phosphorilation and does not lead to final products CO_2 and H_2O.

The normal steady concentration of superoxide [O_2^{*}] is higher in mitochondrial matrix than in cytoplasm and nucleus. Subsequently it is happened Haber –Weiss reaction of iron catalyzed by superoxide transformations which is passed into Fenton reaction (7, 8, 9, 10, 11, 12):

$$Fe^{3+} + O_2^{*-} \rightarrow Fe^{2+} + O_2$$

$$Fe^{2+} + H_2O_2 \rightarrow Fe^{3+} + {}^{-}OH + {}^{*}OH$$

$$O_2^{*-} + H_2O_2 \rightarrow {}^{-}OH + {}^{*}OH + O_2 + Fe^3$$

The formed complex ROS/H_2O_2 pass through mitochondrial membranes and cytoplasm into nucleus and generates superoxide [O_2^{*}] inducing free radicals ($^{*}OH$). Free radicals ($^{*}OH$) react on nuclear DNA [nDNA] and induce process replication via realizing of 2nDNA reaction (11, 12):

$$^{*}OH + H_2\text{-nDNA-DNA} \longrightarrow H_2O + H^{\bullet}\text{-nDNA-DNA};$$

$$O^{*} + 2H_2O \longrightarrow 2H^{\bullet} + 2OH^{-};$$

$$2H^{\bullet}\text{-nDNA-DNA} + 2H^{\bullet} \longrightarrow 2\text{nDNA-H}^{\bullet} + 2\text{nDNA-H}^{\bullet};$$

$$2\text{nDNA-H}^{\bullet} + 2^{*}OH \longrightarrow 2\text{nDNA} + H_2O$$

Thus the free radicals ($^{\bullet}OH$ and $H^{\bullet}$) induce nDNA replication and also are neutralized in final S and G2 phases of cellular cycle via nDNA replication which occurs as in cancer cells as well as in normal cells [4, 6. 7]. However 2nDNA reactions for cells' replications occur considerally more in cancer cells than in normal cells because lack of energy 2nDNA reaction from Basic Internal Energy (E_{bas}) in deep level of the cancer stem cells find other cells of an organism with enough deep level energy for 2nDNA replication from Basic Internal Energy causing mechanisms of Metastasis (see above, part 1).

Highlight of Warburg effect mechanism: As outcome of viral oncogenes operation the huge anabolic processes cause huge consumption energy and Acetyl-CoA and partial suppress catabolic anaerobic processes in cancer tissue due to shift balance anabolic processes & catabolic processes into excessive anabolic processes leading to lack Acetyl-CoA for anaerobic processes in cancer metabolism that causes shift balance Aerobic oxidative processes & Anaerobic processes of oxidative phosphorilation into expression of Aerobic oxidative processes, owing to partial suppression of Anaerobic processes of oxidative phosphorilation, in mitochondria of cancer cells. These processes induce increased ROS/H_2O_2/Free radicals which exert cancer cells' irrepressible proliferative processes for cancer tumor growth and Metastasis. Just Lactic acids accumulate energy for excessive anabolic processes in condition glycolisis metabolism in cancer tissue [7, 8, 9, 10].

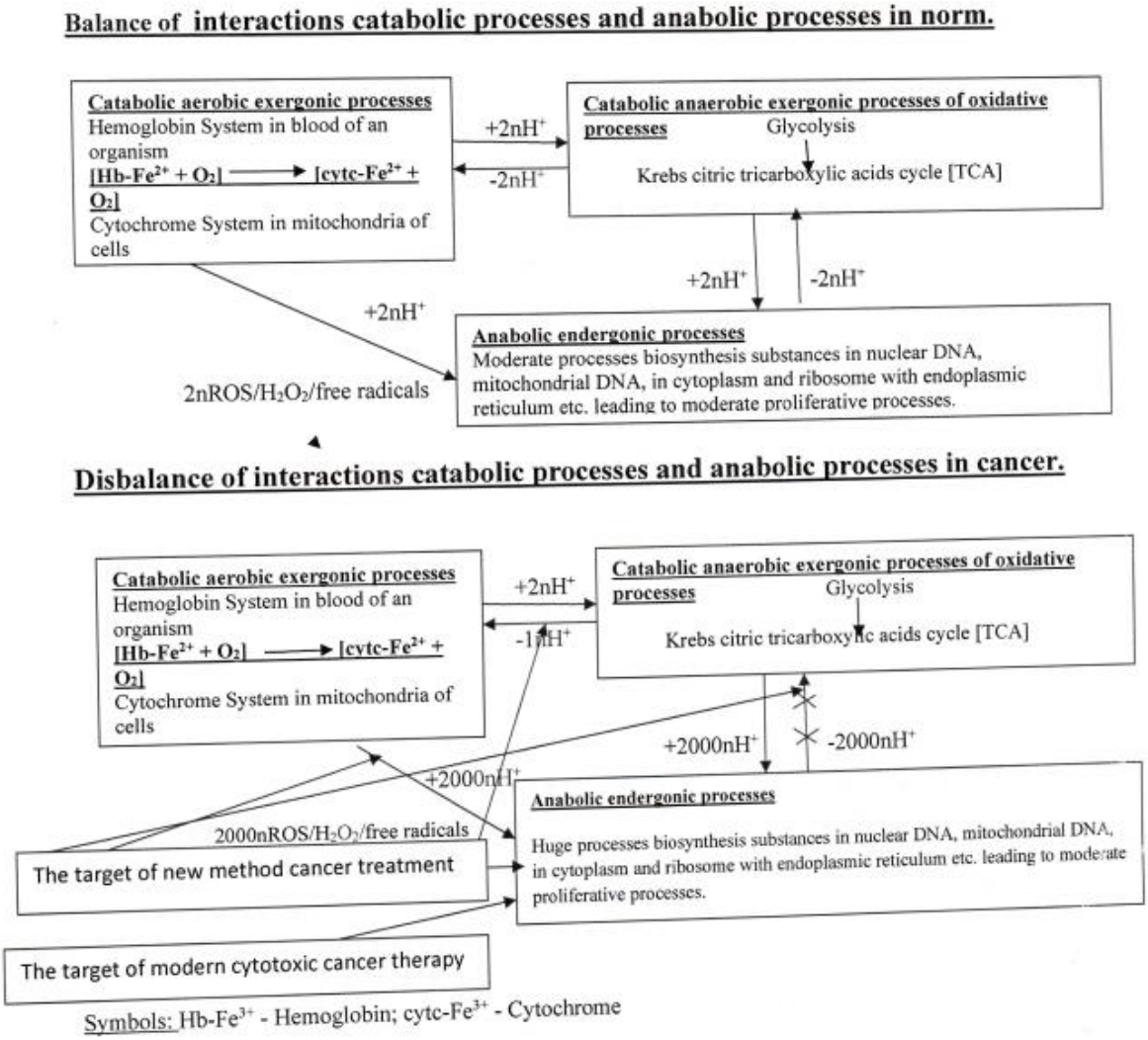


Figure 4: The targets of both the new method of cancer treatment and the modren method of cancer treatment

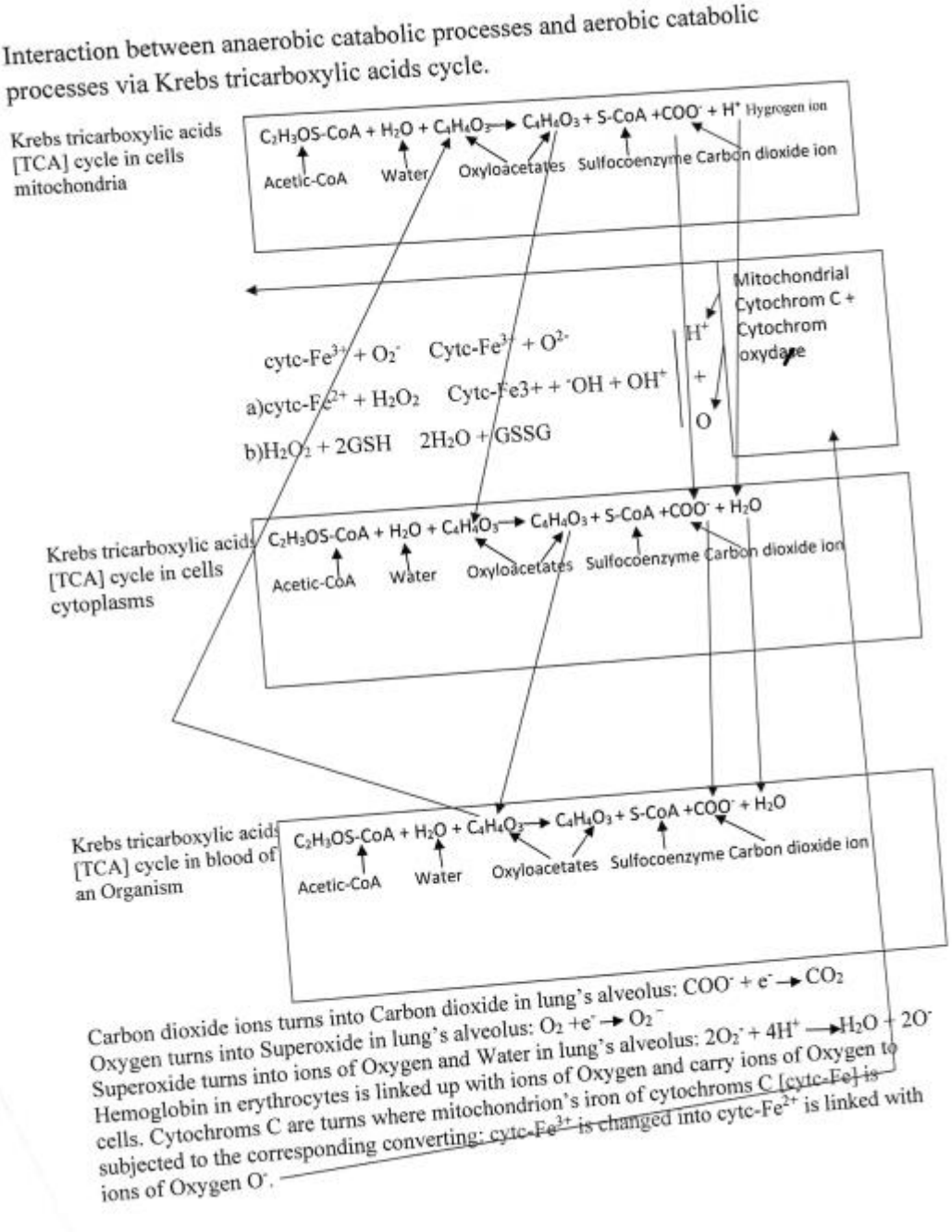
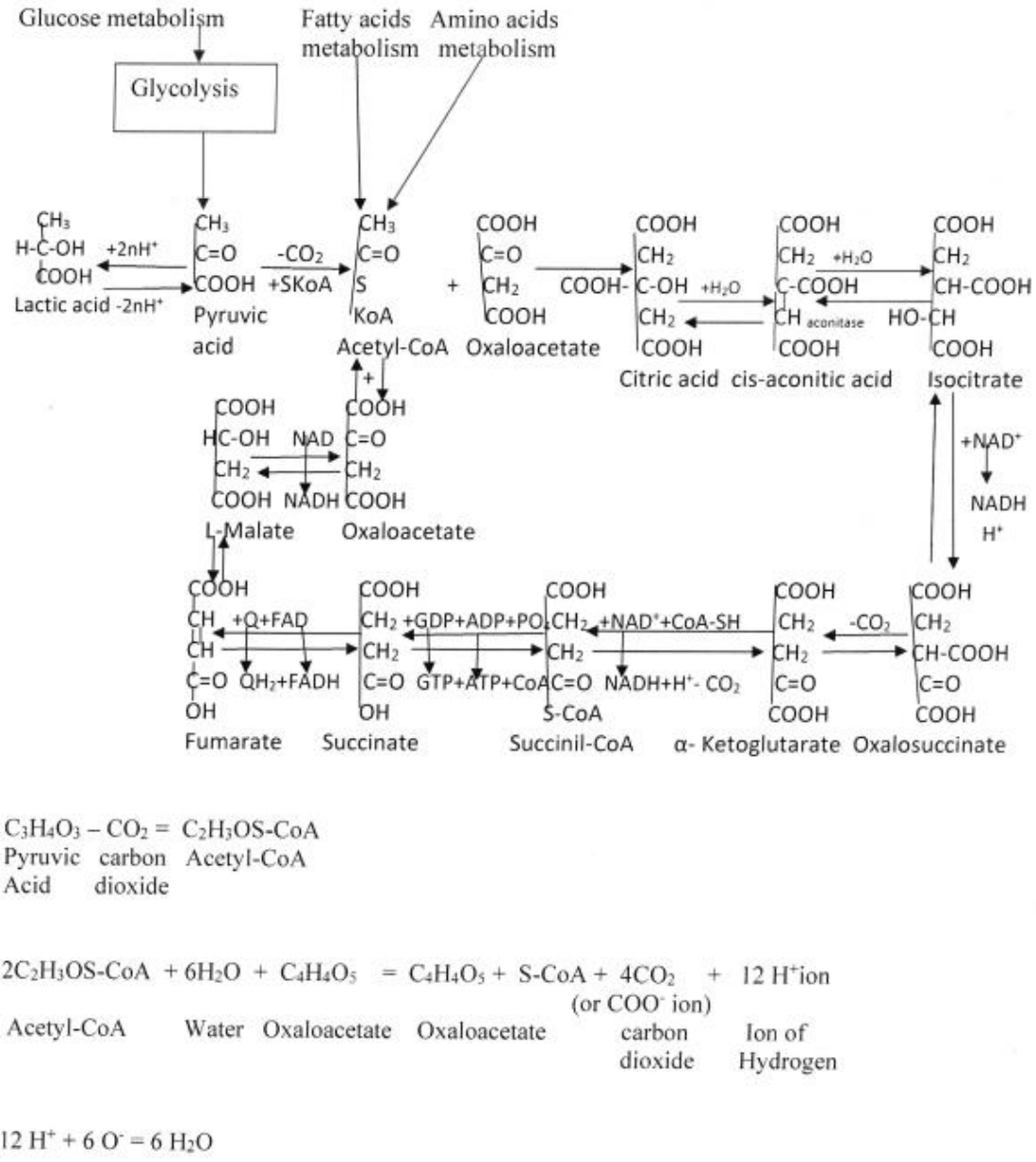


Figure 5: Interaction between anaerobic and catabolic processes and aerobatic processes via Krebs tricarboxylic acids cycle.



$C_3H_4O_3 - CO_2 = C_2H_3OS\text{-}CoA$

Pyruvic Acid — carbon dioxide — Acetyl-CoA

$2C_2H_3OS\text{-}CoA + 6H_2O + C_4H_4O_5 = C_4H_4O_5 + S\text{-}CoA + 4CO_2 + 12\ H^+ion$

(or COO^- ion)

Acetyl-CoA — Water — Oxaloacetate — Oxaloacetate — carbon dioxide — Ion of Hydrogen

$12\ H^+ + 6\ O^- = 6\ H_2O$

Figure 6: Krebs tricarboxylic acids cycle (TCA) in catabolic exoergonic process.

3. The mechanism of new method cancer treatment.

3.1. The detailed description of the use of Herbal Extracts in treatment by "Prolonged Medical Starvation for 42-45 days".

New method cancer treatment uses "Prologed medical Starvation" which is supplemented with considerably decreased dosage cytotoxic substances (13, 14, 15). "Prolonged medical Starvation during 42 - 45 days" of an organism is supported with herb extracts [sage, hawthorn, horse-tail, (stinging-)nettle, ninety-knot, hypericum, ergot, St.John's wort, etc.] providing with small dosage of cytotoxic activity of red cranesbill (Geranium robertianum) and used abundant liquid drink including water up to 1,5-2,0 liter per day (13, 14, 15, 16). The herbal extracts should be filtered through a triple gauze layer in order that any fibre must not remain in the extract. The herbal extracts fill the organism during "Prologed medical Starvation 42-45 days" for supplementing with necessary microelements and vitamins, especially folic acid, that is necessary for hemopoiesis and decreases also acidification in the blood of the organism by "Prolonged medical Starvation". During the "Prolonged medical Starvation" it's necessary to look after the common health state of the person and especially state of gastrointestinal tract that it occurs the bowels open /timely evacuation of excrements/, that there will not be constipation /retention of feces/. The disturbance of gastrointestinal activity should be healed with vegetable laxatives, activated charcoal, medicaments and use an enema if it's necessary. The starvation leaving should been taken place during 7 days with gradual addition of products: juices, then watery decoctions and gels, then vegetable pulps, then baked fruits and vegetables, then liquid kasha (dish of cooked grain), then mashed potatoes, then pair of cutlets-and up to the usual nutrition (14, 15). The diet shouldn't be salted during leaving starvation [14, 15].

3.2. The Healing Mechanism of "Prolonged Medical Starvation 42–45 Days with Very Small Dosage and Weak Cytotoxic Substances".

Cancer tumor is situated 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 depressive organism via treatment by "Prolonged medical Starvation (during 42–45 days)" [13-17]. The treatment by "Prolonged medical Starvation (during 42–45 days)" is providing with small dosage of cytotoxic activity of red cranesbill (Geranium robertianum) and used abundant liquid drink including water up to 1,5-2,0 liter per day [14, 15] causing considerable decrease almost of all depots of an organism exhausting organism's fat and hydrocarbonic depots, that leads to competition between cancer tissue and an organism for the use of remained decreased depot for maintenance stability Internal Energy of a depressive organism (U org) (normal temperature 36.0°C–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 depressive organism become stronger due to support with herbal extracts including also small dosage of cytotoxic activity of red cranesbill (Geranium robertianum), delivering vitamins and microelements into the organism [14, 15]. Besides increase of fat metabolism from fat depot leads to augmentation glutation peroxide GPX and phospholipid hydroperoxide glutathione peroxide (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 excessive proliferative processes of cancer cells [6, 14,15]. Suppression accelerating cellular cycle in cancer cellular cycle leads to decrease anabolic processes in condition of "Prolonged medical Starvation" with small dosage of cytotoxic activity of red cranesbill (Geranium robertianum) which is exerting normal nuclear DNA [nDNA] work, decreased replication via prevailing Mitosis over Meiosis in complex Mitosis-Meiosis phase [6, 13]. Eliminating partial suppression of Anaerobic processes of oxidative phosphorylation by "Prolonged medical Starvation" restores normal balance Aerobic oxidative processes & Anaerobic processes of oxidative phosphorylation in mitochondria of cancer cells decreasing ROS in mitochondria of cancer cells causing suppression of excessive nucleus DNA replication with normalization of cellular cycle of cancer cells and elimination irrepressible proliferative processes of cancer growth [3, 4, 15, 16, 17]. 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 due to prevailing state over diploid Mitosis phase normal cellular cycle [15, 16, 17]. Besides broken covalent bonds between Mitosis and Meiosis, deprive barriering defense of viral pluripotent stem cells function causing normal cellular cycle with activity of diploid Mitosis phase in cancer cells [14, 15, 16, 17]. Expression Mitosis in normal cellular cycles of all cells incite T cells [T lymphocytes] via appearance produced immunoglobulins CTLA-4 and PD-1, and resonance waves of cellular capacitors T memory cells learn and remember waves function of viral substances 21 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 defense of covalent bonds between Mitosis and Meiosis causing loss viral pluripotent stem cells function. Thus, such basic phenomena of the cancer metabolism are inhibited following datum [14, 15, 17]:

1. Mechanism of "Warburg effect."

2. Biochemical and biophysical mechanisms of metastases and non-healing tumor ulcers.

Inhibition of Warburg effect by "Prolonged medical Starvation" leads to cancer cells' depressions which are determined by the following changes:

1. Expression normal cellular cycle and inhibition accelerated cancer cellular cycle.

2. Activated diploid Mitosis phase cellular cycle and suppression haploid Meiosis phase of viral cellular cycle.

3. Stimulated immune phagocytosis of T killer cells and B cells to produce antibodies against the autoantigen IgE substances causing suppression haploid Meiosis phase of viral cellular cycle. Simultaneously the very small dosage and weak cytotoxic substances damage only depressed cancer cells but don't influence an organism's able-bodied immune cell especially T-cells. Thus influences 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 promoting cured an organism. Benefits "Prolonged medical Starvation" contributes to depression of cancer tumor metabolism that helps for efficient anticancer therapy with considerably decreased dosage of cytotoxic drugs. Such approach to anticancer chemotherapy prevents damage Internal Energy (U) and Internal Medium both an organism and cells of an organism, preventing damage of immune and hormonal systems as the links of defensive mechanism of regulative system of an organism.

4. The mechanisms of forming cancer metastases in neglected state of an organism causing treatment as by mechanism of new method cancer treatment as well as by mechanism of modern method cancer therapy.

4.1. The Mechanisms of Cancer Tumor Metastases in neglected state of an organism.

The overload of "nodal point of bifurcation anabolic and catabolic processes" [NPBac] with partial suppression catabolic exergonic anaerobic processes occurs due to shift balance anabolic endergonic processes & catabolic exergonic anaerobic processes into excessive anabolic endergonic processes in cancer metabolism [4, 18, 19, 20, 21, 22] (Figure 3). Thus increased the anabolic endergonic processes in cancer tissues of neglected organism leads to deep losses of considerable decrease almost of all depots of an organism especially exhausting organism's fat and hydrocarbonic depots via their substances because of increased anabolic endergonic processes of cancer tumor in neglected state of a human organism becoming lean [4, 18-22]. Besides this violated balance anabolic biosynthetic processes & catabolic anaerobic processes cause violation balance catabolic aerobic processes & catabolic anaerobic processes into prevalence aerobic processes of respiratory oxidation over partial suppressed anaerobic processes of oxidative phosphorilation in cancer metabolism [4, 6, 18-22]. The prevalence aerobic processes of respiratory aerobic oxidation over anaerobic processes of oxidative phosphorilation leads to disbalance between mitochondrial aerobic respiratory oxidative function and anaerobic oxidative phosphorilation of link Glycolysis-Krebs Tricarboxylic Acids Cycle (TCA) (4-6,18-22) (Figure 6). As concerning of the absence the respiratory electron transport chain with five Complexes in oncologic viruses (v-oncogenes), this prevalence aerobic processes of respiratory oxidation in cancer cells provide oncologic viruses (v-oncogenes) with respiratory electron transport chain by cellular mitochondrial respiratorial electron transport chain. However the oncologic viruses (v-oncogenes) are intensive replicated and find respiratory activity in respiratory electron transport chain of new heathy cells which are affected by oncoviruses of cancer cells via transiting the new cancer calls of metastasis in new organs (Figure 5 and Figure 6). Thus increased quantity metastases create neglected state of cancer ill organism. Just cells' mitochondrial aerobic oxidative function produces stable quantity Oxygen ions [O^{-2}] via operation of cytochrome system [cytochrom C, cytochrom-c-oxidase, cytochrom P450 etc.] in cancer cells because of delivering stable quantity Oxygen (O_2) by Hemoglobin system in blood corresponding to stable Respiratory Index [$CO_2/O_2 = 0,8 - 1,0$] in an organism. Produced in Krebs tricarboxylic acids cycle (TCA) Hydrogen ions (H^+) react with Oxygen (O_2) and form Water (H_2O) that must eliminate Oxygen from liquids of an organism tissue and cells of an organism (4, 6, 9, 10, 18 - 22) (Figure 5 and Figure 6). However the supplementary Oxygen (O_2) does not find sufficiently Hydrogen ion (H^+) to react with Oxygen (O_2) and does not produce supplementary Water (H_2O) [4, 6, 9, 10, 17–22]. Therefore this supplementary Oxygen (O_2) adds electron, due to Reactive Oxygen

Species (ROS) operation, and is transformed into superoxide (O_2 *) which generates free radicals. Free radicals exert DNA replications in G2 phase of cellular cycle via inducing reaction 2nDNA replication (5, 6). Partial suppression catabolic processes of Krebs tricarboxylic acids cycle (TCA) decreases quantity of Hydrogen ions (H^+) production in cancer metabolism. The insufficiency of Hydrogen ions (H^+) production causes abundance superoxide (O_2 *) inducing excessive quantity of ROS/ H_2O_2 /free radicals which exert accelerative DNA replications via inducing accelerative reaction 2nDNA reactions in cancer cells (4, 5, 6, 11, 12, 18-22).

$$^{*}OH + H_2\text{-nDNA-DNA} \longrightarrow H_2O + H^{\bullet}\text{-nDNA-DNA};$$

$$O^{*} + 2H_2O \longrightarrow 2H^{\bullet} + 2OH^{-};$$

$$2H^{\bullet}\text{-nDNA-DNA} + 2H^{\bullet} \longrightarrow 2\text{nDNA-}H^{\bullet} + 2\text{nDNA-}H^{\bullet};$$

$$2\text{nDNA-}H^{\bullet} + 2^{*}OH \longrightarrow 2\text{nDNA} + H_2O$$

The induce nDNA replication in G2 phase cellular cycle, and also the free radicals (*OH and H•) are neutralized in final G2 phase of nDNA replication as in cancer cells as well as in normal cells [5, 6, 11, 12, 18-22]. Then it occurs M phase of cellular cycle, i.e. Mitosis in cell division. Thus moderate cellular replication occurs in norm due to production moderate quantity ROS/H_2O_2/free radicals in able-bodied cells and occurs via $G_\circ$, G1/S, G2, M phases cellular cycle. The accelerated cycle of cancer cell is induced by accelerated cycle of v-oncogene initially and then is continued via affecting cancer nuclei by excessive quantity ROS/H_2O_2 /free radicals produced in cancer cells' mitochondria. The accelerated cellular cycle of cancer cells leads to shortening cancer cellular cycle without $G_\circ$ and G1 phases cellular cycle that creates excessive cellular replication of cancer cells. The perpetual affecting cancer cells by excessive quantity of ROS/H_2O_2 /free radicals cause irrepressible cancer tumor growth which also supports by some growth factors as EGF, FGFs, HGF, HDGF, GDF9, IGFs and so on [5, 6, 11, 12, 18–22]. Furthermore, the irrepressible cancer tumor growth leads to partial suppression catabolic anaerobic oxidative processes due to overloaded "nodal point of bifurcation anabolic and catabolic processes" [NPBac] with consumption great quantity energy and Acetyl-CoA that impede excretion via oxidative destruction of great quantity high-molecular substances which produced by excessive anabolic processes of cancer metabolism [4, 6, 9, 10, 18-22]. Therefore the excretion of great quantity high-molecular substances are produced via huge anabolic processes that occurs within cancer cells (Figure 1). Thus there are formed many metastases in neglected organism. Besides the partial suppression catabolic anaerobic processes in cancer tissue touches also on Krebs Tricarboxylic Citric Acids cycle [TCA] via partial suppression mechanism transferring Oxaloacetates from cancer tissue TCA to cancer cells' TCA [4, 5, 6, 10, 18-22] (Figure 5 and Figure 6). The overload NPBac with partial suppressed mechanism transferring Oxaloacetates from cancer tissue TCA to cancer cells' TCA results in expression mechanism metastasis due to blocking oxidative destruction of synthesized high-molecular substances in cancer tissue [4, 6, 9, 10, 18-22] (Figure 5 and Figure 6). Also operations of an organism cells' cellular capacitors via resonance waves promote movement cancer cells with the synthesized high-molecular substances within them into healthy tissue without overload "Nodal point bifurcation anabolic and catabolic processes [NPBac] and lack of Acetyl-CoA" for oxidative destruction high-molecular substances and cause metastases into the healthy cells of healthy tissues of different organs where these healthy cells are changed itself into cancer cells of cancer tissue.

4.2. The cancer metastases in neglected state of an organism are destructed via creating by efficient treatment of cancer disease by mechanisms of new method cancer treatment.

The state of "Prolonged medical Starvation (during 42–45 days)" bereave of some substances from anabolic biosynthetic processes that prevent to affect of cells by v-oncogenes impeding of shift balance anabolic endergonic processes & catabolic exergonic processes into excessive anabolic endergonic processes [4, 14, 15, 23, 24, 25]. Hence absent of excessive anabolic endergonic processes of cancer tissue and excessive quantity of mitochondria catabolic aerobic electron transport chain processes that lead to absent mechanism forming metastases and development of cancer cells [11,12, 15, 23-25]. Thus overloaded "nodal point of bifurcation anabolic and catabolic processes" [NPBac] with consumption great quantity energy and Acetyl-CoA in "Prolonged medical Starvation (during 42–45 days)" leads to depression cancer development (4, 15, 19, 23-25). Besides it prevents of forming Warburg effect as mechanism of cancer development. Also, the new method cancer treatment use "Prolonged medical Starvation (during 42-45 days)" for depression cancer activity of forming metastases, and use very small dosage of cytotoxic substances which don't suppress activity of immune systems and hormonal systems. Therefore, Hormones how cofactors of an organism's metabolic chemical processes promote maintenance stability Internal Energy (U_{org}) of an organism in state of "Prolonged medical Starvation (during 42-45 days)" that supports stability as balance anabolic biosynthetic processes & catabolic anaerobic phosphorilation of oxidative processes as well as catabolic aerobic oxidative processes & catabolic anaerobic phosphorilation of oxidative processes. Also, very small dosage of cytotoxic substances destruct of some depressed mechanism of cancer development, and then immune T cells phagocytosis with B cells antibodies creates complete destruction of oncologic mechanisms leading to recovery of the organism.

4.3. The cancer metastases in neglected state of an organism are appeared in all organs of an organism including in living organs which create impossible to treatment of cancer disease by modern method cancer therapy with large dosage cytotoxic drugs.

As concerning to modern methods of cancer treatment with large doses of cytotoxic drugs, the both immune system and hormonal system of an organism are suppressed by large dosage cytotoxic drug that reduce possibility of efficient cancer treatment especially of cancer many metastases [6, 26-37]. First of all, chemotherapeutic modern methods cancer therapy use the large dosage cytotoxic drugs which create destruction as great quantity of cancer cells with oncologic viruses (v-oncogenes) in them as well as suppressed both Hormonal processes of an organism's maintenance stability Internal Energy via defending again environmental external powers and Immune processes of T cells and B cells antibodies again external organisms (v-oncogenes) [6, 26-37]. Secondly, the modern methods cancer therapy with large dosage cytotoxic druges can destruct great quantity of oncologic viruses or even all oncologic viruses (v-oncogenes) only in the beginning cancer disease without multiple cancer metastases [6, 26-37]. However the forming multiple cancer metastases in neglected state of an organism are occurred the overload of "nodal point of bifurcation anabolic and catabolic processes" [NPBac] with partial suppression catabolic exergonic anaerobic processes occurs due to shift balance anabolic endergonic processes & catabolic exergonic anaerobic processes into excessive anabolic endergonic processes in cancer metabolism and increased catabolic exergonic aerobic respiratory electron transport chain of supplementary Oxygen (O_2) with adding electron, due to Reactive Oxygen Species (ROS) operation, and is transformed into superoxide (O_2*) that induce reaction 2nDNA replication via exert accelerative DNA replications via inducing accelerative reaction 2nDNA reactions in cancer cells [6, 26-37]. The accelerating state in G2 phase of cellular cycle are supported by oncologic viruses (v-oncogenes) which form supplemental metastasis from healthy cells into cancer cells [6, 26-37]. These activities of cancer development form many new cancer cells which cannot be to destruct all of them even by large quantity of cytotoxic drugs that make neglected state of cancer disease of how incurable organism. This activity of cancer development can be ceased by creating depressed activities of cancer development but which cannot make by large quantity of cytotoxic drugs. However, the depressed activities of cancer development are made by "Prolonged medical Starvation (during 42–45 days) in new method cancer treatment which give opportunity to efficient treatment with very small dosage of cytotoxic substances and supplemental by immune therapy of T cells and B cells Antibodies.

5. The mechanism of forming either resistance cytotoxic drugs or relapse cancer disease in event to cease of treatment after modern methods of therapy with large dosage cytotoxic drugs and the mechanism of preventing as forming resistance cytotoxic drugs as well as appearance relapse cancer disease in new method cancer treatment.

Immune system and hormonal system are the links of system maintenance stability Internal Energy and Internal Medium via determining stability chemical potential Internal Energy (Uμ) of an organism. Therefore, suppressed immune system and hormonal system after long anticancer modern chemotherapy with large dosage of cytotoxic drugs don't prevent both relapse of cancer disease and resistance anticancer cytotoxic drugs which are occurred due to violation stability Internal Energy of cancer cells chemical potential (Uμ*) of an organism [38, 39, 40, 41] (Figure 7).

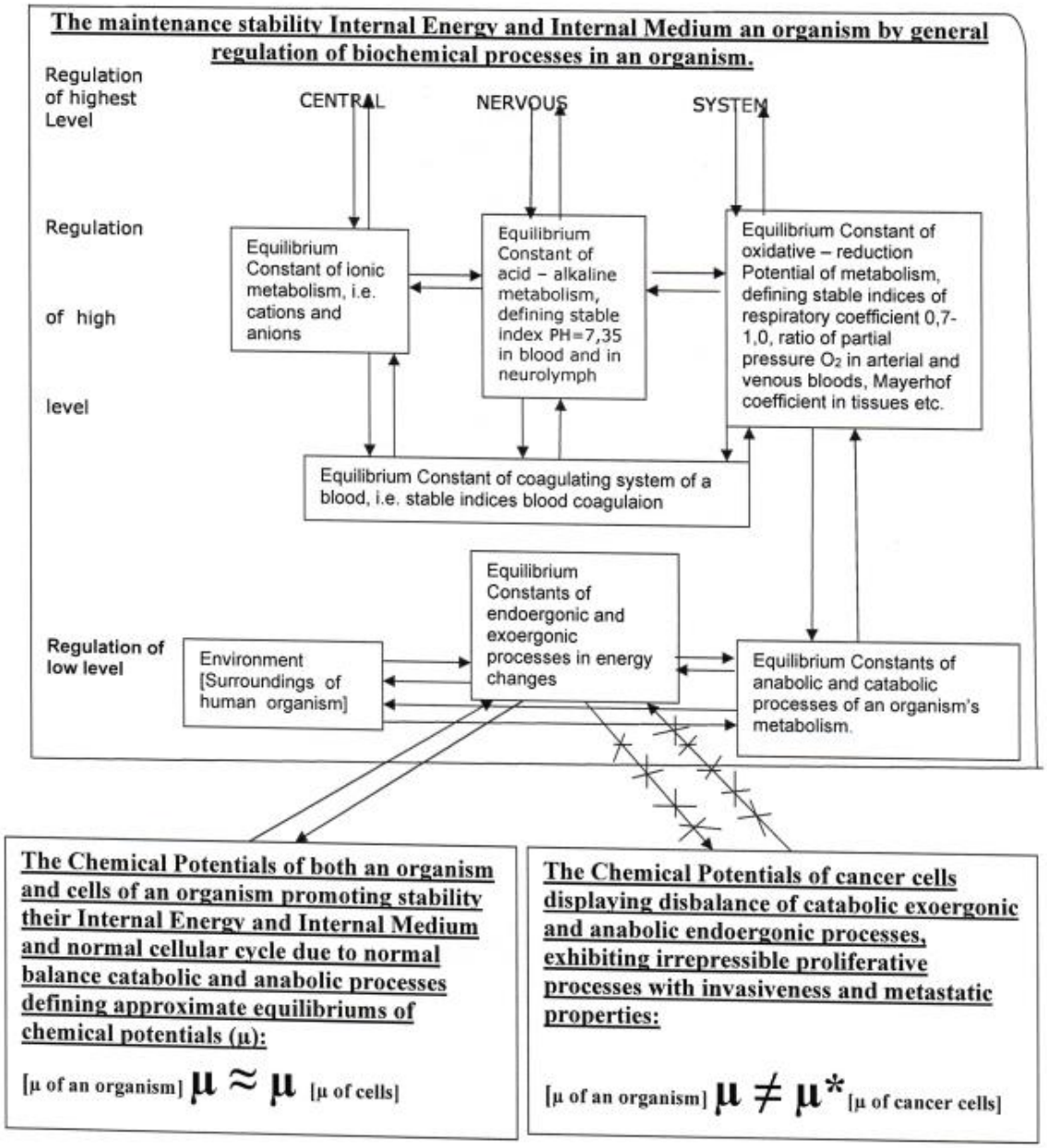


Figure 7: The influences general regulation biochemical processes on Internal Energy determining stability internal chemical potentials of an organism (μ), normal cells (u) and cancer cells (u*)

5.1. The mechanism of forming either resistance cytotoxic drugs or relapse cancer disease in event of the cease after treatment by modern methods of therapy with large dosage cytotoxic drugs.

Cancer tumor is situated 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.) [42, 43] (Figure 8). The modern chemotherapy with large dosage cytotoxic drugs leads to complete destruction of some cancer cells with oncologic viruses within them, and also it makes some suppression defensive mechanisms of immune and hormonal systems [44, 45]. Just the normal development of cellular cycle demand energy for the supplemental anabolic biosynthetic endergonic processes which energy is received from Basic Internal Energy (E_{basic}) in norm of an organism through Basic stem cells (neurons) → Totipotent stem cells → Pluripotent stem cells → Multipotent stem cells → Oligopotent stem cells → Unipotent stem cells → type healthy cells. HThere are occurred oncogenesis also through Basic stem cells

(neurons) → Totipotent stem cells → Pluripotent stem cells → Multipotent stem cells → Oligopotent stem cells → then Unipotent stem cells from normal cells which turn into Unipotent cancer stem cells of cancer pathology because of affected cells by viral oncogenes (v-oncogene). Thus suppressed defensive mechanisms of immune and hormonal systems of an organism leads to exerting of some survived oncologic viruses after pause of intensive chemotherapy which make relapsed cancer cells of appearance cancer disease [6, 44, 45] (Figure 9). As opposed to the relapsed cancer disease, the resistance cytotoxic drugs after pause from intensive modern Chemotherapy is occurred via following reasons: Firstly, normal chemical potentials (μ) of relative G1 → S → G2 phases cellular cycle being affected by survived oncologic viruses create transition normal chemical potentials (μ) through relative G1 → S → G2 phases cellular cycle into cancer pathology chemical potential (μ*) of cancer prokaryotic cellular cycle. Just relative G1 → S → G2 phases of eukaryotic cellular cycle are the mechanisms in which there are realized as driving mechanisms of cellular cycle in norm (μ) as well as driving mechanisms of prokaryotic cellular cycle in cancer pathologic chemical potential (μ*) (Figure 7). Also it is reflected positive fluctuations entropy ($+\Delta_x\beta$) and negative fluctuation entropy ($-\Delta_x\beta$) showing cellular cycle as via G_0/G1/S/G2/Mitosis in normal phases of eukaryotic cellular cycle as well as through G_0/G1/S/G2/Mitosis-Meiosis in oncologic phases of prokaryotic cellular cycle according Glansdorff-Prigogine theory (1, 2), (Figure 1). This mechanism exerts operation Meiosis-Mitosis prokaryotic cancer cellular cycle because of affected both nuclear DNA and mitochondria of an organism's cells [44, 45]. Modern methods cancer therapy use following targets: cancer tumors, cancer cells, cancer cells' nucleus and its DNA, cancer cells' mitochondria, cancer cells' organelle as well as links between them (46, 47). Thus, secondly, there are occurred pause after intensive influence by large dosage cytotoxic drugs on cancer cellular cycles by modern methods cancer therapy [44, 46, 47]. Hence there are subjected the strange DNA of deed cells by large dosage cytotoxic drugs as DNA of deed cancer cells as well as DNA in the glands of immune cells and of hormonal cells of an organism [44, 48, 49]. Therefore some survived Immune T cells of phagocytosis and B cells of antibodies are found via sensitive factors in pause after intensive Chemotherapy as antigens of the decomposed substances of dead cancer cells within the received antigens of cytotoxic drugs [44-49]. The some survived immune T cells of phagocytosis and B cells of antibodies don't react on the decomposed substances of dead cancer cells but react on antigens of cytotoxic drugs causing phagocytosis of destruction these cytotoxic drugs (44 - 49). Thus resistance to cytotoxic drugs creates destruction cytotoxic drugs which repeat exertion of cancer disease [44 -49] (Figure 10). Therefore DNA minor grooves of immune cells and DNA minor grooves of hormonal cells are also connected by Brostallicin (PNU-166196) although normal cells are less exertion than cancer cells [50]. Thus violation immune and hormonal function of an organism causes common disbalance anabolic endergonic processes & catabolic anaerobic exergonic processes & catabolic aerobic exergonic processes of Quasi-stationary pathologic State of an organism via accelerating cancer cellular cycle supplementally. Besides, thirdly, influencing of cancer cells by large dosage cytotoxic drugs can suppress also immune T cells and hormonal cells which are remained on immune sensitive condition to chemical structure of cytotoxic drugs in deed cancer cells. That condition of survived immune T cells leads to resistance of cytotoxic anticancer drugs after recovery from suppressed their states in pause of Chemotherapy. Hence the survived immune T cells create resistance of cytotoxic drugs transiting to relapsed cancer disease after intensive suppressed Chemotherapy with resistance cytotoxic drugs [44-49] (Figure 9 and Figure 10). Thus resistance to cytotoxic anticancer drugs and relapsed cancer disease are occurred after some times of pause intensive chemotherapeutic treatment with large cytotoxic drugs that can affect by survived some cancer cells [v-oncogenes] of nuclear DNA (nDNA) exerting G1/S/G2 phases prokaryotic cancer cellular cycle of Meiosis-Mitosis phase. The suppression of Meiosis-Mitosis phase cancer cellular cycle by large dosage cytotoxic drugs touch on exerting human eukaryotic genome of normal cellular cycle. Just it is occurred resistance antiviral force of cytotoxic drugs over oncologic viral force which can transit Meiosis-Mitosis into Mitosis-Meiosis reflecting prevalence antiviral force of cytotoxic drugs. But retaining Meiosis-Mitosis reflects prevalence oncologic viral force over antiviral force of cytotoxic drugs in which viruses [v-oncogenes] use energy for cancer cells development via accelerating cancer cellular cycle [2, 4]. Just the transition Meiosis-Mitosis into Mitosis-Meiosis reflects prevalence antiviral force of cytotoxic drugs in which rest some hormones activity of hormonal glands and immune T memory cells, T helper cells, T killer cells with B cells are restored activity after some time of intensive cytotoxic drugs treatment [44-49]. Thus also hormones activity restore immune T memory cells, T helper cells, T killer cells. Then T memory cells transmit these data to T helper cells and further to T killer cells. Thus either immune T killer cells and antibodies of B cells destruct cancer cells together with cytotoxic drugs activity or these immune T cells causing resistance to these anticancer drugs [44-49]. Hence retaining Meiosis-Mitosis cancer cellular cycle of survived oncologic viruses [v-oncogenes] retains accelerating cancer cellular cycle which is supported by activity of mistaken survived immune T cells after some time of intensive large dosage of cytotoxic drugs treatment [44-49] (Figure 10). Then it gives possibility some survived oncologic viruses [v-oncogenes] to create relapsed cancer disease after some time pause of intensive cytotoxic drug therapy [6, 44-49] (Figure 9). As concerning to using some hormone activity by survived rest oncologic viruses, it must be explained the following example: In breast cancer cells after intensive cytotoxic therapy are occurred either resistance to cytotoxic drugs or relapse cancer disease because cytotoxic drugs suppress cancer Meiosis-Mitosis cellular cycle and simultaneously suppress as immune T memory cells, T helper cells, T killer cells as well as activity female hormones Estrogens [estrone, estradiol, estriol] and Progesterone hormones. After some time from intensive chemotherapy, it is begun to restore as suppressed immune T memory cells, T helper cells, T killer cells as well as suppressed activity female hormones estrogens [estrone, estradiol, estriol] and Progesterone hormones in which the restored activity of both survived immune cells and hormonal estrogens can make mistakes which lead to either resistance to cytotoxic drugs or to relapse cancer disease (see above).

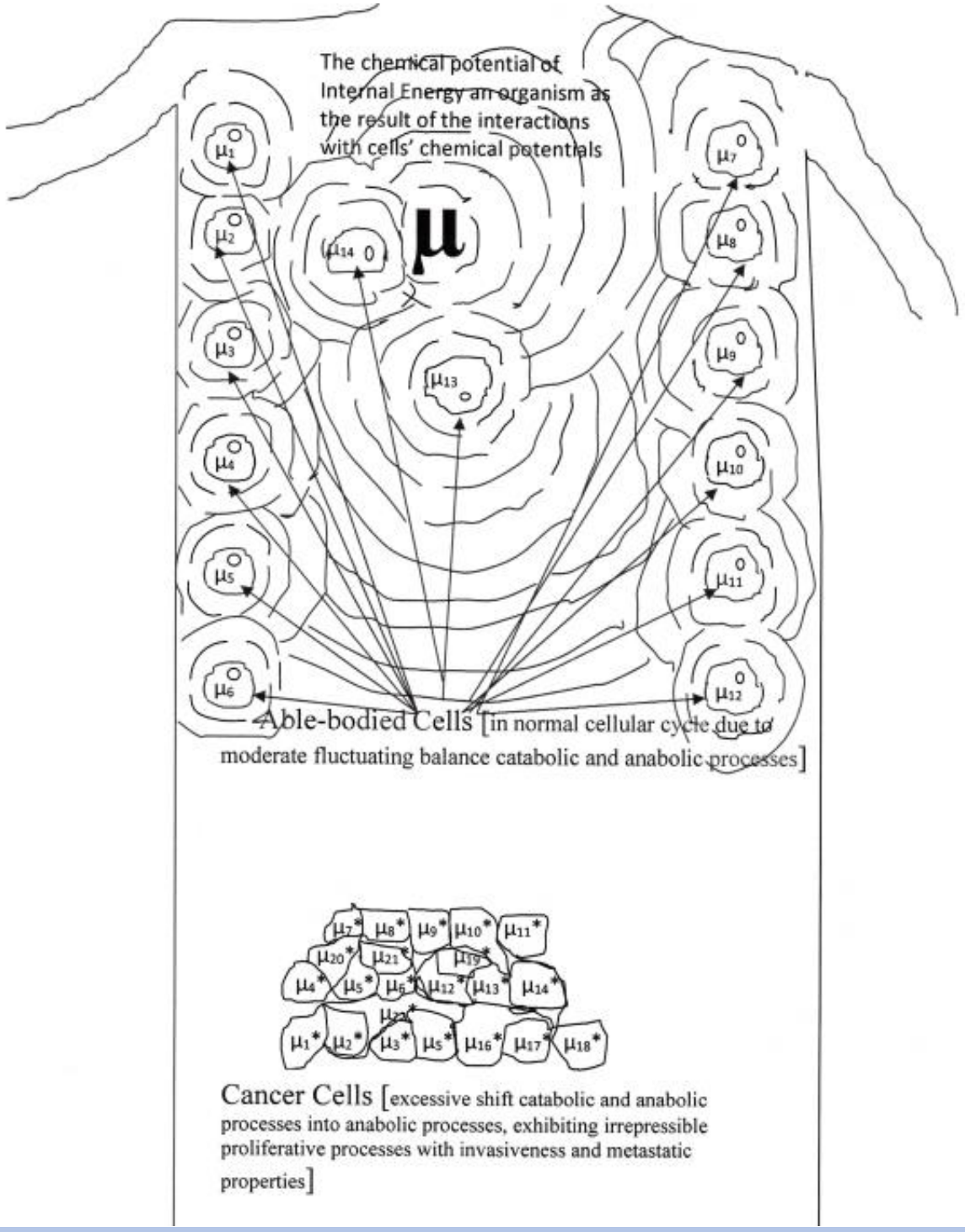

The chemical potential of
Internal Energy an organism as
the result of the interactions
with cells' chemical potentials
μ
μ1
μ2
μ3
μ4
μ5
μ6
μ7
μ8
μ9
μ10
μ11
μ12
μ13
μ14
Able-bodied Cells [in normal cellular cycle due to moderate fluctuating balance catabolic and anabolic processes]
Cancer Cells [excessive shift catabolic and anabolic processes into anabolic processes, exhibiting irrepressible proliferative processes with invasiveness and metastatic properties]

Figure 7:

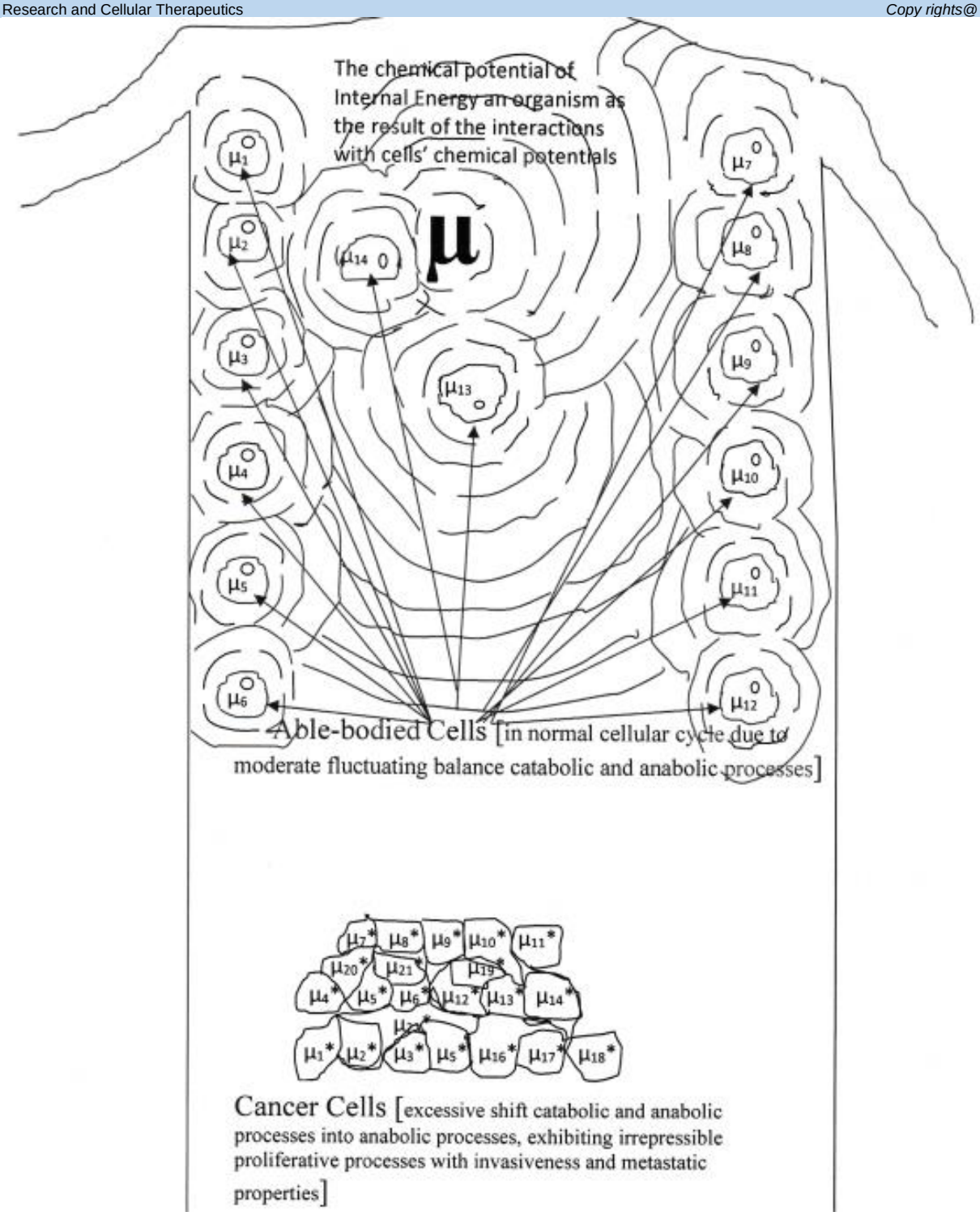


Figure 8: Balance Internal Energy both cells and an organism due to their chemical potentials (u) promoting operation resonance waves of cellular capacitors and disbalance of chemical potentials (u*) cancer cells.

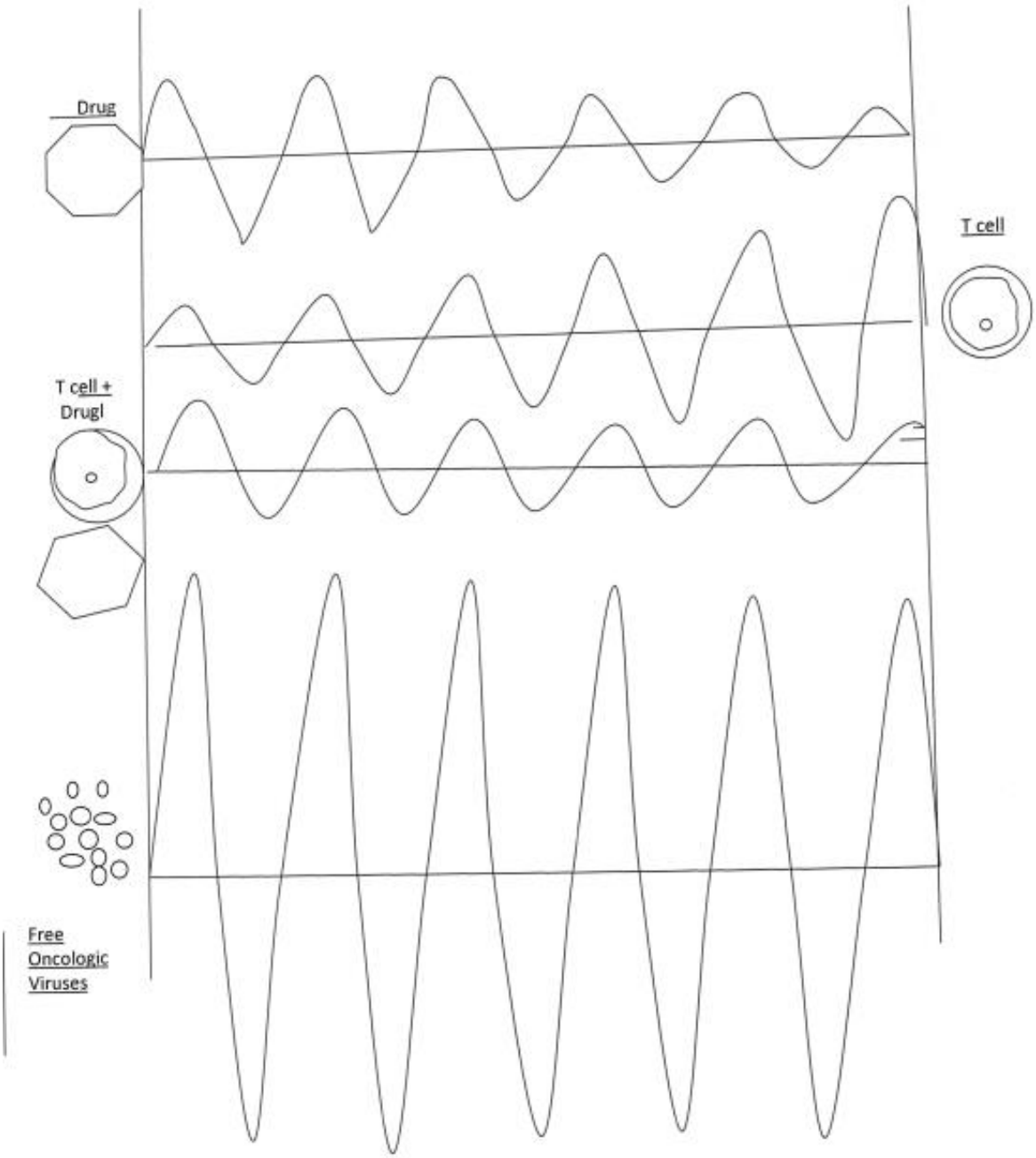


Figure 9: The Mechanisms of Relapse Oncologic Viruses in Cancer Diseases.

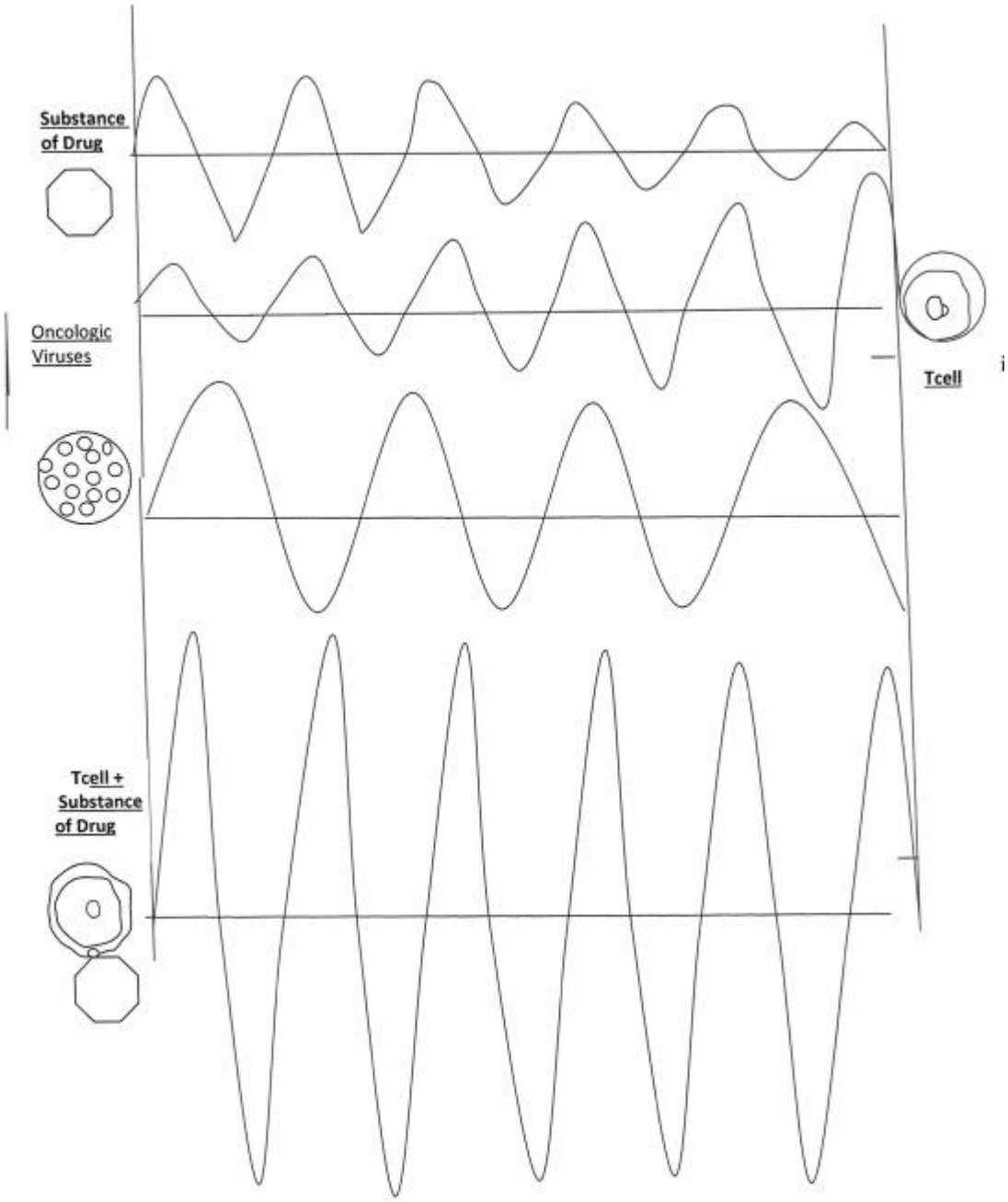


Figure 10: T cell disordered resonance waves on strange Drug's substances causing resistance to cytotoxic Drug.

5.2. The mechanism prevents of forming either resistance cytotoxic drugs or relapse cancer disease in new method cancer treatment.

Cancer tumor is situated 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.) as in normal organism as well as in cancer disease organism (Figure 8). As opposed to modern methods chemotherapy with large dosage of cytotoxic drugs, the new method cancer treatment uses combination "Prolonged medical starvation (during 42-45 days)" with considerably decreased dosage of cytotoxic drugs in new method cancer treatment which don't suppress immune and hormonal systems because of small dosage of cytotoxic drugs [51, 52]. Thus "Prolonged medical starvation 42-45 days" leads to bereave of the substances which are used these substances for anabolic biosynthetic processes in oncogenesis, and this causes suppression activity of cancer cells due to violation mechanism of Warburg effect. As opposite stability Internal Energy and Internal Medium via determining normal stability Internal Energy (μ) of an organism's normal cells, there are occurred violation stability Internal Energy of cancer cells (μ°) of an organism. Besides violation stability Internal Energy of cancer cells (μ°) are stronger than normal cells stability of Internal Energy (μ) because large dosage of cytotoxic drugs suppress immune system and hormonal system after anticancer modern chemotherapy with large dosage of cytotoxic drugs. Just these large dosage cytotoxic drugs cannot cure the neglected state of the cancer disease organism (see above). Besides these large dosage cytotoxic drugs don't prevent both relapse of cancer disease and resistance anticancer cytotoxic drugs. The therapeutic targets Warburg effect by new method cancer treatment using "Prolonged medical Starvation (during 42-45 days)'' and immunotherapy combination with very small dosage weak cytotoxic substances is more efficient method of cancer treatment than modern methods cancer treatments with large dosage cytotoxic drugs [51, 52]. As opposed to modern method Chemotherapy with targeting for destruction cancer cells and suppression of defensive systems immune cells and hormonal cells

causing by large dosage cytotoxic drugs, the new method cancer treatment displays combination "Prolonged medical starvation 42-45 days" with considerably decreased dosage of cytotoxic drugs that leads to destroy mechanism of Warburg effect which is the mechanism of oncogenesis and activity of viral oncogenes (v-oncogene). Just the depressed activity oncologic viruses (v-oncogenes) via depressed cancer cells are arisen by "Prolonged medical starvation 42-45 days" that targets Warburg effect creating violating "aerobic oxidation in Glycolysis" for destructed Warburg effect. The considerably decreased dosage of cytotoxic drugs which exerts activities of immune system of an organism. Hence "Prolonged medical starvation 42-45 days" creates depressed state of metabolic processes in the organism's cells and in the cancer cells because of bereaves of some substances for anabolic biosynthetic processes. Therefore, decreased anabolic biosynthetic processes prevent to affect an organism's cells by v-oncogenes impeding shift into excessive anabolic endergonic processes of balance anabolic endergonic processes & catabolic exergonic processes. The absent of excessive anabolic endergonic processes of cancer tissue and excessive quantity of mitochondria catabolic aerobic electron transport chain processes lead to absent mechanism forming metastases and development of cancer cells. Thus overloaded "nodal point of bifurcation anabolic and catabolic processes" [NPBac] with consumption great quantity energy and Acetyl-CoA in "Prolonged medical Starvation (during 42–45 days)" leads to depression cancer development [4, 5]. Besides it prevents of forming Warburg effect as mechanism of cancer development. Also the new method cancer treatment use "Prolonged medical Starvation (during 42–45 days)" for depression cancer activity of forming metastases, and use very small dosage of cytotoxic substances which don't suppress activity of immune systems and hormonal systems. Therefore hormones how cofactors of an organism's metabolic chemical processes promote maintenance stability Internal Energy (Uorg) of an organism in state of "Prolonged medical Starvation 42–45 days" via supporting with extracts of vegetable herbs via delivering Vitamins, as biochemical cofactors, that supports an organism metabolism creating stability as balance anabolic biosynthetic processes & catabolic anaerobic phosphorilation of oxidative processes as well as balance catabolic aerobic oxidative processes & catabolic anaerobic phosphorilation of oxidative processes. Also, very small dosage of cytotoxic substances destructs depressed mechanism of cancer cells development, and immune T cells with B cells antibodies creates complete destruction of oncologic mechanisms leading to recovery of the normal organism. Thus, as opposed to modern methods chemotherapy with large dosage of cytotoxic drugs, the depressed state of the organism causing by "Prolonged medical Starvation 42-45 days" creates depressed of the mechanism increased anabolic endergonic biosynthetic processes that promotes exerting decreased dosage of cytotoxic drugs with activity of immune and hormonal systems. It causes decreased catabolic aerobic electron transport chain processes and restored balance anabolic biosynthetic processes & catabolic anaerobic oxidative phosphorilation processes of creating destruction Warburg effect by new method cancer treatment and appear Pasteur effect of defensive activity of immune and hormonal systems which resonance waves maintain stability Internal Energy of all organism's cells and an organism [53].

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This article is dedicated to the memory of my daughter T.M. Ponisovska.

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