

Pathogenesis of Cancer: Cancer Reparative Trap

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Abstract

Cancer is one of the leading causes of death in the world while the long-term prognosis is still unfavorable, despite the enormous efforts in the search for effective anti-cancer drugs. We think that the obstacle for creating of effective anti-cancer drugs could be existing idea that the basis of cancer is caused by the damage of the genetic apparatus of the cell. In this paper, we present the pathogenesis of cancer which is based on the formation of the special sustainable pathophysiological state of the organism what we call the state of "cancer reparative trap". The essence of this pathophysiological state of the organism is in the reparative orientation of the immune system of cancer patients, when constant tissue repair is accompanied by systemic suppression of the anti-tumor immunity. Specifically, during the long-term exposure to carcinogens (exogenous and/or endogenous), the continuous tissue damage occurs which induces permanent stimulation of cell proliferation (imbalanced Th1 < Th2 lymphocytes, M1 < M2 macrophages, inflammation, angiogenesis, etc.) in order to repair the tissues damaged. At the same time, tissue repair is necessarily accompanied by the suppression of anti-tumor immunity (increase in T-regulatory cells, imbalanced Th1 < Th2 lymphocytes, M1 < M2 macrophages *et al.*), which creates the necessary conditions for the survival of the malignantly transformed cells, formed by the action of carcinogens. The determining role of the imbalance in the autonomous nervous system (simpathetic/hypersympathetic dominance) in the development, maintenance and generalization of the cancer process has been shown. The explanation of a number of phenomena has been presented: the cell resistance to chemotherapy, and the phenomenon of cancer cell dormancy. The promising approaches for the cancer management in clinical practice have been proposed.

Keywords

Carcinogenesis, Cancer Pathophysiology, Anti-Tumor Immunity, Cancer Reparative Trap

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1. Introduction

At present, in the modern oncology the damage of the genetic apparatus of the cell is considered to be the primary cause of cancer, and the pathogenesis of cancer is seen as a process of transformation of a normal cell into a tumor cell, as evidenced by deep fundamental research of the pathogenesis of cancer, which is held exclusively at the cellular, molecular and genetic levels of the organism [1] [2]. Such a vector of the scientific research based on the concept of cancer as a “genes damage disease” limits the search for effective methods of cancer treatment [3]. The data on the survival of cancer patients against treatment, which for the past 30 years has only increased by 14% (from 50% to 64%) [4] can be considered as the confirmation of the insufficient efficiency of the existing approaches to cancer therapy. In addition, the incidence of cancer globally has increased in just four years from 12.7 million in 2008 to 14.1 million new cases in 2012, when there were 8.2 million deaths. Over the next 20 years, it is expected to hit 25 million a year—a 75% increase [5]. Surprisingly, this unfavorable prognosis has been made while the annual financing of scientific research of the cancer problem in the world is increasing enormously, as well as the scholars’ optimism regarding the rapid creation of effective cancer drugs. Despite the availability of the important basic knowledge about the cancer biology, the obstacle to the creation of effective cancer treatment in humans exists. In our opinion, this obstacle is the lack of the true pathogenesis of malignant tumors.

The purpose of this paper is to present a new systemic view of the pathogenesis of cancer with the hope that it will allow the scientific community to equip the new pathogenetically based treatment strategies in the “war against cancer”.

2. The Current Scientific Knowledge of Cancer Etiology and Etiotropic Cancer Therapy

It is accepted to distinguish three etiological causes of cancer and respectively, three types of carcinogenesis: chemical carcinogenesis (chemical carcinogens—benzpyrene, asbestos and over 800 chemicals) physical carcinogenesis (physical carcinogens—ionizing radiation, ultraviolet radiation, etc.), biological carcinogenesis (biological carcinogens—viruses, bacteria, fungi) [6]. However, in clinical practice it is practically impossible to determine the etiological cause of cancer, and to prescribe the appropriate etiotropic cancer therapy in each case, so the causal cancer treatment does not exist. Moreover, paradoxically, that from the positions of commonly accepted cancer etiology existing and developing modern methods of cancer treatment (chemotherapy, radiation therapy, gene therapy/virotherapy *et al.*) is based on the use of carcinogens! Such an approach is “cancer treatment by carcinogens” reminds the fire being extinguished with gasoline and contradicts one of the fundamental principles of clinical medicine—conducting causal (etiotropic) treatment of the disease.

3. The Current Scientific Ideas about the Pathogenesis of Cancer and Pathogenetic Cancer Therapy

As mentioned above, the commonly accepted basis of the pathogenesis of cancer is the damage to the genetic apparatus of cells (mutation, disturbance of gene expression, activation of tumor promoter gene, inactivation of tumor suppressor genes, etc.) [7] [8]. Based on this, the only pathogenetic cancer therapy is the application of methods of cancer gene therapy (RNAi approaches, drug resistance, hematopoietic progenitor cell gene transfer, cancer stem cells, homologous recombination, ribozyme technology, antisense technology, tumor suppressors, gene delivery systems—viral and non-viral, anti-gene therapy—antisense, siRNA & ribozymes; apoptosis, DNA synthesis and repair), aimed to eliminating the genetic damage and control over cancer cells. However, the methods of cancer gene therapy are only being developed and their use in clinical practice is the matter of the future [9].

4. Modern Treatment of Malignant Tumors

It is considered to have been proven that a number of pathological processes that are typical for various malignant tumors are caused by the activity of the cancer cells in particular. These pathological processes caused by cancer cells are inflammation (cell production of pro-inflammatory cytokines, growth factors, and others.) [10], disruption of the immune system (violation effect or functions of NK cells, cytotoxic lymphocytes, macrophages, the emergence of T-regulatory cells, imbalance of Th1/Th2 *et al.*) [11], immune evasion by tumor cells [12] [13],

the permanent reproduction of tumor cells under the influence of autocrine and paracrine stimulation of cell division [14], metastasis (invasion factors, cell products, impaired intercellular interactions *et al.*) [15], angiogenesis (growth factor production by cells of blood vessels, endothelial cell proliferation, etc.) [16], and oxidative-nitrosative stress (cell production of reactive oxygen and nitrogen species) [16]-[18]. Each of the presented pathological processes becomes a target for the development of different methods of anti-cancer therapeutic effects. For example, the various methods of antioxidant therapy [19], cytokine therapy [20], cell therapy, targeted therapy [21] [22], vaccine therapy, including DNA vaccines [23] [24], methods of blocking neoangiogenesis [25], and others have been offered.

Unfortunately, despite the scientific substantiation and efficiency of the developed methods of treating cancer in preclinical studies, the expected success in clinical practice has not been achieved yet, including the use of anti-cancer vaccines [26]. All the cancer treatments are directed towards suppressing the various manifestations of the activity of cancer cells, so these treatments are symptomatic. Strictly speaking, according to the existing ideas about carcinogenesis, even modern standards of cancer treatment (surgery, chemotherapy, radiation therapy) are also symptomatic because they are only directed towards eliminating malignant tumor cells from the body, rather than at the mechanisms of their occurrence (DNA damage, etc.). One can say that the modern cancer treatment is the struggle with cancer cells, but not with the human disease. In the modern oncology the gap between scientific theory and clinical practice caused by the lack of understanding of the true pathogenesis of cancer is obvious.

5. Common Pathophysiological Mechanism of Cancer Disease

We believe that for all kinds of cancer, regardless of a histological type, there is existence of a common pathophysiological process of malignant tumors in the organism. Based on the analysis of the numerous scientific data and the results of our research it can be claimed that in the development of malignant tumors, along with damage to the genetic apparatus of the cell, the suppression of anti-tumor immunity takes place and is required. It should be noted that the suppression of anti-tumor immunity is one of the natural physiological reactions of the organism, and when this reaction becomes pathophysiological condition of an organism—it results in cancer developing.

Thus, under physiological conditions, the temporary local suppression of antitumor activity of the immune system is one of the links in the natural reparative process, which is always observed when local tissues of the organism are damaged as a result of any chemical, physical or biological impacts [27] [28]. The physiological meaning of the temporary local suppression of anti-tumor immunity is to ensure the successful repair of tissue damaged [29]. The point is that the proliferating tissue cells and tumor cells are similar in structure and properties [30], so the active anti-tumor immunity would block the repair processes of the tissue damaged through elimination of proliferating cells. In this regard, the key factor in the success of tissue repair is a local temporary suppression of anti-tumor immunity [31]-[33] and the activation of immunological reactions, supporting repair [34] [35]. The immunological reactions are developed in hearth lesions that support the inflammatory process and cellular proliferation for successful tissue repair with known cellular, cytokine, and vascular reactions [36]-[39]. Reactivating anti-tumor immunity (specifically, the accumulation of CD8+ cells at the site of injury on completion reparation [40]) to protect the organism from malignantly transformed cells, which are practically always appear in the area of inflammation [10] occurs upon the completion of reparation and reduction of inflammation. The balance of sympathetic and parasympathetic parts of the autonomic nervous system provides for normal physiological flow of the presented processes.

This natural physiological mechanism of tissue repair becomes pathophysiological when multiple foci microdamages occur in the organism caused by the impact of exogenous factors (chemical, physical and biological carcinogens), as well as the presence of imbalance in the autonomic nervous system with sympathetic/hypersympathetic dominance caused the ischemia and tissue hypoxia. As a result of sympathetic/hypersympathetic dominance, in the foci tissue microdamages chronic inflammation with a permanent formation of cancer cell is formed [10]. We believe that the presence of multiple foci tissue microdamages combined with sympathetic/hypersympathetic dominance imbalance immunological reactions in the direction of constant maintenance of cell proliferation for tissue repair occurs [41] [42], which is accompanied by systemic inhibition activity of the anti-tumor immunity [43] [44]. This imbalance of immunological reactions should be designated as a *reparative orientation* of the immune system.

In these conditions, even when NK-cells support the proliferation and angiogenesis [45], malignantly trans-

formed cells have the opportunity for tumor growth [30], and the existing tumor in the organism promotes the relapse or generalization of cancer. For example, stress-induced sympathicotonia leads to 30-fold increase in metastasis to distant tissues [46]. In our view, the constant emergence of multiple foci tissue microdamages and chronic inflammation in the organism may be also caused by the influence of endogenous carcinogens (reactive oxygen and nitrogen species) as a result of chronic psychoemotional stress [47]-[49], which allows to select another type of carcinogenesis, typical only for humans which is psychogenic (stressful) carcinogenesis [50].

In general, the submitted pathophysiological mechanism: multiple permanent (prolonged) tissue microdamages in combination with sympathetic/hypersympathetic dominance provide permanent (prolonged) maintenance of cell proliferation with systemic inhibition of anti-tumor immunity can be called “*cancer reparative trap*” (CRT) of the organism (Figure 1).

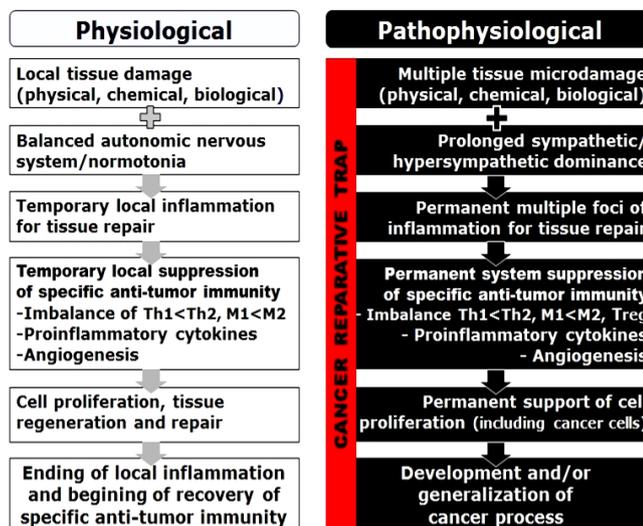


Figure 1. Interconnection between nervous system, tissue damage, inflammation, tissue repair and anti-tumor immunity in health and carcinogenesis.

“Cancer reparative trap” is the resistant pathophysiological condition of the organism that contributes to the appearance, development and generalization of cancer. It should be recognized, that the physiological and pathophysiological processes are shown simplistically in Figure 1, but we have allocated the most important conjugate and sequence of events which reflect the content of the processes. The CRT state is crucial in developing not only solid, but also diffuse malignant tumors, despite a number of features.

6. Comments to the Pathogenesis of Cancer from Positions a New View

6.1. Comment No. 1: DNA Damage and the Appearance of Cancer Cells. Are They Enough for the Development of Cancer Disease?

DNA cells damage is a permanent and natural process in the organism which occurs most intensively in locations of chronic inflammation [10]. These zones of chronic inflammation are a kind of places of less resistance (Latin: locus minoris resistentiae), which always have all the necessary local cellular-molecular conditions for appearance of cancer cells [51]-[53]. The accumulation of DNA damage cells and the number of foci of chronic inflammation inevitably increase with age [54]-[57], but the cancer does not arise at all. Why? From the position of the proposed views on the pathogenesis of cancer, DNA damage and the appearance of cancer cells are not sufficient for developing a cancer disease. The occurrence of cancer is only possible when the pathophysiological state—“cancer reparative trap” is formed in the organism.

6.2. Comment No. 2: Where Do Cancer Cells Come from?

Cancer cells and stem cells are surprisingly similar [58]. One of the common characteristics of cancer cells is the

use of anaerobic glycolysis [59] [60]. It is considered that this singularity of cancer cells is obtained as a result of mutations. At the same time, intense anaerobic glycolysis differ not only cancer cells but also stem cells [61]. There are significant antigenic similarities between cancer cells and stem cells, including the expression of oncogenes, providing the typical cancer phenotype [30] [62]-[64]. Another important similarity is their ability to proliferate without differentiation in hypoxic conditions [61] [65].

In normal conditions stem cells carry out the repair of the damaged tissue by actively dividing with subsequent differentiation [66] [67]. In chronic inflammatory conditions (prolonged damage), in ischemia and hypoxia conditions stem cells proliferate without differentiation [65]. In these conditions DNA of stem cells and, especially, the genes responsible for cell proliferation, are the most susceptible to the damaging influence of carcinogens, therefore, only stem cells which, by the way, are very similar to cancer cells acquire malignancy [63] [68]. Terminally differentiated cells practically are not capable of dividing and transforming into cancer cells. In cancer cells the properties of stem cells by the microenvironment are maintained [69]-[71], which have a reparative orientation, *i.e.* maintain proliferation of cells through the CRT state of the organism. At the same time, when the conditions change the microenvironment, *i.e.* eliminate the CRT state of the organism, cancer cells can become normal [72]-[74].

Thus, cancer cells are stem cells with damaged genetic apparatus, and the CRT state of the organism provides maintenance “stem properties” of cancer cells, *i.e.* their malignancy (proliferation without differentiation, invasiveness and metastasis). Moreover, the CRT state of the organism determines monoclonal origin of malignant tumors (arise from a single transformed cell) by predominance of high activity of any clone of autoreactive T helper-2 lymphocytes with production of cytokines and growth factors in response to high concentration of tissue-specific proteins in the most damaged tissue. In this most of the damaged tissue, stem cell (in various degrees of differentiation), mobilized to repair, but malignantly transformed one will inevitably have an advantage for the proliferation compared to other malignantly transformed stem cells in the less damaged tissues.

6.3. Comment No. 3: There Are Cancer Cells but There Is No Cancer Disease?

It is a well-known fact that cancer cells without cancer exist in a healthy organism [75]. Thus, at autopsy, cancer cells are found in the breast of more than 1/3 of the women aged 40 - 50 years although the breast cancer as a disease is diagnosed in no more than 1% of women in this age group. The malignant cells are detected in almost 100% of cases at histochemical investigations of autopsy material thyroid in people aged 50 - 70 years but the incidence of thyroid cancer is no more than 0.1%. Similar examples of the presence of cancer cells without evidence of growth and without clinical manifestations are also the characteristic of the prostate gland and other organs. Why a cancer disease with presence of cancer cells in the organism is not developed in healthy people?

In our opinion, these data confirm the ideas about permanent formation of cancer cells in the organism, but pathophysiological conditions in the organism—the CRT state is required for the development of cancer disease.

6.4. Comment No. 4: When Are Dormant Cancer Cells Woken up?

It is also a well-known fact about the presence of “dormant cancer cells” in the organism of cancer patients after the treatment which is believed to be the basis for the recurrence and progression of cancer. Due to them there are doubts about the possibility of complete eradication of cancer [76]-[78].

From the standpoint of a new view on the pathogenesis of cancer, if the metastatic cancer cells are in the areas of chronic inflammation, which can be called “incubators for cancer cells” due to the presence of all necessary conditions for their proliferation, these cancer cells survive and give rise to secondary tumors. Otherwise, metastatic cancer cells become “dormant” or die. Indeed, the fact is known that 99.9% of metastatic cancer cells do not generate new cancer tumors [79]-[81], probably because many of them move to the state of “dormancy” [82]. At the same time, any surgery or traumatic event can lead cancer cells from a state “dormancy” and cause a relapse of cancer tumors with rapid growth in the site of damage [83] [84].

In our clinical practice, we often see a recurrence of cancer in the site obtained mechanical trauma of tissues. However, in our opinion, this is not caused by the individual fact of mechanical trauma, and the appearance of trauma on the background of existence CRT state of the organism. Such a combination of trauma (or damage to other tissues, including chemotherapy), and CRT outputs the cancer cells from a state “dormancy” with subsequent progression of cancer disease.

6.5. Comment No. 5: What Avoids What at Cancer or Are Cancer Cells So “Smart”?

Now, it is generally accepted the existence of the phenomenon “immune escape” of cancer cells from immune surveillance [85], *i.e.*, cancer cells are believed to suppress antitumor immunity and establish an immunosuppressive tumor microenvironment [86]. Are the cancer cells really endowed with a kind of “mind”, “insidiousness” and “cunning”?

From the positions of the presented pathogenesis of cancer, inhibition of anti-tumor immunity is an integral part of the repair process and occurs before the appearance of the cancer cells so they are not able to be the cause of suppression anti-tumor immunity. At the same time, the well-known immunosuppressive properties of cancer cells should be considered as a natural nonspecific immunosuppressive activity of proliferating cells in the conditions of the tissue repaired. In this connection, the term “tumor immune escape” does not reflect the essence of the relationship between cancer cells and the immune system. Due to the fact that the protection of the body against cancer is associated with anti-tumor activity of the immune system [87], the main hope of overcoming “immune escape” of cancer cells and the activation of anti-tumor immunity in cancer patients is associated with the creation of cancer vaccines.

However, the clinical efficiency of these vaccines still remains low [88] [89]. Are the cancer cells “smart” that evade from the effects of the vaccine as well? We believe that the reason lies in the reparative orientation of the immune system in a state of CRT, when there is a system maintaining cell proliferation with simultaneous systemic inhibition of anti-tumor immunity. On this background, the application of any cancer vaccines in combination with the known induction and the role of T-regulatory lymphocytes in cancer [90] [91] will be followed by blocking the systemic effects of cancer vaccines [92], therefore, the effects of these vaccines will be limited predominantly to local cellular-molecular effects. This can be proved by the fact that the most effective is the local intratumoral injection of anti-cancer vaccines [93]-[95].

Thus, the cause of cancer intractable problems is not any “cunning” of cancer cells, but the systemic pathophysiological processes in the organism.

6.6. Comment No. 6: What Is behind Cancer Drug Resistance?

It is believed that cancer cells resistance to chemotherapy is the cause of treatment failure of 90% of patients with metastatic cancer and negates all attempts of effective treatment of cancer [96]. In this connection, some researchers focus their efforts on elucidating the molecular genetic mechanisms of chemoresistance of cancer cells in particular [97] [98], other researchers are investigating the role of the microenvironment (stroma) in cancer cells resistance to chemotherapy [99]. It should be noted that the acquired resistance of cells, including cancer cells, to adverse influences (including toxicity) is a natural highly conserved property of cells in order to adapt to the damage and stress [100]-[102]. Along with the natural property of the adaptation of cancer cells, there is another mechanism of cancer drug resistance, which contains the transition of cancer cells into a “dormant” state during chemotherapy [103], in which the cancer cells are not sensitive to chemotherapeutic drugs.

From the standpoint of the view represented in the pathogenesis of cancer, chemotherapy suppresses the components of CRT associated with inflammation and proliferation at the moment of its implementation, so the cancer cells enter the “dormant” state. For example, a continuous long chemotherapy keeps tumor in “dormant” state for several years [104], at the same time, chemotherapy as systemic toxic influence, accompanied by damage of the brain tissue [105], peripheral nerves [106], heart [107], lung [108], gastrointestinal tract [109], the eye [110] and other tissues. After completion of chemotherapy an activation of reparative processes in damaged tissues with possibility of recovery state of CRT, the awakening of “dormant cancer cells” and cancer progression occurs.

6.7. Comment No. 7: Where Is the Key to Understanding the Spontaneous Regression of Cancer?

Spontaneous regression of malignant tumors is defined as the partial or complete disappearance of a malignant tumor in the absence of all treatment or in the presence of therapy, which is considered inadequate to exert a significant influence on neoplastic disease [111]. The phenomenon of spontaneous regression of cancer has been known for hundreds and thousands of years and now is recognized as the undeniable fact [112].

However, the mechanism of this mysterious phenomenon is still unclear, but it is the understanding of the

mechanism of this phenomenon that may appear to be the key to unlocking the whole problem of human cancer. Previously, the various mechanisms for spontaneous regression of human cancer were proposed, which included: immune mediation, tumor inhibition by growth factors and/or cytokines, induction of differentiation, hormonal mediation, elimination of a carcinogen, tumor necrosis and/or angiogenesis inhibition, psychological factors, apoptosis, epigenetic mechanisms or their combinations [113]. In animal models, the spontaneous regressions of cancer occur frequently enough and can reach 50% - 80% [114] [115]. At the same time, in humans the spontaneous regression of cancer are the casuistic cases which occur in 0.00071%, *i.e.* 1 in 140,000 cases of cancer [116]. Why is there such a difference of 100,000 times?

The answer to this question lies in the fundamental difference between human and animals, which is in the presence in human of higher nervous activity (psychic activity) and the second signal system (speech). The psyche of a cancer patients is involved in the formation of pathophysiological state of the organism by activating the CRT state and constant maintenance of sympathetic/hypersympathetic dominance, which provides extremely high stability of the CRT state, which is not observed in animals. Sympathetic/hypersympathetic dominance in cancer patients is the result of chronic stress influence with the development of anxiety and depressive disorders [117] [118], which have a close inverse interconnection with the specific anti-tumor activity of the immune system in cancer patients, regardless of the cancer types [119]. These data to some extent help to explain the cases of spontaneous regression of cancer at disappearance of anxiety and depressive disorders with restoration of balance of the autonomic nervous system and blocking CRT state in the organism that occurred against the background of dramatic change in the patient's outlook on life, religious faith, favorable change in their environment, etc. [120]. Other cases of spontaneous regression of cancer in humans, which occurred on the background of infections, hyperthermia and other states [121] [122], are probably caused by somatogenically reasons of eliminating sympathetic/hypersympathetic dominance and blocking of CRT state of the organism.

We assume that the basis of the mechanism of spontaneous regression of cancer lies in changing the regulation of the autonomic nervous system on the level of suprasedgmental autonomic structures, *i.e.* structures of limbic-reticular complex with the "switching" of sympathicotonia/hypersympathicotonia condition to normotonia/vagotonia condition with blocking CRT state of the organism. The targeted control of the autonomic nervous system in cancer patients enables to control of inflammatory mechanisms and anti-tumor immunity that will allow to create the necessary conditions for manageable cancer regression.

7. Prospects for Clinical Application of a New Approach to the Pathogenesis of Cancer

The application of standard cancer treatment (surgery, chemotherapy, radiotherapy) is aimed at achieving cancer remission/healing. At the same time, paradoxically, but the risk of relapse and progression of cancer after surgery, chemotherapy, radiotherapy is high enough because of the additional damage of tissues of the body and activation of the CRT state. Moreover, all therapeutic methods aimed at improving tissue repair (some modalities of physiotherapy, massage therapy, efferent therapy, relaxation, spa treatment, etc.) are also very dangerous for cancer patients because of the activation of the CRT state. This is the insidiousness of cancer disease which hides the CRT state behind its facade. In this regard, the development of the methods anti-CRT therapy for targeted drug accompaniment of cancer patients during the cancer treatment is required.

From positions of a new view on the pathogenesis of cancer, the search of the medicines including combined ones aimed at blocking CRT state—anti-CRT drugs seems promising. For example, as drugs of anti-CRT therapy the lower doses of cytostatics [123] and low doses of radiotherapy can be used, and the main purpose of their application is to block the inflammation and repair processes, but not necessarily killing of cancer cells. Furthermore, nonsteroidal anti-inflammatory drugs, immunomodulatory drugs with antiangiogenic activity, autonomic and psychotropic drugs (anxiolytics, antidepressants), and various combinations of drugs may be used. It can be assumed that the effectiveness of many existing anti-cancer drugs and treatment methods will be significantly increased if they are used together with the anti-CRT therapy.

8. Clinical Approbation of a New Approach to the Pathogenesis of Cancer

Due to the fact that the elimination of the CRT state leads to remission/cure cancer, the diagnostics of the CRT state especially in dynamics is important for the prognosis of cancer. In our clinical practice for the diagnosis of a number of parameters in the dynamics which indicate of the CRT state, we used the following methods: heart

rate variability (for evaluation sympathetic/hypersympathetic dominance), the delayed type hypersensitivity skin reaction on the tumor-associated antigens (for evaluation activity of antitumor immunity) [119], flow cytometric detection of human CD4+ CD25+ Foxp3+ regulatory T lymphocytes, detection of oxidative stress by spontaneous chemiluminescence in blood plasma, as well as psychometric tests SCL-90 together with the clinical method in order to identify psycho-emotional disorders that are a common cause of imbalance in the autonomic nervous system.

On the basis of the submitted views on the pathogenesis of cancer, we have developed and tested anti-relapse strategy of psychoimmunological rehabilitation of advanced cancer patients in clinical practice [124]. The effective influence on the higher nervous activity with the elimination of psycho-emotional disorders in cancer patients was accompanied by spontaneous activation of specific anti-tumor immunity that indicated on blocking the CRT state. In these cancer patients an increase of life expectancy was observed.

9. Conclusion

It should be recognized that cancer process is still unmanageable due to the lack of systemic representations about the true pathogenesis of cancer. Paradoxically, but unabated scientific research continues to withdraw beyond the scope of understanding of the nature of cancer, deepening the gap between science and clinical practice. The existent molecular-genetic oriented scientific approach to study of cancer problem leads away clinicians 100,000 times further away from the understanding of true pathogenesis of cancer in human. Currently, the damage of genetic apparatus of the cell is considered to be the basis of cancer disease, which in our opinion, is a systemic error in understanding of the nature of cancer. The damage of genes does not necessarily lead to the development of cancer and this pathological process is located only in a number of other well-known cellular-molecular disorders in cancer, and the development and progression of cancer process is only possible at formation specific pathophysiological state in the organism—the state of “cancer reparative trap”. We hope that this view of the pathogenesis of cancer will be allowed to create more adequate models of research and management of cancer process and to develop pathogenetically based approaches to cancer therapy.

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