Journal of Immune Based Therapies, Vaccines and Antimicrobials, 2014, 3, 33-36
Published Online July 2014 in SciRes. http://www.scirp.org/journal/jibtva
http://dx.doi.org/10.4236/jibtva.2014.33005

Scientific Research

Prevention of Cancer and Cancer Re-Occurrences by Immunization, by Using Immune Competent Cells, and by Affecting Molecular Mechanisms of Cancerogenesis

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Received 29 April 2014; revised 29 May 2014; accepted 5 June 2014

Abstract

Primary cancers can be prevented by immunizations. We suggest immunizing healthy people, especially the ones with genetic predisposition to cancer, with a standard oncoantigen. In patients suffering from cancer, immunotherapy can be effective only if it is administered during complete remission. Immune competent cells, like T-lymphocytes and bone marrow, are the most important components for cancer prevention and treatment. Because of the dramatic increase in the incidence of cancer, it is important to offer all adults with absolutely healthy immune system an opportunity to donate their own T-lymphocytes and bone marrow cells and preserve them at −196˚C. These cells can later be used by the same people in auto-system if they develop cancer. Patients who had their cancerous tumors surgically removed can also have their own T-lymphocytes and bone marrow cells collected during remission and then used in auto-system in case of cancer re-occurrence. It is also possible to impact on cancer development during the process of cancerogenesis by administering large amounts of normal DNA and possibly different types of RNA (displacement) together with nucleases (directly into the tumor or blood). In addition, blockers of cytokines that suppress immune system should be administered as well. It is intriguing to think that injection of large amounts of normal DNA and possibly different types of RNA together with nucleases to patients with chronic and hereditary diseases (diabetes Type II, schizophrenia, and other similar diseases) can lead to therapeutic effect.

Keywords

Cancers, Immunization, Immune Competent Cells, Cancer Remission

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How to cite this paper: Skurkovich, S. and Skurkovich, B. (2014) Prevention of Cancer and Cancer Re-Occurrences by Immunization, by Using Immune Competent Cells, and by Affecting Molecular Mechanisms of Cancerogenesis. *Journal of Immune Based Therapies, Vaccines and Antimicrobials*, **3**, 33-36. http://dx.doi.org/10.4236/jibtva.2014.33005

1. Introduction

Immunotherapy of many pathological conditions including cancer can be quite effective [1]-[5]. In 1969 we performed cross-immunization of children in acute phase of acute lymphoblastic leukemia (ALL) with certain success [1]. In another study started in the early 1970s, 54 children with acute leukemia (52 with ALL and 2 with AML) who had achieved complete remission after standard-for-that-time chemotherapy were divided into two groups: 27 received standard maintenance chemotherapy and immunotherapy and 27 received chemotherapy alone. Immunotherapy consisted of a long-term administration of viable cryopreserved at –196˚C allogeneic leukemic cells. We have found that in patients younger than 7 years of age, if immunotherapy was started in the first several months of their remission, it did not exhibit any additional therapeutic effect. However, immunotherapy was effective in children younger than 7 if it was initiated after 1 to 1.5 years of their remission. In children over 7 years of age, if immunotherapy was started after 6 months of remission, it led to its stabilization in all patients. After 5 years of remission all therapy was stopped. As of the beginning of 2013, 8 out of 19 (42.1%) of immunized children achieved remission lasting over 10 years and are considered cured. This study has been run for over 30 years by scientists from the Central Institute of Hematology and Blood Transfusion and of N.N. Blokhin Central Institute of Oncology in Moscow. Interestingly, intrathecal administration of sera of patients who responded to immunotherapy to patients with CNS leukemia resistant to chemotherapy led to sharp decrease in pleocytosis. This is the first report of a cure of children with ALL after addition of immunotherapy into their treatment regimen [3] [4]. In our view, children who responded to immunotherapy had absolutely competent immune system. Although currently there is a lot of success in chemotherapy of acute leukemia in children our data show that immunological methods of treatment of leukemia can achieve remarkable therapeutic effect. In the past, we also proposed to treat acute leukemia with bone marrow transplantation [5]. Although the pathogenesis of acute leukemia differs from that of solid tumors, there are certain common elements that allow us to speculate that immunotherapy could be similarly effective in many forms of cancer. We think that immunotherapy of solid cancer can be successful only in patients in complete remission. It is possible to achieve cure after surgery, e.g., in early stages of lung or breast cancer, if all cancer cells are removed. However, if there are any cancer cells left in the organism, cancer will recur due to the ability of cancer cells to avoid immune recognition. Our data outlined above show that some cancer (leukemia) patients when in full remission have a good immune response to other heterogeneous cancer cells. This suggests that healthy patients with normal immune system will be able to respond to immunizations for the purposes of cancer prevention. There are a lot of cancer vaccines. We believe that one of the most promising vaccine candidates is a standard onco-antigen NY-ESO-1 [6].

At the present time it is well known that T-lymphocytes and bone marrow cells are the best instruments for cancer prevention and therapy. Therefore, it is reasonable to store one's own immune cells in order to use them in auto-system in the future.

Thus, we propose the following: immunization of healthy people, creation of banks of immune competent cells from healthy individuals for their future treatment in auto system if they develop cancer, prevention of reoccurrence of cancer in patients after surgical removal of their tumor, and impact on molecular mechanism of cancerogenesis.

2. Prevention and Immunotherapy of Cancer

2.1. Immunization of Healthy People

Absolutely healthy people with normal immune system who either do or don't carry a genetic marker for cancer susceptibility, or people at high risk for developing cancer (e.g., due to smoking or occupational or environmental exposure) should receive long-term immunizations with a safe standard onco-antigen which elicits immune response to the potential tumor. All these studies should be double-blind, placebo-controlled, and long-term.

Realization of this project will, first of all, dramatically decrease the numbers of breast cancer in women and prostate cancer in men.

2.2. Creation of Banks of Immune Competent Cells from Healthy Individuals for Their Future Treatment in Auto System If They Develop Cancer

Because of a dramatic increase in the incidence of cancer healthy adults who are concerned about developing cancer in the future and wish to have a chance to have it cured, should have their immune competent cells (T-

lymphocytes and bone marrow cells or, if a patient doesn't want to give his/her bone marrow cells then only T-lymphocytes can be taken) harvested every 12 - 15 months, frozen at −196˚C, and stored for many years. We propose two ways of using these cells in case patient develops cancer. One way is to incubate them with a standard cancer antigen at +37˚C for 18 hours prior to freezing them at −196˚C. Before administration cells need to be thawed. The second way is to mix these immune competent cells with a standard cancer antigen right before administering them to the patient. In both instances these immune competent cells should be administered to the patient multiple times. We imagine that every person in the course of his/her adult life should be encouraged to create a bank of his/her own immune competent cells in the same manner as stem cells from umbilical cord blood are currently banked.

This approach will guarantee to the individuals that they will have their own immune competent cells available if they develop cancer. This will undoubtedly give many healthy people a piece of mind and less fear of cancer. Since patients' own cells will be used there will be no complications. It is possible to start taking immune competent cells from people who are 18 - 20 years of age and repeat harvesting 12 - 15 times during their lifetime.

2.3. Prevention of Re-Occurrence of Cancer in Patients after Surgical Removal of a Cancerous Tumor

After surgical removal of the tumor, it is necessary to treat tumor cells with trypsine and formalin and freeze them at −20˚C. When the patient is in full remission for at least 12 - 13 months it is necessary to take his/her T-lymphocytes and bone marrow cells (if a patient doesn't want to give his/her bone marrow cells then only T-lymphocytes can be taken) and then incubate them together with some of his/her own formalinized cancer cells, or onco-antigen, or both at +37˚C for 18 hours. This "therapeutic mixture" (T-lymphocytes, bone marrow cells, formalinized cancer cells and onco-antigens) can then be frozen at −196˚C and then administered to the patient in case of cancer re-occurence. All this takes place in auto-system.

If after cancer surgery a patient is still in remission, it is possible to take T-lymphocytes and bone marrow cells again from this patient 12 - 13 months after the first immune competent cells' withdrawal or 24 - 26 months after surgery. In case of cancer re-occurrence these immune competent cells are mixed again with the rest of the patient's own formalinized cancer cells, or onco-antigen, or both and administered to the patient. If desired, immunogenicity of these cells can be enhanced by incubating them with interleukin 2 (IL-2), interferon-gamma (IFN-γ), or both [7]-[9].

All these activities will considerably decrease the number of cancers in the world.

2.4. Impact on Cancerogenesis

Multiple etiological factors (radiation, viruses, environmental factors, etc.) can lead to cancer. During cancerogenesis a decrease in immune function is observed. The so-called "escape" of the tumor from the immune response is achieved by inducing synthesis of blocking antibodies and secretion of immuno-suppressive cytokines.

Cancerous cells are potentially immortal (the phenomenon of immortalization) due to high activity of telomerase—an enzyme which restores the initial length of telomeres and also due to suppression of apoptosis of malignant cells.

Life cycle of malignant tumors represents an example of biological immortality. Nowadays this phenomenon is only used for production of monoclonal antibodies. It cannot be ruled out that in the future this phenomenon will be used in the system of life prolongation, even if it sounds paradoxical. One should remember that, perhaps, creation of organized biologic structure cannot exist without factors which are responsible for repression of proliferation and morphogenesis.

Qualitative and quantitative changes of the growth factors lead to the decrease or increase in sensitivity of the cancerous cells to physiological regulators of cell growth. Perhaps it is possible to impact on cancerous cells in the period of cancerogenesis (it is better to start from early stages) by injecting locally in tumors or in the body (the phenomenon of displacement) of various components including nucleic acids.

3. Our Suggestion for the Impact on Cancerogenesis

Of course our suggestions are very speculative. We should remember that we deal with cancer and any conversation is justified even if it is wrong because it stimulates thinking how we should manage cancer therapy. We

start from the fact that we should somehow change molecular mechanism of cancerogenesis. Thus, we suggest displacing pathological sites of cancer DNA and RNA with normal components of DNA and various types of RNA. Thus we suggest: 1) Continuous injection of large amounts of normal DNA and messenger RNA and possibly other nucleic acids (locally in the tumors or in the blood). Nucleic acids should be obtained from the normal types of cells of organs where the tumor originated from. These cells can be grown in normal cell cultures in vitro. It is possible that tumor-associated ingredients displaced by normal components will be disintegrated by the patient's immune system which is free from immunosuppressive action of cytokines. We should also continuously administer monoclonal or other types of antibodies and other blockers of nucleases to prevent disintegration of normal DNA and RNA thus allowing DNA and RNA to work. Nucleases specifically recognize and hydrolyze phosphodiester joint right in the center of the nucleotide sequence [10] [11]. Of course methods should be developed in order to allow normal DNA and various types of RNA to penetrate cells. This is one of the biggest problems—penetration of substances into the cell. Maybe it is possible to achieve this by administering substances which temporarily increase penetration of biological components into cells. 2) Injection of substances (into tumor or blood) which block immune suppressive cytokines (it is better to use monoclonal or other antibodies or other methods). We should start our research with the injection of the mentioned components in an animal model and then in women with breast cancer and men with prostate cancer. It is intriguing to think that injection of large amounts of normal DNA and possibly different types of RNA together with nucleases in the organism of patients with chronic and hereditary, genetic diseases (type 2 diabetes [12], schizophrenia [13], and other diseases) can lead to therapeutic effect. Apparently, in these diseases molecular mechanisms are destroyed.

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