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Original Research Article

PREVENTION OF CANCER IN HEALTHY PEOPLE

Simon Skurkovich[1]* Boris Skurkovich[2]

[1]Advanced Biotherapy Laboratories, 802 Rollins Avenue, Rockville, MD 20852, USA.
[2]Warren Alpert Medical School of Brown University, Providence, RI, USA

Abstract: Cancer can be prevented in healthy people. We propose immunizing healthy people with a vaccine containing safe onco-antigens, which are antigenically similar to the oncogenic factors. As a result, healthy organism will develop robust immune response to the vaccine and will be protected against cancer. Immune components of immunized healthy relatives of cancer patients or of paid donors could also be used for adaptive therapy of these patients.

Key words: Cancer prevention, safe onco-antigen, cancer, leukemia, cancer remission, immunization

Introduction: Immune system of the organism is a biological marvel that can disintegrate any foreign non-self-substance, including cancer cells [1-3].There is abundant data that vaccination of humans against two oncogenic viruses - human papilloma virus [4]and hepatitis B virus [5]- can stimulate immune response that is capable of destroying these viruses thus preventing development of cancer. It is also possible to get successful results in healthy people by stimulating their immune response to other etiological factors. It is very possible that viruses mentioned above induce and change synthesis of various types of normal and defective interferons, which probably take part in the pathogenesis of cancer the same way as hyper-production of gamma interferon is the possible etiological factor in multiple sclerosis [6,7].

For Correspondence:
sskurkovich@gmail.com
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Materials and Methods

In 1969, Mathe *et al*[8] treated twenty patients with acute lymphoblastic leukemia who underwent chemotherapy and achieved remission. After that, patients underwent immune therapy with BCG and/or vaccinations from a pool of allogeneic leukemic lymphoblastic cells pretreated with formalin or irradiated *in vitro* (experimental group). After remission induced by chemotherapy, ten patients (control group) did not undergo immune therapy. Out of these ten patients, all

died. Of twenty patients treated with immune therapy, eight patients had long-term remission for 295 days. The longest remission time was 1150 days at the time of publication.

Since 1967, we have been conducting research on the treatment of acute lymphoblastic leukemia (ALL) in children. In 1969, we performed cross-immunization of patients with ALL with leukemic cells with certain degree of success [1] and then treated fifty-four children with ALL with a cryo-preserved vaccine composed of allogeneic leukemic cells that we had created earlier. This clinical research lasted for over 30 years. We tried to achieve remission using chemotherapy preparations of that time.

Out of fifty-four patients, eight survived (remission longer than ten years) [9,10]. This was a huge achievement in immune therapy of leukemia at that time, though nowadays there are data on successful treatment of acute leukemia with modern chemotherapy. Now a number of our survived patients have started their own families. Our data showed that leukemic patients, when in full remission, could mount a robust immune response to other allogeneic leukemic cells. Apparently, full remission is the best time to start immunotherapy. Similar mechanism could take place in solid tumors.

Several approaches to immunotherapy for pancreatic cancer have shown promise in early clinical trials as well [11].

Immunization of healthy people with a safe onco-antigen. It is well known that cancer is caused by various etiological factors. Without talking in detail about mechanisms of cancerogenesis, which have been widely described in the literature and which is not a goal of our work, we should state that its final stage is characterized by a loss of control of cell differentiation thus allowing cells to divide and proliferate without limit which can lead to the death of an individual. In 1975, this phenomenon - "non-stop" cell proliferation - was used to develop monoclonal antibodies [12] which was an important discovery of the 20th century. In the 1970s, one of us (SS) constructed a hybridoma (staphylococcus + myeloma) which produced monoclonal antibodies to staphylococcus. Unfortunately, he did not publish these data because his scientific colleagues had some doubts and persuaded him not to publish. In 1975 Cesar Milstein and others published their work on production of monoclonal antibodies [13]. Probably, in the future the phenomenon of "non-stop" cell proliferation will also be used for prolonging life.

Many attempts to treat cancers are progressive but are not effective enough. It is very difficult to treat this disease after it has already occurred. Much more attention should be paid to cancer prevention in healthy people.

We think that it is necessary to immunize healthy people with a safe onco-antigen so they could develop immune response. Cell structures (immune T-lymphocytes, some bone marrow and other cells) can disintegrate cancer cells. Thus, a healthy organism that has immune defense due to immunization will be ready to attack cancer elements. Immune components of immunized healthy relatives of cancer patients and of paid donors can also be used for adaptive therapy of these patients.

Numerous studies in the 19th century have explored the possibility of cancer treatment with serum antibodies obtained from animals immunized with safe cancer vaccines. However, these attempts were unsuccessful because scientists used humoral antibodies. In most cancers, anti-tumor immunity develops at a cell level – T-lymphocytes, bone marrow and other cells. T-lymphocyte is a working structure, which kills cancerous cells. Active research on the role of lymphatic cells in immunity started in the 20th century. Safe cancer vaccines should be administered to healthy people for stimulation of their immune response (mostly T-lymphocytes, bone marrow and other cells). This immune response targeted against cancer cells may save a person from cancer development in the future. In order to improve immunogenicity of a cancer vaccine, various adjuvants (e.g., BCG) can be used and vaccine can be treated with IL-2 and gamma interferon. It is necessary to create a combined onco-vaccine against various cancer types and use it

as a universal onco-antigen. In many cases, tumor cell culture can be used though it is necessary to continue research on how to obtain these cultures. In other cases, cryo-preserved and trypsinized cancer cells obtained during surgery can be used after they are treated with formalin or other substances.

After immunization, a person with a healthy immune system will develop immune response to the onco-antigen the same way a person has an immune response to a bacterial antigen (vaccine). We think that the first attempt to try this approach should be made for prevention of breast cancer and prostate cancer in healthy people.

To some extent, the choice of cancer antigen can be determined based on tumor markers [14]. Cancer vaccine can be created against a group of cancers or against combined cancer antigens.

There are several safe cancer vaccines. We believe that one of the possible vaccines is a standard onco-antigen NY-ESO-1 which gives specific immune response against melanoma [15]. In our work, synthetic onco-antigens can also be used. However, initially, we should conduct research in volunteer donors who would undergo immunization with the onco-antigen to work out optimal immunization schedules.

Usually, animal studies are performed prior to clinical trials in humans. These animal studies may show good results, mainly while studying infectious diseases. However, results of experiments in animals very often do not predict results in humans. Treatment of systemic lupus erythematosus in mice with antibodies to gamma interferon was successful [16], but in humans, administration of antibodies to gamma interferon caused exacerbation of the disease [17]. Experimental treatment of multiple sclerosis in mice had various results; meanwhile treatment of multiple sclerosis with antibodies to gamma interferon in humans had clearly positive results[6,7]. Certainly, in a number of cases experimental linear tumors in mice developed very differently from tumors in people. Thus, our proposed clinical trial of prevention of cancers in healthy people should be done no matter what the results of experiments in animals are.

When treating cancer, it is necessary to pay attention to the activity of immune-suppressive factors and give antibodies or other blockers against suppressive elements to cancer patients. Immunosuppressive factors, such as some cytokines and other factors play an important role in tumor pathogenesis, and, as we firstly showed, anti-cytokines are widely used for the treatment of autoimmune and other diseases[2,18].

Frequently, malignant cells can develop in the organism of a healthy person. However, these cells are antigenically heterogeneous and are quickly destroyed by the body's immune system. Thus, normal immune system is the main protective factor against the development of cancer. However, persons with a weakened immune system are more likely to develop cancer than the ones with the normal one.

It is also necessary to note that after surgery (breast, prostatic cancers) doctors often think that the patient is in full remission. Nevertheless, to kill tumor cells that might have been left after surgery, patients should undergo chemotherapy because, after treatment, if any tumor cells are left in the organism of a cancer patient these cells induce immune suppression that takes over patient's immune system. Thus, aggressive oncogenic factors either cause or are accompanied by immune suppression in cancer patients. At the time when clinical and laboratory parameters indicate that patient's immune system has returned to normal, he or she should be immunized with a safe onco-antigen which can elicit immune response against patient's tumor cells. Successful use of immunotherapy in cancer patients can be successful if it is performed in remission period when immune system can fully respond to onco-antigens. It is even more advantageous to immunize healthy people with onco-antigens because their immune system is completely intact. This would lead to prevention of cancer in these people. For a possible cancer prevention in immune suppressed patients we suggest administering them typed bone marrow cells, T and B lymphocytes, or whole blood. In our

opinion, this will help prevent cancer in some of them. We also should use a wonderful method of teaching immune cells so they develop immunologic specificity to a particular antigen. Bone marrow cells and T lymphocytes and other immune cells should be introduced to tumor and other antigens during in vitro incubation. This method can be used for prevention and treatment of tumors and other pathologic conditions. It is also important to create onco-antigens containing determinants of tumors removed during surgery. These tumor cells as well as all other immunizing preparations should be treated to eliminate any possibility of cancer transfer to healthy individuals who are immunized in order to prevent the development of some or most cancers.

It is time to work on cancer prevention in healthy people. At first, it is necessary to create a safe combined cancer antigen (vaccine). We are certain that in modern medicine it is possible to create safe combined cancer vaccines that can be used for prevention of cancer in healthy people. For this it is necessary to start organizational activities. Firstly, we should start working with people with healthy immune system who either have, or do not have onco-marker, or people who are at risk for cancer development (such as heavy smokers, cancer-inducing occupations, and people who have genetic predisposition). They should undergo immunization with the safe combined cancer antigen which will elicit immune response. It is necessary to develop immunization schedule which will induce strong immune response against the safe combined cancer antigens. This will ensure that immune ingredients will disintegrate oncogenic factors which will appear in organism of people who underwent immunization. Primarily research (before extensive work) should be done with a control group. After positive trial results, we can start wide research on large groups of people who are afraid of cancer development. In addition, it is necessary to pay more attention to various research in animals which can be used for cancer prophylaxis and possibly treatment in people. A number of wild animals have immune system that differs from humans, i.e. their immune system expression is greater. Various types of sharks, crocodiles, camels, rats, turtles, some types of fish, shellfish, insects, plants and possibly other biological objects should be carefully studied. A number of these animals have higher regeneration rate unlike humans, express bactericidal activity, immunity against aging (lobster and tortoise), and in some cases ability of immune system to destruct cancer cells. These studies are rare, but they indicate that this field should be carefully evaluated in order to extract components for cancer prevention and treatment in humans from the biological objects mentioned above. It is also necessary to think about possibility of the use of metals for cancer prophylaxis and treatment. If we seriously talk about cancer prevention we should not treat any information on cancer skeptically. It is obvious, that mortality rates associated with cancer are higher than mortality rates on battle fields. More money is invested in developing new types weapons than in battle against cancer. It is necessary to establish international centers with international funding, where the objects of research mentioned above can be studied. Each person can invest some money for such centers. This will bring prompt results in cancer prevention and treatment. The heads of these centers should be humane and kind (not heartless bureaucrats) then battle with cancer will be effective and fast.

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