

Stimulation of endogenous stem cells in controlled eosinophilic syndrome against cancer

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1. Summary

While analyzing the influence of immunocompetent cells to malignant neoplasms, we faced a natural deficiency of leukocyte granulocytes in majority of cancer patients. Scientific articles [1-4] prove the efficiency of eosinophil peroxidase toxic proteins in the fight against cancer. It is a natural anti-cancer defense mechanism, open to everyone. However, this mechanism often fails for several reasons. Immunity is trying to fix the problem, but production of immunocompetent cells lags behind the proliferation of cancer cells. There is an urgent need to stimulate endogenous stem cells, or rather to stimulate hematopoietic stem cells to produce more eosinophils, which proved their higher anti-cancer efficiency than T cells. It is also necessary to stimulate hematopoietic stem cells, because it is important to inhibit telomerase [5-11], i.e. to turn immortal cancer cells back into normal ones living by the laws of apoptosis. To effectively meet these challenges it was necessary to raise regenerative activity of stem cells, or hematopoietic stem cells, several-fold.

2. Description of the mechanisms or pathways involved in the stimulation of endogenous stem cells

To avoid the excessive stimulation of stem cells the specific approach was applied which presupposed the shift in the WBC differential count towards the maximum development of eosinophils, leaving the production of other cells at the same level in the reference range. The controlled eosinophilic syndrome immunomodulator (C.E.S.I.) was developed. The drug passed a federal examination and is currently used by an association of Russian enterprises for research and anti-cancer immunotherapy. The paper describes how and at what level the regenerative activity of stem cells was raised. The practice of using the C.E.S.I. showed that it is much easier to raise immunity in healthy people rather than in patients with cancer. The effectiveness of measures taken to enhance the regenerative activity of stem cells is determined by the surplus of the exceeded level of granulocytes over their anti-cancer consumption. The higher stage of cancer, the higher consumption of eosinophils. It is possible to achieve sustainable positive balance of eosinophils in patients with primary oncology through 1-2 courses of treatment (10-20 days). 10 courses of the drug (100 days) are required for the patients with stage IV cancer.

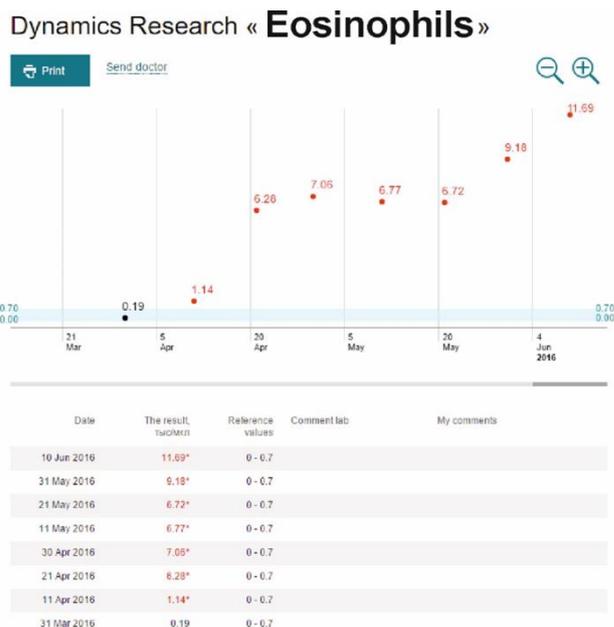


Fig.1. Dynamics of eosinophils (thousand/ μL) while stimulating stem cells. The reference range is 0-0.7 thousand/ μL . The data is provided by the patient of Invitro laboratory.

Figure 1 shows the dynamics of increase in eosinophils as a result of stem cells stimulation. It is Stage I of immunostimulation. Stage II – operational stage – is to sustain the number of eosinophils at the highest possible level until the tumor necrosis and removal of its decay products. It is possible to end stimulation of stem cells at the moment of sustainable drop of tumor markers to the reference values, when they are secured on the lower level of the reference range, for example, the UBC in bladder cancer (Fig. 2).

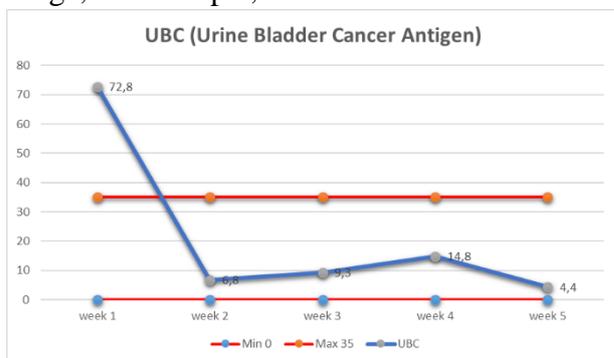


Fig. 2. Dynamics of UBC (mcg/L) of the patient with stage IV urinary bladder cancer

The effectiveness of immunotherapy can be seen in the dynamics of tumor necrosis on the following ultrasound images (Fig.3).

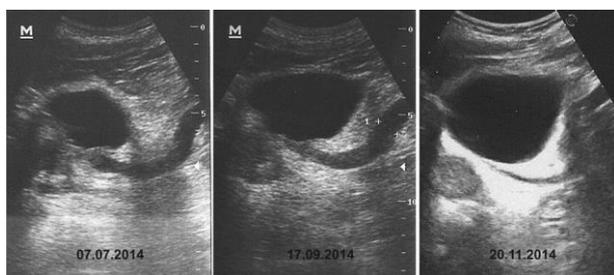


Fig. 3. Dynamics of ultrasound in stage IV cancer during immunotherapy

On the first image of Fig. 3 (07.07.2014) left ureter is dilated throughout from 3 to 11 mm, and there is a 14x9 mm neoplasm in urethral orifice which causes almost complete stenosis of the ureter. The diagnosis of the Moscow Oncology Research Institute is multiple primary synchronous cancer: 1. Stage I bladder cancer, T1NxM0, status post transurethral resection of 8

intravesical doses of doxorubicine. 2. Stage IV left ureter cancer, T4NxM0. Severe disorders of excretory function of the left kidney. The patient was supposed to undergo left nefrurerectomy with a resection of the bladder and paraaortic lymphadenectomy. The patient refused to undergo surgery in favor of immunomodulator “C.E.S.I.” (discharge summary from 08.08.2014). During immunotherapy, MRI was conducted on 10.07.2014 and 22.09.2014, which showed increase in the size of the neoplasm and dilatation of left ureter up to 13 mm. The second image of Fig. 3 shows the results of ultrasound from 17.09.2014 – dynamics is confirmed. Ultrasound on the third image of Fig. 3 (end of Stage 2 of immunotherapy) shows improvement. The ureter was reduced to norm (3 mm). Ureteral activity is intense. The function of the left kidney is restored. The patient returned to normal activities. During immunotherapy without surgery and chemotherapy we achieved tumor necrosis and elimination of its decay products, restoration of the affected organs – kidneys, ureter, urinary bladder.

3. Experimental evidence that the approach is feasible

We have been using the above described method of stem cells stimulation and anti-cancer immunotherapy for many years. The technology has been successfully tested to eliminate large solid tumors (Fig.4).



Fig.4. MRI and ultrasound of a solid tumor in urinary bladder

During stem cells stimulation regenerative activity was increased 61.5 times (Fig.1). As a result, the tumor was eliminated without surgery; pieces of necrotic tissue were removed naturally (Fig.5).



Fig.5. Pieces of necrotic tissue

The principles of evidence-based medicine are proved by means of Student’s paired t-test with a significance point $p < 0,001$. In July 21, 2015 the Library of Congress United States Copyright Office (101 Independence Avenue SE Washington, DC 20559) registered a new technology called “Controlled Eosinophilic Syndrome Against Cancer. Scientific Discovery and Practical Aspects of Immunotherapy” (Registration Number TXu 1-974-907) [12].

4. Experimental plan to validate the hypothesis or find new pathways

It is possible to test the above described method of stimulating regenerative activity of stem cells at any time. The interested party (to work as the collaboration partner will be considered) can form a study group of patients and make a request for immunostimulation to the Scientific Production System “Fertility & Ecology” (e-mail: fertility.ecology@gmail.com). A representative sample is 10 people. There are the following options: 1) healthy people who want to lift their immunity, i.e. protection against external pathogenic conditions, such as doctors. The course takes 10 days. The location is the city of Izhevsk, Russia. Immunostimulation and

accommodation in a sanatorium. Specific terms of boarding and lodging with pictures and prices, depending on the requirements of the patients, are available upon request. The expected results are activation of stem cells, increase in the level of protective immunocompetent cells and immunity on the whole in several times – it is measured before stimulation, after it, and in a month. After 10 days the partner receives the group of patients to do a follow-up. 2) cancer patients with stages I-IV, wishing to achieve remission, i.e. to eliminate metastases, solid tumors, to reduce tumor markers to the reference range, to get protection from relapse, according to the individual programs. The cycle of immunostimulation takes up to 10 courses (up to 100 days). As a result, the partner receives the group of patients for further research to prove the efficiency of stem cells stimulation.

To find new pathways, we are interested in cooperation in terms of genomic research. It is highly important for the partners in joint studies to realize the effect of stem cells stimulation on the changed (mutated) genome of people with cancer. Our proposals were published in *Science*, April 4, 2016 «Invitation to the concluding phase 2 of anti-cancer research» [13]; 21 April 2017 «Stimulation of endogenous stem cells in controlled eosinophilic syndrome against cancer» [14].

5. Funding request for a research collaboration

Research Plan.

1. The partner tests the technology of stem cells stimulation in accordance with Section 4.
2. Joint genomic research of stem cells stimulation. The main objective is to identify changes at the genetic level, caused by stem cells stimulation at different stages of cancer.
3. Establishment of a Joint Center for Immune Research and delivery of personalized medical care. The production sector (manufacturing of biomaterials and drugs) + research sector (development and improvement of technologies) + provision of personalized health care.

Costs of the Research Plan are determined by the cost estimate, formed in the development of certain components of the Research Plan and the Center's Project. Costs will vary depending on the region of realization of the Project (any place in the world upon request of the partner). The Project capacity depends on the interests and abilities of the partner. The Project should follow the principle of replicability, i.e. nonrecurring costs should bring multiple financial results.

6. References

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