

ONCOLOGY IN THE MAINSTREAM OF THE NATIONAL ACADEMY OF SCIENCES OF UKRAINE: TO THE 100th ANNIVERSARY OF THE ACADEMY

Fluctuation of time is determined by the order and sequence of historical events of global and/or local scale, the harmonization of which reflects the dynamics of the development of society. The top of universal values of this process was and remains the academic science, which is based on the principles of an inextricable triad: education, science and culture. The intellectual and creative “explosion” of the 20th and the beginning of the 21st century has fundamentally changed human consciousness and priority values. Along with the knowledge of physical, natural phenomena and the search for energy sources, man has become not only a subject, but also an object of research. The pace of development of the life sciences reached the apogee. The struggle for higher expectancy and quality of life is a priority of modern science. The key problem of biomedical research has been and remains malignant neoplasms, which dynamics becomes a threat of civilizational scale.

An important role in actualization of fundamental and applied research in the field of experimental and clinical oncology belongs to the National Academy of Sciences of Ukraine. At the beginning of the 20th century, the issue of the causes, progression of tumor disease and the search for ways to treat patients was actively debated by scientists and biologists. Expansion of the front of experimental research has greatly accelerated the acquirement of knowledge of the biology and morphology of the tumor cell. The undeniable achievement of Ukrainian academic science was the concentration of research on experimental carcinogenesis, initiated by the school of V.V. Pidvysotsky. His disciples were talented scholars, including future presidents of the Ukrainian Academy of Sciences D.K. Zabolotny and O.O. Bogomolets.

Creation of the Institute of Experimental Biology and Pathology in Kyiv in 1930 made it possible to con-



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centrate a considerable amount of research on the problem of reactivity and antitumor resistance of the organism. Election of O.O. Bogomolets as President of the Ukrainian Academy of Sciences contributed to the significant deepening and expansion of research on the problems of experimental and clinical oncology. Speaking at the I Congress of Oncologists of Ukraine (Kyiv, May 25–30, 1938) with an introductory speech “Topical Problems of Oncology”, he emphasized the need to systematize knowledge about malignant tumors, further study of etiology, pathogenesis, local and general predisposition to the emergence and development of cancer. Particular emphasis was placed on the need to increase the reactivity of the organism and antitumor immunity, regardless of the causes of their impairment, which is the

basis of prevention and basic principles of treatment of cancer patients. From the standpoint of the present, these theses were the forerunner of strategy of modern therapy. Further intensification of studies on nonspecific protective regulatory mechanisms in carcinogenesis showed the role of the factors of the homeostasis system in the formation of antitumor resistance of the organism at different stages of the development of tumors. World recognition of the priority and achievements of Ukrainian scientists in the study of the relationship between tumors and the organism was the inclusion in the program of the VIII International Cancer Congress (1962) a separate section meeting devoted to this topic, headed by R.E. Kavetsky, who summarized the results of his scientific research in the monographs “Tumour and Host” (1962) and “Interaction of Host and Tumor” (1977).

In the 1980s, molecular mechanisms of leukemogenesis, biophysical aspects of blastomogenesis were studied in depth, as well as new models of precancerous and tumor processes were developed. The central place in the research was the problem

of anti-carcinogenesis, which allowed to substantiate the theoretical possibility to stop the processes of transformation of a normal cell into a cancer cell and to prevent the tumor progression. In particular, the effect of interferon on the process of chemical carcinogenesis and tumor metastasizing was discovered in the experiment. Intensive development has begun on the search for natural antitumor substances of plant and bacterial origin. These works demonstrated the reversibility of carcinogenesis and the ability of the tumor cell to differentiation. Investigation of humoral and cellular reactions of antitumor immunity allowed to reveal the characteristic features of the immune response of the body when cancer was induced by chemical carcinogens and oncogenic viruses. It has been found that antitumor humoral reactions not only inhibit the proliferation of transformed cells, but also could stimulate the development of tumors.

The role of cellular RNA in the transformation of normal hematopoietic cells in leukemias was first established. It was shown that the action of different types of leukemogenic agents is realized on the level of stem hematopoietic cells and progenitor cells. In this regard, original research on ultrastructural identification of polypotent stem hematopoietic cells has been conducted. And already in 1977 in Kyiv, the Institute of Oncology Problems hosted the I International Conference “The Role of Stem Cells in Leukemo- and Carcinogenesis” with the participation of leading specialists from many countries of Europe and the USA (in 1983 — II International Conference was held). In 1978, the Institute organized Soviet-French symposium on ultrastructure and histochemistry of normal and tumor cells. It is important that, after 40 years, in 2017, in R.E. Kavetsky Institute of Experimental Pathology, Oncology and Radiobiology of National Academy of Sciences took place a significant event — the III International Conference “Normal and Tumor Cells: Discovery, Diagnosis and Therapy” with the participation of scientists from 14 countries, discussing the following main issues: normal stem cells (the methods of their isolation, and their use in medical practice); identification of stem tumor cells in tissue culture and tumors in experimental animals; tumor stem cells and mesenchymal stem cells in human tumors.

Today, in the structure of the National Academy of Sciences of Ukraine, R.E. Kavetsky Institute of Experimental Pathology, Oncology and Radiobiology is a powerful center for scientific research on the urgent problems of experimental pathology, biotechnology and molecular oncology, which made a significant contribution to the treasury of world oncology.

In particular, for the first time, molecular mechanisms, which determine the peculiarities of the course of chronic lymphocytic leukemia, are disclosed. The role of CD150 and CD180 receptors in the regulation of signaling pathways in malignantly

transformed B-lymphocytes has been proved. The Institute has prioritized the discovery of a new isoform of CD150 — nCD150 — the sequence of which was submitted to GeneBank (GenBank accession number: BankIt1650007 CD150v3 KF471075).

New biomolecular markers of early and differential diagnosis were discovered and certain mechanisms of epithelial-mesenchymal transition of cell were determined, probiotic agents and monoclonal antibodies, which directly influence the key stages of differentiation, transformation and apoptosis of cells, were investigated.

For the first time, the S18-2 protein, a representative of the mitochondrial protein family, has been identified, which is involved in mechanisms for regulating the uncontrolled proliferation of malignantly transformed cells. The obtained data allow to consider it as one of the potential oncogenes, which opens up prospects for finding out its role in the mechanisms of the tumor-host interactions.

Up to the world standards, studies are being conducted aimed at a detailed study of lineage-specific and differentiating antigens of cells of hematopoietic and lymphoid tissues of adults and children. In particular, it has been shown for the first time that the cell-analogue of acute leukemia, which appears during the progression of myelodysplastic syndromes, irrespective of their primary form, is a leukemic-modified stem cell of level 3 (CD117⁺, CD33⁺, CD34⁻, HLA-DR⁻), which is normally the progenitor of the myelomonocytic line of hemopoiesis. The obtained data are crucial for the prognosis of the disease, the formation of high-risk groups among patients and the appropriate treatment.

Currently, the study of the role of metal-containing proteins in the pathogenesis of the most common tumors is actively ongoing.

These and other studies are aimed at early detection and timely destruction of cancer cells, taking into account the individual characteristics of the course of tumor disease and maximizing the preservation and rehabilitation of the antitumor resistance system of the organism.

In our time, we received a new understanding of the problem of tumor-host interaction. The view of the tumor as a local process has changed to the perception of the disease of the whole organism, which is reflected in the approach to the treatment of cancer patients.

An original technology for the creation of a personalized treatment — cancer autovaccine, which includes biotechnologically modified tumor-associated proteins of autologous tumor material and products of microbial synthesis, is developed. The mechanism of its action is based on the formation of a long-term immune response in a patient that is capable of inhibiting the development of the tumor process due to the ability of the killer cells of the immune system to recognize tumor antigens and thus prevent the development of relapse and metastases. This inno-

vative development passed a complete cycle of pre-clinical and phase III clinical trials. The technological industrial regulations for its production have been elaborated. It took many years before we got the widespread recognition of scientific achievements of the Institute's scientists at the highest level — the 2017 award of the State Prize of Ukraine in the field of Science and Technology “Fundamental Basis of the Realization of Mechanisms of Antitumor Defence of the Organism”.

High hopes rely on photodynamic therapy of tumors — an innovative method for treating patients with malignant neoplasms, which is based on the administration of a special photosensitizer that can accumulate primarily in tumor tissue sensitizing it to the following laser irradiation.

In the Institute there have been developed the new types of hemo- and enterosorbents, which have unique properties to remove exo- and endogenous toxins of different molecular weights, and are used in clinical practice. The newest adsorption band on the basis of activated carbon fibrous materials achieved recognition at the International Festival of Innovative Projects Sikorsky Challenge 2017.

Modern immunocytochemical methods of diagnosing malignant diseases of the hematopoietic and lymphoid tissues have been introduced in accordance with the new WHO classification (2017) using the panel of Ukrainian monoclonal antibodies.

Another important activity of the Institute is the creation of a new generation of nanocomposites for improving the effectiveness of cancer treatment and overcoming resistance to cytostatics, which com-

bines therapeutic and diagnostic properties in one nanosystem.

Recently, scientific interests are concentrated around the study of miRNAs as an important factor in the epigenetic regulation of gene expression, which allows predicting the course of the oncological process with high accuracy.

In particular, the unique technologies of early diagnosis of cancer (Onco-Check-up) and prognosis of the sensitivity to medical treatment (Onco-Drug-test) have been developed. The developed technologies are based on the identification of certain panels of selective tissue-specific epigenetic oncomarkers (circulating miRNAs). The introduction of Onco-Check-up and Onco-Drug-test in a wide clinical practice allows not only to carry out population screening of the most widespread malignant neoplasms, but also to develop personalized programs for prevention, diagnostics and therapy of cancer.

Oncology is one of the most important, most complex, multi-vector and socially important direction of modern medical and biological science. The successful development of fundamental and applied knowledge may be achieved only due to the concentration of efforts and the fruitful consolidation of many scholars from various fields of science within the National Academy of Sciences of Ukraine.

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