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The history of the development of scientific activity in the Kazakh Institute of Oncology and Radiology: To the 60th anniversary of the Institute

The article describes the history of the establishment of scientific activity in the cancer service of the Republic of Kazakhstan during 60 years of existence of the Kazakh Institute of Oncology and Radiology. The author offers citations from historical documents, highlights the role of individual scientists who stood at the origins of the development of the scientific activity, shares the current scientific achievements of the Institute's staff, and emphasizes the main priorities of further scientific research.

Keywords: the oncology development history, cancer service.

The Kazakh Institute of Oncology and Radiology (hereinafter – the Institute, KazIOR) was founded by the Resolution of the Council of Ministers of the Kazakh SSR No. 962 dated 24 September 1959, and Order of the Minister of Health of the Kazakh SSR No. 1-15-33 dated 5 July 1960.

Its establishment started from scratch on the basis of the Obstetrics and Gynecology Chair of the Faculty of Advanced Training for Doctors of the Alma-Ata State Institute, at the 2nd Municipal Clinical Hospital. The Institute had no working space, no scientific workers in oncology and radiology. From the first days, we had to start working in different directions: design, preparation of construction estimates, on-job training of specialists at workplaces through postgraduate and resident courses provided at the central institutes of Moscow and Leningrad.

Extract from an address of the Institute's employee to graduate students, November 1960 (4.5 months after the Institute was established): "On 29 October, we celebrated the 43rd anniversary of the October Revolution; the solemn part was followed by a comradely dinner and dancing. Our team is good and friendly. Now, we have 65 persons in the Institute ... Saken Nugmanovich (S.N. Nugmanov, the First Director of the Institute) referred me to you asking you to send us a list of equipment and instruments available of the laboratories where you are working now."

Extract from the note of the Chief Physician of the Republican Oncological Dispensary A.A. Korzun to the Chairman of the State Planning Committee of the Kazakh SSR, 1961: "The number of patients diagnosed with malignant neoplasms in the Republic is increasing every year. If we take the incidence in 1950 as 100%, it went up to 192.1% in 1955 and 273.1% in 1958. ...In the 1960s, advanced forms of cancer account for 30.6% in the Republic ...I ask you to provide real help in scheduling the construction in regional centers of oncological dispensaries with boarding houses and radiological departments."

This document initiated an intensive formation of cancer service in Kazakhstan and the opening of oncology dispensaries in every region.

The main purpose of the Institute was to organize the cancer service in the Republic and to develop domestic science. *Extract from Resolution of the Council of Ministers of the Kazakh SSR No. 962, 1959: "... it is required: 1. to coordinate the research on cancer in one research plan combining the efforts of all departmental research institutions. 2. The research plan should include experimental and hygienic studies in cancer etiology and pathogenesis and the determination of carcinogenic factors influencing the general population. 3. Research for the most advanced methods of early cancer diagnostics and effective treatment of malignant neoplasms should be intensified."*

Since the early days of the Institute, there has been a clearly defined research plan. Its intensity is evident in the research and development report delivered by the Institute after a year and a half of its existence.

Extract from the Institute's R&D report for 1961: "For 1961, the Republican Research Institute of Oncology and Radiology of Ministry of Healthcare of the Kazakh SSR has planned scientific researches ...including the following problems: 1) Etiology and pathogenesis of malignant growth, 2) Prevention of tumors, 3) Diagnostics and treatment of malignant tumors, 4) Organization of anti-cancer fight..., which are transitional within the five-year scientific research plan. Besides, along with scientific research, 13 scientific staff members initiated their independent research under the Institute's plan."

Saken Nugmanovich Nugmanov headed the Institute from 1960 to 1970. A decade of purposeful intensive work for the Institute's benefit with the support of the Government of the Kazakh SSR enabled the creation of an excellent basis for further development of cancer science and service. The personnel trained in targeted areas subsequently became leading scientists of the CIS and the world. Since the Institute's establishment, the organization of laboratories, departments, the scientific activity, and the specialists' training were constantly financially supported by the state; the Institute received assistance and advice from the USSR central oncology and radiology institutes and their scientists.

However, the financial situation in the Republic at that time was not easy, as can be seen from some documents. *Extract from the Order of the Ministry of Health Care of the KazSSR on additional financing, 1965: "The Department of Medical Statistics (besides the list of planned mandatory expenses) should allocate funds for the procurement of high-quality paper and at least three desktop multi-key counting machines of the Rheinmetall or Vyatka type."*

We should highlight a highly appropriate selection of scientific personnel and their hard work. The staff conducted 39 scientific-medical expeditions to various climatic and geographical zones of Kazakhstan; over 300 specialists in oncology of Kazakhstan underwent advanced training and specialization; 9 doctoral theses and 98 candidate theses were defended during the first decade of the Institute's existence. On the 10th anniversary of the Institute (1970), the Academic Council's report stated that *"...except for planned and fulfilled, 27 doctoral and 67 candidate theses in oncology were defended in Kazakhstan; the authors or scientific supervisors of those theses were the Institute's employees."*

At that time, 19 out of the Institute's 60 structural units were purely scientific laboratories (according to the Institute's structure for 1970). Other clinical departments combined therapeutic activity with the search for new methods of cancer diagnostics, treatment, and prevention.

From the first days of the Institute's existence, biologists, chemists, physicists, engineers, and other experts were involved in scientific research along with medical workers.

In the first decades, the development of new diagnostic methods of pre-tumor states and cancer of certain localization, studying epidemiology and elaborating scientific grounds for preventing malignant tumors were the main scientific directions. The Institute organized scientific and practical medical expeditions to various climatic and geographical zones of Kazakhstan and visited the regions for preventive examinations. Extensive research has been carried out in radiobiology (particularly radiosensitivity and radiosensitivity of tumors), experimental oncology, biorhythms, carcinogenesis, immunology, geographical pathology, precancerous and cancer epidemiology.

Over the years, each field has developed into separate schools, producing its students and followers. The national government highly appreciated the Institute's staff professional level. Many veterans recall the satisfaction from receiving medals and diplomas of the USSR Exhibition of Economic Achievements, from the inclusion of their research results in the All-Union Plan of Implementation of Scientific Achievements in Public Healthcare Practice, preparation of guidelines, patents, and monographs.

Radiotherapy for cancer of certain localizations, also while taking antioxidants, was first developed and introduced in the Republic under Academician Saim Baluanovich Balmukhanov and later Professor Gazis Sergazinovich Kanafyanov. The Institute has reached the world level through the conducted radiosensitivity studies of malignant neoplasms. Academician S.B. Balmukhanov, the founder of radiology and radiobiology in Kazakhstan, made a valuable contribution to cancer service develop-

ment in Kazakhstan. S.B. Balmukhanov was awarded many high governmental awards and the honorary title of the International Peace Prize Laureate for his contribution to the fight for a nuclear-free world.

The new scientific directions related to the study of the role of immunity and endocrine-metabolic shifts in the breast, genital, and prostate tumors developed under the leadership of Prof. S.A. Baisheva enabled the elaboration of modern methods of predicting the clinical course of the disease and choosing the treatment method, including immune hormone therapy. During the existence of the Institute, its Immunology Laboratory staff has authored over 40 patents.

In the study of clonal-structural bases of radiochemical resistance and radio-modification of tumors at various stages of the metastatic process, a group of scientists led by Professor Bulat Ismailovich Ismailov developed unique experimental models and created a multi-level theory of carcinogenesis.

Boris Saimovich Balmukhanov supervised biophysical research at the Medical Physics Laboratory. They established the role of blood electrolytic components non-equilibrium states while developing an erythrocyte test system for primary drug selection.

The Laboratory of Experimental Chemotherapy for Tumors, headed by Professor Adak Kabiev and later by Dr. Gulnara Gadilevna Ushbayeva, was developing new anti-tumor drugs based on Kazakhstani plants. More than 150 plants with revealed anti-tumor activity were investigated. Such enormous work was possible only because preclinical studies of new domestic medicines with pronounced anti-tumor activity were routinely conducted at that time.

The Laboratory of Carcinogenic Agents of the External Environment under the leadership of Prof. Murat Abdulkhaevich Karimov ("Honoured Inventor of the USSR," "Honoured Worker of Kazakhstan") studied the toxic, carcinogenic, and leukemic potential of various chemical compounds, industrial wastes, and lifestyle factors in the epidemiology of malignant tumors defined the content of carcinogenic agents in the environment in the regions of Kazakhstan with challenging environmental conditions (Mangistau, Atyrau, West Kazakhstan, North Kazakhstan, East Kazakhstan, Pavlodar, Kyzylorda and Almaty regions). The research results were immediately used to develop measures to improve public health in the studied regions and prevent malignancies.

For the first time in the Soviet Union, the Experimental Oncology and Tumor Radiobiology Laboratory headed by Prof. Mikhail Lvovich Efimov and later by Galina Semenova Vasilyeva developed and implemented into practice of many departments the tumor radiation and chemotherapy techniques based on regular biorhythmic fluctuations of the tumor and body sensitivity and resistance during the day. The developed techniques utilized the body reserve forces to significantly increase the radiation and chemotherapy effectiveness while reducing and even eliminating toxic and adverse body reactions.

Prof. Roza Khusainovna Mustafina headed the study

of the tumor's systemic action on body biochemistry, the search for ways to correct metabolic disturbances, and the investigation of early cancer signs and cancer prevention. The nature of the tumor's systemic action on the body was established for the first time based on glycolysis and the Krebs cycle.

We would also like to recall the beginning of using cryosurgical techniques in organ-saving and plastic surgery in the complex treatment of sarcomas and soft tissues, the development and introduction of reconstructive-plastic operations under the leadership of Alikhan Kamovich Kosayev (later - Dosbul Khaynazarovich Savkhatov, Gani Amangeldiyevich Serikbayev), as well as unique operations on the lung in metastasis, carried out by Prof. Azat Akimkulovich Beisebayev and his team; the introduction of intratumor radiosensitization for cervical cancer patients in the Intracavitary Gamma Therapy Department under the leadership of Zhenis Saryevich Mustafin; the development and implementation of systemic radiotherapy technique to treat malignant lymphoma, brain tumors, breast cancer, skin melanoma, and the use of fast electrons in the Clinical Radiology Department under the leadership of Prof. Nariman Azhilayevich Azhilayev.

I would also like to mention doctor Serik Khamitovich Kobikov. For a long time, he was in charge of the Children's Unit, the first medical setting in Kazakhstan to investigate and treat malignant neoplasms in children's nervous systems. I should also recall doctor J.D. Zhumagazin who supervised introducing the complex and combined treatment of urogenital tumors in the Oncurology Department.

A big team of the Pathomorphology and Geographical Pathology of Tumors' Laboratory headed by Prof., USSR State Prize Laureate Nelly Ivanovna Kolycheva studied tumor morphological features in background diseases, as well as pre-cancer and cancer histotypes variability over time in various regions of Kazakhstan and different age, gender, and ethnic groups. Those researches allowed revealing the specifics of esophageal, breast, intestine, uterus, and other cancers' frequency and prevalence in Kazakhstan.

Cytology laboratory headed by Prof. Azat Ilyasovna Shibanova has developed and introduced quantitative and qualitative cytology methods for accurate diagnostics and disease prognosis using cytological material, elaborated a set of new optic-geometrical criteria for cytological preparations.

Dr. Vladimir Ivanovich Filipenko has introduced Colour Doppler Mapping at the Ultrasound Diagnostics Department for volumetric liver masses' differential diagnostics.

The Tumour Molecular Biology Laboratory at the Radiation Genetics Group, headed by Prof. Zhanalyk Niyazovich Abdrakhmanov and later Prof. Saule Alikhanovna Yermekova, investigated the mutational effects of low radiation doses on DNA structural organization and initiated the introduction and development of PCR-based molecular genetic methods in experimental and clinical practice. At present, two scientific centers of the Institute continue these studies.

The X-ray Diagnostics Department, headed by Associate Professor A.T. Turganbayev and later by Prof. A.H. Khamzin, introduced intra-arterial prolonged infusion polychemotherapy. Later, Prof. Zhamilya Zholdybayevna Zholdybay supervised many radiological, mammographic, computed tomographic, magnetic resonance, angiographic, scintigraphic clinical, and scientific studies.

I would also mention Prof. Gaziza Jumageldinovna Seitkazina, who contributed a lot to experimental radiobiology. The Laboratory for Scientific Organization of Anti-Cancer Fight she established at the Information-Analytical Centre was responsible for conducting the hospital and population cancer registers. The population cancer register is still the backbone of the entire cancer service system.

Some of our veterans still work at the Institute. I have to name Prof. Galym Bazenovich Adilbayev, who was the first to perform reconstructive and plastic surgery in the treatment of head and neck tumors; Prof. Nino Apollonovna Chichua, our permanent chemotherapist, who developed chronochemotherapy approaches in the treatment of cancers of various localisations, taking into account individual body parameters; Doctor of Medical Sciences Isa Tazhedinovich Tazhedinov, who is introducing new radiopharmaceuticals, radioisotope diagnostics; Prof. Raimkul Karakulovich Karakulov, who continues introducing new methods of hematological diseases treatment.

The Dissertation Advisory Committee was functioning at the Institute till 2010. More than 90 doctoral and more than 250 candidate's theses were prepared and defended during its existence.

Since the Institute's foundation, its scientists have published more than 70 collections and materials of conferences, more than 90 monographs in the Kazakh and Russian languages, dozens of manuals, over 200 guidelines, more than 8000 scientific papers in national and international journals. More than 300 copyright certificates and patents were received. Every year, our scientists participate and make oral and poster presentations at congresses, international conferences, and forums.

The global and national scientific knowledge has grown tremendously over the semicentenary. The priority research areas, our Institute's structure, and the whole cancer service were changing considering the development trends. Nine directors replaced each other over the past time. I want to remind all the directors who worked from the Institute's foundation to the present day. Professor Saken Nugmanovich Nugmanov (headed the Institute in 1960-1970), Professor, Academician of the National Academy of Sciences of the Republic of Kazakhstan, Honored Scientist Saim Baluanovich Balmukhanov (1970-1974), Professor, Honorary Member of the Academy of Medical Sciences of the Republic of Kazakhstan, Honored Doctor of the Kazakh SSR Argyn Arynovich Suleimenov (1974- 1983), Professor Odak Kabievich Kabiev (1983-1987), Professor, Honored Worker of the Republic of Kazakhstan Agzat Akimkulovich Beisebayev (1987-1990), Professor, Full Member of the National Academy of Sciences of the Republic of Kazakhstan, Honored Worker of the Republic of Kazakhstan Zhanalyk Niyazovich Abdrakhmanov (1990-2001), Professor, Acade-

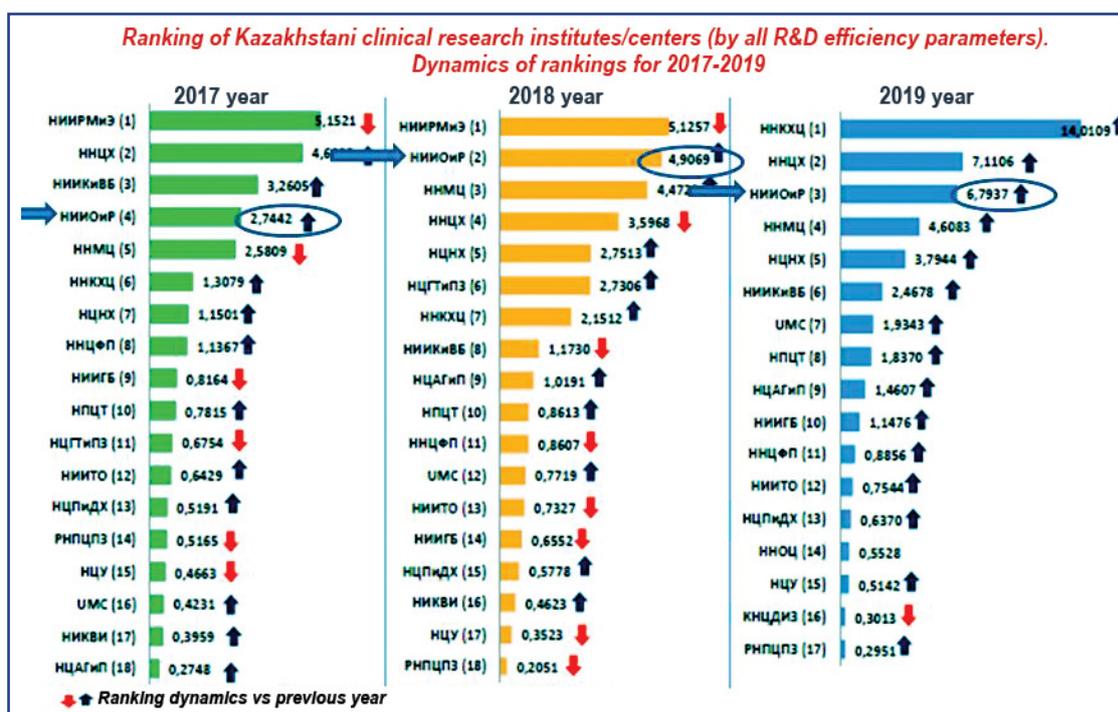
mician of Russian Academy of Medical Sciences, Academician of National Academy of Sciences of the Republic of Kazakhstan Zhetkergen Anesovich Arzykulov (2001-2011), Doctor of Medicine Sciences Kuanysh Shadybaevich Nurgaziev (2011-2016), Doctor of Medical Sciences, academician of National Academy of Sciences of the Republic of Kazakhstan Dilyara Radikovna Kaidarova (2016-till today) – each of them made an invaluable contribution to the formation of the Institute and oncology in general.

Currently, oncology is a dynamically developing branch of healthcare in Kazakhstan. The Institute is the central institution providing oncological assistance to the Kazakhstani population; it heads the cancer care network consisting of 14 regional, two regional, and two municipal oncological dispensaries.

More than 700 employees work at the Institute today. The Institute has become a large, internationally recognized scientific organization and a training center for the country's oncological staff. The Academic, Radiological, Diagnostic, Chemotherapeutic and Surgical Councils and eleven scientific-methodical centers established at the Institute are engaged in clinical and scientific work.

Day hospitals and a drug supply center have been opened for the patients' convenience and increasing throughput. For more than a decade, our Institute annually trained residents in 3 specialties: "Oncology, including pediatric oncology," "Radiation diagnostics," and "Radiation therapy." Our alumni have joined the ranks of clinical staff in the periphery and became a reliable reserve for further development of Kazakhstani oncological science.

Currently, the Institute led by the Chairman of the Board, Doctor of Medicine, Academician of the National Academy of Sciences of the Republic of Kazakhstan Dilyara Radikovna Kaidarova continues at a high level the traditions established 60 years ago – the aspiration to be an advanced center, known in international scientific circles and possessing a high scientific potential for further development. The Institute stands out for the active development of fundamental, methodological, scientific, and organizational foundations of oncology with a wide range of practical applications. In recent years, the Institute ranks among the top 18 research institutes and research centers of clinical profile in Kazakhstan by R&D activities (Figure 1). It produces many scientific and technical products each year (Figure 2).



Legend: List of institutes/centers (column 2017, top down): НИИРМиЭ – Scientific-Research Institute for Radiation Medicine and Ecology, ННЦХ – A.N. Syzganov National Scientific Center for Surgery, НИИКиВБ – Scientific Research Institute of Cardiology and Internal Medicine, НИИОиР – Kazakh Institute of Oncology and Radiology, ННМЦ – National Scientific Medical Center, ННХЦ – National Research Cardiac Surgery Center, НЦНХ – National Center for Neurosurgery, НЦЦФП – National Scientific Center of Phthisiopulmonology, НИИГБ – Research Institute of Eye Diseases, НПЦТ – Research and Production Center for Transfusiology, НЦГТИПЗ – National Center for Occupational Hygiene and Occupational Diseases, НИИТО – Research Institute of Traumatology and Orthopedics, НЦПидХ – Scientific Center of Pediatrics and Pediatric Surgery, РНПЦПЗ – Republican Scientific and Practical Center of Mental Health, НЦУ – Academician B.U. Dzhharbusynov Scientific Center of Urology, УМС – University Medical Center Corporate Fund, НИКВИ – Kazakh Scientific Center of Dermatology and Infectious Diseases, НЦАГиП – Scientific Center of Obstetrics, Gynecology and Perinatology

Figure 1 – Ranking of Kazakhstani clinical research institutes/centers (by all R&D efficiency parameters). Dynamics of rankings for 2017-2019

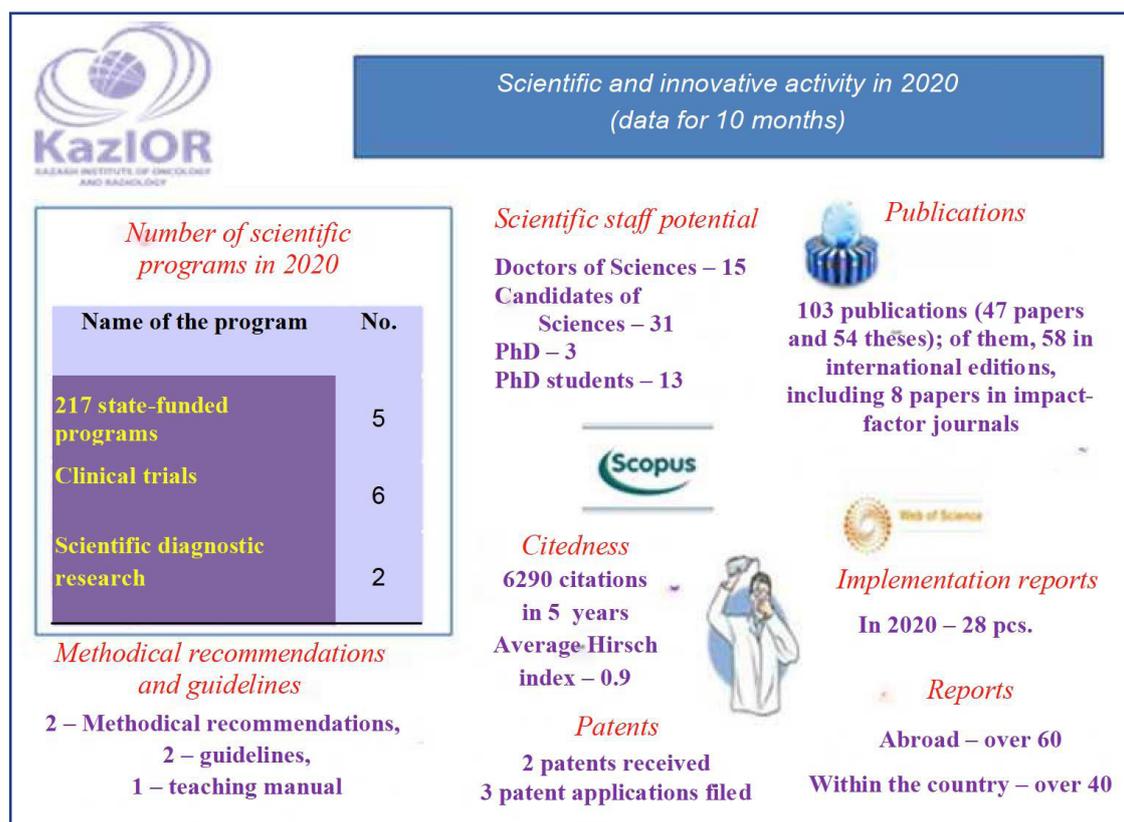


Figure 2 – Scientific and innovation activities of KazIOR during 10 months of 2020

Research projects completed in 2020:

- “Prognostic value of clinical-genetic and immune histochemical characteristics of colorectal cancer” (2018-2020);
- “Possibilities to determine T-lymphocyte markers in lung and breast cancer early diagnostics and prediction” (2018-2020);
- “Prognostic stratification of differentiated thyroid cancer based on genetic analysis” (2018-2020);
- “Development of new molecular-genetic methods for prostate cancer aggressive forms preclinical diagnostics” (2018-2020);
- “Gene expression profiling to identify non-Hodgkin B-cell lymphomas molecular subgroups in Kazakhstan” (2018-2020).

The following priorities shall be implemented by the Institute in the next three years:

- National personalized and preventive medicine introduction program in the Republic of Kazakhstan
- Hyperthermic intraperitoneal chemoperfusion in ovarian cancer treatment
- Neuropsychological rehabilitation of cancer patients with CNS tumors and bone and soft tissue tumors, with post-amputation phantom pain syndrome
- The role of microsatellite instability in patients with resectable colorectal cancer in personalizing treatment and predicting the course of the disease
- New approaches to presymptomatic diagnostics of malignant neoplasms using modern radiological and genetic technologies
- Optimization of treatment protocols based on the study of molecular-genetic characteristics of multiple primary myelomas

- Implementation of personalized treatment for ovarian cancer based on molecular-genetic characteristics
- Study of the tumor cells energy metabolism under the influence of natural polyphenols in combination with chemotherapeutic drugs
- New approaches to cancer patients’ medical rehabilitation during radiation therapy

Conclusion: Over the 60 years of its existence, the Kazakh Institute of Oncology and Radiology has produced evident scientific results. Kazakh oncologists have made a significant contribution to improving the efficiency of cancer diagnostics and treatment. The results of basic research, scientific, organizational, and methodological work in oncology, radiation diagnostics, radiation therapy, and nuclear medicine allow every year to expand the local population’s treatment options and increase the Institute’s competitiveness in the global market. A positive trend has been achieved in increasing cancer patients’ survival rate, improving their quality of life and social activity.

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ТҰЖЫРЫМ

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¹«Қазақ онкология және радиология ғылыми-зерттеу институты» АҚ, Алматы, Қазақстан Республикасы

Қазақ онкология және радиология ғылыми-зерттеу институтында ғылыми қызметтің қалыптасу тарихы. Институттың құрылғанына 60 жыл

Бұл мақалада Қазақ онкология және радиология ғылыми-зерттеу институты құрылған күннен бастап 60 жыл ішінде Қазақстан Республикасының онкологиялық қызметіндегі ғылыми қызметтің қалыптасу тарихы ұсынылған. Тарихи дереккөздерден алынған дәйексөздер келтіріліп, ғылыми қызметті дамытудың бастауында тұрған кейбір ғалымдардың рөлі атап өтілді, институт ғалымдарының қазіргі кездегі жетістіктері мен болашаққа арналған ғылыми зерттеулердің негізгі белгіленген басым бағыттары көрсетілді.

Түйінді сөздер: онкологияның даму тарихы, онкологиялық қызмет.

АННОТАЦИЯ

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История становления научной деятельности в Казахском научно-исследовательском институте онкологии и радиологии. К 60-летию создания института

В данной статье представлена история становления научной деятельности в онкологической службе Республики Казахстан за 60 лет со дня образования Казахского научно-исследовательского института онкологии и радиологии. Приведены цитаты из исторических источников, отмечена роль некоторых ученых, стоявших у истоков развития научной деятельности, показаны достижения ученых института на настоящее время и основные намеченные приоритетные направления научных исследований на будущее.

Ключевые слова: история развития онкологии, онкологическая служба.