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INTERVIEW

"Development of gerontology would be more effective under governmental support": an interview with Vladimir N. Anisimov

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Introduction

The Editor-in-chief of "Biogerontology" Suresh Rattan asked me to interview Prof. Vladimir Anisimov (Fig. 1), Head of Department of Carcinogenesis and Oncogerontology, N. N. Petrov National Medical Research Center of Oncology, St. Petersburg, Russian Federation, founder and president of Gerontological Society of Russian Academy of Sciences (1994–2022), who was the first receiving in Bologna, Italy, 2011 medal and Honorary Diploma for the excellence and achievement of the science of Aging in recognition of the outstanding contribution to the development of Gerontology in Europe (Biology of aging) from European Regional Branch International Association of Gerontology and Geriatrics.

Professor Vladimir Anisimov's extensive research on the effects of melatonin, metformin, rapamycin and other substances on aging and longevity in animals has significantly contributed to our understanding of the biological processes that underlie aging. His work has opened up new avenues for developing anti-aging interventions. In one of his topics, Professor Anisimov focused on the effects of melatonin on aging, particularly its antioxidant properties. As a hormone that regulates sleep–wake cycles, melatonin has also been shown to have anti-inflammatory and anticarcinogenic effects. Anisimov's research on mice and rats has shown that melatonin supplementation improved cognitive function and increased lifespan. Another area of Professor Anisimov's research is the anti-diabetic drug metformin, which has potential anti-aging effects. In a study on mice, Anisimov found that metformin could increase lifespan and delay the onset of age-related diseases such as cancer and infection disease. Professor Anisimov's research on light exposure and its effects on aging suggests that exposure to light during the night may have pro-aging effects and increase the risk of cancer. Furthermore, as one of the founders of the field of oncogerontology, Professor Anisimov has made significant contributions in the intersection of cancer and aging. His work in this field has helped to identify the biological processes underlying both diseases and has led to the development of new interventions. I have

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Fig. 1 Anisimov Vladimir Nikolaevich, 2020

had the pleasure of knowing Professor Vladimir Anisimov for over 20 years, and it was a great honor to interview this distinguished researcher. While our initial conversation took place over the phone, the majority of the interview was conducted through written communication.

Alexey Moskalev (AM): can you describe your memory experience from your childhood and adolescence?

Vladimir Anisimov (VA): "Become a doctor, invent pills against aging," my mother told me when I was very young. She entered the 1st Leningrad Medical Institute in 1940. But a year later the war began and one course of medical, although higher, education was not enough to become a nurse, but enough to collect the dead right on the streets or in frozen houses and take them to the morgue. When my mother began to develop dystrophy, a classmate and friend of her older sister called them to a military unit stationed in her native village. My mother became a soldier, and the soldier's ration was more than the worker's. In this part, which equipped shells with fuses and explosives for the Leningrad Front, she served until the end of the war. My father, Nikolai Alexandrovich, in 1936, following the Komsomol call, entered the Leningrad Artillery and Technical college, from which he graduated in 1939, becoming a specialist in ammunition, explosives and fuses. My father spent the entire blockade in besieged Leningrad. First, he cleared unexploded enemy bombs and shells, and then served in a military unit that (apparently in order to preserve military secrets) had a peaceful name—PSM-21 (Mobile Equipment Workshops). It was in this unit, which supplied ammunition to the defenders of the city, that the failed doctor Masha met with Captain Nikolai Anisimov, whom she married. In December 1945 I was born. Then my father was sent to Magdeburg in Germany, where in 1948 my sister Tatyana was born. Then my father was transferred to Kaliningrad, and only in 1952 did we return to Leningrad. With two small children, it was impossible to study at the medical institute. Mom entered the law college, where university professors read her and other frontline soldiers a university course for 2 years. So, my mother became a lawyer and worked all her life in a large industrial association. She often said that she really wanted to become a doctor, and, apparently, she embodied this unfulfilled personal dream in me.

I went to school in Kaliningrad in 1952. I remember that the school and the house where the families of officers lived were the only surviving buildings in the street—all the rest were in ruins. That is why they didn't want to send me to school. By that time I did not reach 7 years of age yet. But all my friends went to the 1st grade, and I cried so much that they took pity on me and took me—they say, let it be like that for now. Six months later, we returned to Leningrad and I was accepted into the 334th male school, which is on Tkachey Street behind the Nevskaya Zastava. We lived on the same street in a large house, which everyone called the "railroad", because it was inhabited mainly by the families of workers and employees of the Proletarian steam locomotive repair plant. Before the war, my maternal grandfather and his two brothers worked as blacksmiths at the plant. The blacksmiths had reservation for conscription, but three brothers volunteered for the front and all the three were killed.

In 1955, my father was sent to serve in the Far Eastern Military District. We got on the train and traveled for 9 days across the country to Khabarovsk. It was a grandiose journey, we crossed the border between Europe and Asia, then saw boundless Siberia.

In 1959, when I was in the 7th grade, it was announced that 11 years of education were introduced

Fig. 2 Student of Medical Nurses College, 1960

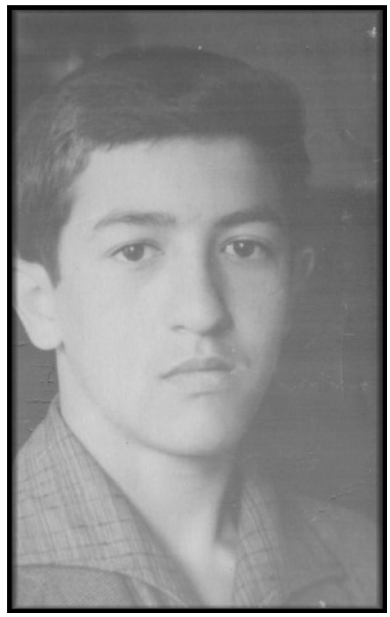

Fig. 3 Student of 1-st I.P.Pavlov Leningrad Medical Institute, 1962

in schools. For some reason, the idea came to my mind to enter a medical assistant's school in order to have a specialty in the same 4 years. Despite the fact that I was not yet 14 years old, I made a decision myself and went to submit documents to the Khabarovsk Paramedic college. In 1960 Nikita Khrushchev reduced the size of the army by more than a million, my father was demobilized, and we returned to Leningrad. There were no paramedical colleges here, and only nurses and paramedical laboratory assistants were trained in medical schools. Somewhere they enrolled only girls, somewhere they didn't want to count the one year that I had already studied in Khabarovsk. Finally, I was admitted to the 2nd Leningrad Medical college, located at the Karl Marx hospital near the Freedom Bridge (Fig. 2).

I studied at the nurse's school with pleasure, I was dreamed of becoming a surgeon. With a friend in the study group Valery Yatsenko, who also dreamed of becoming a surgeon, we were on duty at night at the surgical department of the hospital, mastering the profession of an operating room nurse. I remember that the teacher of surgery told us that if we want to be surgeons, we need to learn how to knit sutures with the left and right hands and, in general, develop the left hand. She advised me to learn how to play ping-pong with my left hand, which I still know how to do. I remember the day when Yuri Gagarin flew into space—we went out into the street in white coats to rejoice. I remember how they underwent obstetric practice in the Snegirev maternity hospital and the first time I accepted birth—I was then 15 years old … They taught us very well. We were taught how to fold gowns properly, how to give injections, how to give enemas, how to do dressings, and as a result we were well trained in nursing and nursing skills. In the 3rd year of the college, I realized that the knowledge for entering the institute is not enough, it is necessary to improve my knowledge in physics and chemistry. Therefore, I entered an evening school—a school for working youth, as they were then called. After classes at the school, I rode a tram through the whole city home to Tkachey Street, and then ran evening school.

I graduated from college with a "red" diploma, that is, with top marks, which gave me the right to immediately, without a 3-year working off, to enter the institute. It was 1962. I successfully passed all the entrance exams to the 1st Leningrad Medical Institute named after Academician I. P. Pavlov (1st LMI), where my mother studied in the pre-war year. I even wrote an essay "Why I choose the profession of a doctor" evaluated on top level (Fig. 3).

Group mates Oleg Paykin and Rezvan Ibragimov introduced me to the sport. Oleg once announced

the creation of a handball section at the institute. In those years, many students from the German Democratic Republic (GDR) studied at the Faculty of Dentistry. In East Germany, handball was very popular, and German students asked to organize a sports section. A good coach was invited, a playground was equipped next to the building of the Department of Physical Education and an entry into the section was announced. Rezvan played handball in the army and immediately enrolled himself and brought me and some friends to the section. I liked the game, the lessons in the section were interesting and intense. Thanks to regular training and participation in handball competitions, I got physically stronger and participated with pleasure in numerous institute cross-country skiing competitions.

I remember well the day when I first time visited came to the Institute of Oncology. The reason for visiting was the article "Torches on the fingers" that interested me about the Kirlian effect in a book published by "Komsomolskaya Pravda" in the popular science series "Eureka". The Kirlian spouses discovered that when exposed to microwave fields, biological objects emit some luminous fields that can be registered when photographed. At the same time, the nature of this glow, including its color and intensity, depended on the functional state of a particular organ or tissue. I was especially struck by the fact that the luminescence of the human skin was different in different areas and was distributed over the Ged's zones, and changed significantly in diseases. I was a 3rd year student and it occurred to me that this method should be effective for diagnosing cancer. Without thinking twice, I took a book with an article, waved my hand at the lectures, and went to the Institute of Oncology. Fortunately, it was then located very close to the 1st Med, on Kamenny Island. Having logically assumed that such a proposal should be addressed to the laboratory of biophysics, I went to its head—Professor Pavel Polikarpovich Dikun—I made inquiries at the institute's registry. Pavel Polikarpovich met me well, listened patiently in his usual manner. But when I dried up, he said that his laboratory was engaged in the detection of carcinogens in the human environment and, if I was interested, he was ready, despite the fact that I was a medical student, and not a biophysicist or at least a biologist, to teach me this, because the problem is becoming more and more urgent. I thanked him politely, saying that I was still interested in applying the Kirlian method in oncology. "It seems that Nikolai Pavlovich Napalkov was interested in this problem," Pavel Polikarpovich said thoughtfully. That's how I first heard the name of a person whose meeting dramatically changed and determined my whole subsequent life. "Which room is it in?" Pavel Polikarpovich explained that the laboratory of tumor strains, which was headed by Nikolai Pavlovich, had already moved to one of the premises of the complex of the new institute buildings built in the village of Pesochny, near Leningrad. In 1965, our laboratory and the laboratory of chemical carcinogens moved to a new building. Experimental tumor laboratories were located at the premises in the middle of the 3rd floor of the laboratory building. The neighbors were the laboratory of endocrinology on the one hand and the laboratory of cytology on the other. Other laboratories of the experimental sector of the Institute began to move from Kamenny Island. When the Institute of Oncology was located on this island, it included the Department of Experimental Oncology, which was headed by academician Leon M. Shabad. Then Shabad was invited to head the Department of Carcinogenesis at the newly established Institute of Experimental and Clinical Oncology in Moscow. Professor Nikolai V. Lazarev, a prominent pharmacologist and toxicologist, was invited to head the Department of Experimental Oncology at the Leningrad Institute of Oncology. When the construction of a new building in Pesochny was completed, a decision was made to expand the staff of the institute. New laboratories were created, which were then headed by very young research workers of the department—P. P. Dikun (Laboratory of Biophysics), N.P. Napalkov (Laboratory of Experimental Tumors), V.M. Dilman (Laboratory of Endocrinology), G. B. Pliss –(Laboratory of Chemical Carcinogens), T.A. Korosteleva (Laboratory of Immunology), M. P. Ptokhov (Laboratory of Cytology), A. N. Parshin (Laboratory of Biochemistry), S.F. Serov (Laboratory of Pathomorphology), A.L. Remizov (Laboratory of Organic Synthesis). N.V. Lazarev headed the Laboratory of Pharmacology and Toxicology.

The Laboratory of Tumor Strains was renamed the Laboratory of Experimental Tumors, since work with transplanted tumor strains occupied a very modest place in the research conducted there. The main direction was the study of patterns of transplacental carcinogenesis. The impetus for them was the sensational

Fig. 4 Volunteer at Laboratory of Experimental Tumors, 1966

story in 1958 with thalidomide, the pills with a hypnotic effect, were taken by pregnant women in Germany. These women began to give birth to children with various malformations. A huge scandal erupted. Everyone rushed to study the teratogenicity of drugs. However, even more dangerous was the development of malignant neoplasms in children whose mothers were exposed to certain chemicals during pregnancy, including drugs. The leaders in research on this problem were the laboratories of A. Druckrey in Germany, J.M. Rice in the USA and our laboratory, which in 1964 was headed N.P. Napalkov, student of L.M. Shabad. He had already begun research on the carcinogenicity of thyreostatics, enormous in scale, over a number generations. In one of the experiments, rats and their offspring have been receiving drugs during 17 generations!

In the fourth year of the 1st Leningrad Medical Institute, I restricted classes in the sports section. I spent all my free time in Pesochny, at the Institute of Oncology (Fig. 4). True, sometimes I participated in competitions in handball, skiing, and even the institute's football championship. Two "newcomers" appeared on the course—two students transferred from the Chelyabinsk Medical Institute—Oleg Kisselev (he became of academician of RAMS) and Viktor Fedorov. They were excellent students, they wanted to do science, and they chose the 1st LMI as a launching pad for entering the temple of science. It so happened that we quickly became friends. Victor worked at the Department of Faculty Therapy, and Oleg Kisselev at the Department of Forensic Medicine studied the role of choline esterase in the brain during stress. Once he set up a great experiment and asked him to help immobilize the rats. We tied them with bandages by the paws, stretching several rats on the boards, and left them for several hours. The rats obviously did not like it, they desperately resisted and squeaked. One of the results of the experiments was the establishment of the phenomenon of greater resistance to stress in female rats in comparison to males. One had to look in the literature to see how new this was. Surprisingly, we were able to find very little data on this issue in the literature. We found a work in which, using a classical physiological model of an isolated neuromuscular preparation of a frog, it was shown that, in response to stimulation with an electric current, the female muscle responded much longer than the male muscle. We found the book of the founder of the theory of stress Hans Selye—"Essays on the Adaptation Syndrome" in the scientific library of the institute, carefully studied it, but did not find any indications of the existence of gender-dependent dimorphism in the reaction to stress. Then the idea occurred to me to turn to address Selye himself. The address of the classic was found in the Public Library, and I wrote him a letter asking him to send the prints of his works on this subject. After some time, a weighty package came to my name at the institute, which contained a catalogue, if I am not mistaken, about 2,000 publications of the great scientist. In a cover letter, Selye thanked me for my interest in his work and expressed his readiness to send reprints of any articles I need, indicating only their serial numbers in the catalog, since he himself does not remember which work contains the answer to my question. The letter was typed on a typewriter in English, but signed in Russian "Hans Selye". Selye was Czech but lived and worked in Canada. I was very proud of this letter, I showed it to my friends. It is still kept in my papers among the letters dear to me. Then I was struck that a scientist of this level answered a student. I always try to follow the example of H. Selye to respond to letters from students, novice researchers and doctors, who quite often reachout to me by e-mail in the era of the Internet.

Once, having arrived from another foreign business trip, Napalkov instructed me to find the work of the american pathologist Bilshovsky, whose report he listened to at the conference. Bilshovsky discovered that female rats, which were castrated and one of the ovaries transplanted into the tail, developed the

so-called persistent estrus syndrome—that is, instead of cyclic production of estrogen and regular (every 4–6 days) ovulation, sex hormones were secreted by the ovaries constantly, which manifested itself constantly keratinization of the mucous membranes lining the genital tract of animals, and follicular cysts developed in the ovaries. The idea was that against the background of such a syndrome, after a short-term administration of any carcinogenic substance, it would be possible to reveal the carcinogenesis-promoting (accelerating) action of the constant production of endogenous hormones in the target tissue. I "dived" into the State Public Library, checked the volumes of Index Medicus for many years, an excellent abstract publication, and quickly found Bilshovsky's article, ordered a photocopy and brought it to the boss. "Here is what you will do!"—said Nikolai Pavlovich. I sat down with ovarian transplant operations and pretty quickly learned how to perform them in 3–4 min each and a lot in a day. Large groups of operated rats were quickly recruited, and I learned how to take and evaluate vaginal smears, which recorded the stages of the estrous cycle in rats (equivalent to the menstrual cycle in women).

By the end of the 5th course, I already knew for sure that the proposed N.P. and I want to deal with it. After the 5th course, we had to divide into 3 streams—therapeutic, surgical and obstetric-gynecological. Since I worked with the Bilshovsky model, it was easy for me to make a choice—I went to the specialization in obstetrics and gynecology. And here again I became lucky. Our group in the 6th year of the was led by Ph.D. Ekaterina Timofeevna Vasilyeva, a wonderful teacher and person. At the Department of Obstetrics and Gynecology, she was a specialist in endocrinology and I learned a lot from her. She also introduced me to the pathologist Olga Ivanovna Topchieva, who worked at the Department of Obstetrics and Gynecology. Olga Ivanovna was a major specialist in the diagnosis of endometrial scrapings and knew the morphology of the ovaries very well. I climbed into her cramped office under the roof of the obstetric clinic and spent hours studying under the microscope preparations of ovarian tissue removed during the operation of wedge resection at Stein-Leventhal syndrome, normal ovaries removed during various surgeries, histological preparations of the endometrium, cervix and vagina, which Olga Ivanovna gave me the large quantities. What I did at the Institute of Oncology in the experiment was of practical importance for the clinic of obstetrics and gynecology. The knowledge that I received, sitting for hours in the libraries of the Institute of Oncology and the 1st LMI, the Library of the Academy of Sciences and swallowing a huge amount of literature on the physiology and pathology of the reproductive system, was firmly deposited in my head. I willingly shared them with my group mates, making reports that Ekaterina Timofeevna entrusted to me. She encouraged my passion and enthusiasm. I am deeply grateful to her for her support and always sympathetic criticism of my sometimes emotional speeches.

The Laboratory of Endocrinology of the Institute of Oncology was headed by a young, but already very famous scientist Vladimir M. Dilman. In those years, he was just over 40 years old, he was the author of a number of books, brilliant lecturer with his wide erudition and ability to connect the unconnected. His speeches at the meetings of the academic council or at scientific conferences have always gathered a large audience. The youth were fascinated by his ideas.

Having met and made friends with a cheerful and friendly Laboratory of Edocrinology, I also got to know Vladimir Mikhailovich himself, who was aware of what I was doing, and advised me to study the hormonal status of my rats with persistent estrus. I got some special exchange cages for rats, collected urine from them. Bilshovsky's model really turned out to be a very successful model of the Stein-Leventhal syndrome. In rats, hormonal disorders characteristic of accelerated aging rapidly developed, and the frequency of tumors was increased. When Dilman published his book entitled "Aging, Menopause and Cancer" I got copy of it, in which there is an inscription made by Vladimir Mikhailovich: "To Volodya—my comrade in science" and the date February 2, 1968. I was extremely proud of this inscription then, and even now, after so many years, I'm proud of her.

AM: when did you become interested in the scientific problem of aging? What was your path to gerontology?

VA: In 1964, while still a 3rd year student of the 1st Leningrad Medical Institute, I began to engage myself in scientific work at the Laboratory of Experimental Tumors of the N.N.Petrov Research Institute of Oncology, under the supervision of N.P. Napalkov. After graduating from the institute in 1968, I was accepted as postdoc at the Research Institute of

Oncology, after which I was enrolled in the staff of his laboratory. Under his guidance, I completed and in 1972 defended my Ph.D. dissertation on the topic "Blastomogenesis in rats with constant estrus." The work was able to show that in rats with impaired estrous function induced by ovarian autotransplantation into the tail after ovariectomy (a model of the Stein-Leventhal syndrome—sclerocystic ovary syndrome), hormonal and metabolic changes characteristic of natural ageing develop at a young age already. It was also found that carcinogen 20-methylcholanthrene also causes accelerated ageing in female rats, and when the two effects are combined, a sharp increase in carcinogenesis is observed. I performed the endocrinological part of the work in Dilman's laboratory. After defending my dissertation, I received an invitation from Dilman to continue our successful cooperation as a researcher in a new group (laboratory) of ageing mechanisms, which he organized based on the Institute of Experimental Medicine. I informed on this invitation my teacher N.P.Napalkov, who in 1970 went to work at the World Health Organization (WHO) and until 1974 headed the Oncology Unit at the WHO headquarters in Geneva. Nikolai Pavlovich recommend me to accept this proposal, motivating me to continue and deepen my work on the topic that has become the main one in my scientific life—carcinogenesis and ageing. I followed his advice and in 1973 I was elected as junior researcher. In 1976, the headquarters of the Laboratory of Ageing Mechanisms and its employees from the Institute of Experimental Medicine were transferred to the Research Institute of Oncology.

For 50 years my major research was focused on studying interaction between ageing and carcinogenesis, mechanisms and modifying factors of these processes, development of new means aimed at cancer and premature ageing prevention. Proliferative activity of a target tissue was established to be a critical factor determining age-associated sensitivity to carcinogenic agents of different nature (chemical, physical, biological), while other factors (xenobiotic metabolisms, interaction of proximal carcinogens with receptors, DNA repair, immune system activity, etc.) play a secondary modulating role.

(Fig. 5) In 1984 I defended DSc dissertation "Experimental study of the peculiarities of carcinogenesis in different age periods", scientific consultant of which was Napalkov, who since 1974 headed the

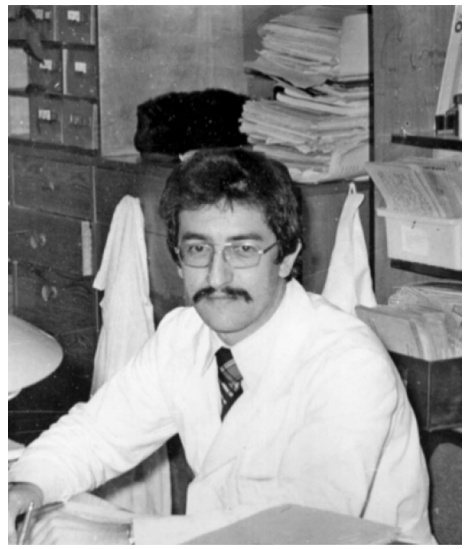

Fig. 5 Researcher at Laboratory of Experimental Tumors. 1980

Research Institute of Oncology. In 1987, in connection with the departure of N.P. Napalkov to Geneva as Assistant Director General of the WHO, at his suggestion I was elected as a head of the Laboratory of Experimental Tumors, the oldest experimental oncological laboratory in Russia, founded back in 1926 by N.N. Petrov. In 1998, the laboratory was renamed the Laboratory of Carcinogenesis and Ageing, and in 2000 it became a part of the newly organized Department of Carcinogenesis and Oncogerontology, of which I was elected as the head.

I traveled a lot for to participation in international meetings on oncology and gerontology, give lectures in the USA and European countries, China and Japan, short-term internships and carry out joint projects. Among them, a special place is occupied by cooperation with the International Agency for Research on Cancer (IARC) (Lyon, France), in which I was the co-chair of two international conferences (1983,1988). In 1991–92 I was a member of the IARC scholarship committee, carried out a number of joint scientific projects. In particular, in experiments with the synthetic analogue of thymidine, 5-bromodeoxyuridine, evidence was obtained for the sufficiency of isolated DNA damage in initiating carcinogenesis and premature aging (Napalkov et al., 1989, Anisimov, 1994).

As part of my collaboration with the WHO International Programme on Chemical Safety, I was the

co-coordinator of the project for the preparation of the guidelines "Principles for Evaluating Chemical Effects on the Aged Population" (Anisimov et al., 1993), published in Geneva. At the invitation of the United Nations Aging Program, since 1998, I participated in the work of the expert group on the preparation of the "Agenda for Research on World Aging in the 21st Century", which was adopted at the UN World Assembly on Aging in Madrid in 2002 and is widely known as the Madrid United Nations International Action Plan on Aging (Andrews et al., 2001). This work was continued in the preparation of the Agenda for Research on Aging in Europe in the 21st Century (2006) and the FUTURAGE project of the European Community, of which I have been a member of the Scientific Council since 2011.

From 1998 to 2009, at the invitation of the Director of the Max Planck Institute of Demographic Research (Rostock, Germany) J.W.Vaupel I participated as the co-coordinator in the implementation of the “Cancer Rates Over Age, Time, and Place” project. The project, along with the staff of the Max Planck Institute, involved a group of talented Russian mathematicians from the Institute of Control Sciences and the Institute of Computational Mathematics of the RAS, and Ulyanovsk State University. The result of this project was the development of new mathematical approaches to the analysis of the kinetics of the processes of carcinogenesis and aging, their computer modeling, which was reflected in a series of articles (more than 20) in leading international scientific journals, including Nature Reviews Cancer, Biogerontology, Experimental Gerontology, Mechanisms of Ageing & Development, and publication of the book “Gerontology in silico*:* the emergence of a new discipline. Mathematical models, data analysis and computational experiments” (Marchuk et al., 2007). In 2005–2007, at the invitation of the European Commission, I was the co-chair of the SENECA-2007 project, which finished in Warsaw in October 2007 with the European Conference "Cancer and Aging". The proceedings of this conference were published in a special issue of the journal "Mechanisms of Aging & Development" (Anisimov, 2009) (Fig. 6).

AM: gerontology as a science in Russia has deep roots; what major historical milestones would you single out?

VA: There are several key events in the history of Russian gerontology. First of all, there is a book by

Fig. 6 Head of Laboratory Carcinogenesis and Aging, 2000

Ilia Mechnikov «Etudes sur la nature humaine: Essai philosophie optimiste» (1903), where he introduced the term «gerontology» and put the cornerstone of the scientific discipline in biology and physiology of ageing. In the 1920’s of the twentieth century the works of N. A. Belov, A. A. Bogdanov, S. A. Voronov, I. I. Schmalhausen not only evoked interest towards the investigation in the processes of ageing per se, but also raised the question on the possible increase in the life span of animals and humans. One of the followers of the views of I.I. Mechnikov was an outstanding scientist V.G. Korenchevsky. After graduating from the Military Medical Academy in St. Petersburg in 1903, V.G. Korenchevsky worked at the medical faculty of Moscow University, where in 1909 he defended his dissertation for the degree of Doctor of Medicine. In 1910 he was invited by I.P. Pavlov to St. Petersburg to work in the Physiological Department of the Institute of Experimental Medicine and at the Department of Physiology of the Military Medical Academy. In 1919 V.G. Korenchevsky left Russia and spent many years in the UK. In 1945, he founded the Gerontological Laboratory in Oxford, organized the "Ageing Club" in Great Britain, which was renamed the "British Society for the Study of Ageing", and in 1950 in Liège, Belgium, opened the first international gerontological congress, becoming the founder of the International Association of Gerontology. In his fundamental monograph "Physiology and Pathology of Aging" (1961), he wrote: "The goal is not only to

prolong life, but also to strengthen it—to add life to years, not years to life, also to prevent the manifestation of deterioration, to alleviate pathological symptoms that are not necessarily associated with normal aging, as they are not detected in most rare cases of less pronounced pathological aging. Since presented as another, more perfect aging begins very early, it is realistic to see that physiologically normal processes change and, consequently, human life changes, and therefore, probably, in the future, a person will be being".

Another direction of life extension at the end of the nineteenth century, and at the beginning of the twentieth century, was the application of extracts of the sex glands. It was based on the obvious relationship between health and sexual activity, i.e., it was believed that stimulation of sexual function could lead to life extension. The emergence of interest in this method is associated with the name of the French physiologist C. Brown-Séquard (1818–1894), who injected himself (albeit after experiments on animals) of extracts from the testes of dogs and rabbits and claimed that he was 30 years younger. The method has been used to a limited extent. Subsequently, the Austrian surgeon O. Steinach (1861–1944) tried to stimulate the functions of the testes in a surgical way, including the transplantation of animal testes. The Russian surgeon (who worked mainly in France) S. Voronov (1866–1951) introduced the transplantation of the testes of great apes into widespread practice.

The effectiveness of such methods is mainly short-term, there is not enough data on the increase in lifespan because of their use, although they contained a rational grain and experiments on the use of tissue and hormonal therapy continue.

It should be noted that in Russia, interest in the use of gonadal extracts has resulted in serious research related to the possibility of regulating the aging process, the continuation of which at present time has led to the development of fairly effective methods for extending life.

The beginning of these studies can be attributed to the work of Professor A. Pehl. At the Institute of Opotherapy he created in St. Petersburg (a term used to denote the use of extracts of organs or the consumption of those organs on which they wanted to have a therapeutic effect, patients were injected with the drug spermine, isolated from seminal fluid of animals. Later at the beginning of the twentieth century under the direction and with the participation of S. I. Metalnikov studied the processes of aging in cell cultures of protozoa, and discussed the possibilities of regulating aging at the cellular level. A.V. Dogel, based on the results of his studies of the sympathetic nervous system, concluded that its degeneration in old age leads to a weakening of the trophic influences of the nervous system on tissues and metabolic disorders occur in them. N. A. Belov developed a systematic approach to the body, where an important role belongs to the regulatory interactions between its parts. E. Bauer believed that aging is a consequence of growth restriction, which in turn follows from the properties of protein molecules. The consequence of his ideas about the body as a non-equilibrium system was the importance of regulatory processes to maintain its stability. I. I. Schmalhausen, in his early work, also substantiated aging by processes that regulate growth. He believed that life can be extended by hormonal influences.

At the same time, an idea began to take shape of the important role of the central nervous system in the development of practically all pathologies (which arose largely as a response to R. Virchow's theory of cellular pathology). Its origin is associated with the works of I. M. Sechenov, who influenced S.P. Botkin, who, in turn, attracted I. P. Pavlov. His own research, as well as the work of his students (A. V. Tonkikh, L. A. Andreev, D. I. Soloveichik, A. D. Speransky, M. K. Petrova, etc.) laid the foundations for the idea of the body as a self-regulating system, about uneven changes in nervous regulation with age (Duplenko, 1985). M. K. Petrova, summarizing the results of many years of experiments of the Pavlov's school on the study of age-related physiology, concluded that the nervous system plays a leading role in the genesis of aging.

Another option for activating body functions and, accordingly, prolonging life, since the Middle Ages, was considered the use of human blood (it was considered a carrier of "vital heat"). At that time, attempts were also made to transfuse blood, but without success. On the other hand, at the beginning of the 1920 there was a popular theory that the immortality of unicellular organisms can be explained by their ability to conjugate with each other (in the modern sense, to carry out gene exchange). It was also believed that mobile blood elements could conjugate with each other. From this followed the logical conclusion that

the conjugation of blood cells from different people can lead to the extension of their life. The study of this possibility relates to the works of the Russian doctor, philosopher (the founder of systems theory) and revolutionary A.A. Bogdanov (1873–1928). Bogdanov believed that aging is caused by random disturbances in the activity of individual organs, which weaken individual links (parts of the system) of the body. Moreover, the weakest link is the most critical to such violations. Therefore, acting on it, you can effectively slow down the aging process. He considered the weakest link to be the subsystem that connects other body systems—the circulatory system. To influence it, he chose the exchange of blood between two people in order to carry out the conjugation of blood elements. To implement his concept, Bogdanov, being one of the prominent revolutionaries and having sufficient opportunities, founded the Institute of Blood Transfusion in 1926. But soon he died, carrying out an experiment on himself.

His student, the famous Soviet gerontologist, academician A.A. Bogomolets (1881–1946), having adopted his main ideas, modified them somewhat. In his opinion, the leading role in aging belongs not only to blood, but in general to the entire connective tissue of the body. He also modified the method of combating aging. It was the activation of connective tissue functions by introducing antibodies to this tissue. In this case, the decay of some cells as a result of the immune response leads to the activation of other cells of this tissue. In fact, this mechanism is similar to cell therapy, and like the latter, the effectiveness of the Bogomolets method for extending life is not at all obvious. Subsequently, this method was replaced by hormonal therapy and immunostimulation (Duplenko, 1985).

1930–40 s are characterized by the formation of the first gerontological schools in the USSR–Kiev, Kharkov (A. Bogomolets, D. Chebotarev, A. Nagorny, I. Bulankin), Leningrad (Z. Frenkel, E. Bauer, L.Shtern,V. G. Baranov). In 1957, on the initiative of Z. Frenkel, the country's first scientific and practical urban gerontological society was created in Leningrad. The same year, V. Alpatov organized the gerontological section of the Moscow Society of Naturalists. In 1958, the Research Institute of Gerontology of the USSR Academy of Medical Sciences was organized in Kiev. In 1963, the first All-Union Conference (Congress) on gerontology and geriatrics was held in Kiev, and the All-Union Scientific and Medical Society of Gerontologists and Geriatrics was established. In 1970, the first department of geriatrics in the country was opened at the Kiev Institute for the Postgraduate Medical Education. This period is characterized by the active development of gerontology and geriatrics both in Ukraine (D.F. Chebotarev, V.V. Frolkis, V.N. Nikitin), and in Russia and in other regions of the USSR—in Leningrad (I. Likhnitskaya, N. Kosinskaya, M.D. Alexandrova, V.M. Dilman), in Moscow (I.A. Arshavsky, N.M. Emanuel, B.F. Vanyushin, I.V. Davydovsky, L.V. Komarov), in Tbilisi (N.N. Kipshidze), in Kishinev (V.Kh. Anestiadi), in Minsk (T.L. Dubina), Novosibirsk (Yu.P. Nikitin). An important role was played by the seminars on the fundamental problems of aging organized in Moscow by N.M. Emanuel (1970–1984). The Group (Laboratory) of Mechanisms of Aging was created by V. M. Dilman in 1973 at the Institute of Experimental Medicine in Leningrad. Four All-Union Congresses on Gerontology and Geriatrics were held (1972-Kiev, 1976-Kiev, 1982-Kishinev, 1988-Tbilisi).

The collapse of the USSR led to the complete disintegration of all-Union structures and the almost complete cessation of systematic research on gerontology and geriatrics in the Russian Federation. Almost anew, both the association of specialists and research institutions of this profile had to be created. In Nizhny Novgorod in 1989, the first regional Gerontological Center was created, in St. Petersburg in 1994—the City Geriatric Center. In 1992 V.Kh. Khavinson founded St. Petersburg Institute of Bioregulation and Gerontology.

In close connection with the experimental-physiological direction of research on the connection between nervous activity and pathological processes (including those associated with aging), clinical studies developed. The main support of this direction was given by the outstanding Russian clinician G.F. Lang. Although the main topic of his research was hypertension (he is the author of the neurogenic theory of hypertension), he also paid attention to the mechanisms of atherosclerosis, diabetes, and other diseases. His student V.G. Baranov created the Leningrad school of endocrinologists. V.M. Dilman considered himself a disciple of G.F. Lang.

On the initiative of the Gerontological Society a scientific specialty «Gerontology and Geriatrics—medical and biological sciences» has been

introduced into the official list of specialties of the Russian Federation Ministry of Industry and Science in 2001. More 300 dissertations were defended on the new specialty since this event. It is worth noting that numerous researchers from Belarus, Ukraine, Kazakhstan, Kirgizia, Uzbekistan, Equador, Syria and Sweden held their dissertations at the Dissertation Councils in Russia. The award and mutual recognition of scientific degrees in different countries will foster education and training of researchers and finally, progress of gerontological studies. In 1990 in Kiev the first issue of the All-Union (further Ukrainian) Journal "Problems of Ageing and Longevity" saw the light.

Disintegration of the USSR resulted in the collapse of all former All-Union structures and actual closure of systematic studies in gerontology and geriatrics on the territory of the Russian Federation. Practically anew, we started looking for professionals and establishing research and practical institutions of this profile. The convocation of the Russian founding conference «Medical and social aspects in gerontology and geriatrics» organized by the St. Petersburg Scientific Gerontological Society in 1994 in St. Petersburg became a crucial moment in the modern history of Russian gerontology. Gerontological Society of the Russian Academy of Sciences (RAS) united leading scientists in gerontology and geriatrics around the country irrespective of their agency belonging. In 1996 Gerontological Society joined European Regional Branch of International Association of Gerontology (IAG). The same year at the premises of the Samara Regional Hospital for War Veterans there was opened a research institute «International Centre for the Problems of the Elderly». In 2007 the Institute was reorganized into geriatric center. Regular issuing of the information bulletin «Herald of the Gerontological Society of RAS» (www.gersociety.ru) started since 1996. The same year the first issue of the journal «Advances in Gerontology» (St. Petersburg) and the 1st issue of the journal «Psychology of Maturity and Ageing» (Moscow) were published. The Russian Congresses of Gerontologyt and Geriatrics were held in 1999 (Samara), 2003 (Moscow) and 2012 (Novosibirsk). In 2000, Saint Petersburg hosted the 2nd European Congress on Biogerontology with 300 participants from 33 countries. In J 2002 in Moscow there was held the 6th European Congress of Clinical Gerontology. The 6th European Congress of IAGG held on 5–7 July 2007 in St. Petersburg was an event of utmost importance for European and Russian gerontology. It gathered over 1500 participants from 70 countries of the world (Fig. 7).

Fig. 7 Head of Department of Carcinogenesis and Oncogerontology, 2017

The first regional gerontological center was set up in Nizhny Novgorod in 1989, then followed city geriatric center in St. Petersburg in 1994. In 1992 there was founded the Institute of Bioregulation and Gerontology in St.-Petersburg. Gerontological Society of the Russian Academy of Sciences united leading scientists in gerontology and geriatrics around the country irrespective of their agency belonging. In 1994 there was set up a Chair of Gerontology and Geriatrics at the Russian Medical Academy for Postgraduate Education in Moscow. In 1995, by the resolution of the Russian Health Ministry there was adopted a new medical specialty «physician-geriatrist». The same year the first issue of the Journal «Clinical Gerontology» (Moscow) and the manual for physicians «Practical Geriatrics» (Samara) saw the light. In 1998 Scientific council on gerontology and geriatrics of the RAMS and Russian Ministry of Health, international centers for older people on the basis of regional hospitals for war veterans in Ulyanovsk and Yaroslavl were set up and started their work. The first Russian Congress of Gerontologists and Geriatrists was held in 1999 in Samara. Resolution of the Russian Ministry of Health No. 297 of 28 July 1999 «On the improvement of medical assistance to old and senile citizens in the Russian Federation» played a significant role in the development of national geriatric service. This document provided for organization

of geriatric centers throughout the country, departments of medical and social assistance to the elderly within out-patient clinics and other important measures, including those on professional training. In 2000 Saint Petersburg hosted the 2nd European Congress on Biogerontology with 300 participants from 33 countries. Scientific Journal "Bulletin of Experimental Biology and Medicine" has a permanent section «Biogerontology». Since 2001 annual almanac «Gerontology and Geriatrics» has been issued by the Russian Research Institute of Gerontology.

As it was noted above, the first in the country Chair of Gerontology and Geriatrics was organized in 1970 on the basis of the Research Institute of Gerontology of the USSR Academy of Medical Sciences in Kiev. In 1994, the Chair of Gerontology started its work at the faculty for postgraduate education of the Moscow Medical Dentistry Institute. Later on, in 1995 it was re-subordinated to the Russian Medical Academy for Postgraduate Education. There were elaborated qualification requirements to physician geriatrist in 1995 with its second edition in 1998; statute of physician-geriatrist in 1996, with its second edition in 1998; qualification tests for specialty physician-geriatrist in 1996 with its second edition in 1998; uniform program for postgraduate training of physicians in gerontology and geriatrics (1997).

Along with the Department of Gerontology at the Russian Medical Academy for Postgraduate Education other institutions carry out postgraduate training in gerontology and geriatrics. Thus; I. M. Sechenov Moscow Medical Academy has the Department of Geriatrics and Hematology. Chair of Gerontology and Geriatrics of the I. I. Mechnikov North-Western Medical University conducts training in clinical gerontology and medical-social expertise, as well as rehabilitation of old and senile patients. Advancement cycles are held for geriatrists and therapists with subsequent examination for the certificate of specialist—geriatrist, as well as for paramedical personnel with further exam and award with the certificate of geriatric nurse. Chair researchers carry out substantial scientific and practical work on age-related pathology of cardio-vascular, gastro-intestinal and genitourinary systems. In St. Petersburg, the license for educational activity in the area of professional (postgraduate and additional) training in gerontology and geriatrics was granted also to the St. Petersburg Institute of Bioregulation and Gerontology. Chairs or courses in gerontology and geriatrics are open in medical higher schools in Ekaterinburg, Yoshkar-Ola, Nizhny Novgorod, Novosibirsk, Rostov-on-Don, Yaroslavl and other Russian cities. As for undergraduate training, there should be first of all noted a tremendous work carried out by the Department of Geriatrics of Samara State Medical University.

Demographic aspects are included into the course "Social politics", the issues of pensioners' rights protection—into the course "Legal coverage of social work", gender issues—into the course «Genderology and Feminology». According to the state educational standard, professional social work embraces population social protection, work with different social, age, gender and ethnic groups, individuals in need of social assistance and protection. Basic curricula include humanitarian, socio-economic and natural sciences.

This multidisciplinary training has an integrative character. Postgraduate courses for social workers in the field of gerontology are open in many national universities. A personnel training for social and medical gerontology is well organized in Republic Bashkortostan at the Institute for Postgraduate Studies of the Medical University, Bashkir State University, Medical colleges. During several years professional training in social gerontology is carried out at the M. V. Lomonosov Pomorsky State University in Arkhangelsk. Future progress in the education in geriatrics we will wait from The Institute of Postgraduate Medical Education established at 2014 at the North University. International schools in gerontology launched in Russia gave a new impulse to personnel training. Bearing in mind acute interest at the national level towards geriatric oncology and contribution of Russian gerontologists to the development of this issue, European school of oncology «Cancer in the elderly: achievements and prospects» was organized in November 2001 at the N. N. Blokhin Russian Cancer Research Center of the RAMS (Moscow). In 2002–2020 there were held 7 International schools on gerontology and geriatrics organized by the Satellite Centre of the International Institute on Ageing—UN, (Malta) in Saint Petersburg formed by INIA, St. Petersburg Institute of Bioregulation and Gerontology and City Geriatric Medical and Social Centre. Joint Finland—St. Petersburg projects «Personnel training for geriatric services» and «Development of geriatric services in St. Petersburg» may serve a vivid example

of international collaboration in professional training. Within the framework of these projects doctors, nurses and social workers take postgraduate course in gerontology in Finland (Turku and Tampere).

AM: how was the Russian Gerontological Society created?

VA: In 1992 in Moscow, on the initiative of MD, PhD L.D. Itkina, who worked as a geriatrician in the Central Polyclinic and was listed mainly as a freelance specialist in gerontology and geriatrics of the Ministry of Health and Medicine of the Russian Federation, the Moscow, which became interregional, Association "Gerontology and Geriatrics" was created. It mainly brings together practical doctors working in the field of geriatrics and in hospitals for veterans of the Great Patriotic War. Itkina was the president of this association. I. I. Likhnitskaya was the vice-president of the Association, and we expected that the main identified activities of this organization were seminars to improve the skills of doctors in the network in the field of geriatrics. In most economically (and scientifically) developed countries (USA, Great Britain, Italy, Germany, France and others), with geriatricians, that is, doctors, hospitals that cover elderly and senile people, large teams of scientists work in the field of aging biology, develop means of prevention of accelerated aging. Special attention paid to health manifestations of the elderly population. It is no coincidence that the executive committee of the International Association of Gerontologists includes three sections: the biology of aging, clinical gerontology (geriatrics) and the section of the behavioral and social sciences of aging. We are invited to follow just such a union of specialists of all those who are interested.

I introduced my friend the head physician of the St. Petersburg Medical and Social Geriatric Center E. Pushkova (the daughter of I. I. Likhnitsksya) to the director of the St. Petersburg Institute of Bioregulation and Gerontology V. Khavinson, we discussed the action plan, and things went well. In 1993, we published an appeal to medical doctors and specialists in gerontology and in the journal “Physician” and “Medical Newspaper” about the need to create a Russian Gerontological Society. We set the date for the founding conference—March 31, 1994, compiled lists of people who were engaged in gerontology and geriatrics—whom we knew personally from various conferences, and by publications, sent out invitations. V. Khavinson proposed to invite academician F. I. Komarov, as the patron of the conference, who was at that time Vice-President of the RAMS and actively supported research on peptide bioregulators. Ella Pushkova enlisted the support of Prof. A.V.Shabrov, the rector of the I. I. Mechnikov St. Petersburg Medical Academy. Of course, we invited L.D. Itkina. Academician Yu. P. Nikitin, director of the Research Institute of Therapy of the Siberian Branch of the RAMS, arrived from Novosibirsk. For the conference, R.Sh. Bakhtiyarov prepared an exhibition about Z. G. Frenkel in the Russian National (Public) Library, I organized an exhibition of publications by Russian scientists on gerontology and geriatrics, which we placed in the foyer of the conference hall of the boarding house where the event was held.

The conference went great. About 100 people came from seven cities of Russia. Academician of the RAMS Fedor I. Komarov opened the conference. They chose the board, which, at his suggestion, elected me as president, vice-presidents—academician of the RAMS Yu.P. Nikitin, V.Kh. Khavinson, a student of academician N.M. Emanuel L.K.Obukhova. E.S. Pushkova and a student of V.M.Dilman—E.V. Tsyrlina were elected as scientific secretaries of the Society (Fig. 8). I remember that Leonid Gavrilov (he moved with his wife Natalya from Moscow to the USA and works in the Illinois University, Chicago), referring to the organization of a gerontological society, asked why I need all this? I answered him that time had come, and asked a counter question: if not we, then who would do it? I did not receive an answer to my question.

There were many organizational problems. It was necessary to prepare and approve the Charter of the company, register and open a bank account. Bearing in mind that the All-Union Society of Gerontologists and Geriatricians was part of the system of scientific and medical societies under the patronage of the USSR Ministry of Health, we wrote a letter about the creation of the Gerontological Society to the Ministry of Health but received no answer. The Ministry of Health, which was headed at that time by General of the Military Medical Service E.A. Nechaev, he failed to find time for scientific societies. An appeal to the RAMS also remained unanswered. Valuable advice was given by F. I. Komarov, who advised me to apply to the Russian Academy of Sciences (RAS). The issue of creation was included in the program of meetings

Fig. 8 The first Council of Gerontological Society, St. Petersburg, 31 March, 1994

of the Bureau of the Branch of Physiology of the RAS. We prepared the necessary documents, arrived at the appointed time in Moscow. The meeting of the bureau of the Branch of Physiology, to which V. Kh. Khavinson, L. K. Obukhova, and myself were invited, passed without problems. I made a brief report on the state of gerontology in the country, the history of the issue and the founding conference held in March 1994. Academicians Yu.V.Natochin and P.V.Simonov supported the idea of organizing Gerontological Society at the RAS, no one expressed objections or doubts about the expediency of creating the Gerontological Society at the RAS, and the decision was made.

Without a doubt, the creation of the Gerontological Society, which brought together the leading gerontologists and geriatricians of the country, regardless of their departmental affiliation, was a turning point in the recent history of Russian gerontology, which gave impetus to the development of gerontology in the country. In 1994, the Department of Gerontology and Geriatrics of the Russian Medical Academy of Postgraduate Education in Moscow was established. In 1995, by order of the Ministry of Health of the Russian Federation, a new medical specialty "geriatrics" was approved, the first issue of the journal "Clinical Gerontology" (Moscow) and a manual for physicians "Practical Geriatrics" (Samara) were published. In 1996, on the basis of the Samara Regional Hospital for War Veterans, the Research Institute "International Center for the Problems of the Elderly" was opened. Since 1996, the Herald of the Gerontological Society of the RAS began to appear regularly. At the December 2022 250th issue of this information bulletin was published. In the Department of Clinical Medicine of the RAMS, elections were held for the first time in the specialty "geriatrics" (V. S. Gasilin). In August 1997, at the XVI World Congress of Gerontology in Adelaide (Australia), the Gerontological Society was admitted to the International Association of Gerontology and Geriatrics" (IAGG) and the 1st issue of the journal "Psychology of Maturity and Aging" (Moscow), the abstract collection "Gerontology and Geriatrics" began publishing. In 1998, the Interdepartmental Scientific Council for Gerontology and Geriatrics of the RAMS and the Ministry of Health of the Russian Federation was created and began to work, and International Centers for the Affairs of the Elderly in Ulyanovsk and Yaroslavl were organized based on regional hospitals for war veterans. In 1999, the 1st Russian Congress of Gerontologists and Geriatricians took place in Samara. This event stimulated interest to gerontology and geriatrics and in few years more than 30 new regional branches of Gerontological Society were created over the country. Among most active regional branches, it is worthy to note Arkhangelsk, Kursk, Nizhny-Novgorod, Syktyvkar, Yakutsk, Jaroslavl, Volgograd, Samara, Novosibirsk. Great number of excellent conferences including international were organized, inducing involvement of new members of Society in active work.

In recent years, the Russian National Scientific and Practical Gerontological Center at the N.I.Pirogov

Russian Medical University, headed by Prof. O.N.Tkacheva, who is the main freelance specialist-geriatrician of the Ministry of Health of the Russian Federation and the President of the Russian Association of Gerontology and Geriatrics.

AM: which of your research do you consider the most important?

VA: My main scientific activity relates to the study of patterns and mechanisms of the relationship between ontogenesis and carcinogenesis. In this regard, I am developing the directions founded by my teachers—N. P. Napalkov and V. M. Dilman.

My first studies were devoted to the study of the features of the occurrence of tumors in conditions of disturbed hormonal balance in the body. In experiments on mice and rats it was found that exposure to various chemical carcinogenic agents is accompanied by an accelerated development in the body of animals of hormonal and metabolic disorders that are characteristic of natural aging and contribute to the implementation of the process of carcinogenesis. Induction in female rats of the syndrome of permanent estrus, which is also accompanied by a number of signs of accelerated aging, had a promoting effect on the development of neoplasms (Anisimov. 1972). These observations became the key to all my subsequent scientific activity.

I experimentally established the main patterns of the modifying influence of age on the body's sensitivity to the action of various exogenous and endogenous carcinogenic agents, which underlie the mechanism of the age-related increase in the frequency of malignant neoplasms. The role of age-related dynamics of the activity of enzyme systems that metabolize carcinogens, DNA repair systems, proliferative activity of target tissues in changes in their sensitivity to the initiating action of carcinogenic agents of various nature (chemical, radiation, hormonal) has been identified and characterized. It has been shown that hormonal-metabolic and immunological disorders that develop in the body with aging contribute to the promotion of carcinogenesis. It has been established that with age, cells accumulate in body tissues that have undergone accidental exposure to carcinogenic agents and have passed, in accordance with the multi-stage model of carcinogenesis, more than one stage on the way to its complete malignancy. Exposure of these cells to late-stage carcinogens and tumor promoters in older animals invariably induces neoplasms in target tissues at a higher rate and with shorter latency than in younger animals. The results of these studies were summarized by me in the chapter "Carcinogenesis and Aging", published in 1983 by Academic Press in the 40th volume of "Advances in Cancer Research", then in 1987 in the USA in the two-volumes "Carcinogenesis and Aging" CRC Press, which became the recognized guide to the problem. In recent years, I have formulated the concept of accelerated aging syndrome that develops in the body under the influence of various carcinogenic environmental factors. Later I published the books "Cancer in the Elderly" (St. Petersburg, 2006) and the manual for physicians "Oncogerontology" (St. Petersburg, 2017) and chapters devoted to this problem in the manuals on geriatric oncology published in the USA and Great Britain (1992, 1994, 1998, 2012, 2017, 2018, 2020).

In a series of fundamental studies with the synthetic analogue of thymidine 5-bromodeoxyuridine, I, in collaboration with A.Ya. Likhachev, N.P. Napalkov and L. Tomatis, established for the first time that isolated DNA damage is sufficient to initiate a tumor process and accelerate the aging process in vivo. The results obtained are essential arguments in support of the mutational theory of carcinogenesis and the mutational theory of aging (Napalkov et al. 1989; Anisimov 1994).

It is shown that, on completion of sexual maturity, the level of estrogens required to suppress hemicastration-induced compensatory ovarian hypertrophy is raised in female rats, as age advances. This suggests an age-associated elevation of the threshold of sensitivity of the tonic center of the hypothalamo-pituitary complex to inhibition by estrogens. It is shown experimentally that such factors as the age-connected decline in the hypothalamic level of catecholamines, decreased estrogen uptake by the anterior and mediobasal hypothalamus, diminished activity of the pineal gland and a shift toward predominant utilization of free fatty acids for energy supply play a key role in the mechanism of this hypothalamic phenomenon. Some external environmental factors (constant lighting, carcinogenic chemicals, transplantable tumors) serve to raise the hypothalamic threshold of sensitivity, too. Hypothalamic sensitivity to estrogen inhibition was normalized in old rats by administration of L-dopa, phenformin, dilantin, polypeptide pineal extract and succinic acid. Resumption of estrous cyclicity in old rats with constant estrus due

to administration of some drugs provides another proof in support of the hypothesis on the regulatory nature of ageing and, particularly, the mechanism of age-associated switching-off of reproductive function (Dilman and Anisimov, 1979).

Developing the ideas of academician N.M. Emanuel about the kinetic approach to the study of aging processes, in 1981 I proposed a new classification of geroprotectors according to the type of aging deceleration they cause and the mechanism of their action, which ultimately determines the nature of the development of age-related pathology in the population, including cancer. Studies of the kinetic parameters of the aging of populations and the development of tumors in their representatives made it possible to establish the fundamentally important fact of a direct correlation between the type of retardation of aging caused in it by one or another geroprotector and its effect on the occurrence of neoplasms (Anisimov 1983, 1987, 2003, 2018). It has been shown that substances that delay the onset of aging of the population as a whole to a later age increase the latent period of tumor development without significantly changing the frequency of their occurrence. Agents that slow down the rate of population aging reduce the frequency and increase the latent period of development of neoplasms, while under the influence of agents that accelerate the aging of the population, an increase in the incidence of tumors and a number of other diseases is naturally observed. These experimental data were confirmed in epidemiological studies in the USA, Germany, Denmark and Sweden, published in 2000–2018.

It was found that the use of drugs that normalize the hormonal, metabolic and immunological changes that develop with aging and, thereby, slow down the implementation of the genetic program of aging, can give the most significant geroprotective and tumor-preventing effect. For the first time, the ability of antidiabetic biguanides (phenformin, buformin and metformin) to increase life span and inhibit the development of spontaneous and chemical carcinogen-induced tumors in animals was revealed, which gave impetus to the development of a whole area of modern gerontology and oncology—the study of the role of the insulin-insulin-like growth factor-1 system. glucose in the mechanisms of aging and carcinogenesis, the use of metformin for the prevention of tumor development and premature human aging (Anisimov 1980, 1983, 2003,2005, 2017; Anisimov, Bartke, 2013; Golubev, Anisimov, 2019).

Fundamentally important were the results of studying the role of the pineal gland in tumor growth and the aging process. In joint experiments with V.Kh. Khavinson and V.G. Morozov we established a high geroprotective, anticarcinogenic and antitumor activity of pineal gland peptides. In our experiments with I.A.Vinogradova and D.Sh.Beniashvili it was shown that maintaining under constant light/dark regimen and exposure to low-frequency electromagnetic fields accelerated aging and promoted the development of neoplasms, while light deprivation, the administration of the pineal hormone melatonin or pineal peptides had the opposite effect. For the first time, melatonin's ability to inhibit the development of cancers of the breast, colon, cervix, vagina, lung, skin, and soft tissues has been revealed in my laboratory. In a series of experiments, the role of clock genes as factors determining the development of neoplasms under various light conditions was revealed. The results of these studies formed the basis of the evidence base for the IARC to recognize light pollution carcinogenic to humans (Anisimov et al., 2020).

In close cooperation with academician V. P. Skulachev, the geroprotective and anticarcinogenic properties of potent scavenger of free radicals SkQ1 preparation were studied in our laboratory. At a very low dose of 5 nmol/kg, it significantly reduced age-related mortality in SHR mice, especially in the first half of their life. At the same time, morbidity and mortality from infections were significantly reduced, and the aging of the reproductive system was slowed down. At the same time, the drug had no effect on the development of spontaneous breast tumors in SHR mice and in HER2/neu transgenic mice (Skulachev et al., 2009). Our results were confirmed by studies of SkQ1 mice of different strains at Moscow State University, Sweden, and the USA, podospore fungi, and branched crustaceans. A feature of the geroprotective action of SkQ1 is that the maximum life span does not increase so much as its quality improves (Skulachev et al., 2009).

The technique for studying the geroprotective properties of pharmacological preparations in mice, developed and tested in our laboratory, has received international recognition and is included in the manual "Biological aging: methods and protocols" published in 2007 and republished in 2013 in the USA

(Anisimov et al., 2007, 2013). In total, throughout my scientific career, I participated in tests for the geroprotective and anticarcinogenic effects of more than 30 different substances, including various antioxidants, melatonin, rapamycin, SkQ1, enterosorbents, immunomodulators, and peptides from various tissues.

We had fruitful collaboration with Prof. G. M. Zharinov from the Russian Scientific Center for Radiology and Surgical Technologies, who created a unique database on the life expectancy of people of creative professions (artists, musicians, artists, writers, athletes, scientists), numbering more than a half million people listed in Wikipedia (Anisimov and Zharinov, 2006).

It was shown that the mean age-at-death among writers and poets was significantly lower than that in visual artists, musicians, and scientists whereas scientists lived longer than representatives of other categories. Women lived longer than men of any studied categories. It was shown that the mean age-of-death gradually but irregularly increased since the first century A.C. until the twentieth century in any professional cohort. Visual artists-men in twentieth century lived longer than in previous historical periods. Scientists both females and males in twentieth century lived longer than those of the nineteenth century. The first five places of long-livers among men belong to Nobel prize winners (78.8 years.), academicians (72.7 years.) and corresponding members of the RAS (71.7 years.), conductors (71.1 years.) and scientists (71.0 years.). Rock-musicians, author's song singers and poets lived less other categories (43.6; 53.6 and 61.6 years. respectively). Among women leading long-livers were conductors (83.2 years.), harp-players (80.9 years.), academicians of the RAS (80.3 years.), clavecin-players (79.1 years.) and violinists (78.2 years.). Among women, less lived rock-musicians (37.6 years.), author's songs singers (51.4), horns and woodwind instruments players (59.0 years.). Relative number of nonagenarians (90+) was much higher among women as compared to men. The values were as 43.76% of harp-players, 33,33% of conductors, 29.17% of architects, 20% of violinists and viola-players and 18.99% sculptors for women, and 16.67% of Nobel prize winners, 12.12% of conductors, 7.51% of academicians, 7,44% of violinists, and 7,0% of scientists survived 90+ years among men. Centenarians were 8.33% of academicians and architects, 6.25% of harp-players and 4.22% of writers-poets among women, and only 0.76% of pianists, 0.45% of scientists and 0.42% of violinists were centenarians among men. Our data agree with the opinion that high intellect and education directly correlate with longer life span and longevity (Anisimov, Zharinov, 2013, Anisimov et al., 2020).

I am the author of more than 800 scientific papers, including 20 monographs and manuals published both in Russia and abroad (Germany, USA, France, Switzerland, etc.), I have 12 patents for inventions. I am one of the most cited Russian scientists (RSCI: 15,248 citations; Hirsch index h = 56; WoS = 43; IC = 4327, h = 36; SCOPUS citation index: h = 41; Google scholar citation index: h = 61).

I was invited by the United Nations Aging Program to serve on the international group of experts preparing the "Agenda for Research on World Aging in the 21st Century", which formed the basis of the International Plan of Action adopted at the UN World Assembly in 2002 in Madrid, and then also in the preparation of the research program on aging for the European Region. I was repeatedly invited as an expert by the WHO Programme on Chemical Safety, the IARC was organizer and chair for a lot of conferences and symposia on the problems of "cancer and aging", "light regimen, melatonin and cancer", "pineal gland and cancer" at many major international and domestic congresses on oncology and gerontology in recent years, was president of the 2nd European Congress of Biogerontology (St. Petersburg, 2000) and president of the 6th European Congress of Gerontology (St. Petersburg, 2007). Since 1997 I have been a member of the Council of the IAGG and a member of the Council of its European branch, a member of the Scientific Council of the FUTURAGE Program of the European Community.

On my initiative, in 1994, the Gerontological Society (GS) was established at the RAS, of which I was the president until December 2022 and currently I am the honorary president of the GS RAS. I am also the editor-in-chief of the Russian journal "Advances in Gerontology" and, it version in English, and the newsletter Herald of the Gerontological Society of the Russian Academy of Sciences", deputy editor-in-chief of the journal "Clinical Gerontology", a member of the editorial boards of several international journals.

I was repeatedly awarded the State Scientific Scholarship of the Russian Federation (1994–1996; 1997–1999; 2000–2002), I received grants from the President of the Russian Federation for state support of leading scientific schools (2003–2005, 2006–2007 and 2012–2014). In 1997 I was awarded the medal of P.L. Kapitsa "To the author of a scientific discovery", in 2001—awarded the diploma V.Kh.Vasilenko of the Presidium of the RAMS, in 2002 was awarded the medal "For Services to Domestic Health Care" by the Ministry of Health of the Russian Federation, in 2003—a diploma and a medal of the Interdepartmental Scientific Council for Gerontology and Geriatrics of the RAMS and Ministry of Health of the Russian Federation for the contribution to the development of gerontology and geriatrics in the Russian Federation in 1999–2003, in 2005—the P. Erlich medal and the diploma "For special merits in preventive and social medicine" by the European Academy of Natural and Social Sciences (Hannover, Germany). In 2009—awarded diploma of the State Duma of the Federal Assembly of the Russian Federation, in 2011—a medal and an honorary diploma of the European Branch of the International Association of Gerontology and Geriatrics "For outstanding achievements in the study of aging and contribution to the development of gerontological science in Europe" in the nomination "biology of aging"

AM: who are the most significant teachers on your scientific path?

VA: My main teachers were the outstanding Russian scientists, academician of the RAMS N.P. Napalkov and Prof. V.M. Dilman. Many years of cooperation with following Russian scientists gave me a lot: A.Ya. Likhachev, M.A. Zabezhinsky, K.P. Pozharisski, V.A.Alexandrov,V.B. Okulov, E.S. Pushkova, V.Kh. Khavinson, I.G. Popovich, O.N. Mikhailova, A.M.Olovnikov, V.P.Skulachev, M.N.Kondrashova, B.F. Vanyushin, A.G.Golubev, M.N.Ostroumova, L.M. Berstein, A.M. Michalsky, A.V.Arutyunyan, A.A.Romanyukha, I.A.Vinogradova, V.S.Turusov, as well as cooperation with leading gerontologists from Ukraine: V.V. Bezrukov, G.M. Butenko, L.A. Bondarenko; Austria: A.V.Sidorenko; Canada: T.Fulop; Denmark: S.I.S.Rattan; France: Y.Touitou; Germany D. Gupta;Great Britain: R.Peto; Italy: C.Franceschi; Israel: I.N.Zusman; USA: L.Balducci, L.S.Birnbaum, M.V. Blagosklonny, D.K.Ingram, R.S.Reiter, J.M.Rice, G.S.Roth, J.M.Ward, J.W.Vaupel, J. Vijg, A.Yu.Yakovlev, A.I.Yashin; Switzerland: W.Pierpaoli, and many others whom I was lucky to work and communicate with, and from whom I learned a lot.

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