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## Nucleosides, Nucleotides and Nucleic Acids

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## Biographical Sketch

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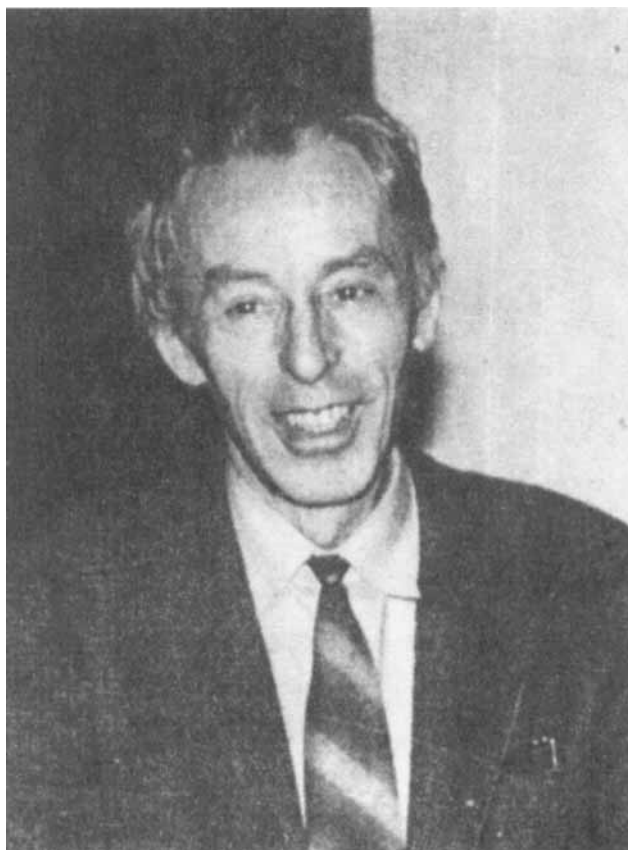
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#### BIOGRAPHICAL SKETCH



**Professor Alexander Krayevsky PhD, (1932-1999)**

On August 24, 1999, Russian science suffered the loss of an outstanding scientist and a great man, professor Alexander Krayevsky, an esteemed member of the Russian Academy of Sciences. He was referred to by those who knew him well in Russia as Sasha and by those who knew him well abroad as Alex. He was a renowned scientist who made innumerable contributions to the fields of nucleic acid chemistry and the chemistry of other biologically active compounds such as alkaloids, fatty acids and lipids. Many cutting-edge areas of



Photo 2.

Maryla Krayevsky (Alex's mother) was sent into exile in 1937; Anton Krayevsky (Alex's father) was executed in 1937.

bioorganic chemistry and molecular biology bear notable signs of his contributions. In his lifetime, he published more than 250 works, and these publications tell us more about his accomplishments than any memoir. But what the scientific publications do not tell us about Alex is the remarkable story of his difficult life, and his extraordinary ability to overcome adversity.

Alex was born in Moscow in 1932 during a challenging time for Russia, a time of political repression under Stalin's rule. This repression had a severe impact on his family. His parents (photo 2), Polish immigrants, were professional communists who worked for Communist International (Comintern). In 1937, Alex's father Anton (Vladislav) Krayevsky, a member of the Governing Board of Comintern, was executed. Shortly thereafter, his mother Maryla was arrested and sent to exile to the Vorkuta region in the Far North, where she remained until 1945. Alex's friend Inga Poletaeva remembers: "Sasha had mixed feelings when talking about



Photo 3.

Alex with his nanny, Marusya Markova, who saved him from Stalin's orphanage in 1937. Marusya stayed with Alex family till her death in 1989 at the age of 86.

the profession of his parents. He appreciated a joke popular in the later years of communism among intellectuals: three characteristics are common among Soviet people – intelligence, integrity, and Communist Party membership – and any two of these are incompatible with the third. I remember his opinion that his parents' emotional infatuation with socialist and communist ideas prevented them from understanding the real meaning of the events happening in their adopted country. Sasha used to say, 'There is one thing I would never become - a communist'."

After his parents were arrested, Alex - at five years old - was ordered to be sent to a special orphanage school for children of political prisoners. Instead, at the last moment he was rescued by his nanny, Marusya Markova (photo 3), who took him to a small village 200 km away from Moscow. This is where Alex went to primary and secondary school and spent the

years during World War II. Bronislav Gursky, Alex's friend, remembers, "We went to school in the second shift<sup>1</sup>. The school was a one-story building that resembled a barracks, which was typical for the North around that time. There were not enough classrooms, and often a teacher had to teach two different grade levels and/or subjects in the same room at the same time. I was amazed by Sasha's vast knowledge of literature and poetry. He recited them so naturally, as though he knew the characters personally. He understood the smallest details of the situations described by the author. I could only regret that I did not understand the interpersonal relationships in the story as well as the story teller (Alex)." In 1945, when the exile of Alex's mother was over Alex was able to join his mother in the Far North, where they remained until the Rehabilitation<sup>2</sup> that followed Stalin's death.

In 1950, Alex entered the Lomonosov Institute of Fine Chemical Technology in Moscow. After graduating from the Institute, Alex worked for four years at the All-Union Institute of Medicinal and Aromatic Plants located in a small village near Moscow. The Institute was home to many chemists, botanists, and pharmacologists. While Alex was there, he played an instrumental role in establishing an experimental production facility. His scientific research during that time was focused on isolating and studying alkaloids. He remembered this period of his life very fondly, and was very proud of his achievements during this time. His friend from the Institute, A. Belikov, remembers, "Sasha had a great memory, his mind was unencumbered with debris, and he was unbelievably personable. He never complained about his problems, although there were many, including: his inability to return to and work in Moscow<sup>3</sup>, to find housing, and to clear his father's name."

Four years later, in 1959, Alex returned to the Institute of Fine Chemical Technology in Moscow, where he worked productively on the synthesis of unsaturated fatty acids. In 1963, he defended his PhD thesis under the supervision of Professor Nicolai Preobrazhensky. After several years of successful research and teaching at the Institute, Alex realized the promise and importance of developing the field of molecular biology, a branch of science relatively unknown at that time. He accepted a position at the Engelhardt Institute of Molecular Biology, the institution to which he would devote the rest of his life. In the beginning of this most fruitful period of his career, he studied the catalysis of peptide bond formation at the ribosome peptidyl transferase center. His research included development of methods for the synthesis of amino acid and peptide derivatives of nucleotides and RNA, as well as the design

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<sup>1</sup> Because space and teachers were scarce during this time, the school day was broken up into two shifts, morning and afternoon, to accommodate all of the children.

<sup>2</sup> After Stalin's death, when Khrushchev came to power, he set a new policy of "Rehabilitation" or "Reform Communism" in an attempt to humanize the Soviet system

<sup>3</sup> Because his father was executed for political reasons, Alex's family ties limited his freedom to live and work in Moscow.

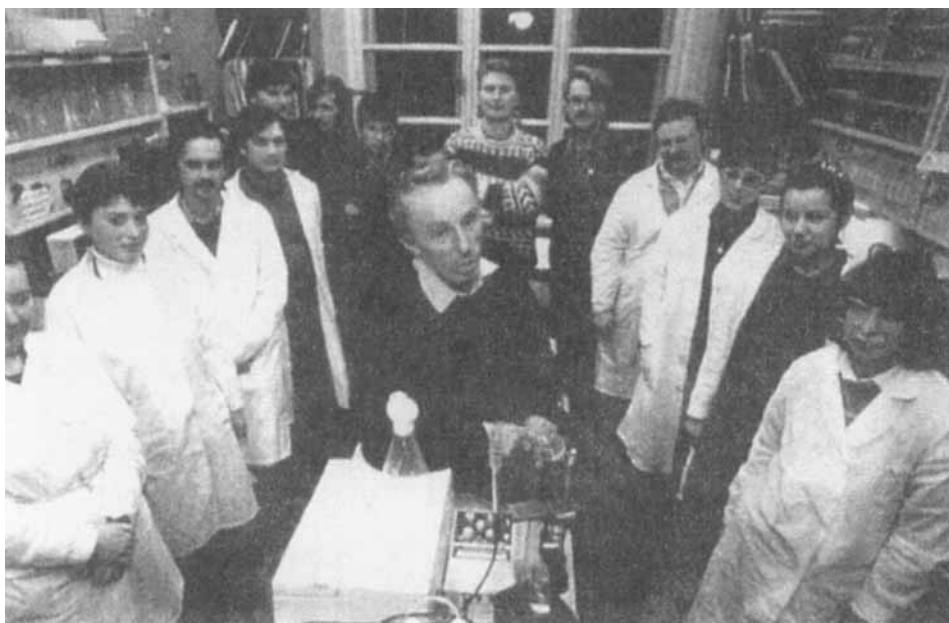


Photo 4.

Alex in his laboratory in 1990s, Engelhardt Institute of Molecular Biology, Russian Academy of Sciences, Moscow.

of experimental systems for studying the active center of ribosomes. As a result of his research, Alex proposed an original model for studying the peptidyl transferase center of the ribosome that used minimal donors and acceptors functioning as aminoacyl- and peptidyl-tRNA. For this work, Alex received awards from the Academies of Science of the USSR and Czechoslovakia. This research also became the basis of his thesis for his Doctor of Sciences degree<sup>4</sup>. In 1985, Alex was appointed the Head of the Laboratory of Chemical and Biological Analysis of Biopolymers and Cells (photo 4). In 1990, he was elected a Corresponding Member of the Russian Academy of Sciences and in 1994, he became a Full Member. Then in 1995, he was appointed the Deputy Director of the Institute.

The last 20 years of his life were devoted to studying the biosynthesis of nucleic acids. His research focused on the function of human, bacterial, and viral DNA polymerases. A large number of substrate analogues for these enzymes were designed, synthesized, and tested

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<sup>4</sup> This degree is the next higher level degree after PhD, and is awarded to a select group within a field for significant contributions in the field, such as development of an original theory, new concept, or entirely novel area of research.



Photo 5.

Alex, his grandson Sasha, Dr Kyo Watanabe, and Dr Hikoya Hayatsu at the 3-th International Engelhardt Conference on Molecular Biology, 1997.

under Alex's direction. Based on the obtained results, Alex developed principles of selective inhibition of DNA polymerases and retroviral reverse transcriptases. In turn, these principles were used in his lab to design several antiviral drugs. The fight against AIDS, which came to the international forefront in the mid-1980s, demanded collaboration from scientists working across many different fields. Alex united the efforts of the chemists and enzymologists in his lab with virologists, clinical researchers and chemical technologists from many other Russian and international institutions to lead this research. Despite the difficult conditions of post-Soviet Russia, Alex established a manufacturing facility and technology for Azidothymidine. His most recent achievement was the development of a novel inhibitor of HIV replication, phosphazid (Nicavir). In 1999, phosphazid was approved for the treatment of AIDS patients across Russia.

Alex worked in many institutions abroad and made friends around the world (photos 5-7). Many of his international colleagues abroad quickly recognized and appreciated his talent, extraordinary abilities, and friendly nature, and they became his friends. Alex had long-lasting scientific contacts with Prof. E. DeClercq and Prof. J. Balzarini (Rega Institute, Belgium),



Photo 6.

Alex and Dr. Knud Niehaus ( Max-Plank-Institute, Berlin) at the 4-th International Engelhardt Conference on Molecular Biology, 1999.

Prof. K. Watanabe and Prof. B. Polsky (Sloan-Kettering Cancer Research Center, USA), Prof. Ya. Gluzman (Cyanamid Company, USA), Prof. W. Prusoff and Prof. Y.C. Cheng (Yale University, USA), Prof. K.Nierhaus (Max-Plank Institute, Germany), Prof. J.L. Imbach and Prof. G. Gosselin (Université de Sciences et Techniques, France), Prof. M. Wainberg (McGill AIDS Centre, Jewish General Hospital, Canada), Prof. N. Johansson (Medivir AB, Sweeden),



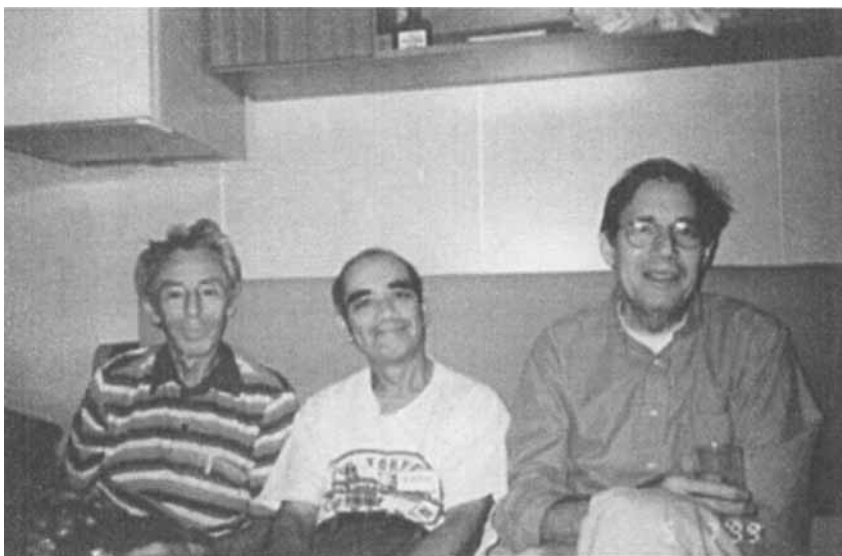


Photo 7.

Alex, Dr Watanabe, and Dr G. Ellestad at the 4-th International Engelhardt Conference on Molecular Biology, 1999.

Prof. S. Roberts (Liverpool University, England) and many others. From the memoir of Dr. Knud Nierhaus: "I liked him from the very first moment when we met about 25 years ago. We had a common interest in the ribosomal peptidyl transferase center, and his view as a chemist was complementary to my biochemical approach. I learned a lot from him, and his excellence as a chemist and his modest and friendly character made him many friends, and I am happy that I was one of them. I mourn with you for this great and incorruptible man who had an unerring judgment".

Alex is not only remembered for his research, the dozens of students who received their PhD degrees under his direction and those who worked in his lab remember him as an inspiring and involved mentor (photo 8). Almost every afternoon, all the members of the lab would gather with Alex in his office for tea so that everyone could take a break from their busy day. Sometimes, they would discuss their research and other times they would just unwind before going back to work. No matter how busy everyone was, the tradition never ceased. Dimitri Semizarov, former student of Alex, remembers: "He made my first experience in research the most memorable. His intense passion for science and his incredible personality inspired me to devote myself to science. He created a warm atmosphere in the lab that stimulated everyone to work closely together, which is uncommon in today's research community, where



Photo 8.

Alex is lecturing using the pointer sized for the Soviet-era demands.

competition is prevalent. Although he was a great mentor, my greatest times with him were spent talking about literature, politics, and life in general, as well as him telling me stories from his life”.

Alex was an amazing personality, the standard for honesty, scrupulousness, and virtue. He always had time for those who needed help, advice, or support. He lived simply and was indifferent to the material side of life. In a field where some only want acknowledgment, he openly shared his knowledge, ideas, and scientific plans with everyone. In addition to being a great scientist, he also loved literature, deeply understood music, wrote poetry and poetic

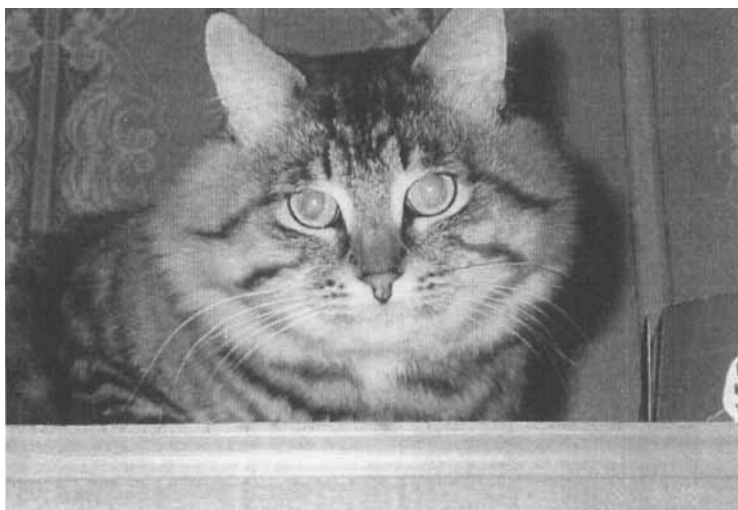


Photo 9.

Alex's cat Mishka. This image is quite familiar to many who knew Alex.

letters to friends, and had a very special sense of humor. His beloved cat Mishka (photo 9) was featured on many of his holiday postcards, and was a prominent image in many science labs around the world. When Alex was asked about his health which was generally poor, he would reply with his favorite saying, "The good parts aren't sick, bad ones I don't feel sorry for". He was very perceptive with people. After meeting someone, if he said that the person had "lively eyes", it meant that the person intrigued and interested him. His unique skill of discerning and recognizing people at first sight never left him.

Alex's house was always crowded with his close friends. While Alex was working at the Moscow Institute of Chemical Technology, he initiated the Society of Chemistry Enthusiasts for his fellow scientists. The Society meetings were held at his house on the last Friday of each month. Typically, the meeting would begin with a presentation related to chemistry or biology, but quite often expand to include music, poetry, or literature. The presentations were always followed by a discussion amongst the members. Alex's wife and long-time partner, Elena Krayevsky (photo 10), who died shortly before him, was the gracious host. She actively participated in the discussions and served a homemade meal to the entire group after the discussion. These meetings attracted and united a very diverse group of people who worked in many different areas of science. Of course, the founder (Alex) was the heart and soul of the Society, his opinion was critical to every one of its members. Although it may be hard to



Photo 10.

Alex and his wife Elena Krayevsky in 1953 and 45 years later.

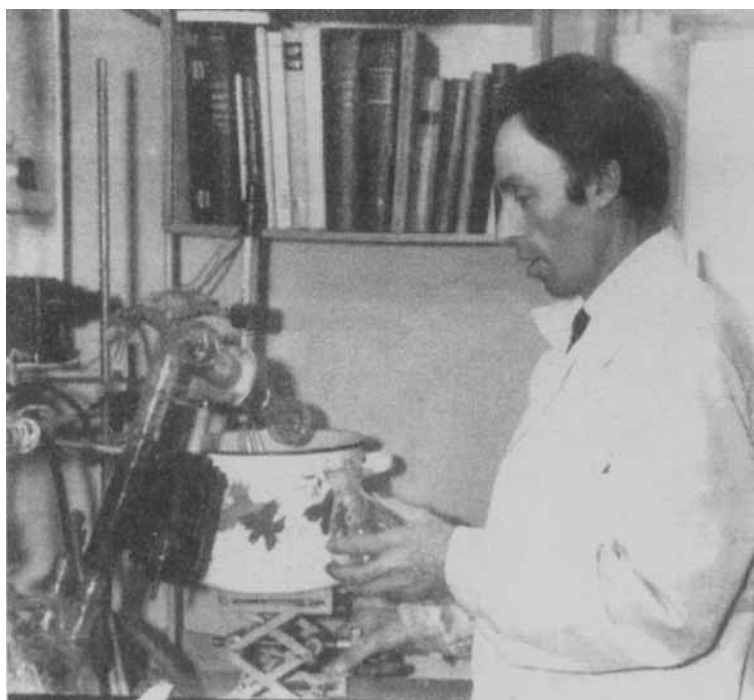


Photo 11.

Alex's greatest pleasure was experimental work in which he was very skillful and creative, 1980s.

believe, the meetings of this Society were held consistently for almost 40 years in the Krayevsky home.

He was happiest when he was conducting an experiment, and loudly singing a wild mixture of songs from all times and origins, from arias to folk ballads (photo 11). When Alex left us, he was still at the peak of his creativity, and never ceased working until his last day. As we say in Russia, "until his last day, he did not let the pen drop from his hand". On his desk, he left behind a draft of a presentation for an upcoming conference and several unfinished papers on which he had been working on. His death has left everyone who was touched by him with a feeling of irreversible loss. Family, friends, students, and colleagues of Alex are sincerely grateful to all of the people who sent an outpouring of letters to the Institute to commemorate him (photo 12).

Dr. Alexander Krayevsky lived during a very turbulent time in his country. Despite the unstable time, a time of contradictions between words and reality, Alex was able to realize

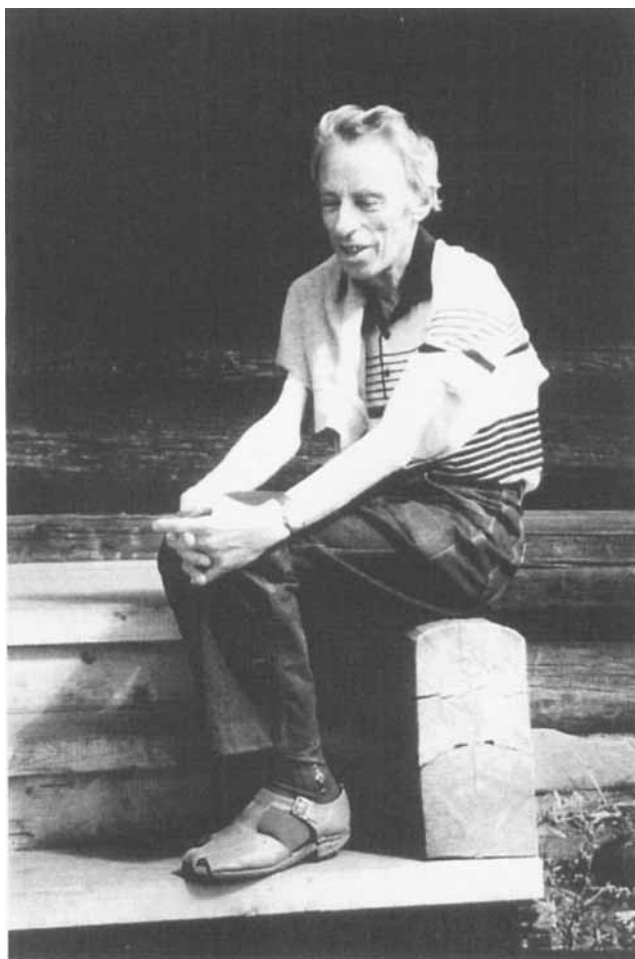


Photo 12.  
Alex's last photograph, July 1999.

and reveal his unique and important talents. Alex is survived by his son Slava and his grandson Sasha. He has left a deep impression that will never be forgotten.

On behalf of Dr. A. Krayevsky's colleagues and friends,  
Marina Kukhanova, Ph.D. and  
Natalia Tarussova, Ph.D  
Institute of Molecular Biology,  
Russian Academy of Sciences