

HISTORY OF OUR CONTRIBUTION TO BIOCHEMISTRY

Selected Pages of the History of Soviet Biochemistry

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I was inspired to write this paper by the conference at Moscow State University dedicated to the 100th anniversary of Academician Sergey Severin's birth (December 21, 2001).

My first remembrances of Sergey Severin are related to the opening ceremony of the memorial plaque dedicated to his teacher, Vladimir Gulevich, who died in 1933. Sergey Severin opened this plaque right at the entrance to the building at the corner of Bolshaya Nikitskaya and Mokhovaya streets where Gulevich was the Head of the Department of Biochemistry. (After Gulevich's death Professor Boris Zbarsky (1885–1954) became the Head of the Department of Biochemistry and Analytical Chemistry at the 1st Medical Institute. He was also the Head of the Laboratory at the Lenin Mausoleum. In 1952 Zbarsky was arrested, and he was released only in 1954.)

I was working at this department as an assistant for five years (from 1936 to 1941) and some people working with Gulevich still remained there. I will never forget Assistant Professor N. F. Tolkachevskaya, who discovered anserine together with Gulevich [1]. The Department of Biochemistry moved to the building at Sadovaya street and the memorial plaque dedicated to Gulevich was lost. However, in the 70s Sergey Severin opened a new memorial plaque dedicated to Gulevich at the building of the Zoological Museum of Moscow State University.

My personal acquaintance with Academician Severin began in 1955 during our participation in the first Soviet delegation to the III International Biochemical Congress in Brussels. Academician Alexander Oparin (1894–1980), Director of the Bach Institute of Biochemistry, Academy of Sciences of the USSR, the author of the well-known book "The Origin of Life on the Earth" was the Head of the Soviet delegation. I was a member of that delegation. It was our first experience in the West, and we all were very impressed.

Participation in the VI International Biochemical Congress in New York (1964) was another important event of that period. The Organizers paid respect to our country by inviting Academician Severin to give a plenary lecture, which was focused on the mainstream of his studies, investigation of biological activity of imidazole derivatives [2]. Academician Severin not only extended

Gulevich studies but also deepened them. Severin found tight links of imidazole containing dipeptides, anserine and carnosine, with processes of skeletal muscle contraction and also with reaction of substrate and oxidative phosphorylation.

In that plenary lecture Sergey Severin introduced results of his younger colleague, Vladimir Skulachev, on mechanisms of oxidative phosphorylation. Skulachev also presented a separate paper at the VI Biochemical Congress [3]. In contrast to Paul Boyer [4], Skulachev proposed that during oxidative phosphorylation the amino group of an adenine moiety of ADP plays a central role in ATP synthesis. The audience was impressed by Skulachev's presentation. Later Mitchell proposed the chemiosmotic hypothesis of energy coupling [5], and mechanisms of oxidative phosphorylation were revised.

After the Congress Britton Chance, one of the leading American biochemists and a high class yachtsman, invited many participants of the Congress to visit his "farm" in the countryside. Sergey Severin invited me and one female member of the Bulgarian delegation to join his car. Young participants (including V. Skulachev) took the train and Chance picked them up at the railway station as the driver of his "farm car". Women and older guests settled in large (two floor) wooden house and young guests were distributed over the territory of Chance's "rancho" in tents and sleeping bags. At Chance's rancho there was a seminar on current problems of bioenergetics after which we came back to New York.

The Soviet delegation also visited the Center of Biological Studies in Boston. Although members of the Soviet delegation were strongly recommended to walk in New York only in groups, A. Petrova (1906–2001, Doctor of Sciences in Biology, coworker of Ya. Parnas and B. Stepanenko) and I visited the highest building in New York.

The Congress granted each participant with 100 USD for subsistence. However, members of the Soviet delegation could not use this money even for chemicals. According to tough instructions of that time we had to give money to the Head of the Soviet delegation professor S. Mardashev (Head of Gulevich's Department of Biochemistry after B. Zbarsky; he died in 1974) and he passed this money to the Soviet government.

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In 1969 the Soviet delegation participated in the VI FEBS Congress. At that time the USSR and Spain had no diplomatic relations due to the Franco regime and we had to go to Spain semi-legally (via France). After the Congress in Madrid participants were invited to a bullfight and the male part of our delegation visited this rough show. Being in Madrid it was impossible to ignore the famous Prado museum keeping paintings of such great artists as El-Greco, Tizian, etc. On Madrid square I saw a famous sculpture of Don Quixote and Sancho Panza. Besides Madrid, our delegation visited the old Spanish city Toledo where El-Greco used to live. This city is also known for its hand-made metal goods.

After the congress participants visited a large cemetery located inside the mountain where Franco supporters and Spanish revolutionaries were buried. We were impressed by this magnificent construction.

At the end of 1958 the Laboratory of Physiological Chemistry, Academy of Sciences of the USSR was closed. This laboratory remained after the arrest and death (in 1949) of academician Ya. Parnas, distinguished biochemist who made substantial contribution in studies of phospho-carbohydrate and nucleic acid metabolism and who discovered glycogen phosphorylation. During the period from 1949 to 1958 Professor B. Stepanenko (Doctor of Sciences in Chemistry, expert in carbohydrate metabolism, died in 1981) was the head of this laboratory. Part of this laboratory was taken to Bach Institute of Biochemistry, another part joined the Institute of Biological and Medical Chemistry, Academy of Medical Sciences of the USSR. In the group of Professor Stepanenko, I was sent to the Bach Institute of Biochemistry, where the Carbohydrate Laboratory (with Professor Stepanenko as its Head) was organized.

In 1960 Professor D. Mikhlin (a pupil and follower of A. Bach) who studied redox processes in plants died and I won a competition for position of the head of Laboratory of Biological Oxidation, a direct heritage of A. Bach. I employed R. Zvyagilskaya as my PhD student. She graduated from the department of Academician A. Belozersky, School of Biology of Moscow State University. (A. Belozersky, Vice-President of Academy of Sciences of the USSR, Head of the Department of Physico-Chemical Biology of this Academy, died in 1972.) She was one of the top students but Belozersky preferred to work with male colleagues. In that period I established tight cooperation with the laboratory of Professor M. Meysel (1901-1987; Head of the Department of Functional Cytology of Microorganisms at the Institute of Microbiology, Academy of Sciences of the USSR). His laboratory studied morphology of yeast mitochondria [6].

One of the major goals of the Laboratory of Biological Oxidation consisted in isolation of yeast mitochondria. R. Zvyagilskaya and I developed the method for isolation of intact mitochondria from the yeast

Endomyces magnusii. It was important to compare energy metabolism of yeast mitochondria with that of higher eukaryotes. In 1963 Zvyagilskaya successfully defended her PhD thesis and in 1973 we published a monograph on biochemistry of yeast mitochondria [7]. However, in spite of these evident achievements I had no opportunity not offer her the position of Senior Researcher, but a lucky chance helped me.

In 1977 there was an International Symposium on Membrane Bioenergetics on Spezia island (Greece). The Soviet delegation consisted of five members: Vice-President of Academy of Sciences of the USSR Yu. Ovchinnikov (1934-1988; after Belozersky he was the Head of the Department of Physico-Chemical Biology of Academy of Sciences of the USSR), V. Skulachev with his wife, Galya Tikhonova (research officer of Bach Institute of Biochemistry who died in car crash in 1982) and myself.

When we arrived to Athens our Embassy in Greece warmly met us and invited us to the concert of Krasnoyarsk Ensemble of Folk Dance which was on tour in Greece. It was a well organized performance and Yu. Ovchinnikov (who lived in Krasnoyarsk in his childhood) presented a large bunch of roses to the Ensemble. It was a wonderful evening.

All major schools of bioenergetics were involved to the symposium on Spezia island. Ernster (Sweden), Skulachev (USSR), Papa, Azzone (Italy), Ovchinnikov (USSR), Azzi, Shatz (Austria), Griffiths (UK), Klingenberg (Germany), and others presented their papers. My presentation was about peculiarities of energy metabolism in yeast *Endomyces magnusii*.

I asked Skulachev to join me in my efforts to persuade Ovchinnikov to find a possibility to establish position of Senior Researcher for R. Zvyagilskaya. During one breakfast Ovchinnikov agreed with our arguments and after our returning to Moscow Zvyagilskaya received the requested position.

At the end of our stay on Spezia island Ya. Ovchinnikov damaged his leg during a session of underwater swimming. He had constantly high temperature and we had problems with him on our return trip to Moscow.

I should say that the Laboratory of Biological Oxidation of Bach Institute of Biochemistry studied not only yeast energy metabolism. My colleagues K. Sholz and I. Gorskaya (she died in a car crash in 1993) studied oxidative phosphorylation of rat liver mitochondria using specific inhibitors of respiratory chain and coupling (e.g., rotenone, antimycin A, oligomycin, and some membrane active polypeptides). Studies of membrane active polypeptides, gramicidin C and melittin, revealed that uncoupling effect of these inhibitors is realized via increase of mitochondrial membrane permeability for monovalent cations. This effect of gramicidin C was called the "canalogenic effect" [8]. K. Sholz developed kinetic methods for studies of coupling between proton

translocation and ATPase of H^+ -ATPase complex. Using these methods and various inhibitors we found [9] the absence of tight coupling between H^+ -translocase and ATPase activities, which was proposed by P. Mitchell. Sholz et al. determined stoichiometry of proton translocation via H^+ -ATPase [10]. In rat liver mitochondria the stoichiometry value was 3.3 H^+ per ATP.

In 1982 Bach Committee invited me to give the 38th Bach Lecture. The topic of my lecture was "Energy metabolism in yeast". Five years later Academician Severin, the Chairman of Bach Committee of Academy of Sciences of the USSR, nominated Zvyagilskaya and me for the Bach Prize due to our contribution to studies of Biochemistry of yeast mitochondria. We received this Prize at the Annual General Meeting of the Academy of Sciences of the USSR on 17th of March 1988.

I am deeply grateful to the great man and scientist academician Sergey Severin for his constant support of me and my studies.

REFERENCES

1. Tolkachevskaya, N. F. (1929) *Z. Physiol. Chem.*, **185**, 28.
2. Severin, S. E. (1964) *Proc. Plenary Sessions Sixth Int. Congr. Biochem.*, pp. 1-17.
3. Skulachev, V. P. (1964) *Sixth Int. Congr. Biochem.*, **32**, 758.
4. Boyer, P. (1963) *Science*, **141**, 1147.
5. Mitchell, P. (1966) *Chemiosmotic Coupling Oxidative and Photosynthetic Phosphorylation*, Glenn Research.
6. Meysel, M. N. (1950) *Functional Morphology of Yeast Organisms* [in Russian], Academic Press of the USSR, Moscow.
7. Kotelnikova, A. V., and Zvyagilskaya, R. A. (1973) *Biochemistry of Yeast Mitochondria* [in Russian], Nauka, Moscow.
8. Sholz, K. F., Aliverdieva, D., and Kotelnikova, A. V. (1983) *Abst. III Soviet-Swedish Symp. on Biological Membranes*.
9. Gorskaya, I. A., Sholz, K. F., Moreva, S. A., and Kotelnikova, A. V. (1979) *Biokhimiya*, **44**, 975-982.
10. Sholz, K., Gorskaya, I., and Kotelnikova, A. (1983) *Eur. J. Biochem.*, **196**, 129-134.