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Comparative Genomics, Genosystematics, and the Scientific School of A.S. Antonov

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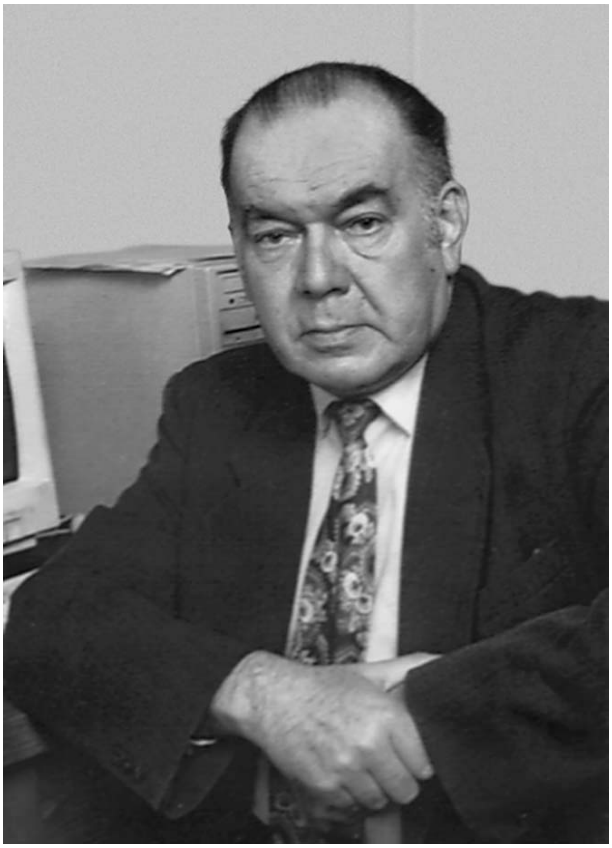

Andrei Sergeevich Antonov (1936–2008).

Some more than a year has passed since the memorial scientific conference was organized by the Belozersky Institute for Physicochemical Biology, the Faculty of Biology of Moscow State University, and the Kharkevich Institute for Information Transmission Problems of the Russian Academy of Sciences [1]. The conference commemorated the 50th anniversary of the research area conceived by A.N. Belozersky and his direct followers [2–5]. Not an average field in science deserves such the occasion. This was the case: the school of Belozersky indeed pioneered the onset of comparative and evolutionary genomics, which have become leading areas in science, and by no means continues overflowed by current knowledge influx. The honorees of the conference, A.S. Spirin, the full member, and B.F. Vanyushin, the corresponding member of the Russian Academy of Sciences, explained the youth about the legacy of then conceived ideas for modern top research [3, 4]. The journal *Biokhimiya* (Biochemistry) dedicated a special issue to cover the event. Andrei Sergeevich Antonov was in the heart of organizing the celebration. He was inviting speakers and authors, compiling the scientific program, settling the accommodation of conference guests, chairing at the round table and tallying up the glorious achievements of the half-century history of genosystematics [5]. A.S. Antonov was already aware of his incurable disease. Today we look back to remember this great scientist, and have an important, although grievous, reason to revisit the events of the past within the context of modern science.

The Antonov's main interest in science had always been the comparative studies of genomes, which evolved through pioneer works on DNA base composition into the modern area with state-of-the-art techniques. The ideology of comparative and evolutionary studies of DNA has emerged before the advent of sequencing methods when no gene was known. It was created in great anticipation of the future perspectives for the widest range of biological disciplines, which began to fully unfold only recently, in the age of complete genome sequencing. This amazing transformation in fact took place within the lifetime of its creators.

In the 20th century the experimental biology broke through traditional descriptive science into trying to understand the fundamental forces driving the living cell. Modern comparative genomics carries this creative nomothetic impulse compensating a relative simplicity of experiments with a more sophisticated deduction. It generates new knowledge in at least four branches of molecular biology. As the seminal work [2] predicted the basic genetic information flow from DNA through RNA, comparative genomics reveals the mechanisms of the genetic machinery. Armed with the computer, it identifies genes, gene families, gene paralogs, regulatory structures, transcriptomes and regulons, annotates gene structurally and functionally. The clusters of orthologous groups of proteins (COGs) [6] become meaningful and predictive only when they are built using phylogenetic criteria [7]. Entire metabolic pathways can now be compared. Comparative studies play en ever increasing role in modern biology. Experimental proof of the *in silico* predictions still requires more effort and funding, while bioinformatic tools became truly public. Their use in various fields of genomics allowed functional studies of the evolution of genetic systems during phylogenesis and ontogenesis, e.g. the emergence of the immune system in vertebrates or carcinogenesis [8].

The second field, which deeply adopted the comparative methodology, is structural studies. The secondary structure of large biopolymers, like ribosomal RNA, was predicted with amazing accuracy on the basis of co-variation of RNA sites in different organisms [9, 10] long before the X-ray structural data arrived. Even today crystallographic studies do not explain the functional importance of some evolutionary conserved regions, which directs and fuels future research.

The third field is genetic identification of biological objects. It has well established in practice outside academia: in forensic science, express diagnostics of pathogens in medicine and epidemiology (including the yet to be developed early detection of biohazard agents), affiliation of paternity, genetic barcoding of important agricultural objects, identification of spawning and feeding fish stocks (the major subject of international fisheries conventions and the establishment of exclusive economic zones), ingredient identification in complex food products, discovering illegal ingredients and tracing poaching sites, and many others. DNA diagnostic methods offer efficient solutions in distinguishing naturally breeding populations without their field monitoring, recognition of cryptic species at any stage of development including larvae. Large-scale barcoding of life is now a perspective [11, 12]. With the evolution of technologies, smallest bits of biological material will suffice for taxonomic profiling of various biocommunities, and the methods will become affordable to a wide research audience. For the first time ecologists will be able to study prokaryotic and eukaryotic biodiversity in nature, rather than in culture.

Finally, the forth endeavor is the ambitious attempt to unveil the past, recover the course of the natural history on earth, reconstruct the phylogenetic tree of life based on its genetic record and apply this knowledge to understand the fundamental traits of molecular and morphological evolution.

Long before the term *genomics,* was coined, A.S. Antonov considered these four branches of comparative genomics in unity [13, 14] as different facets of genosystematics [15], which he saw necessary to describe versatile life in the mirror of the genotype. Definitely, he was fond of the fourth one the most. A follower of A.N. Belozersky and A.S. Spirin, A.S. Antonov devoted his life to the establishment and promotion of genosystematics. Strikingly unlike today, in the past 1960s and 1970s this emerging science was not valued for its scientific merit but faced massive resistance in the minds of the classic school, particularly in botany. A.S. Antonov appeared to be the one to sally forth in the defense of the new paradigm. He explains, disputes, gives scholarly and public lectures, writes popular papers and books, directs student and postgraduate works – all with his exuberant energy. With the rhetoric talent and scientific ultimatism, A.S. Antonov always excited the audience and was long remembered by the opponents.

A.N. Belozersky and A.S. Antonov edited and issued the first volume on comparative genomics in the USSR [16], which also appeared among the first in the world literature. The second volume came out [17], and the succession of other books followed, up to his last remarkable monograph *Plant Genosystematics* [18]. After the decease of A.N. Belozersky, A.S. Antonov takes over the Department of Evolutionary Biochemistry at the Institute for Physicochemical Biology (at that time, Interfaculty Special Research Laboratory) of Moscow State University and becomes the leader of a large national school of thought. Although there was no concept of "principal organization" in academia, the Department became the standard maker in national research and collaborated with more than fifty institutions from around the Soviet Union. As an organizer of science, A.S. Antonov was exceptionally open-minded in the support of younger initiatives. Research in the Department spanned the phylogenetic studies of butterflies, sea urchins, yarrows, whitefishes, bacteria and human races. Concurrent projects included studies of the chloroplast genome organization, distribution of repeated and unique DNA in vertebrate and invertebrate genomes, DNA synthesis during mammalian meiosis and the effect of polyploidy on the rate of molecular evolution. The interests reached from the level of speciation to the relationships of phyla. With his authority and administrative powers, A.S. Antonov could have easily had cut the subjects to focus on one hot problem and succeed immediately. He possessed a gift to recognize the promise in science, which his colleagues testified every time they moved into a field or adopted a technique recommended by A.S. Antonov long before. Forcing on the nearest key problem is the practice in today's science, which gradually turns into a production of knowledge. A.S. Antonov, however, cherished and promoted the diversity of individual interests and supported the young talents in understanding the importance of the academic and multidisciplinary approach to advance scientific frontiers. Shall that not be, we would have had another comparative and evolutionary genomics in the country and another scientific school with another human core.

Like A.N. Belozersky, his teacher, who "consigned" branches of molecular biology to his followers and "kept" genosystematics, A.S. Antonov "kept" only large-scale genosystematics of land plants. That was the time of the advent of RNA sequencing, a state-of-the-art technique in the mid-1980s. His research team published a series of works, which retain their impact today. It was the criticism of the molecular clock hypothesis [19], establishment of the monophyly of gnetophytes and gymnosperms [20, 21], which refuted the old textbook hypothesis of the anthophyte origin of angiosperms, the proof of the closest relationship between hornwort mosses and higher plants [22] together with other remarkable achievements in bryophyte phylogenetics, comparative studies of different genes' information value in phylogenetics [20, 23], etc.

During recent years A.S. Antonov critically revisited the ideology of the comparative approach in molecular phylogenetics warning against weakly supported hasty inferences and outlined future development of the theoretical framework for genome comparisons [14, 18, 23].

Andrey S. Antonov never avoided public and educational activities. For many years he worked with the journal *Molekulyarnaya biologiya* (Molecular Biology) as an author, reviewer, and translator. Five doctorate and about fifty candidate dissertations were successfully defended under his supervision, his learners work actively today across the country and abroad, his scientific school has been officially acknowledged as leading and received funding from different sources. His last project was the establishment of a professional oriented laboratory at the Faculty of Biology – a unified platform for education and science to support student works and independent researchers in genomics from and outside the University. Along with scientific legacy, Antonov left us the lessons of leadership. A responsive guide, he was intolerant to narrow-mindedness in its every display, always faced it and never traded for diplomacy.

In our hearts Andrei S. Antonov will live as a prominent figure in science and remarkable personality, brilliant polemist and narrator, whose mental horizons and personal charisma fascinated people around him. In the testimony of deep respect to Andrei S. Antonov, this issue is dedicated to him by his friends, learners, and followers.

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