
OBITUARY

***In memoriam* Andrei Darievich Mirzabekov
(1937–2003)**



On July 13, passed away Andrei Darievich Mirzabekov, an outstanding molecular biologist, Full Member of the Russian Academy of Sciences, Director of the Engelhardt Institute of Molecular Biology and former Editor-in-Chief of this Journal.

Born October 19, 1937 in Baku, Andrei was brought to Moscow in 1943 by his parents. When he was still a student of the Lomonosov Institute of Fine Chemical Technology, Mirzabekov started working as a laboratory assistant in the Institute of Radiation and Physicochemical Biology founded by W.A. Engelhardt (now Engelhardt Institute of Molecular Biology, EIMB); ever since, his life in science has been inseparably linked with this Institute. In EIMB he got his Ph.D. and D.Sc. degrees, as a staff member of EIMB in the early seventies he went to train and work in the

leading laboratories of the world (Cambridge, Pasadena, Harvard), which was not the least thing in his making as a scientist.

In 1973 Mirzabekov was appointed Head of the Lab of Chromosome Molecular Organization, in 1984 he succeeded to the deceased W.A. Engelhardt as the Director of EIMB, and headed the Institute till the last day of his life.

A.D. Mirzabekov authored more than 300 published works and inventions; his achievements were acknowledged with several State awards, and the Engelhardt Gold Medal from the Russian Academy of Sciences (for chromatin studies, 1999). In 1981 he was elected Corresponding Member of the RAS, and became Full Member in 1987. From 1988 to 1990 he was the Academician Secretary of the Division of Biochemistry, Biophysics, and Chemistry of Bioactive

Compounds of the RAS. He actively collaborated with A.A. Bayev in launching the National Program on the Human Genome, he was Deputy Chairman of the Scientific Council of this program (1989–1994), and of course participated in the International Human Genome Project, being Vice President of HUGO (1989–1993) and heading its regional office in Moscow. His works have gained worldwide recognition, and he was a member of the Academies of several countries.

For more than a quarter of a century A.D. Mirzabekov led his research team, and in parallel, for over 15 years he headed the Chair of Molecular Biophysics at the Moscow Physical and Technological Institute; many of his students and followers have grown into well-known scientists.

As the Director of EIMB, Mirzabekov urged the staff to concentrate efforts on the most important problems of molecular biology and biotechnology, and helped organize new research teams that could obtain domestic and foreign grants; the latter, in its turn, has helped the Institute survive the dramatic cuts in budget financing of the Russian science.

A.D. Mirzabekov was a member of Editorial Boards of several respected Russian and international Journals, and Editor-in-Chief of *Molecular Biology* for a decade (1986–1996).

The scientific interests of A.D. Mirzabekov have for many years been focused on the structural-functional study of tRNA, chromatin, and DNA-protein complexes, as well as on developing methods for examining the disposition of proteins on DNA and identifying the nucleotide–amino acid interactions in nucleosomes. Together with researchers from various labs of the Institute he studied the interaction of low-molecular-weight ligands with DNA at its minor and major grooves, using his method of DNA modification with dimethyl sulfate. In a joint work with W. Gilbert and A. Maxam to locate the contacts of the *lac* repressor with operator DNA, a technique was conceived whereby one could determine the consecutive disposition of adenylic and guanylic residues; this had been the basis for further development of the sequencing approach that led Maxam and Gilbert to the Nobel Prize.

For several times, A.D. Mirzabekov abruptly changed the direction of his research, intuitively choosing the most promising trends and seeking his own way. He has established nucleosome organization at high resolution, including that for particular active and repressed genes; determined for a number of genes the detailed dynamics of chromatin decondensation due to consecutive removal of histones; revealed the changes in chromatin condensation with distance and suppression of transcription by repressed genome regions; simultaneously located on DNA and

identified the promoter interaction sites of RNA polymerase and the H4 and H5 residues in nucleosomes and chromatin. These original data gave birth to novel notions on chromatin superstructure and conformational dynamics of chromatin and the RNA polymerase–promoter complex, as well as confirmed the earlier hypothesis of Mirzabekov and Rich about the mechanism of DNA bending caused by lateral neutralization of its phosphates by proteins. These studies were done within the Mirzabekov's general strategy: detailed location of proteins and their particular sites on DNA in the entire genome and isolated nucleoproteins, using his method of DNA–protein crosslinking combined with gene engineering and immunochemical techniques.

Since 1988, A.D. Mirzabekov focused his efforts on theoretically substantiating, developing, and implementing a novel approach to the analysis of biological macromolecules, first of all DNA and proteins: the biochip technology. For a long time, this direction was thought to hold little promise; most of the prominent scientists in the nineties did not believe it would be possible to miniaturize the biochemical assays and combine on a minute surface a vast set of probes that could independently and specifically interact with the query substance. And it took the inexhaustible energy of Andrei Darievich, his confidence in overcoming any difficulties, his remarkable organizer abilities to find the ways and means of realizing his ideas in those hard times for Russian science. His new research team was one of the first to implement the biological microchip production technology. The first basic patent for biochips with gel pads belongs to EIMB. In 1993 Mirzabekov was invited to continue the work in the Argonne National Laboratory. He advanced a basically novel setup of joint research, namely, creation of two identical labs in his Institute in Moscow and in the USA. This idea proved to be very fruitful and ensured rapid theoretical and technological progress. In a short time the team published dozens of papers in renowned journals and secured a score of international patents. The biochips thus developed are broadly used in research, and some diagnostic versions (such as one for drug resistance in the causative agent of tuberculosis) are now attested by the Ministry of Health. A special product is the “generic” biochip of 4096 cells with the exhaustive set of hexanucleotides, which allows analysis of any nucleic acid sequences, detection of hereditary mutations and genomic polymorphism, assessment of the specificity of DNA interaction with proteins and drugs.

A.D. Mirzabekov really could find original solutions to seemingly insoluble problems. His famous response to expressed doubts in the feasibility of a task was, “Don't tell us why this is impossible to do; had it been easy, it would have already been done.”

With support from the Presidium of RAS and the Academy of Medical Sciences, Mirzabekov established the Biochip Technology Sharing Center at EIMB to make this powerful tool available to the broad community engaged in basic and applied research.

Andrei Darievich was a many-sided man. He read a great lot, he was at home in classical literature, poetry, and keen on philosophy (though saying that the researcher should experiment rather than philosophize). He was a good skier, mountaineer, swimmer; at quite an adult age he mastered the really circus feat

of riding a unicycle, which made him very famous among American colleagues.

Remarkable was Andrei Darievich's stamina and courage in his terminal disease. He was fully aware of what he was facing and what little time he had; he never complained, he did not ask for sympathy, he only wanted to work. Despite dwindling strength, to his very last day he discussed the research matters with his co-workers, edited manuscripts, settled organizational questions—did everything for his cause to live after him.

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