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**FINAL REPORT  
OF THE  
NATIONAL ACADEMY OF SCIENCES-  
ACADEMY OF SCIENCES OF THE USSR  
WORKSHOP ON STRUCTURE OF THE EUCARYOTIC GENOME  
AND REGULATION OF ITS EXPRESSION  
OCTOBER 16-27, 1989  
TBILISI, GEORGIA, USSR**

**MASTER** *EP*

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## I. EXECUTIVE SUMMARY

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From October 16 to 27, 1989, in accordance with the Agreement on Scientific Cooperation Between the National Academy of Sciences (NAS) and the Academy of Sciences of the USSR (ASUSSR), a scientific workshop was held in Tbilisi, Georgia, USSR, entitled "Workshop on the Structure of the Eucaryotic Genome and Regulation of its Expression." The workshop was organized by Dr. Alexander Rich (NAS), Massachusetts Institute of Technology; Dr. Gary Felsenfeld (NAS), National Institutes of Health; Academician Andrei Mirzabekov (ASUSSR), Engelhardt Institute of Molecular Biology; and Dr. M. Zaalishvili, Institute of Molecular Biology and Biological Physics, Academy of Sciences of the Georgian SSR (ASGSSR). Originally Dr. Rich was the American Chair, but due to health complications, Dr. Felsenfeld served instead.

The workshop itself took place October 16-20, and was followed by one week of visits to various institutes in Leningrad and in the Moscow region. Included were visits to the Institute of Cytology in Leningrad; the Institute of Molecular Biology, Institute of Molecular Genetics, and Institute of Crystallography in Moscow; and the Institute of Protein Research in Pushchino.

The workshop was organized as a follow-up to a 1975 bilateral symposium in Kiev which focused on the structure and function of nucleic acids. The first bilateral USSR-USA Symposium was organized by Dr. Rich; Alexei Bayev, Institute of Molecular Biology, ASUSSR; and G. Matsuka, Institute of Molecular Biology and Genetics, Academy of Sciences of the Ukrainian SSR (ASUKSSR).

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## II. COMMENTARY ON THE WORKSHOP AND SITE VISITS

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### A. Scientific Appraisal of the Workshop

Immediately following the workshop, the NAS requested scientific comments from Dr. Felsenfeld, on the quality of the Soviet presentations and the state of the field of complex systems in the Soviet Union in general. The following is a summary of his report and those of other members of the NAS delegation.

#### General Impressions:

There seemed to be little or no problem as far as language was concerned. All the Soviet presentations were made in English, and presentations were comprehensible to the Americans. Additionally, the Soviet participants evidenced no difficulties in understanding the American presentations.

The attendance at the meeting was lower than expected, averaging only 80 scientists at any one time. The NAS participants suggested several possible explanations: 1) many of the post-doctoral candidates and graduate students may not have possessed the English language skills to derive any benefit from the workshop; 2) the workshop's venue in Georgia may have made it financially inaccessible to many scientists in Moscow, where there is a strong concentration of research in microbiology and biochemistry; 3) the average young Soviet scientist is so intensely specialized that they attended only those sessions which directly impact on their area of specialization.

This narrow specialization, in the opinion of the NAS participant who made this observation, might prevent the Soviet scientists from seeing the "'big picture' of gene expression and control." In an attempt to explain this phenomenon, the participant posited, "[i]t may be that the average junior Soviet scientist doesn't have the rich diet of visiting seminar speakers that our students and post-docs profit from in the States, and thus don't [sic] develop a broad perspective. On the other hand, within their 'specialties' they seem to be well informed, recalling things from our papers that we didn't remember ourselves. At this level, there were some intense question-and-answer sessions between young Soviet scientists and individual members of the delegation."

By far the largest concern of the American participants was, however, that there were not enough young participants in the workshop. Those young scientists that did manage to attend the workshop seemed hesitant to participate in the formal discussions. Fortunately, the delegation was able to interact with these and other younger scientists at informal discussions during the workshop and in seminars arranged during post-workshop site visits in Moscow. More information on these site visits is presented below.

In assessing the overall effectiveness of the workshop, several of the participants compared it to an interacademy conference which had taken place in 1975 in Kiev with many of the same participants. At this initial meeting the primary objective was establishing contact, and the level of the Soviet work presented was assessed as "uneven." Additionally, there were virtually no presentations in the field of genetics (an unfortunate result of the Lysenkoism of previous decades).

At the 1989 workshop, judging from their limited contacts, the participants were much more impressed with the improvement in Soviet capabilities in genetics, molecular biology, and biochemistry. Stated one participant, "[s]everal of the Soviet talks were in fact excellent." Another participant equated the 'mood' of the workshop with that of any small international meeting and stated that "[t]he quality of Soviet research in this field is greatly improved, and therefore the exchange of information was stimulating and valuable." An additional noticeable improvement was in the ability of Soviet graduate students to conduct quality experiments. In 1975 this was practically non-existent; the emphasis was much more theoretical.

Also in stark contrast to the 1975 meeting, most of the Americans were quite familiar with their Soviet counterparts, having either hosted them in the United States or encountered them at international conferences.

There was a general consensus among the American participants that the Soviet delegation was the best that the country had to offer in the field of molecular biology. Several delegation members judged the stature of the delegation within the Soviet Union to be roughly comparable to that of the American delegation in the U.S. The American participants used terms ranging from 'able' to 'outstanding' to describe their counterparts. Once again using the comparison with the 1975 meeting, one of the participants stated that the Soviet delegation seemed "somewhat younger and more energetic" at the 1989 meeting. In addition to the leading scientists from Moscow institutes, there were also a few participants from outlying locations such as Novosibirsk and Tartu and, of course, Tbilisi.

Despite these impressive comments, the American delegation still came to the conclusion the quality of science reflected by the Soviet presentations was far below the that reflected in the American presentations. In the words of one participant, "[t]he symposium reinforced past impressions that with a few exceptions, like Frank-Kamenetsky, the USSR does not have groups doing truly innovative molecular biology like that represented by essentially all of the U.S. participants. However, two of the major USSR groups, Georgiev and Spirin, were unrepresented."

## Effectiveness of Meeting Scientific Objectives

The American participants in the activity variously stated their scientific objectives as 1) exchange scientific information among major contributors in the field of Eucaryotic Genome Structure, 2) determine the level of Soviet capabilities in this field, 3) explore possible avenues for collaboration and exchange of students.

At least some of the participants expressed satisfaction at having achieved the first two of these objectives.

In terms of future collaboration, the outcome was generally positive, with several researchers expressing varying degrees of interest in placing postdoctoral researchers and senior researchers in their own laboratories from the Institute of Molecular Biology and the Shemyakin Institute of Bioorganic Chemistry. Areas cited for possible research collaboration included mapping of genes on human chromosome 1 (with Sverdlov's group at the Shemyakin Institute) and investigating the interaction between GCN4 protein and its DNA recognition sequence (with Konstantine Ebalidze of the Institute of Molecular Biology). This latter collaboration would take advantage of the relatively better U.S. understanding of reagents as well as the strong Soviet capabilities in chemical crosslinking.

Additionally, one of the NAS participants also made progress during the workshop in improving computer communications links for the purpose of collaborating on the Human Genome Project.

### B. Scientific Site Visits

Following the workshop, the American delegation travelled to Moscow to make site visits to a number of related scientific institutes. A full list of these institute visits is appended to this report. Below, some of the more interesting observations from three of these institutes are summarized.

#### **Institute of Molecular Biology (Director, Andrei Mirzabekov)**

The participants who visited this institute praised its large, active, and highly professional research groups. They attributed this success, in part, to the frequent visits which the leading scientists at the Institute had made to the West. One participant favorably compared the visit to one he might make to a laboratory in the United States, and, just as in the U.S., he spent a considerable amount of time reviewing individual research projects with students.

Following are some individual comments on laboratories visited:

"[Mirzabekov's] group continues to extend the method developed by . . . [him] . . . years ago for cross-linking proteins bound to DNA in vivo. Though this ought to have been an exhausted subject, recent improvements are giving very valuable and unique information about regulation of gene expression.

"Andreyeva has solved the crystal structures of aspartic proteases and is currently working on the structure of a phenylalanyl-tRNA synthetase and its complex with tRNA<sup>Phe</sup>. The laboratory facilities that she has are completely inadequate but she does have access to synchrotron X-ray facilities in Germany. They appear to be quite capable scientists suffering from completely inadequate computational and crystallographic facilities."

Other researchers who the participants singled out for their outstanding work included Georgi Georgiev and M. Volkenshtein in the senior group and V. Ivanov among the younger scientists.

**Institute of Molecular Genetics (Profs. Sverdlov and Frank-Kamenetsky)**

Unlike the Institute of Molecular Biology, the scientists at this institute have only been allowed to travel freely to the West since 1987. As a result, the institute is smaller and not as well known to U.S. counterparts. Nonetheless, the NAS participants cited excellent work by a few of the groups they visited. Specific comments are listed below.

"Frank-Kamenetsky and his colleagues do excellent studies of variant DNA structures (H-DNA, cruciform, effects of DNA supercoiling), a field in which they are among the world's leaders. Nikiforov's group, working in the area of bacterial genetics, is very active in mutational studies of RNA polymerase and in studying the interaction of protein overproduction with the heat shock system, where they have obtained some striking results."

### 3. Institute of Crystallography (Director: Boris Vainshtein)

The research on protein crystallography was rated by the American participant who visited this institute as "reasonably good." Nonetheless, while the institute has better x-ray facilities than the Institute for Molecular Genetics, it lacks adequate computing facilities.

Partly as a result, the participant speculated that there might be more research going on in his own laboratory on macromolecular crystallography than in the entire Soviet Union.

#### Conclusions Drawn From Site Visits

At all of the institutes visited, the American scientists noted that the laboratory facilities and equipment were outdated by U.S. standards, but, in some cases, still functional. Commented one participant "[i]t is evident that much effort goes into maintaining equipment that we would tend to replace." Another participant compared the facilities to those found in Spain, Italy or "provincial" American or British Universities. They were, nonetheless, superior to those found in China.

In addition to these technical shortcomings, however, one of the participants also observed that Soviet progress in crystallography and molecular biology was being held back by the failure of scientists in these two disciplines to interact more effectively with each other. Another participant noted that the Soviet scientists were generally much stronger at chemical rather than biological aspects of their field. The same participant noted in his Soviet counterparts a lack of "appreciation of modern concepts in molecular genetics, and cellular and developmental biology." Nevertheless, he was impressed by their knowledge of scientific literature and willingness to try new and untested approaches--a refreshing change from the "factory-like mentality" engendered by better scientific conditions in the U.S. In sum, however, he assessed the majority of work as less than fundable quality by U.S. standards.

#### C. Recommendations:

Upon their return to the United States, the American delegation made several recommendations for improving the structure of future activities on this topic. Some of the more commonly voiced comments are cited below.

1. A Different Meeting Format: Several participants stated that they felt constrained by the rather formal seminar format of the meeting and the large number of total participants. One opted for a more open U.S. style workshop limited to 30-40 participants. As this participant, noted, however, the quality



of Soviet science would have to improve for a meeting of this type to be successful.

2. Better Planning of the Site Visits: While the seminar was too formal for some participants, many others stated that the Soviet approach to the site visits was too casual. Specifically, they requested that future activities include more scientific site visits, pre-arranged one-on-one visits with specific individual scientists sharing similar research interests, and prior announcement of mini-seminars at these institutes to ensure that they are well attended by interested researchers, particularly the younger ones. It was acknowledged, however, that communications difficulties still make fulfilling these requests difficult.

3. Choosing a More Accessible Venue: As mentioned above, almost all of the participants believed that the choice of venue (Tbilisi) had prevented many of the best younger scientists as well as some senior ones from attending the workshop. For this reason, they suggested Moscow as a venue for future activities. Recognizing that this would make it difficult for scientists from outlying areas to attend, they suggested that subgroups of the delegation could go to outlying scientific centers to give mini-workshops after the main workshop.

## APPENDIX I

### LIST OF PRESENTATIONS FROM NAS--ASUSSR WORKSHOP ON THE STRUCTURE OF THE EUCARYOTIC GENOME & REGULATION OF ITS EXPRESSION October 14-27, 1989

#### U.S. Presentations:

- J. Abelson, "RNA Splicing in Yeast"
- B. Alberts, "The Properties of a Model Multiprotein Complex that Functions on DNA"
- C. Cantor, "Problems and Progress in Making Maps of the Human Genome"
- D. Crothers, "DNA Bends and Bendability"
- G. Felsenfeld, "Taxon-Specific Crystallins"
- M. Gellert, "Novel Aspects of V(D)J Recombination in Lymphoid Cells"
- M. Oettinger, "RAG-1: A Gene Encoding or Activating the V(D)J Recombinase"
- M. Simon, "The Mechanisms of Signal Transduction"
- C. Smith, "Long Range Structural Patterns in Simple Chromosomes"
- J. Steitz, "Mammalian snRNPs: Diversity in Form and Function"
- T. Steitz, "Structure of Glutamyl-tRNA Synthetase Complexed with tRNA<sup>Gln</sup> and ATP"
- J. Strominger, "Mutants of HLA-A2 in the Analysis of its Structure and Function"
- K. Struhl, "Molecular Mechanisms of Transcriptional Regulation in Yeast"
- P. von Hippel, "The Structure, Regulation, and Mechanisms of Action of the RNA Transcript Elongation and Termination Complexes of E. Coli"

Soviet Presentations:

- V. Agol, "5' Nontranslation Region of the Picornaviral Genome: Unusual Translation Control"
- A. Bogdanov, "Conformation of Ribosome-Bound Messenger RNA"
- K. Ebalidse, "Mapping of the DNA-Histone Interface in the Nucleosome by Chemical Cross-Linking"
- A. El'skaya, "The Translational Mechanisms of Gene Expression Control in Eukaryotes"
- M. Frank-Kamenetsky, "Structure of Telomeric Sequence  $(C_4A_2)_n$   $(T_2G_4)_n$  Under Superhelical Stress"
- E. Gren, "Structural Organization of the Hepatitis B Virus Core-Antigene Gene and Corresponding Proteins"
- V. Ivanov, "Sequence-Dependent Energetics of the B to A Transition in DNA A-Philic Sites in the Eucaryotic Genome"
- L. Kisselev, "Tryptophanyl-tRNA Synthetases: Studies with Mabs"
- V. Lipkin, "Calmodulin-Independent Adenylate Cyclase Bovine Brain cDNA Nucleotide Sequence and Partial Structure of the Human Gene"
- E. Lukanidin, "Structure of Gene MTS1 Transcribed in Metastatic Mouse Tumors"
- T. Maimets, "Oncoprotein p53 Modulates DNA Replication"
- G. Matsuka, "Influence of 2'-5' Oligoadenylates on the Secondary Structure of Nucleic Acids"
- A. Mirzabekov, "An Oligonucleotide Hybridization Approach to DNA Sequencing"
- S. Nedospasov, "Genes, Coding for Tumor Necrosis Factors: Genome Organization and Regulation of the Expression"
- L. Ovchinnikov, "Features of Translation of Informosomes in Cell-Free Systems of Protein Biosynthesis"
- D. Prangishvili, "Eukaryotic Features of Molecular Organization of Archaeobacteria"

- S. Rasin, "DNA Sequences, Located in the Vicinity of Replication Origin in the 5'-Upstream Region of the Domain of Chicken Alpha-Globin Genes, Contain an Enhancer and Recognition Sites for DNA-Binding Proteins"
- R. Salganik, "Molecular Mechanisms of Genomic Rearrangements: Predetermined Mutations Triggered by the Double-Strand DNA Breaks"
- M. Speek, "Structural and Functional Analysis of the Highly Repeated Long Interspersed DNA (Line) in Rat"
- E. Sverdlov, "The Family of Human Na,K-ATPase Genes"
- V. Vlassov, "Reactive Derivatives of Antisense Oligonucleotides as Gene Directed Drugs"
- T. Zaalishvili, "Study of ADP-Ribosylation in Rat Brain Nuclei"
- E. Zaychikov, "Tick-Borne Encephalitis Virus Replication Complex"

## APPENDIX II

### LIST OF PARTICIPANTS IN NAS-ASUSSR WORKSHOP ON THE STRUCTURE OF THE EUCARYOTIC GENOME

#### NAS PARTICIPANTS

Gary Felsenfeld (NAS)  
National Institutes of Health  
Building 2, Room 301  
9000 Rockville Pike  
Bethesda, MA 20892  
301/496-4173

John Norman Abelson (NAS)  
Division of Biology 147-75  
California Institute of Technology  
1201 East California Boulevard  
Pasadena, CA 91125  
818/356-3945

Bruce M. Alberts (NAS)  
Department of Biochemistry & Biophysics  
University of California  
San Francisco, CA 94143-0448  
415/476-4132

Charles R. Cantor (NAS)  
Director, Human Genome Center  
Lawrence Berkeley Laboratory  
Donner Lab, Room 459  
University of California  
Berkeley, CA 94720  
415/486-6800  
Fax 415/486-5717

Donald Morris Crothers (NAS)  
Department of Chemistry  
Yale University  
225 Prospect Street  
New Haven, CT 06511  
203/432-5204

Martin F. Gellert (NAS)  
Section on Metabolic Enzymes, LMB, NIDDK  
National Institutes of Health  
Building 2, Room 322  
9000 Rockville Pike  
Bethesda, MD 20892  
301/496-5888

Melvin I. Simon (NAS)  
Biology Division 147-75  
California Institute of Technology  
Pasadena, CA 91125  
818/356-3944 or 356-2143

Joan Steitz (NAS)  
Department of Molecular Biophysics & Biochemistry  
Yale University  
260 Whitney Avenue (P.O. Box 3333)  
New Haven, CT 06510  
203/785-4585

Thomas Steitz  
Department of Molecular Biophysics & Biochemistry  
Yale University  
260 Whitney Avenue (P.O. Box 6666)  
New Haven, CT 06511  
203/432-5617 or 203/432-5598

Jack Leonard Strominger (NAS)  
Fairchild Biochemical Laboratories  
Harvard University  
7 Divinity Avenue  
Cambridge, MA 02138  
617/732-3083

Kevin Struhl  
Harvard Medical School  
Department of Biochemistry & Molecular Pharmacology  
240 Longwood Avenue, C1-210  
Boston, MA 02115  
617/732-2104

Peter von Hippel (NAS)  
Institute of Molecular Biology  
Klamath Hall 297  
University of Oregon  
Eugene, OR 97403  
503/686-5151

### Soviet Participants

A. Mirzabekov (Chair)

Engelhardt Institute of Molecular Biology

V. Agol

Institute of Poliomyelitis and Viral Encephalitides

A. Bogdanov

Belozersky Laboratory of Molecular Biology and Bioorganic Chemistry

K. Ebalidse

Engelhardt Institute of Molecular Biology

A. El'skaya

Institute of Molecular Biology and Genetics, Kiev

M. Frank-Kamenetsky

Institute of Molecular Genetics

E. Gren

Institute of Organic Synthesis, Latvian SSR

V. Ivanov

Engelhardt Institute of Molecular Biology

L. Kisselev

Engelhardt Institute of Molecular Biology

V. Lipkin

Shemyakin Institute of Bioorganic Chemistry

E. Lukanidin

Engelhardt Institute of Molecular Biology

T. Maimets

Estonian Biocenter

G. Matsuka

Institute of Molecular Biology and Genetics, Kiev

S. Nedospasov

Engelhardt Institute of Molecular Biology

L. Ovchinnikov

Institute of Protein Research

D. Prangishvili

Institute of Molecular Biology and Biological Physics, Georgia

S. Rasin  
Engelhardt Institute of Molecular Biology

R. Salganik  
Institute of Cytology and Genetics, Novosibirsk

M. Speek  
Estonian Biocenter

E. Sverdlov  
Shemyakin Institute of Bioorganic Chemistry

V. Vlassov  
Novosibirsk Institute of Bioorganic Chemistry

T. Zaalishvili  
Institute of Molecular Biology and Biological Physics, Georgia

E. Zaychikov  
Omsk Institute of Natural-Foci Infections



### APPENDIX III

#### Site Visits in Moscow

##### Wednesday, October 25:

Site Visit: Engelhardt Institute of Molecular Biology  
Host: Academician Andrei Mirzabekov, Director  
U.S. Talks: Peter von Hippel, Martin Gellert, Gary Felsenfeld,  
Bruce Alberts

##### Thursday, October 26: Site Visits in Moscow

Site Visit: Engelhardt Institute of Molecular Biology  
Host: Dr. Andreyeva  
U.S. Talks: Thomas Steitz

Site Visit: Institute of Molecular Genetics  
Host: E. Sverdlov, Director  
M. Frank-Kamenetsky  
U.S. Talks: Gary Felsenfeld, Martin Gellert, Bruce Alberts,  
Kevin Struhl

Site Visit: Institute of Crystallography  
Host: Dr. Vainshtein  
U.S. Talk: Thomas Steitz

Site Visit: Belok Protein Institute, Pushchino  
Host: Pyotr Privalov  
U.S. Talks: Peter von Hippel, Donald Crothers

##### Friday, October 27:

Site Visit: Engelhardt Institute of Molecular Biology  
Host: A. Mirzabekov, G. Georgiev  
U.S. Talks: Donald Crothers, Kevin Struhl, Marjorie Oettinger

**END**

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