OCT 20 1992

Institute of Gene Biology
Russian Academy of Sciences
Nikolai V. Gnuchev, Ph.D
Vice Director

Vavilov str., 34/5 Moscow 117984, Russia, Tel. 135-6089
[redacted]

10/14

Dr Guyer

Mark

These are the names etc of the Director and Vice Director of the Inst of Gene Biology I discussed at EPMC this morning

George

Institute of Gene Biology
USSR Academy of Sciences

Prof. Georgii P. Georgiev
Director

[redacted]

WASHINGTON UNIVERSITY SCHOOL OF MEDICINE
AT WASHINGTON UNIVERSITY MEDICAL CENTER

CENTER FOR GENETICS IN MEDICINE

12 June 1992

Dr. Jane Peterson
Chief, Res. Centers Branch,
National Center for Human Genome Research, Dept of HHS
PHS - NIH, Building 38A, Rm 610
9000 Rockville Pike
Bethesda, MD 20892
[redacted]

Dear Jane,

This is to give your some details of conversations that I have had with Dr. John Bruer of the McDonnell Foundation about possible Foundation support for 1 or 2 Russian investigators. The notion of the Foundation is to screen requests coming from one of the current grantees -- in this case, me -- which would permit them to assign funds to a North American university that would then be transferred directly to active Russian genome investigators, either as specie[illegible] credit or as reagents and equipment. The possible mechanism would be that after our visit to Russia, I could prepare two proposals in concert with individual Russian investigators, on the order of $40-50,000 each. This would be sufficient to give a real level of material support to those laboratories. One advantage of this proposed mechanism is that the sole beneficiary would be the actual investigator in Russia. Thus the funds would be used neither for unknown purposes nor for the support of émigré scientists (who would thus be benefiting primarily an American laboratory). One disadvantage is that only 1 or 2 Russian laboratories could benefit, but other Foundations might conceivably join in similar activities. Of course, I expect to confer with NCHGR staff and particularly with you about any potential grantees.

Sincerely yours,

David

David Schlessinger

Box 8232
4566 Scott Avenue
St. Louis, Missouri 63110
(314) 362-1199 FAX: (314) 362-3203

WASHINGTON UNIVERSITY SCHOOL OF MEDICINE
AT WASHINGTON UNIVERSITY MEDICAL CENTER

CENTER FOR GENETICS IN MEDICINE

✓ cc: Jane Peterson

SEP 14 1992

September 10, 1992

Dr. John T. Bruer
President
James S. McDonnell Foundation
1034 South Brentwood Boulevard, Suite 1610
St. Louis, MO 63117

Dear John,

The NIH Genome Center-sponsored trip to St. Petersburg was an eye opener. Overall it was discouraging to find that very few of the institutions in Moscow/St. Petersburg have currently viable programs, and in addition, they have retained a power structure in which a few people expect to have control over fund distribution (rather than basing the award and distribution of funds on the merit of scientific proposals). Although I did my best to speak with a number of groups and tried to arrange interactions, my conclusion is that it would be difficult for the Foundation to find unmistakably worthwhile projects or groups to sustain at the present time.

In several cases the groups have remained on a high level, but even in those cases the cadres between the level of young students and older administrators/group leaders were largely de-populated. The intermediate level scientists of talent have simply moved to the west. Our task was especially difficult because few if any young people who have left have had any contact with Genome Research. In that respect, the Foundation might have better prospects for supporting infrastructure there in connection with neuroscience or cell biology groups. No doubt you may hear from others about such possibilities.

For my part, I am continuing active discussions and managing of letters and plans with one of the scientists I met, Dr. Nikolai Tomilin, and it might be that an interesting proposal will develop involving a new technology based on DNA fibers tethered to a matrix. It seems best at this time to let that percolate into a proposal to be considered under the NIH

Box 8232
4566 Scott Avenue
St. Louis, Missouri 63110
(314) 362-1199 FAX: (314) 362-3203

program for support of Eastern European science. NIH would be a logical agency since any such proposal will take some time to develop and would specifically need the benefit of peer review.

Sincere regards,

David

David Schlessinger

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Center for Human
Genome Research
Bethesda, Maryland 20892

Building 38A, Room 610
(301) 496-7531
(301) 480-2770 (Fax)

September 10, 1992

James D. Watson, Ph.D.
Director
Cold Spring Harbor Laboratory
PO Box 100
Cold Spring Harbor, NY 11724

Dear Dr. Watson:

I have been meaning to write to give you a report of the Human Genome Meeting in St. Petersburg, but have been delayed by vacation and preparation for the upcoming Council. I found the meeting to be very useful in many ways, although it will be some time before it is apparent whether or not any meaningful collaborations between U.S. and Russian scientists have been established. Overall, I think the Russians, particularly young scientists who rarely go abroad, appreciated our coming to Russia to discuss genome science. Unfortunately, most of these young people want to leave Russia as soon as possible. Dr. Nikolsky told me that in his view Russian science has lost a whole generation of scientists to the west.

I found Dr. Bayev to be a particularly interesting figure. Some of the young scientists told us that they believe he has a broad and fair view of genome science and they do not look forward to the prospect of his retirement. He gave an eloquent speech at the banquet, talking about his life and his vision for the program. Many of the Russian scientists at the upper levels of the Institutes have been in positions of power for some time (during communist rule) and their intentions are not clear.

The American participants seemed to enjoy the meeting, but felt frustrated that we can do so little given the enormous problems faced by Russian science. Two problems were identified that we can help with: providing the Russians with scientific journals and names and addresses of U.S. genome scientists. A number of potential U.S.-Russian collaborations were established and I hope that we will see some applications for support in the near future. There was some discussion of a future meeting, but we agreed that it we should wait to determine if useful collaborations were begun at this meeting.

I am enclosing the "official" report from the meeting, a poster and a pin made for the meeting and the program. I am sorry you were unable to attend the meeting as I believe it accomplished many of the scientific goals you envisioned and was extremely interesting culturally.

Sincerely yours,

Jane L. Peterson, Ph.D.
Chief, Research Centers Branch

cc: Dr. Michael Gottesman
Dr. Elke Jordan

bcc: Dr. Guyer , Board

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Center for Human
Genome Research
Bethesda, Maryland 20892

Building 38A, Room 610
(301) 496-7531
(301) 480-2770 (Fax)

September 10, 1992

Nikolai Nikolski
Institute of Cytology of the
Russian Academy of Sciences
194064 St. Petersburg
Tikhoretsky Avenue 4
Russia

Dear Dr. Nikolsky:

I want to thank you, somewhat belatedly, for hosting the U.S.-Russian Human Genome Meeting in St. Petersburg this past July. I personally found the meeting to be very rewarding scientifically and culturally and appreciate all of your efforts in making the meeting a success. I have spoken to a number of the U.S. participants who shared my enthusiasm for the meeting and agreed that you and the Institute of Cytology played a critical role in making it a success. I hope that through the meeting, the Russian participants were able to make meaningful contacts with U.S. genome researchers and that successful and productive collaborations will result.

The problem with the lack of scientific journals in Russia was agreed to be a critical one with which we could assist. I have submitted to Human Genome News an article about the meeting mentioning the need for journals. Additionally I contacted the American Society of Human Genetics and found that their journal program includes only the Journal of the ASHG. Dr. Zelenin sent me a list of contacts at each Russian institute which I have sent to the U.S. participants for their use if they are able to identify a source of journals to be sent to Russia.

I have not received any information as to whether the funds that were provided by NIH have been received in St. Petersburg. If there remains any problem with the payment, please let me know so that I can try to find the problem with the transfer.

Again, thank you for your hospitality and participation in the planning of the meeting. I look forward to future Human Genome meetings where the results of collaborations that began at this meeting are discussed.

Sincerely yours,

Jane L. Peterson, Ph.D.
Chief, Research Centers Branch

cc: Dr. Michael Gottesman
Dr. Elke Jordan
bcc: Dr. Guyer, Board

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Center for Human
Genome Research
Bethesda, Maryland 20892

Building 38A, Room 610
(301) 496-7531
(301) 480-2770 (Fax)

September 9, 1992

Vladimir Larionov
National Institutes of Environmental
Health Sciences
Research Triangle Park
Mail Drop E 404
PO Box 12233
Research Triangle Park, NC 12233

Dear Dr. ~~Larionov~~ Vladimir:

I want to thank you, somewhat belatedly, for your assistance in organizing the joint U.S.-Russian Human Genome Meeting. I felt that overall the meeting was quite successful and hope that some successful collaborations with U.S. genome scientists have been established. Your help was critical for me in making the preparations for the meeting and ensuring its success. I thoroughly enjoyed my stay in your country both professionally and personally. The mix of scientific sessions and tours was, in my opinion, balanced perfectly. I hope that I will have the opportunity to visit Russia again sometime in the future.

The lack of scientific journals in Russia was agreed to be a critical problem with which the United States scientific community could assist. I have submitted to Human Genome News an article with information about the meeting and the need for scientific journals. Additionally, I contacted the American Society of Human Genetics and found that their journal program includes only the Journal of the ASHG. Dr. Zelenin sent me a list of contacts at each Russian Institute which I have passed on to the U.S. participants should they be able to identify a source of journals to be sent to Russia.

I hope the remainder of your trip went well. I look forward to interacting with you and Natasha in the future, as participants in the Human Genome Program. Thank you again for your help.

Sincerely yours,

Jane L. Peterson, Ph.D.
Chief, Research Centers Branch

cc: Dr. Michael Gottesman
Dr. Elke Jordan

bcc: Dr. Guyer , Board

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Center for Human
Genome Research
Bethesda, Maryland 20892

Building 38A, Room 610
(301) 496-7531
(301) 480-2770 (Fax)

September 10, 1992

Ardrei Mirzabekov
Engelhardt Institute
of Molecular Biology
Vavilov Street 32
Moscow 117984
Russia

Dear Dr. Mirzabekov:

I want to thank you, somewhat belatedly, for agreeing to host the U.S. Russian Human Genome Meeting in St. Petersburg and your valuable participation in organizing it. I felt that the meeting was successful in many ways and I anticipate that some meaningful collaborations have been established between scientists in our two countries. I personally found the meeting to be very rewarding scientifically and culturally and hope that I will be able to visit your country again in the future.

The problem with the lack of scientific journals in Russia was agreed to be a critical one with which we could assist. I have submitted to Human Genome News an article about the meeting mentioning the need for journals. Additionally I contacted the American Society of Human Genetics and found that their journal program includes only the Journal of the ASHG. Dr. Zelenin sent me a list of contacts at each Russian institute which I have sent to the U.S. participants for their use if they are able to identify a source of journals to be sent to Russia.

Another request from the participants was for us to exchange lists of U.S. and Russian scientists involved in research in the Human Genome. I have prepared such a list and will send it to you for distribution. I would welcome your providing us with a list of Russian scientists that I could distribute to those scientists who participated in the meeting.

Again, thank you for your assistance with the meeting and I look forward to the prospect of the establishment of new U.S.-Russian collaborations.

Sincerely yours,

Jane L. Peterson, Ph.D.
Chief, Research Centers Branch

cc: Dr. Michael Gottesman
Dr. Elke Jordan

bcc: Dr. Guyer, Board

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Center for Human
Genome Research
Bethesda, Maryland 20892

Building 38A, Room 610
(301) 496-7531
(301) 480-2770 (Fax)

September 9, 1992

Maria Sippola-Thiele, Ph.D.
University of Michigan
Medical Center
Department of Internal Medicine
Division of Medical Genetics
Ann Arbor, Michigan 48109-0652

Dear Dr. ~~Sippola-Thiele~~ Maria:

I want to thank you, somewhat belatedly, for your help in transferring the meeting funds to St. Petersburg for the U.S.-Russian Human Genome Meeting. Your willingness to assist NCHGR in this process was greatly appreciated. I believe that the U.S. participants felt that the meeting was worthwhile, although it is difficult to know yet if the type of assistance the NIH can provide will make a difference in helping to maintain Russian science.

I am sorry to hear that you will soon be leaving the University of Michigan Genome Center. I have enjoyed working with you and your management of the Michigan Center has made much of NCHGR's work easier. I wish you well in your new position and hope that you will continue to be involved in the biotechnology aspects of the Human Genome Project.

Sincerely yours,

Jane L. Peterson, Ph.D.
Chief, Research Centers Branch

cc: Dr. Gottesman, Dr. Jordan
bcc: Dr. Guyer, Board

Department of Human Genetics

THE UNIVERSITY OF UTAH

AUG 3 1 1992

August 13, 1992

Dr. Jane L. Peterson, Ph.D.
National Center for Human Genome Research
Bldg. 38A, room 610
9000 Rockville Pike
Bethesda, MD 20892

Dear Dr. Peterson

We wanted to give you our impressions of the Russian genome meeting in St Petersburg as we are actually quite disturbed by the conclusions that we reached.

Foremost is the overwhelming desperate state of science in Russia. We felt that our Russian colleagues tried very hard to put on a good face but just underneath was panic. As we understood only later, researchers are being let go, research institutes such as the Engelhart have to pay their employees in cash and the promised operating funds are not forthcoming from the government. Moreover the crucial reagents and supplies must be purchased from the west and the exchange rate makes doing business almost prohibitive. We have the strong impression that their science is going downhill fast and is virtually at a standstill already.

However there is some good genome-related research being done. There are a number of people involved in mapping and human genetics who are well trained and know just what to do but are hampered by their circumstances. Genetically, there are very interesting family resources that must result from the ethnic and geographical isolation of various populations. We heard of one group with very high consanguinity that is turning up interesting diseases. These would be very interesting to develop. We were impressed with the sequencing by hybridization where physical chemistry considerations have been used to equalize hybridization rates for differing GC contents. Also, the work from Mirzebekov's group on chromosome structure and organization is first rate. Other efforts were much harder to evaluate. Even when the work was of questionable or unclear merit, however, the investigators were often of high quality.

The group discussion of how the U.S. could help distressed and perplexed us. You gave a good account of the NIH options including collaborative projects with U.S. scientists and direct, competitive application for RO1 funding. But, our Russian colleagues are used to direct support of institutes rather than individual projects. Neither are they at all experienced with NIH-style peer review, or the mysteries of RO1 proposal writing. And although many of these scientists are clearly capable of becoming RO1-competitive, for many historical reasons, few of them now are. The discussion immersed them immediately in our system of project funding where they feel uncomfortable, which got us off to a bad start. Also, our behavior exhibited little sign of the immediacy or gravity of the problem. Discussion of

(continued)

Office of the Co-Chairman
Room 6160
Eccles Institute of Human Genetics
Salt Lake City, Utah 84112 U.S.A.
Phone (801) 581-5190
FAX (801) 585-3910

collaborative opportunities was reasonable but we sensed that not very many arrangements would grow out of the meeting despite much discussion. The Russians seemed understandably reluctant and defensive.

We sense that these feelings are due to their confusion about where to start and concern about not being competitive especially when faced with the representatives of our large genome centers. There was also a strong fear that their scientists would be exploited by moving to U.S. labs. The alternatives are, however, also problematic. We note the embarrassing moment when one Russian participant pointed out that they <u>were</u> a source of cheap labor and that we should put them to work. (This minority view disturbed most of the other Russian participants.) The discussion of competitive RO1 funding only heightened concerns of competitiveness and was quite unfortunate. We think that few, if any, of the Russian scientists felt that they were in a position to compete for grants. Thus, rather than leaving the meeting with a sense of hope, we believe that the vast majority of the Russian scientists left very discouraged about the possibility of getting any help from the U.S. science establishment.

What can be done? Even modest financial help to the Russian labs could save their science from disaster. Salaries for scientists are very low (U.S.$ equivalent of some $15-30/month!) so that help for keeping scientists employed would be trivial. Equipment and supplies, on the other hand, must be purchased at western rates. However, even small amounts of supplies would be a great improvement. A $50,000 annual award would be <u>very</u> substantial.

The collaborative arrangements will often be interpreted as exploitive. Competitive RO1 funding will not succeed in most cases and more importantly the process is too slow - the help would come too late. The problem is urgent, as the science community faces needs for today and tomorrow - not next year.

Supporting sabbatical visits of Russian scientists to U.S. labs would be very helpful but again does not help in the short run. Vigorous recruiting of young scientists to U.S. labs will likely results in just stealing their new talent.

We need to find a way to support their science in their country with real urgency. Can the argument be pushed that there are unique opportunities here that are not available in the U.S.? We do not see a way to do what is needed through the normal NIH channels.

I think that the meeting was a good effort but will fail to accomplish its goal unless some other effort is made. If we sit back and wait for grants to come in it will be too late and too little.

Sincerely,

R. F. Gesteland

E. Branscomb

RFG:tia
cc: Dr. M. Gottesman

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Center for Human
Genome Research
Bethesda, Maryland 20892

August 30, 1990

TO: Director, FIC

FROM: Deputy Director, NCHGR

SUBJECT: Opportunities for Collaboration with USSR Academy of Sciences

We would be happy to interact with those laboratories interested in human genome mapping and sequencing. I have noted the following in your materials:

1. Professor Lev Kisselev, Laboratory of Molecular Bases of Carcinogenesis

2. Shemyakin Institute of Bio-organic Chemistry

3. Andrei Mirzabekov, Molecular Organization of Chromosomes Laboratory, Engelhardt Institute of Molecular Biology

4. Vladimir M. Zakharyev, Engelhardt Institute of Molecular Biology

More detailed information would be needed before recommending specific scientists for collaboration. A brief abstract of the work ongoing would be helpful. We would also be pleased to invite Russian scientists to some of our meetings where their scientific interests match.

Elke Jordan

Elke Jordan, Ph.D.

bcc: Dr. Watson
Dr. Guyer

DEPARTMENT OF HEALTH & HUMAN SERVICES

AUG 23 1990

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892
Building : 31
Room : B2C39
(301) 496- 1415

August 20, 1990

TO: Addressees

FROM: Director, FIC

SUBJECT: Opportunities for Collaboration with USSR Academy of Sciences--Request for Comments

Earlier this year, I met with officials of the USSR Academy of Sciences to explore mutual interests in establishing direct ties between the basic biological science institutes of the Academy and NIH. The idea was first broached by former Soviet Ambassador Dubinin during his visit to NIH last year. Subsequently, Dr. James Mason asked me to represent PHS at the first Joint Commission meeting under the U.S.-USSR Basic Sciences Agreement, which would provide a mechanism for the establishment of collaboration between NIH and the Soviet Academy. At the time, several ICD Directors indicated a strong interest in direct ties with certain institutes of the Academy. In July, two representatives of the Academy visited NIH and informed us that their President, Guriy Marchuk, shared this interest.

At our request, we recently received information from several of the Academy's leading institutes describing their research priorities and proposing several topics for collaboration with NIH. Most of the descriptive general information is in Russian and we will share it with you after it is translated. Attached for your review at this time are suggested topics for collaboration, along with English bibliographies of key publications, from the Engelhardt Institute of Molecular Biology, the Institute of Molecular Genetics, the Shemyakin Institute of Bio-organic Chemistry, and the Human Genome Program of the State Committee for Science and Technology.

Recognizing the limitations of the attached material, I would appreciate comments on:

- your ICD's interest in the Soviet proposals (where appropriate);
- extramural investigators that may be interested, particularly in areas of research where intramural involvement is limited or nonexistent;
- any topics you may wish to propose for collaboration that were not included in the Soviet proposals.

I have been invited to join an OSTP delegation to the Soviet Union in late September and, depending on your reactions, could visit these institutes to convey your preliminary comments and obtain additional information. I would appreciate hearing from you no later than September 5 regarding the attached material.

Please call me if you have any questions.

Philip E. Schambra, Ph.D.

Attachments

Addressees:
Dr. Broder, NCI
Dr. Fauci, NIAID
Dr. Goldstein, NINDS
Dr. Gorden, NIDDK
Dr. Kirschstein, NIGMS
Dr. Lenfant, NHLBI
Dr. Watson, NCHGR

cc:
Dr. Welsch, NCI
Dr. Western, NIAID
Dr. Porter, NINDS
Dr. Cummings, NIDDK
Dr. Rivera, NIGMS
Dr. Hegyeli, NHLBI
Dr. Jordan, NCHGR

LABORATORY FOR FUNCTIONAL MORPHOLOGY OF CHROMOSOMES
ЛАБОРАТОРИЯ ФУНКЦИОНАЛЬНОЙ МОРФОЛОГИИ ХРОМОСОМ

Заведующий лабораторией - доктор биологических наук А.В.Зеленин
Head of laboratory - Doctor of Biological Sciences A.V. Zelenin

1. *Sedman J., Shostak N.G., Kupriyanova N.S., *Serenkova T.I., *Felgenhauer P.E., *Lind A.Ja., Timofeeva M.Ja. 5S rRNA genes of loach (*Misgurnus fossilis L.*). Heterogeneity of the primary structure // Macromolecules in the functioning Cell. Proceeding of 5th Symposium USSR - Italy, Pavia Sept. 22-24, 1986: Roma. 1988. P.15-26.

2. Skuridin S.G., Badaev N.S., *Dembo A.T., *Lortkipanidze G.B., Yevdokimov Yu.M. Two types of temperature induced transition of poly(I).poly(C) liquid crystals // Liquid Crystals. 1988. Vol.3, N 1. P.51-62.

3. *Chiryaeva O.G., Amosova A.V., *Efimov A.M., *Smirnov A.F., Kaminir L.B., *Yakovlev A.F., Zelenin A.V. Cytogenetic mapping of cattle (*Bos taurus L.*) using quantitative analysis of the RBA map prometophase chromosomes // Cytogenetics of animals / Ed. C.R.E. Haltman. C.A.B. International. UK, 1989. P.211-219.

4. Dubovec N.I., Badaev N.S., Bolsheva N.L., Badaeva E.S., *Shcherbakova A.M., *Bormotov V.E., Zelenin A.V. Regularities of karyotype formation in tetraploid triticale // Cereal Res. Communic. 1989. Vol.17, № 3-4. P.253-257.

5. *Mendel R.R., *Schulze I., *Muller B., Kolesnikov V.A., Zelenin A.V. Delivery of foreign genes to intact barley cells by high-velocity microprojectiles // Theoretical and Applied Genetics. 1989. Vol.78, № 1. P 31-34.

6. Prudovsky I.A., Gumeniuk R.R., Yegorov Ye.E., Poletaev A.I., Chumakov P.M., Zelenin A.V. Immortalized phenotype and the presence of active oncogenes correlate with the capacity of culture cells to induce reactivation of DNA synthesis in macrophage nuclei in heterokaryons // Cell Different. 1989. Vol.26, № 3. P.221-228.

7. Prudovsky I.A., Gumeniuk R.R., Yegorov Ye.E. Resident

macrophages specifically inhibit DNA synthesis in the nuclei of transformed cells in heterokaryons // Int. J. of Cancer. 1989. Vol.44, № 6. P.1005-1008.

8. Zelenin A.V., Prudovsky I.A. Regulation of DNA synthesis in heterokaryons of dividing and non-dividing cells // Int. Rev. Cytol. Submitted. 1989. Vol.117. P.178-214.

9. Zelenin A.V., Titomirov A.V., Kolesnikov V.A. Stable transformation of animal cells by means of high velocity mechanical DNA-injection // FEBS 19th meeting. Rome, 2-7 July 1989. Abstract book, 1989. MO 39.

10. Zelenin A.V., Titomirov A.V., Kolesnikov V.A., *Zelenina I.A. *Barmintsev V.A., Zhadanov A.V., Grashchuk M.A.,*Gorodetsky S.I., *Alimov A.A., *Kazansky A.V. *In vivo* transfection of fish and rodent cells with the aid of high-velocity mechanical DNA injection // Structure of eukaryotic genome and regulation of its expression: Abstr. of second bilaterial symp. USSR-USA. Tbilisi, October 16-20. 1989. Moscow, 1989. P.66-67.

LABORATORY OF NUCLEIC ASID BIOSYNTHESIS

ЛАБОРАТОРИЯ БИОСИНТЕЗА НУКЛЕИНОВЫХ КИСЛОТ

Заведующий лабораторией - академик Г.П.Георгиев

Academician G.P. Georgiev

S.V.Razin, M.G.Kekelidzė, E.M.Lukanidin, K.Scherrer, G.P.Georgiev. Replication origins are attached to the nuclear skeleton.Nucl. Acids Res. 1986, 14, 8189-8207.

S.V.Razin, V.V.Chernokhvostov, E.S.Vassetsky, M.V.Razina, G.P.Georgiev. The distribution of tightly bound proteins along the DNA chain reflects the type of cell differentiation. Nucl.Acids Res. 1988, 16, 3617-3633.

Y.S.Vassetsky, S.V.Razin, G.P.Georgiev. DNA fragments which specifically bind to isolated nuclear matrix in vitro interact with matrix-associated DNA topoisomerase II. Bioch.Biophys. Res.Commun. 1989, 151, 1263-1268.

S.V.Razin et al. Transcriptional enhancer in the vicinity of a replication origin within the 5'-region of the chicken alpha-globin domain. J.Mol.Biol. 1990, in press.

A.N.Luchnik, T.A.Hisamutdinov, G.P.Georgiev. Inhibition of transcription in eukaryotic cells by X-irradiation: relation to the loss of topological constraint in closed DNA loops. Nucl.Acids Res. 1988, 16,5175-5190.

N.A.Tchurikov et al. Mobile elements and transposition events in the cut locus of D.melanogaster. Mol.Gen.Genet.. 1989, 219, 241-248.

N.A.Tchurikov, A.K.Ebralidze, G.P.Georgiev. The suffix sequence is involved in processing the 3'-ends of different mRNAs in Drosophila melanogaster. EMBO J. 1986, 5, 2341-2347.

G.P.Georgiev et al. Mobile genetic elementsin Drosophila melanogaster. Genome 1989, 31, 920-928.

D.A.Kramerov, S.V.Tillib, G.P.Shumjatsky, G.P.Georgiev. The most abundant poly(A)$^+$RNAs are transcribed by RNA polymerase III in murine tumor cells. Nucl. Axids Res. 1990, in press.

S.A.Nedospasov et al. Tandem arrangement of genes coding for tumor necrosis factor (TNF-α) and lymphotoxin (TNF-β) in the human genome. Cold Spring Harbor Symp. Quant. Biol. 1987, 51, 611-624.

M.S.Grigorian, D.A.Kramerov, E.M.Tulchinsky, E.S.Revasova, E.M.Lukanidin. Activation of putative transposition intermediate formation in tumor cells. EMBO J. 1985, 4, 2209-2215.

A.Ebralidze, E.Tulchinsky, M.Grigorian, A.Afanasyeva, V.Senin, E.Revasova, E.Lukanidin. Isolation and characterization of a gene specifically expressed in different metastatic cells and whose deduced gene product has a high degree of homology to a Ca^{2+}-binding protein family. Genes and Developm., 1989, 3, 1086-1093.

E.Tulchinsky, M.Grigorian, A.Ebralidze, N.Milshina, E.Lukanidin. Structure of gene mts1, transcribed in metastatic mouse tumor cells. Gene 1990, 87, 219-223.

PROPOSALS

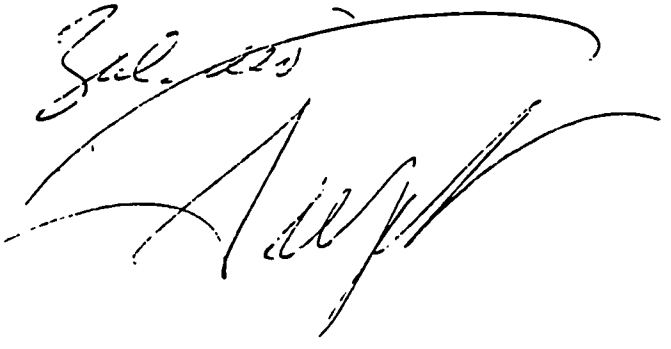
1) Studies on the size of domains containing individual genes in human chicken and D. melanogaster genome.

from US: Prof. R.Martinson (UCLA, Los Angeles)

2) Further studies on the role of mts1 gene product in determination of tumor metastatic behaviour.

from US: Dr. S.Zein (Rochester Univ., Rochester NY)

3) Studies on the functional organization of replication origins in eukaryotes.



Лабороратория молекулярных основ онкогенеза (зав. лаб. - проф. Л.Л.Киселев) работает в следующих основных направлениях

1. Структура генома человека
   физическое картирование 3-ей хромосомы человека с использованием геномных, прыжковых, связующих и других клонотек
   конструирование новых векторов для исследования структуры гнома человека и других высших организмов
   идентификация новых генов, их молекулярное клонирование, картирование, и изучение структуры во взаимосвязи с функцией
2. Регуляция активности генов.
   изучение регуляции транскрипции гена c-myc человека in vitro и in vivo; выделение новых факторов транскрипции
3. Молекулярная и клеточная онкология
   выяснение роли генома вируса гепатита В в возникновении эмбриональных опухолей у детей и бесплодия у мужчин; изучение взаимодействия вируса гепатита В с непеченочными тканями человека

Laboratory of molecular bases of carcinogenesis (Head, Prof. Lev Kisselev) is focused in the following main directions:

1. Human genome structure
   physical mapping of the chromosome 3 by means of genomic, jumping, linking and other libraries
   construction of new vectors for studiing the structure of human genome and other higher eukaryots
   identification of new genes, their molecular cloning, mapping and structural studies in relation with function

2. Regulation of gene activity
   regulation of human c-myc transcription in vitro and in vivo; isolation of new transcription factors
3. Molecular and cellular oncology,
   evaluation of the role of human hepatitise B viral HBV genome in development of embryonal tumors in children and infertility of men
   studies on interaction of HBV with non-hepatic human tissues

Список публикаций:

1. Berdichevsky F.B., Chumakov I.M., Kisselev L.L. Transcription of *son* and K51 *loci* in human and rat tissues // Proceedings of the 5th soviet-italian symposium. Pavia, Sept. 22-24, 1986. /Ed. A.Castellani, C. Balduini and P. Volpe. Roma. 1988. P.35-36.

2. Beresten S.F., *Rubikaite B.I., Kisselev L.L. A general approach to the localization of antigenic determinants of a linear type in proteins of unknown primary structure // J. of Immunol. Methods. 1988. Vol.113. P.247-254.

3. *Mordovtsev V.N., *Starkov I.V., Zabarovsky E.R., Kisselev L.L. Expression of the protooncogenes in psoriatic lesions // Arch. Dermatol. Res. 1988. Vol.280. P.8-11.

4. *Mordovtsev V.N., *Starkov I.V., Zabarovsky E.R., Kisselev L.L. Expression of the protooncogenes in psoriatic lesions // Dermatology Digest. 1988. Vol.6. P.4-13.

5. Zabarovsky E.R., Turina O.V., *Allikmets R.L., Nurbekov M.K., *Filippov S. A., *Dobrynin V. N., Kisselev L.L. λSK3 and λSK5 vectors for constructing genomic libraries derived from λEMBL3 and λEMBL4 by insertion of lac gene // Nucl. Acids Res. 1989. Vol.17, № 8. P.3310.

6. Zabarovsky E.R., Turina O.V., Kisselev L. L. λSK9 - a diphasmid for constructing genomic libraries capable of converting inserts into plasmid and single stranded forms // Nucl. Acids Res. 1989. Vol.17, № 11. P.4407.

7. Zabarovsky E.R., Turina O.V., Nurbekov M.K., Kisselev L.L. SK18 diphasmid for constructing genomic libraries with blue/white selection, multiple cloning sites and with the M13 and λori // Nucl. Acids Res. 1989. Vol.17, № 8. P.3309.

8. Zabarovsky E.R., *Zagorskaya E.G., Kisselev L.L. λSK15 - a diphasmid for construction expression cDNA libraries at BamHI and EcoRI sites with selection against non-recombinant and false recombinant phages // Nucl. Acids Res. 1989. Vol.17, № 11. P.4408.

9. Itkes A.B., Imamova L.A., Alexandrova N.M., Favorova O.O., Kisselev L.L. Expression of c-*myc* gene in human ovary carcinoma cells treated with vanadate // Experimental cell research. 1990. Vol.88. P.169-171.

Временный научный коллектив "Иммунохимия и гибридомы"
Unit "Immunochemistry and hybridomas"
Руководитель - кандидат биологических наук С.М.Воробьев
S. M. Vorobiev

1. Vengerov Y.Y. Semenov T.E., Streltsov S.A. et al. Triple rings - a new type of compact structure of circular DNA // J. Mol. Biol. 1985. Vol.184. P.251-255.

2. Vengerov Y.Y., Semenov T.E., Streltsov S.A. et al. Torus-shaped particles formed due to intermolecular condensation of circular DNA upon interaction with synthetic tripeptide // Febs Lett. 1985. Vol.180. P.81-84.

3. Vengerov Y.Y., Semenov T.E., Surovaya A.N. et al. Electron microscopic and physico-chemical studies of DNA complexes with synthetic oligopeptides: binding specificity and DNA compact structures // J. Biomol. Structure & Dynamics. 1988. Vol.6, P.311-330.

Тема по которой могло бы вестись сотрудничество с учеными из США:
"Изучение организации модельных нуклеопротеидных комплексов и их структурной гомологии с клеточными макромолекулярными образованиями"

Предполагается комплекс подходов, включающий аналитическую биохимию, использование специфических антител, физико-химические методы и электронную микроскопию.
Выбор конкретного белка или лиганда пептидной природы, образующего функционально интересные комплексы с ДНК должен учитывать цели и возможности сотрудничающих сторон.

"The study of organization of model nucleoprotein complexes and their structural homology with cellular macromolecular systems.

It's suggested to apply complex approach including analytical biochemistry, specific antibody arising, physico-chemical methods, electron microscopy.

The choice of particular protein or peptide ligands forming complexes of functional importance with DNA should be done taking into account scientific interests of the collaborating groups.

Сотрудники ВНК "Конденсированное состояние нуклеиновых кислот" опубликовали в международных журналах ряд работ, имеющих прямое отношение к одному из новейших разделов биотехнологии, а именно, к созданию биодатчиков для биосенсорных устройств. Эти работы опубликованы в:

The scientific team "Condensed state of nucleic acids" is involved in experimentation for the newest biotechnology, ax namely, creating of biosensors (biosensing units) based on liquid crystals of double-stranded nucleic acids. Our activity in this field is reflected in the following papers;

1. Yevdokimov Yu., Skuridin S., Salyanov V.
"The Liquid-Crystalline Phases of Double-Stranded Nucleic Acids in vitro and in vivo". (Invited Article).
(1988) Liquid Crystals, vol. 3, N 11, pp. 1443-1459.

2. Yevdokimov Yu.M., Skuridin S.G., Salyanov V.I., Rybin V.K Palumbo M.
"Biosensing Units Based on Liquid Crystals of Double-Stranded Nucleic Acids".
(1990) J. Mol. Recogn., (in press).

3. Skuridin S., Badaev N., Dembo A., Lortkipanidze G., Yevdokimov Yu.
"Two Types of Temperature Induced Transitions of Poly(I) Poly(C) Liquid Crystals".
(1988) Liquid Crystals, vol. 3, N 1, pp. 51-62.

4. Yevdokimov Yu.M., Skuridin S.G., Salyanov V.I.
"Biosensors Based on Double-Stranded Nucleic Acid Molecules".
The First World Congress on Biosensors. Singapore, 2-4 May, 1990.
(1990), Abstracts, p. 65.

5. Yevdokimov Yu., M., Salyanov V.I.
"Reformation of Liqiud-Crystalline Phases of Circular Superhelical DNA Upon the Action of Nuclease".
(1990) Liquid Crystals, (in press).

6. Yevdokimov Yu.M., Skuridin S.G., Salyanov V.I., Damaschun G., Damaschun H., Misselwitz R., Kleinwächter V.
"Effect of Platinum(II) Chemotherapeutic Agents on Properties of DNA Liquid Crystals".
(1990) Biophys. Chem., (in press).

Считаю, что исследования в области фундаментальных основ конструирования новых типов биодатчиков являются актуальными. Такие исследования могут не только представить интерес для ученых Национального научного фонда США, но и проводиться совместно с этими учеными в рамках темы "Биотехнология".

I suppose that the creating of new types of bisensors (biosensing units) based on nucleic acids or their complexes with different compounds interesting from practical point of view is important. Cooperation in this field with american scientists seems to me very possible.

Руководитель ВНК: /Ю.М.Евдокимов/

25 июня 1990 г.

Laboratory of Genom Mobility

Themes: Regulation of gene activity, molecular biology of gene.

Main publications

1. Arkhipova I.R., Mazo A.M., Cherkasova V.A., Gorelova T.V., Schuppe N.G., Ilyin Y.V. (1986) The steps of reverse transcription of Drosophila mobile dispersed genetic elements and U3-R-U5 structure of their LTRs Cell 44, 555-563

2. Zelentsova E.S., Vashakidze R.P. Krayev A.S., Evgeniev M.B. (1986) Dispersed repeats in *Drosophila virilis* elements mobilized by interspecific hybridization Chromosoma 93, 469-476

3. Mizrokhi L.J., Georgieva S.G., Ilyin Y.V. (1988) Jockey, a mobile *Drosophila* element similar to mammalian LINEs, is transcribed from the internal promoter by RNA-polymerase II Cell 54, 685-691

4. Priimagi A.F., Mizrokhi L.J., Ilyin Y.V. (1988) The *Drosophila* mobile element jockey belongs to LINEs and contains coding sequences homologous to some retroviral proteins Gene 70, 253-262

5. Mazo A.M., Mizrokhi L.J., Karavanov A.A., Sedkov Y.A., Krichevskaya A.A., Ilyin Y.V. (1989) Suppression in *Drosophila: su(hw)* and *su(f)* gene products interact with a region of *gypsy* (mdg4) regulating its transcriptional activity EMBO J. 8, 903-911

6. Vashakidze R.P., Zelentsova E.S., Korochkin L, Evgeniev M.B. (1989) Expression of dispersed 36 up sequences in *Drosophila virilis* Chromosoma 97, 374-380

7. Lyubomirskaya N.V., Arkhipova I.R., Ilyin Y.V., Kim A.I.

(1990) Molecular analysis of the *gypsy* (mdg4) retrotransposon in two *Drosophila melanogaster* strains differing by genetic instability Mol.Gen.Genet. in press

The collaboration between american scientists and our laboratory is possible in investigation of structural organization and expression of *Drosophila* mobile elements, the processes of their transposition. During the last few years there were found all the intermediates of reverse transcription of several *Drosophila* retrotransposons and the initiation sites of their transcription were determined. For *Drosophila* mobile element *gypsy* (mdg4) it was shown, that it contains two closely spaced nuclear proteins binding regions which are negative and positive regulators of transcription. For *Drosophila* LINE jockey it was demonstrated that its transcription is performed by RNA polymerase II and is controlled by an internal promoter. Recently we have shown, that many other *Drosophila* retrotransposons have similar organization of promoters. Now we also investigate the instable mutator strain of *Drosophila melanogaster*, characterized by high frequency of transpositions of *gypsy* and *hobo* elements, while other mobile elements are not transposing in this *Drosophila* strain.

P.G. Georgiev, T.I. Gerasimova. Novel genes interacting with expression of the *yellow* locus and the mdg4 (*gypsy*) in *Drosophila melanogaster*. Mol. Gen. Genet. 1989, 220, 121-126.

P.G. Georgiev et al. Mitomycin C induces genomic rearrangements involving transosable elements in *Drosophila melanogaster*. Mol. Gen. Genet. 1990, 220, 229-233.

P.G. Georgiev, S.L. Kiselev, O.B. Simonova, T.I. Gerasimova. A novel transposition system in *Drosophila melanogaster* depending on the *Stalker* mobile genetic element. EMBO J. 1990, July issue.

PROPOSALS

1) Studies on novel genes involved in control of bristles and hairs—(periphery nervous system) development discovered in the system with a mobilized *Stalker*, namely *suppressor of scute*, *pseudoscute* and some others.

2) Studies on cloning, structure and mechanism of functioning of genes involved in control of the *yellow* locus expression, *enchancers of yellow*.

USSR labs are in the Engelhardt Institute of Molecular Biology and Institute of Gene Biology, Ac.Sci. USSR, Moscow.

The research group from US side is Prof. Victor Corces, Johns Hopkins University, Baltimore.

COMPARATIVE STUDY OF VARIOUS DNA-POLYMERASES FROM ANIMALS AND VIRUSES (RETROVIRUSES)

(a head of the lab. Prof. A.A,Krayevsky)

The main topics: The principles of substrate selection by different DNA polymerases; inhibitor analysis of DNA polymerases; construction of selective inhibitors of DNA synthesis catalyzed by various DNA polymerases in cell- and free-cell cultures; investigation of drug resistence.

Proposed collaboration with the USA

Comparative study of DNA-polymerase in mammals (humans) and viruses (retroviruses). Principles of substrate selection by DNA-polymerase, inhibitory analysis of DNA-polymerase, synthesis of selective inhibitors of DNA-polymerase for acellular and cellular systems. Enzyme study of the onset of resistance to medications.

лекарствам.

Литература:

1 R.Sh.Beabealashvilli, A.V.Scamrov, T.V.Kutateladze, A.M.Mazo, A.A.Krayevsky, M.K.Kukhanova "Nucleoside 5'-triphosphates modified at sugar residues as substrates for calf thymus terminal deoxynucleotidyl transferase and AMV reverse transcriptase", Biochim.Biophys.Acta 868, 136, 1986.

2.G.Chidgeavadze, R.Sh.Beabealashvilli, A.A.Krayevsky, M.K. Kukhanova "Nucleoside 5'-triphosphates with modified sugars as substrates for DNA polymerases" Biochim.Biophys.Acta, 868, 145, 1986.

3. A.A.Krayevsky, M.K.Kukhanova, R.Sh.Beabealashvilli, Z.G. Chidgeavadze "Some aspects of DNA polymerase functioning", in "Biophosphates and their analogues - Synthesis, Structure, Metabolism and Activity", Eds., K.S.Bruzik, W.J.Stec, Elzevier Science Publishers, Amsterdam, 1987, p.379-390.

4. N.Dyatkina, S.Minassyan, M.Kukhanova, A.Krayevsky, M.von Janta-Lipinsky, Z.Chidgeavadze, R.Beabealashvilli "Properties of 2',3'-dideoxy-2',3'-didehydrothymidine 5'-triphosphate in terminating of DNA synthesis catalyzed by several DNA polymerases" FEBS Letters, 219, 151, 1987.

5. A.A.Krayevsky, M.K.Kukhanova, A.M.Atrazhev, N.B.Dyatkina, A.V.Papchikhin, Z.G.Chidgeavadze, R.Sh.Beabealashvilli "Selective inhibition of DNA chain elongation catalyzed by DNA polymerases" Nucleosides and Nucleotides 7, 613, 1988.

6. G.V.Pyrinova, E.A. Kuzminova, R.I.Salganik, A.A.Krayevsky, M.K.Kukhanova "Selective inhibition of the reverse transcription in the retroviral A-type particles from rat liver by thymidine derivatives", FEBS Letters 247, 57, 1989.

7. T.Rozovskaya, N.Tarussova, Sh.Minassyan, A.Atrazhev, M. Kukhanova, A.Krayevsky, Z.Chidgeavadze, R.Beabealashvilli "Pyrophosphate analogues in pyrophosphorolysis reaction catalyzed by DNA polymerases", FEBS Letters 247, 289, 1989.

8. D.Z.Chinchaladze, D.A.Prangishvilli, A.V.Scamrov, R.Sh.Beabealashvilli, N.B.Dyatkina, A.A.Krayevsky "2'-Deoxynucleoside 5'-triphosphates modified at sugar residue as substrates for DNA polymerases from Thermoacedophilic archebacterium" Biochim.Biophys.Acta <u>1008</u>, 113, 1989.

9. A.A.Krayevsky, M.K.Kukhanova "Physicochemical aspects of functioning of DNA polymerases" Sov.Sci.Rev.B.Chem. <u>13</u>, 3-67, 1989.

10. N.B.Tarussova, A.A.Khorlin, A.A.Krayevsky, M.N.Korneyeva, D.N.Nosik, N.B.Kruglov, G.A.Galegov, R.Sh.Beabealashvilli "Inhibition of HIV production in cell cultures by 5'-phosphonates of 3'-azido-2',3'-dideoxynucleosides" Mol.Biol.. Moscow <u>23</u>, 1716, 1989.

Лаборатория химич. и биохимич. анализа,
зав.

2. VII – 1990, А. Краевский (А.А. Краевский)

С П И С О К

основных научных статей сотрудников ИМГ АН СССР, опубликованных за последние несколько лет в международных журналах

I. Dept. of Molecular Embryogenetics and Cell Differentiation
Отдел молекулярной эмбриогенетики и клеточной дифференцировки

1 H.G.Gazaryan.

Transplantation of Nuclei and Genes into Animal Ova.

Soviet Scientific Reviews. F. Physiology and General Biology. Vol. 1. P. 703-780. 1987. Harwood Publishers GmbH, United Kingdom.

2. Tarantul V.Z., Kucherjavy V.V., Makarova I.V., Baranov Yu.N., Begetova T.V., Andreeva L.E., Gazaryan K.G.

Rearrangements of microinjected recombinant DNA in the genome of transgenic mice.

Molecular and General Genetics. Vol. 203. P. 305-311. 1986

3. K.G.Gazaryan, S.D.Nabirochkin, E.N.Shibanova, A.G.Tatosyan, F.L.Kisselev

Unstable visible mutations induced in Drosophila melanogaster by injections of oncogenic virus DNA into the polar plasm of early embryos.

Molecular and General Genetics. Vol. 207. P. 130-141. 1987.

II. Dept. of Animal Molecular Genetics
Отдел молекулярной генетики животных

1. Yu.Ya.Shevelev, M.D.Balakireva, V.A.Gvozdev. Heterochromatic regions contain similar arrangements of moderate repeats with inserted copia-like elements (MDGI). Chromosoma, 1989, 98, 117-122.

2. E.S.Pasyukova, E.S.Belyaeva, V.A.Gvozdev. Outcross-dependent

transpositions of copia-like mobile genetic elements in chromosomes of an inbred Drosophila melanogaster stock.
Molec. Gen. Genet., 1988, 212, 281-286.

3. A.A.Kramerov, D.V.Mukha, E.V.Metakovsky, V.A.Gvozdev.
Glycoproteins containing sulphated chitin-like carbohydrate moiety are synthesized in an established Drosophila melanogaster cell line. Insect. Biochem., 16, 417-432, 1986.

III. Dept. of Molecular Bases of Human Genetics
Отдел молекулярных основ генетики человека

1. Limborska S.A., Korneev S.A., Maleeva N.E., Slominsky P.A., Jincharadge A.G., Ivanov P.L., Ryskov A.P.
Identification of some Alu+poly(A)+ RNAs in a variety of human normal and tumor cells.
FEBS Lett., v.22, p.208, 1987.

2. Ryskov A.P., Jincharadze A.G., Prosnyak M.I., Ivanov P.L., Limborska S.A.
M13 phage DNA as a universal marker for DNA fingerprinting of animals, plants and microorganisms.
FEBS Lett., v.233, p.303, 1988.

3. Limborska S.A., Fedorov A.N., Bukhman V.L., Prosnyak M.I.
Detection of globular intron mutation in a -talassemic patient from Azerbaijan.
In: "Metabolism and enzymology of nucleic acids including gene manipulation".
Plenum Press, N-Y, p.197-201, 1988.

4. Slominsky P.A., Maleeva N.E., Buyakova O.I., Pchukarova L.G., Panina T.V., Ryskov A.P., Limborska S.A.
A sequence from human brain cDNA that is expressed actively in neural and tumor cells.
FEBS Lett., in press, 1990.

1. O.L.Lomovskaya, S.Z.Mindlin, Zh.M.Gorlenko and R.B.Khesin.
A nonconjugative mobilizable broad host range plasmid of Acinetobacter sp. that determines HgCl-2 resistance.
MGG, 1986, 202:286-290.

2. E.S.Bogdanova, S.Z.Mindlin, E.S.Kalyaeva, V.G.Nikiforov.
The diversity of mercury reductases among mercury-resistant bacteria.
FEBS Lett., 1988, 234:280-282.

3. E.S.Bogdanova and S.Z.Mindlin.
Two structural types of mercury reductases and possible ways of their evolution.
FEBS Lett., 1989, 247:333-336.

4. M.V.Kashlev, A.L.Goldfarb, V.G.Nikiforov et al.
Transdominant RNA-polymerase mutation blocking initiation-to--elongation transition.
Science, 1990, may.

5. M.V.Kashlev and A.I.Gragerov.
Heat-stock response in E.coli promotes assembly of plasmid encoded RNA-polymerase.
MGG, 1989, 216:469-474.

6. O.N.Danilevskaya, E.V.Kurenova, B.A.Leibovich, I.A.Bass, M.N.Pavlova.
A family of Drosophila telomere-associated repeats: properties, polymorphism and sequence.
Genetics, 1990, in press.

7. A.I.Gragerov, O.N.Danilevskaya, S.A.Didichenko, E.N.Kaverina.
An ARS element from D.melanogaster telomeres contains the yeast ARS core and band replication enhancer.
Nucl. Acid Res., 1988, 16: 1169-1179.

Dept. of Genome Issues

У. Отдел проблем генома

1. A.G.Antoshechkin, V.Yu.Tatur, O.M.Perevedentseva and L.A.Maximova Determination of human fibroblasts metabolism in vitro by gas chromatography-mass spectrometry of cell-excreeted metabolism. - Anal. Biochem. 169(1988) 33-40.
2. A.G.Antoshechkin, V.Yu.Tatur and L.A.Maximova. Discovery of methoxyacetylcarbamide in the urine of normal adults and phenylketonuric children.- Clinica Chemica Acta 177(1988) 239-244.
3. Belitsky G.A., Khovanova E.M., Budukova I.V., Shapurits H.G. Micotoxin induction of somatic mosaicism in Drosophila and DNA repair in mammalian liver cell cultures. - Cell Biology and Toxicology, V.1 (1985) N3, p.133-143.

Dept. of Genome Expression

УI. Отдел экспрессии генома

1. S.M.Mirkin, V.I.Lyamichev, K.N.Drushlyak, V.N.Dobrynin, S.A.Filippov and M.D.Frank-Kamenetskii. "DNA H form requires a homopurine-homopyrimidine mirror repeat", Nature 330, 495-497 (1987).
2. V.I.Lyamichev, S.M.Mirkin, M.D.Frank-Kamenetskii and C.R.Cantor. "A stable complex between homopyrimidine olidomers and the homologous regions of duplex DNA": Nucl. Acids Res. 16, 2165-2178 (1988).
3. O.N.Voloshin, S.M.Mirkin, V.I.Lyamichev, B.P.Belotserkovskii and M.D.Frank-Kamenetskii. "Chemical probing of homopurine-homopyrimidine mirror repeats in supercoiled DNA": Nature 333, 475-476 (1988).
4. V.I.Lyamichev, S.M.Mirkin, O.N.Danilevskaya, O.N.Voloshin, S.V.Dalatskaya, V.N.Dobrynin, S.A.Filippov and M.D.Frank-Kamenetskii "An unusual DNA structure detected in a telomeric sequence under superhelical stress and at low pH": Nature 339, 634-637 (1989).

Laboratory of Somatic Cell Genetics

УП. Лаборатория генетики соматических клеток

1. Cherepakhin V.V., Jakubov L.Z., Ibraghimov A.R., Rokhlin O.V., Allelic exclusion frequency analysis and molecular characteristics of immunoglobulins secreted by the hybridomas expressing both allelic genes. - Immunol. Letters 15, 33-39 (1987).
2. Ibraghimov A., Jakubov L., Mayushina R., Mogilevsky L., Maisurian N., Rokhlin O. Appearance of necantigen in mouse IgG_1 upon reduction of interchain disulfide bridges: assessment of local and general conformational rearrangements by using monoclonal antibody and small-angle X-ray scattering. - J. Biomolec. Struc. Dynamics 5, 1, 177-185, 1987.
3. Jahn S., Grunov R., Kiessig S., Bogachova G., Arsen'eva E., Hlinak A., Rohlin O., Baehr R. Cell biology of human IgM-producing hybridomas derived from a fusion of human spleen lymphocytes with mouse myeloma cells. - Hybridoma 6, 679-687, 1987.

Ученый секретарь ИМГ АН СССР,
кандидат биологических наук А.Е. Хализев

Shemyakin Institute of Bio-ORGANIC CHEMISTRY

Перечень возможных направлений сотрудничества Института биоорганической химии им.М.М.Шемякина АН СССР с учреждениями США

Receptor proteins

1. The structure-functional study of receptor and signal transducing systems (proteins of visual and adenylatecyclase systems, photoreaction centers and photoreceptors of plants, ATPases).
2. The search for and study of new proteins, participating in signal trunsduction.
3. Cloning of their genes and the study of regulation of their expression.

Neurochemistry

1. Search for and structural study of the brain neuropeptides.
2. The study of brain neuroreceptors.

Molecular immunology and hematopoiesis

1. The study of structure-function relationship of new proteins, participating in immune reactions and hematopoiesis.
2. The cloning, elucidation of structure and expression of their genes.
3. The study the receptors binding these proteins on target cells.
4. The study of molecular mechanisms of leukemia development.

Human genom

The study of human genom structure.

Synthetic vaccines

1. Development of new adjuvants, in particular muramylpeptide based compounds, and the study of molecular mechanism of their biological activity.
2. Development of peptide-based synthetic vaccins to wide-spread diseases.

Monoclonal antibodies

Development of monoclonal antibodies to

- receptor proteins
- growth and differentiation factors
- phytoviruses

and their use in structure-functional studies and in diagnostics.

1. I.Schwartz, A.A.Gol'tsov, O.K.Kaboev, A.A.Alexeev, G.Yu. Solovyev, V.L.Surin, A.V.Lukianenko, S.V.Vinogradov, Yu. A.Berlin. A novel frameshift mutation causing -thalassaemia in Azerbaijan // Nucl. Acids Res. - 1989 - v. 17 - N 10 - 3997

2. G.V.Shpakovski, M.H.Karakashly, Yu.A.Berlin. plac10 transducing bacteriophage: DNA primary structure of the region of the abnormal exision //FEBS Lett. - 1989 - v. 258 - N 1 - 171-174

3.J.S.Sacck, S.D.Trakhanov, I.N.Tsigannik, F.A.Quiocho. Structure of L-leucine-binding protein refined at 2.4 A resolution and comparison with the Leu/Ile/Val-binding structure //J.Mol.Biol. - 1989 - 206 - 193-207

4.V.V.Demin. Spatial structure of membrane proteins according to electron microscopic data // Comments on Molecular and cellular Biophysics - 1989 - 5(6) - 314-342

5. E.V.Yurkova, I.N.Tsygannik, A.G.Zargarov, A.S.Zolotarev, N.G.Abdulaev, V.V.Demin. Crystallization of photosynthetic reaction centers from Chloroflexus aurantiacus //FEBS Lett. - 1989 - 256 (1,2) - 167-169

6. E.I.Frolova, G.M.Dolganov, M.N.Markelov, B.Zhumabaeva. Close localizaation of the genes for GM-CSF and IL-3 in human genome//IN: Moderm trends in Human Leukemia. VIII - eds.R.Neth, R. C.Gallo, M.F.Greaves, G.Gaedike, S.Gohla, K.Mannweiler, I.Ritter - Springer-Verlag - 1988 - 390-392

7. N.M.Arzamazova, E.A.Arystarkhova, N.M.Gevondyan, N.M.Luneva, R.G.Efremov, N.A.Aldanova, V.A.Nesmeyanov, N.N.Modyanov. Sequence analysis of exposed domains of membrane-bound Na,K-ATPase. Model of transmembrane arrangement In: The Na,K-Pump.Part A: Molecular Aspects - New York - Alan R.Liss - 1988 - 57-64

8. A.Huth, K.E.Petrukhin, N.N.Modyanov, T.A.Rapoport. SRP-Dependent membrane integration of the -subunit of Na,K-ATPase //Biomed.Biochim.Acta - 1989 - 48 - 77-84

9. E.D.Sverdlov, D.A.Bessarab, I.V.Malyshev, K.E.Petrukhin, Yu.V.Smirnov, Yu.A.Ushkaryov, G.S.Monastyrskaya, N.E.Broude, N.N. Modyanov. Family of human Na,K-ATPase genes. Structure of the putative regulatory region of the .-gene //FEBS Lett.- 1988 - 244 - 481- 483

10. E.A.Aristarkhova, O.E.Lakhtina, N.N.Modyanov. Immunodetec-

tion of Na,K-ATPase .III-isoform in renal and nerve tissue // FEBS. Lett. - 1989 - 250 - 545-548

11. E.N.Chertova, S.V.Lutsenko, N.B.Levina, N.N.Modyanov. Probing the topography of the intramembrane part of Na,K-ATPase by photolabelling with 3-(trifluoromethyl)-3-(m [125J] iodophenyl) diazerin. Analysis of the hydrophobic domain of the .-subunit //FEBS.Lett. - 1989 - 254 - 13-16

12. N.M.Gevondyan, V.S.Gevondyan, E.E.Gavrilyeva, N.N.Modyanov. Analysis of the sulfhydryl groups and disulfide bonds in Na, K-ATPase //FEBS.Lett. - 1989 - 255 - 265-268

13. E.A.Aristarkhova,O.E.Lakhtina,N.B.Levina N.N.Modyanov. Immunoaffinity isolation of Na,K-ATPase .3 isoform from pig kidney //FEBS Lett. - 1989 - 257 - N 1 - 24-26

14. N.E.Broude, N.N.Modyanov, G.S.Monastyrskaya, E.D.Sverdlov. Advances in Na,K-ATPase studies from protein to gene and back to protein //FEBS.Lett. - 1989 - 257 - N 1 - 1-9

15. V.Grishin, T.M.Volkova, A.S.Arseniev.Isolation and structure analysis of components from venom of the spider Argiope lobata //Toxicon - 1989 - v.8 - N3 - 541-549.

16. E.V.Grishin, T.M.Volkova, A.S.Arseniev.New antagonists of glutamate receptors// J.Protein.Chem - 1989 - v.8 - N 3 - 320-322

17. T.M.Volkova, N.A.Avetisyan, T.G.Galkina, A.B.Kudelinn, E. M.Makhmudova, M.M.Soloviev, B.A.Tashmuchamedov, E.V.Grishin. Isolation of argiopin-binding protein from bovine brain //J.Protein Chem. - 1989 - v.8 - N 3 - 322-324

18. S.Yu.Zaitsev, S.V.Dzekhtser, V.P.Zubov. Polymer membranes with immobilized bacteriorhodopsin //Stud. Biophys. - 1989 - v. 132 - N 1-2 - p. 105-110

19. E.P.Lukashev, S.Yu.Zaitsev, A.A.Kononenko, V.P.Zubov. Photoelectrical properties of bacteriorhodopsin in langmuir films //Stud. Biophys. - 1989 - v. 132 - N 1-2 - p. 111-118

20. V.M.Lipkin, N.V.Khramtsov, S.G.Andreeva, M.V.Moshnyakov, G.V.Petuchova, T.V.Rakitina, R.A.Feschenko, K.A.Ischenko, S.F.Mirzoeva, M.N.Chernova, S.M.Dranytsyna. Calmodulin-independent bovine brain adenylate cyclase. Amino acid sequence and nucleotide sequence of the corresponding cDNA //FEBS Letters - 1989 - v. 254 - N 1,2 - p. 69-73

21. S.F.Mirzoeva, S.M.Dranitsyngf, M.N.Chernova, A.N.Obukhov, N.V.Khramtsov, V.M.Lipkin, Yu.A.Ovchinnikov. Partial amino acid sequence of calmodulin-independent bovine brain adenylate cyclase //J. of Protein Chem. - 1989 - v. 8 - N 3 - p. 402-404

22. V.M.Lipkin, O.M.Shamborant, V.V.Gubanov, K.G.Muradov, I. P.Udovichenko, V.A.Bondarenko, M.Yu.Natoshin, N.P.Skiba. Structural and functional studies of cyclic GMP phosphodiestarase // J. of Protein Chem. - 1989 - v. 8 N 3 - p. 406-408

23. V.Z.Slepak, A.N.Pronin, O.G.Kiselyov, V.L.Voeikov, E.I.Frolova, V.M.Lipkin . Structure and function of the subunit of the GTP-binding protein go from bovine cerebellum // J. of Protein Chem. - 1989 - v. 8 - N 3 - p. 436-438

24. I.L.Barsukov, A.S.Arseniev, V.F.Bystrov. 2D H-MNR study of conformational flexibility of L,D-peptides. Gramicidin A and its analog //Peptides 1988 - eds. G.Jung, E.Bayer, Walter de Gruyter - Berlin - p. 471-473

25. I.R.Nabiev, R.G.Efremof, G.D.Chumanov. Surface-enhanced Raman scattering and its application to the study of biological molecules //Sov.Phys. Usp. - 1988 - 31 - 241-262

26. R.G.Chumanov,R.G.Efremov, I.R.Nabiev. Surface-enhanced Raman spectroscopy of biomolecules. I. Water-soluble proteins, dipeptides and amino acids //J.Raman Spectrosc. - 1989 - 1- - 124 -130

27. R.G.Chumanov,R.G.Efremov, I.R.Nabiev. Surface-enhanced Raman spectroscopy of biomolecules. II. The application of short and long-rang components of SERS to study the structure and function of the membrane proteins //J.Raman.Spectrosc. - 1989 - 10 - 131-140

28. S.Nie, C.G.Castillo, K.L.Bergbauer, J.F.R.Kuck, I.R.Nabiev, Yu.N.-T.Surface-chaneced Raman spectra of eye lens pigments //Applied Spectrosc. - 1989 - 28 - 28-29

29. J.Foldi, M.Horanyi, J.G.Szelenyi, S.R.Hollan, E.A.Aseeva, I.N.Lutsenko, V.A.Spivak, O.Toth, B.V.Rozynov. Hemoglobin siriraj found in the hungarian population //Hemoglobin - 1989 - v. 13 - N 2 - 178-180

30. Yu.A.Ovchinnikov, N.G.Abdulaev, B.E.Shmukler, A.A.Zargarov, M.A.Kutuzov, I.N.Telezhinskaya, N.B.Levina, A.S.Zolotarev.

Photosynthetic reaction centre of Chloroflexus aurantiacus. II.Primary structure of M-subunit //FEBS Lett. - 1988 - v. 323 - p. 364-368

31. A.A.Bukharov, B.L.Kolosov, O.N.Klezovich. Nucleotide sequence of rye chloroplast DNA fragment comprising psbD, psbC and trnS genes// Necl. Asids Res. - 1989 - v. 17 - p. 798

32. V.L.Kolosov, O.N.Klezovich, A.S.Zolotarev. Nucleotide sequence of rye chloroplast DNA fragment comprising psbE and psbF genes// Necleic Asids Research - 1989 - v. 17 N 2 - p. 1760

33. A.A.Bukharov, B.L.Kolosov, A.S.Zolotarev . Nucleotide sequence of rye chloroplast DNA fragment encoding D1 protein of photosystem II // Necleic Asids Research - 1989 - v. 17 - 4 N - p. 1759

34. S.A.Zozula, V.V.Gurevich, T.A.Zvyaga, I.L.Dumler, M.N.Garnovskaya, B.E.Shmukler, M.Yu.Natochin, E.P.Shirokova, P.R. Badalov. In vitro synthesis of visual rhodopsin for a protein engineering study //J.Protein Chem. - 1989 - v. 8 - N 3 - p. 380-382

35. Yu.N.Utkin, E.M.Lazakovich, I.E.Kasheverov, V.I.Tsetlin. .-Bungarotoxin interacts with the rat brain tachykinin receptors / /FEBS Lett. - 1989 - 255 - N 1 - 111-115

36. A.A.Kaydalov, Yu.N.Utkin, T.M.Andronova, V.I.Tsetlin, V.T.Ivanov. Muramyl peptides bind specifically to rat brain membranes //FEBS Lett. - 1989 - 248 - N 1,2 - p. 78-82

37. V.P.Shevchenko, V.V.Bezuglov, N.M.Gretskaya, G.S.Kogteva. E.M.Manevich, N.F.Myasoedov. Synthesis of fluoroscent derivatives of tritium labelled prostaglandins // Synthesis and application of isotopically labelled compounds 1988 (pub. 1989) - Eds. T.A.Baillie, J.R.Jones - p. 573-575

38. V.P.Shevchenko, V.V.Bezuglov, E.M.Manevich, N.F.Myasoedov. Synthesis of tritium labelled fluorescent eicosapolyenoic acids // Synthesis and application of isotopically labelled compounds 1988 (pub. 1989) - Eds. T.A.Baillie, J.R.Jones - p. 569-571

39. V.P.Shevchenko, V.V.Bezuglov, I.Yu.Nagaev, N.F.Myasoedov. The introduction of tritium label into natural and modified prostaglandins // Synthesis and application of isotopically labelled compounds 1988 (pub.1989) - Eds. T.A.Baillie, J.R.Jones -

p. 561-564

40. A.G.Tonevitsky, E.M.Manevich, O.S.Zhukova, E.L.Arsen'eva, G.T.Bogacheva, L.D.Bergelson. A new approach to studies of cell-antibody interaction using fluorescence, distance geometry and molecular dynamics ..FEBS Lett. - 1988 - 236 - 315-317

41. V.V.Tertov, T.S.Sayadyan, G.F.Kalantarov, J.G.Molotkovsky, L.D.Bergelson, A.N.Orekhov. Use of lipophylic fluorescent probes for the isolation of hybride cells in flow cytometry //J.Immunol. Methods - 1989 - 118 - 139-143

41. V.M.Lipkin, O.N.Shamborant, V.V.Gubanov, K.G.Muradov, I.P. Udovichenko, V.A.Bondarenko, M.Yu.Natochin, N.P.Skiba, Structural and functional studies of cyclic GMP phosphodiesterase //J.Prot.Chem. - 1989 - v. 8 - N 3 - p.406-408

42. O.M..Vol'pina, A.Yu.Surovoi, V.M.Gelfanof, E.S.Kahn, V.T. Ivanov. Novel foot-and-month disease protective peptides //Technological advances in vaccin development - Alan.R.Liss Inc. - 1988 - p. 391-400

43. A.Yu.Surovoi, V.M.Gelfanov, L.A.Grechyaninova, A.V. Yarov, O.M.Vol'pina, V.T.Ivanov. Towards peptide vaccine against the foot-and-month disease //Peptides 1988. Eds. G.Jung, E.Bayer, Berlin-New-York: Walter de Gryter and Co - 1989 - p. 692- 694

44. Yu.A.Ushkaryov, G.S.Monastyrskaya, N.E.Broude, N.N.Nikiforova, D.A.Bessarab, M.Yu.Orlova, K.E.Petrukhin, N.N.Modyanov, E.D. Sverdlov. Human Na,K.-ATPase genes -subunit gene family contains at least one gene and one pseudogene. FEBS Lett., 1989, 257, 439-442.

45. Sverdlov E.D., Tsarev S.A., Markova S.V., Vasilenco S.K., Chishikov V.E., Petrov N.A., Kusov Yu.Yu., Nastashenco T.A., Balayan M.S. Cloning and expression of hepatitis A virus genome in E.coli cells. - Life Sci. Advantage (ser. "Molecular genetics"), 1987, 6, 129-133.

46. Reverdatto S.V., Andreeva A.V., Buryakova A.A., Chakhmakhcheva O.G., Efimov V.A. Nucleotide sequence of the 5.2 kbp barley chloroplast DNA fragments, containing psbB-psbH-petB-petD cluster, Nucl. Acids Res., 17, 7, 2859-2860.

47. Chakhmakhcheva O.G., Andreeva A.V., Buryakova A.V., Buryakova A.A., Reverdatto S.V., Efimov V.A. Nucleotide sequence

of the barley chloroplast psbE, psbF genes and flanking regions. Nucl. Acids Res. 1989, 17, 7, 2858.

48. Reverdatto S.V., Andreeva A.V., Buryakova A.A., Chakhmakhcheva O.G., Efimov V.A. Nucleotide sequence of the barley chloroplast psbC gene. Nucl. Acids Res. 1989, 17, 10, 3996.

49. Vol'pina O.M., Surovoi A.Yu., Ivanov V.T. Protection against viral infections with the aid of synthetic peptides. Foot-and-mouth disease as an example. Biomed. Sci. 1990, 1, 1, 23-32.

50. Lunev V.E., Lukin Yu.V., Kazennykh N.V., Belyaev S.V., Zubov V.P., Nesmeyanov V.A. Latex-agglutination analysis of human recombinant interleukin-2 with monoclonal antibodies. Biomed. Sci. 1990, 1, 1, 68-72.

51. Nesmeyanov V.A., Khaidukov S.V., Komaleva R.L., Andronova T.M., Ivanov V.T. Muramylpeptides augment expression of Ia-antigens on mouse macrophages. Biomed. Sci. 1900, 1, 2, 155-159.

Soviet-American Cooperation in Basic Sciences.

Proposal.

Research Group "Eukaryotic Gene Expression" (Head-S.A. Nedospasov, Ph.D; Engelhardt Institute of Molecular Biology, USSR Academy of Sciences).

Field: Molecular biology of tumor necrosis factors; regulation of transcription; human genome).

Summary

Previously in collaboration with other groups we have cloned and expressed human and animal genes coding for tumor necrosis factors (TNF), established their chromosomal localization and characterized genomic loci. We started international collaborative effort to study regulation of gene expression for two pleiotropic cytokines: TNF and lymphotoxin. At the present time we study molecular mechanisms of regulation of their expression, as well as genomic polymorphism of TNF locus located in the middle of *HLA* and its possible linkage to autoimmune diseases.

Proposal

To organize, starting from July, 1991, a Soviet-American laboratory for the period of 5 years to study the following mutually related problems:

(1) molecular mechanisms, controlling physiological expression of tumor necrosis factors in healthy organism and in the disease as well as in the course of anticancer or antishock treatments (including control of TNF receptor expression and TNF gene expression);

(2) molecular-genetic analysis of TNF locus inside *HLA* and search for a possible linkage to autoimmune diseases;

(3) evolution of TNF genes.

In addition to the scientists from this group we plan to hire on the temporal basis several research fellows from the USSR as well as young American scientists. The research can be done in parallel in the USSR (Engelhardt Institute of Molecular Biology) and in the USA (NIH, of one of the Universities having working contacts with our group). We hope to get financial support from the USSR Academy of Sciences and from American Foundations.

References

Nedospasov, S.A., Shakhov, A.N., Turetskaya, R.L., Mett, V.A., Azizov, M.M., Georgiev, G.P., Korobko, V.G., Dobrynin, V.N., Filippov, S.A., Bystrov, N.S., Boldyreva, E.F., Chuvpilo, S.A., Chumakov, A.M., Shingarova, L.N. and Ovchinnikov, Y.A.: Tandem arrangement of the genes coding for tumor necrosis factor (TNF-α) and lymphotoxin (TNF-β) in the human genome. Cold Spring Harbor Symp.Quant.Biol. 51 (1986a) 611-625.

Nedospasov,S.A., Hirt,B., Shakhov,A.N., Dobrynin,V.N., Kawashima, E., Accolla, R.S. and Jongeneel,C.V.: Genes coding for tumor necrosis factor and lymphotoxin are tandemly arranged on the chromosome 17 of the mouse. Nucleic Acids Res. 14 (1986b) 7713-7725.

Spies, T., Morton, C.C., Nedospasov, S.A., Fiers, W., Pious, D. and Strominger, J.D.: Genes for the tumor necrosis factors α and β are linked to the human major histocompatibility complex Proc.Natl.Acad.Sci.USA 83 (1986) 8669-8702.

Muller, U., Jongeneel, C.V., Nedospasov, S.A., Fisher Lindahl, K. and Steinmetz, M.: Tumor necrosis factor and lymphotoxin genes map close to *H-2D* in the mouse major histocompatibility complex. Nature 325 (1987) 265-267.

Semon, D., Kawashima, E., Jongeneel, C.V., Shakhov, A.N. and Nedospasov, S.A.: Nucleotide sequence of murine *TNF* locus including the *TNF-α* (tumor necrosis factor) and *TNF-β* (lymphotoxin) genes. Nucleic Acids Res. 15 (1987) 9083-9084.

Jongeneel, C.V., Shakhov, A.N., Nedospasov, S.A. and Cerottini, J.C.: Molecular control of tissue-specific expression at the mouse *TNF* locus. Eur.J.Immunol. 19 (1989) 549-552.

Nedospasov, S.A., Turetskaya, R.L. and Shakhov, A.N.: Cloning and characterization of the rabbit lymphotoxin (*TNF-β*) gene and its tight linkage to the gene coding for tumor necrosis factor. Nucleic Acids Res. 16 (1988) 3112.

Seregina T.M., Turetskaya R.L., Mekshenkov M.I. and Nedospasov S.A.: An autocrine growth factor constitutively produced by a human lymphoblastoid B-cell line is serologically related to lymphotoxin (TNF-β). Mol. Immunol. 26 (1989), 339-342.

Shakhov, A.N., Collart, M., Vassali, P., Nedospasov, S.A. and Jongeneel, C.V.: *κB*-type enhancers are involved in LPS-mediated transcriptional activation of the *TNF-α* gene in primary macrophages. J. Exp. Med. 171 (1990), 35-48.

Shakhov A.N., Kuprash D.V., Azizov M.M., Jongeneel C.V. and Nedospasov S.A.: Structural analysis of the rabbit TNF locus, containing the genes encoding TNF-β (lymphotoxin) and TNF-α (tumor necrosis factor). Gene (1990), in press.

Руководитель временного научного коллектива
доктор биологических наук

С.А. НЕДОСПАСОВ

Head of the group

S.A. NEDOSPASOV

Engelhardt Inst. of Molecular Biology

Molecular organization of chromosomes laboratory

Chairman Professor Andrei D. Mirzabekov

Topics for cooperation:

1. Structure of DNA-protein complexes in chromatin.
2. Regulation of gene activity.
3. DNA sequencing and human genome studies.

1. Mirzabekov A., Bavykin S., Belyavsky A., Karpov V., Preobrazhenskaya O., Shick V., Ebralidse K. Mapping DNA-protein interactions by crosslinking. In: **Methods in Enzymology** /1989/, **170** (Nucleosomes), 386

2. Karpov V., Preobrazhenskaya O., Mirzabekov A. Chromatin structure of hsp 70 genes, activated by heat shock: Selective removal of histones from the coding region and their absence from the 5'-region. **Cell** /1984/, **36**, 423

3. Nacheva G., Guschin D., Preobrazhenskaya O., Karpov V., Ebralidse K., Mirzabekov A. Change in the pattern of histone binding to DNA upon transcriptional activation. **Cell** /1989/, **58**, 27

4. Bavykin S., Undritsov I., Usachenko S., Strokov A., Bogdanov Yu., Mirzabekov A. The primary organization of nucleosomal core particles from actively dividing cells of lily. **FEBS Letters** /1988/, **228**, 149

5. Ebralidse K., Grachev S., Mirzabekov A.. A highly basic histone H4 domain bound to sharply bent region of nucleosomal DNA. **Nature** /1988/, **331**, 365

6. Manning G., Ebralidse K., Mirzabekov A., Rich A.. An estimate of the extent of folding of nucleosomal DNA by laterally assymetric neutralization of phosphate groups. **J. Biomol. Structure & Dynamics** /1989/, **6**, 877

7. Studitsky V., Belyavsky A., Melnikova A., Mirzabekov A. The structure of nucleosomal core particles within transcribed and repressed gene regions. **Nucl. Acids Res.** /1988/, **16**, 11187

8. Lysov Yu., Florentiev V., Khorlin A., Khrapko K, Shick V., Mirzabekov A. DNA nucleotide sequence as determined by oligonucleotide hybridization. **Proceed. USSR Acad. Sci.** /1988/ **303**, 1508

9. Khrapko K., Lysov Yu., Khorlyn A., Shick V, Florentiev V., Mirzabekov A. An oligonucleotide hybridization approach to DNA sequencing. **FEBS Letters** /1989/, **256**, 118

10. Khrapko K., Lysov Yu., Khorlin A., Chernov B., Florentiev V., Mirzabekov A. A fast method for DNA sequencing by hybridization with oligonucleotide matrix. **Science** (submitted for publication)

11. Mirzabekov A., Pruss D., Ebralidse K. Chromatin superstructure-dependent crosslinking with DNA of the histone H5 residues Thr-1, His-1, and His-62. **J. Mol. Biol.** /1990/, **211**, 479

12. Bavykin S., Usachenko S., Zalensky A., Mirzabekov A. Structure of nucleosomes and organization of internucleosomal DNA in chromatin. **J. Mol. Biol.** /1990/, **212**, 495

The Department of Sequencing and Mapping of Human Genome in the Engelhardt Institute of Molecular Biology was organized at the end of 1989. The main aim of our Department is to study on the human genome and to development and improve all aspects of the DNA sequencing methodology. The Department consist of two groups: a).- the group of cloning and mapping of the human genome, and b).- the group of sequencing and primary analysis of sequence data. At the present time we start to cloning and sequencing the several regions of the humen chromosomes, containing the humen oncogenes. The Department is opened to collaboration and ready to carry on the teamworks with the groups, studing on the structure of humen genome and working in this field.

Head of Department

Dr. Vladimir M. Zakharyev

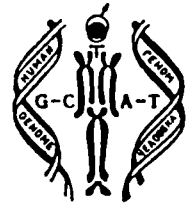
FYI 6/10/92

Leslie,

She is a good contact for the USSR HGPard is the secretary of the Russian National HUGO. She has the responsibility of keeping Scientists there involved in the project and has obtained everything we have on the HGP.

Betty

To Comrade McMillen.



Nina N. BELYAEVA, Ph. D.

Senior researcher
Scientist secretary of
Scientific council
on The State Scientific-Technical
Programme
«HUMAN GENOME»

Engelhardt Institute
of Molecular Biology
USSR Academy of Sciences

Vavilov str., 32
Moscow 117984, USSR
tel. (7)-095-1357445
fax (7)-095-1351405
telex 411755 MOLBI SU

The Human Genome Project in the USSR: a difficult start

A. A. Bayev and A. D. Mirzabekov

In this article the authors describe the establishment of the State Human Genome Project in the USSR, and show how its organization has been conditioned both by past experience and present structural and socio-economic factors.

In 1988 research in human genetics in the USSR received a powerful stimulus in the form of the establishment of a State Human Genome Scientific-Technical Project, one of fourteen such State programmes at the time.

Genetical research in this country has not always been either easy or smooth. Its heyday in the thirties, with such brilliant scientists as N. I. Vavilov and N. K. Koltsov heading research laboratories, gave way to hard times. Progress was severely handicapped by the Michurinian genetics expounded by Lysenko and fortified by the ideological pressures of political leaders who supported his doctrines and tried to rehash all science according to their canons.

For this reason the development of genetics in the USSR was interrupted for a long period, during which time it became impossible for new generations of scientists to appear and hardly possible for those who were on the scene to work, for fear of reprisal.

Stalin's death in 1953 changed the situation for only a short time and unfortunately not in any fundamental way. During his short time in power Khrushchev was to become the new protector of Lysenko.

Nearly 25 years have passed since that time, yet Lysenko's influence can still be felt through his followers and their disciples. The sham ideas of Michurinian genetics have been transformed and still exist in disguised form. However, the breakthrough has now been made and progress in genetics currently involves other, mostly financial, difficulties.

It is for the reasons outlined above that the impetus for progress in molecular genetics in this country has come from molecular biologists. The double helix structure of DNA was discovered by Watson and Crick in the very year that Stalin died, so that molecular biology and molecular genetics almost escaped the vigilance of

Academician A. A. Bayev is Councillor of the Presidium of the USSR Academy of Sciences and Chairman of the State Human Genome Scientific-Technical Project of the USSR. Author of more than 300 scientific papers, he has carried out research in various areas of molecular biology and on the development of new methodologies in genetic engineering. His co-author, Academician A. A. Mirzabekov, is Director of the W. A. Engelhardt Institute of Molecular Biology of the USSR Academy of Sciences and Vice-President of the Human Genome Organization.

The authors may be contacted through Professor Mirzabekov at the W.A. Engelhardt Institute, 32, Vavilov Street, 117894 Moscow, USSR.

ideological advocates (with a few dangerous exceptions which luckily were not pursued to their tragic end). Genetic engineering had appeared and developed within this same scientific community. It is not surprising therefore that the idea of human genome studies was born in this very environment, and that the Institute of Molecular Biology of the USSR Academy of Sciences was a source of inspiration to the Project.

The Human Genome Project in its original form is comprised of seven elements:

(i) collection of cell cultures and the isolation of individual chromosomes;
(ii) clone libraries and the physical mapping of human chromosomes;
(iii) human genome DNA sequencing;
(iv) structural–functional analysis of the human genome;
(v) medical genetic mapping and gene therapy;
(vi) software; and
(vii) instruments, reagents and probes.

This list deserves some comment (in particular, concerning functional studies). One might think that the Project could have been confined to human genome mapping and sequencing, as in the US National Project. Yet it was believed that genetic texts would also have to be decoded in functional terms sooner or later, i.e. a transition from genome syntax to semantics must occur. Moreover, most of molecular genetic studies in this country have a structural–functional framework and are not supported by specific programmes. Apart from other things, scientists prefer to solve such problems through the efforts of small groups over a reasonably short period of time. Human genome sequencing can take up to 15 years and will require a great number of people, whose personal scientific interests likely to be somewhat ignored. Such factors have to be taken into consideration while realising the Project.

The Project also involves medical genetic research. This too is not supported by other programmes, although hereditary pathology is a field where the Human Genome Project can first of all find practical application.

Thus it can be seen that many special circumstances have had to be taken into account in setting up the Project. According to our traditions, the Project does not cover conferences, workshops, schools and other educational programmes, publications, appeals to public opinion, and so on, although all these do actually exist. The cost of examining the moral and ethical issues raised will also apparently need to be met.

The USSR State Committee for Science and Technology allotted 25,000,000 roubles for the fiscal year 1989 and 32,000,000 roubles for 1990. It is not possible to say how much this represents in dollars because prices are inconsistent and the rouble-to-dollar exchange rate keeps varying. Nevertheless, some indication can be had by taking the following example. Within the USSR Academy of Sciences, a molecular biological institute with a scientific staff of some 250 people has an annual budget of about 6,000,000 roubles. Thus, 32,000,000 roubles would suffice for 4–5 institutes of this size and can be considered as quite generous. The Project also receives 5,000,000 roubles per year in hard currency for the purchase of instruments and reagents abroad. The money is distributed through two channels: to basic institutes and as grants to individual researchers and small groups.

The basic research institutes are those which have noticeably contributed to the development of molecular genetics and gene engineering, and have made themselves responsible for realising the Human Genome Project. One should bear in mind here

that progress in human genome studies cannot eventually be made without developing closely related fields of knowledge. Therefore, the creative power of a range of highly qualified experts will be needed to reach the objectives of the Project.

All in all, twenty basic institutes are being financed at the present time. Grants to individual scientists and groups are given on a competitive basis: about 300 grants in 1989 and 1990. The grants are rather small: from 10,000 to 40,000 roubles each.

It should be noted that State national projects are financed over and above the normal budget for each scientific institution in this country which meets salary expenses, the purchase of instruments and reagents, etc. In other words project financing is additional and aimed at stimulating those lines of research that are considered to be of highest priority. The same can be said of grant holders: their salaries and other research expenses are covered from the budgets of their respective institutes. The grant represents additional money and so can be rather modest.

Such a financing system has appeared as a result of the transitional state of our economy during the process of *perestroika* and will doubtless undergo further changes. The system of grants cannot yet operate to its full extent because the country has no free market in instruments and reagents, and researchers are not given a free hand to manage their grants. It remains unclear therefore how effective this system can be right now. Yet one has every reason to claim that the progress of molecular genetics in general and that of the Human Genome Project in particular has been made possible because it was financed by the State.

Hard currency is of crucial importance for research science in this country, especially where modern physico-chemical biology is concerned and instruments and reagents play a key role. Virtually no industry exists here to provide for experimental research in biochemistry, molecular biology and molecular genetics. This does not mean to say that nothing has ever been done along these lines, but whatever it was came from scientists (prototypes of instruments and samples of materials and reagents) rather than from the industrial sector. This accounts for the fact that experiments in biochemistry, molecular biology and molecular genetics still cannot be carried out without imported instruments and reagents. Hard currency funds allotted to the Human Genome Project are therefore extremely important for its realisation.

The Project is not subordinate in fact to either the USSR State Committee for Science and Technology or the USSR Academy of Sciences, although of course both bodies can influence it. The Project is answerable to a Council of 25 members, whose Chairman is Academician A. A. Bayev. The working body of the Council is its Board which is in charge of all routine business. National projects all have the same framework (a new word in science management in the USSR).

The Project has existed for one-and-a-half years and one is bound to admit that it has hardly been through the preliminary stage. Only now have prerequisites for its realisation appeared, but rapid progress is not to be expected. Such a situation can be attributed to several factors. First of all, researchers could not switch to the Project instantaneously; they had to finish previous work and to consider how to solve these new problems. Apparently, some kind of psychological barrier also had to be overcome.

Moreover, others were frightened by the fact that the Project was planned for a long time and that it involved an enormous amount of routine analytical work. Only recently have some scientists come to realise that this rather dull analytical work hides golden possibilities.

We have already mentioned that imported instruments and reagents are essential for human genome experiments. Because of various bureaucratic formalities, it may take as long as eighteen months to two years from the time an instrument or a reagent has been ordered for it to arrive at the institute.

Indeed, the reorganization of our science may be likened to an ocean liner which has to manoeuvre into a narrow harbour: the process needs skill and takes time. ■

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

Note to Dr. Jordan

Subject: Visit of Soviet Academy of Sciences Delegation

We now have the final confirmed dates for the visit of the Soviet Academy of Sciences delegation and biodata for the key members of the delegation (attached). They will be available for meetings as follows:

1. Academician Mirzabekov, Director of the Institute of Molecular Biology, and Academician Georgiev, Director of the Institute of Gene Biology, have specifically requested to meet with you and Dr. Mark Guyer. They will be available February 1, 4 and 5. We were holding February 1 at 3:45 on your calendar, but now the entire afternoon is free and the lunch is cancelled, because the rest of the delegation will arrive the following week. We were also holding February 4 at 1:30. Please let me know the time(s) you would prefer and for how long.

2/1 - a.m.
2/4 - all day
2/5 - before 3

prefer Jan 4 1:30

2. The rest of the delegation (including the Vice President of the Academy Rem Petrov and Academician Ivanov, head of the Shemyakin Institute of Bioorganic Chemistry, will be available February 6-8. We are tentatively planning a formal Stone House lunch on February 6 and hope you or your representative can attend (12-1:30). Do you wish to meet with anyone other than Mirzabekov and Georgiev?

YES lunch

No for oth

Please let me know as soon as possible what your preferences are. Thank you very much.

Alex Stepanian

Alexandra Stepanian
Program Officer for the Soviet Union
and East Asia
Fogarty International Center

Attachments

Academician Andrey Daryevich Mirzabekov

Academician A.Mirzabekov is a prominent scientist in the field of molecular biology.

He was born in 1937, got Ph.D. in Chemistry, then became a professor, member of the Academy of Sciences of the USSR.

Now academician A.Mirzabekov is a director of the Institute of Molecular Biology of AS USSR.

He is an author of 120 scientific publications. His main research interests are in interpreting structure and structural-functional investigations of nuclein acids, nucleoproteids and genome of eucariotic cells.

Academician A.Mirzabekov was awarded with USSR State Prize and International Prize of Federation of European Biochemical Societies.

Academician A.Mirzabekov [redacted] a member of many scientific societies, committees, editorial boards of scientific magazines.