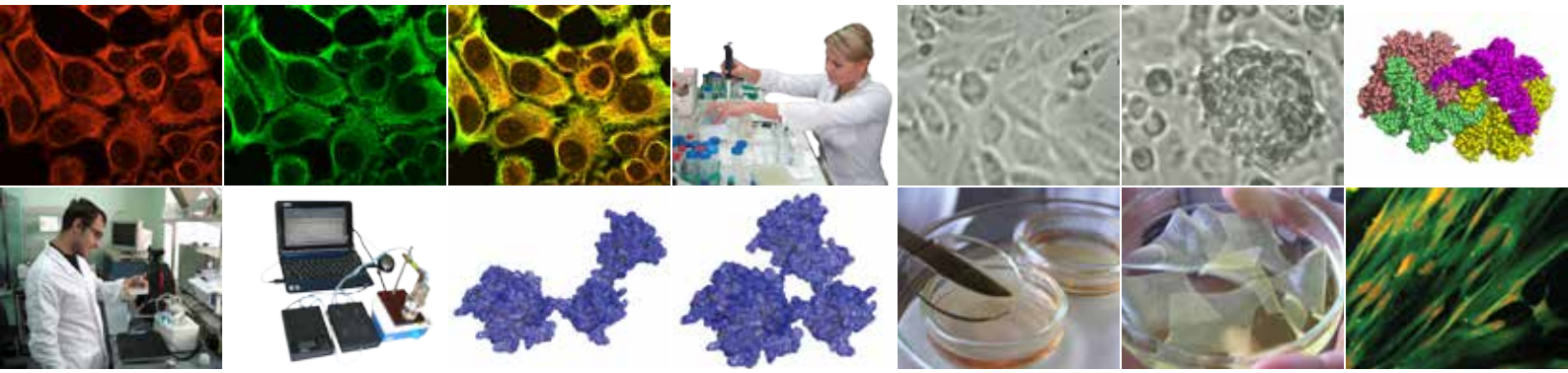
INSTITUTE OF MOLECULAR BIOLOGY AND GENETICS

NATIONAL ACADEMY OF SCIENCES OF UKRAINE



COMBIOM
SEVENTH FRAMEWORK PROGRAMME

Introduction

The Institute of Molecular Biology and Genetics (IMBG) of the National Academy of Sciences of Ukraine (NASU) was founded in 1973. Director of the Institute is a Full Member of NASU Professor Anna V. El'skaya. The staff comprises 433 employees, among them 272 scientists in the field of molecular biology, genetics, molecular biophysics, microbiology, medicinal chemistry and biotechnology, including 31 Doctors of Sciences (Dr.Sci.) and 136 Doctors of Philosophy (Ph.D.), two Full Members of NASU, one Full Member of National Academy of Medical Sciences of Ukraine (NAMSU), and 9 Corresponding Members of NASU.

Scientific research programme of the Institue is focused on the central trends of molecular biology, genetics and biotechnology.

Research areas:

- structural and functional genomics
- proteomics and protein engineering
- molecular and cell biotechnologies
- bioinformatics, computational modeling and design.

IMBG actively participates in many national and academic scientific programmes: "Fundamentals of genomics and proteomics", "Sensor devices for medicine, ecology and industry: metrological support and trial operation" (2013–2017), "Fundamentals of developing nanostructural systems, nanomaterials and nanotechnologies" (2010–2014), "New technologies of developing national medicines and diagnostics for human healthcare and veterinary" (2011–2015), etc.

The Institute is very efficient in international cooperation. For many years IMBG scientists successfully collaborate with their colleagues from Germany, France, USA, Great Britain, Poland, Italy, Greece, Japan, Russia, Belarus and others. At present, IMBG is involved in four 7th Framework Programme (FP7) Projects: "Improving Diagnoses of Mental Retardation in Children in Eastern Europe and Central Asia through Genetic Characterization and Bioinformatics/Statistics", CHERISH, (FP7-HEALTH, SICA), "Nanosensors based on nanomaterials" (FP7-PEOPLE, IRSES), "Transnational Access to NMR" (FP7 East-NMR programme) and "Strengthening Cooperation in Molecular Biomedicine between EU and Ukraine", COMBIOM, (FP7-INCO-2011-6, ERA-WIDE). The IMBG scientists have also other international grants including those of CNRS, NATO, STCU, etc. IMBG has strong long-time bilateral relations with the institutions of CNRS and Polish Academy of Sciences. During this period over 90 conferences, forums, scientific schools including international ones were hosted.

Presently over 100 young employees (under 35 years old) are working at IMBG and their number is growing yearly. Annually more than 30 young researchers are studying in the postgraduate school of IMBG. In the frame of "Molecular Biology" specialization of the Biochemistry Department, IMBG provides several courses on molecular biology and genetics for students of Educational and Scientific Centre "Institute of Biology" of Taras Shevchenko National University of Kyiv.

The IMBG scientists permanently lecture and give seminars for students of Taras Shevchenko National University of Kyiv, National University of "Kyiv-Mohyla Academy", National University of Food Technologies, National Technical University of Ukraine "Kyiv Polytechnic Institute", etc.

There are 2 Joint Departments of IMBG with the Universities:

- Department of Molecular Biology, Biophysics and Biotechnology, Institute of High Technologies (Taras Shevchenko National University of Kyiv)
- Department of Biomedical Engineering of Intercollegiate Medical Faculty of Engineering (National Technical University of Ukraine "Kyiv Polytechnic Institute").

The Council of Young Scientists supported by the IMBG Scientific Council holds the young scientists conferences for international and Ukrainian participants on the modern aspects of molecular biology, genetics and oncology.

Over 5000 scientific articles were published by the Institute scientists, of which more than 1200 – in international journals, among them "Nature", "Science", "Gene", "EMBO J.", "J. Biochem.", "Progr. Nucleic Acid Res. Mol. Biol.", "Nucleic Acids Res.", "Molecular and Cellular Biology", "J. Cell Science", "Biotechnology Current Progress", "Structure".

During 40 years the IMBG scientists achievements were awarded 30 State Prizes of USSR and Ukraine in Science and Technology, 3 Prizes of the Verkhovna Rada for young scientists, 4 Prizes of the Cabinet of Ministers of Ukraine for young scientists, 20 Prizes of the President of Ukraine designated for young scientists, 13 Personal Prizes of NASU. In 2003 IMBG was awarded the Honorary Certificate of the Cabinet of Ministers of Ukraine for its valuable contribution into the development of scientific research in the field of gene engineering and therapy, elaboration and introduction of novel biotechnologies and medicinal preparations. In 2009 IMBG was awarded the European Quality Award and the Europe Business Assembly diploma for scientific achievements of the European level.

Three scientific journals: "Biopolymers and Cell" (*www.biopolymers.org.ua*), "Ukrainica Bioorganica Acta" (*www.bioorganica.org.ua*), "The Bulletin of Vavylov Society of Geneticists and Breeders of Ukraine" (*www.utgis.org.ua*) are being published. In 2002 IMBG created and launched the first version of Web portal in bioinformatics, genomics, structural biology, and molecular medicine (*www.bioua.org.ua*).

Address: 150, Zabolotnogo Str., Kyiv, Ukraine, 03680
Phone: +380 (44) 526-11-69
Fax: +380 (44) 526-07-59
www.imbg.org.ua

Scientific Departments

The Institute of Molecular Biology and Genetics consists of 15 scientific departments and 10 laboratories.

Department of Cell Regulatory Mechanisms

Founded in 1969
Head – **Vitalii A. Kordium**
Dr.Sci. (microbiol.), Professor, Corresponding Member of NASU, Full Member of NAMSU

Department of Cell Signaling

Founded in 1973
Head – **Valeriy V. Filonenko**
Dr.Sci. (mol. biol.), Professor

Department of Translation of Genetic Information

Founded in 1978
Head – **Anna V. El'skaya**
Dr.Sci. (mol. biol.), Professor,
Full Member of NASU

Department of Molecular Genetics

Founded in 1978
Head – **Gennadiy D. Telegeev**
Dr.Sci. (mol. biol.), Senior Research Scientist

Department of Human Genetics

Founded in 1980
Head – **Lyubov L. Lukash**
Dr.Sci. (mol. genetics), Professor

Department of Molecular Oncogenetics

Founded in 1982
Head – **Volodymyr I. Kashuba**
Dr.Sci. (mol. biol.), Senior Research Scientist

Department of Nucleic Acids Biosynthesis

Founded in 1983
Head – **Vadym M. Kavsan**
Dr.Sci. (mol. biol.), Professor,
Corresponding Member of NASU

Department of Protein Synthesis Enzymology

Founded in 1989
Head – **Mykhaylo A. Tukalo**
Dr.Sci. (mol. biol.), Professor, Corresponding Member of NASU

Department of Cell Population Genetics

Founded in 1989
Head – **Viktor A. Kunakh**
Dr.Sci. (genetics), Professor, Corresponding Member of NASU

Department of Molecular and Quantum Biophysics

Founded in 1990
Head – **Dmytro M. Hovorun**
Dr.Sci. (mol. biol.), Professor, Corresponding Member of NASU

Department of Functional Genomics

Founded in 1992
Head – **Alla V. Rynditch**
Dr.Sci. (mol. biol.), Professor,
Corresponding Member of NASU

Department of Synthetic Bioregulators

Founded in 1998
Head – **Igor Ya. Dubey**
Dr.Sci. (bioorg. chem.), Senior Research Scientis

Department of Protein Engineering and Bioinformatics

Founded in 2001
Head – **Olexander I. Kornelyuk**
Dr.Sci. (mol.biol.), Professor,
Corresponding Member of NASU

Department of Human Genomics

Founded in 2002
Head – **Ludmyla A. Livshits**
Dr.Sci. (mol. genetics), Professor

Department of Medicinal Chemistry

Founded in 2003
Head – **Sergiy M. Yarmoluk**
Dr.Sci. (bioorg. chem.), Professor

Administrative Staff

Director

Anna V. El'skaya
Doctor of Science (molecular biology), Professor,
Full Member of National Academy of Sciences of Ukraine
Phone: +380 (44) 526-07-49
Fax: +380 (44) 526-07-59
E-mail: *anna.elskaya@yahoo.com*

Deputy Directors in Scientific Work

Dmytro M. Hovorun
Doctor of Science (molecular biology), Professor,
Corresponding Member of National Academy of Sciences of Ukraine
Phone: +380 (44) 526-20-14
Fax: +380 (44) 526-07-59
E-mail: *dhovorun@imbg.org.ua*

Mykhaylo A. Tukalo
Doctor of Science (molecular biology), Professor,
Corresponding Member of National Academy of Sciences of Ukraine
Phone: +380 (44) 200-03-35
Fax: +380 (44) 526-07-59
E-mail: *mtukalo@imbg.org.ua*

Yaroslav I. Korpan
Doctor of Philosophy (biotechnology),
Leading Research Scientist
Phone: +380 (44) 522-28-24
Fax: +380 (44) 522-28-24
E-mail: *yaroslavkorpan@yahoo.com*

Deputy Director of General Affairs

Valery M. Kharchenko
Research Scientist
Phone: +380 (44) 526-11-59
Fax: +380 (44) 526-07-59
E-mail: *kharchenko@imbg.org.ua*

Scientific Secretary

Yanina R. Mishchuk
Doctor of Philosophy (molecular biology),
Senior Research Scientist
Phone: +380 (44) 526-11-29
Fax: +380 (44) 526-07-59
E-mail: *mishchuk@imbg.org.ua*

Department of Cell Regulatory Mechanisms

Head
Vitalii A. Kordium
Dr.Sci. (microbiology), Professor,
Corresponding Member of National Academy
of Sciences of Ukraine,
Full Member of National Academy
of Medical Sciences of Ukraine
Phone: +380 (44) 526-55-96
Fax: +380 (44) 526-07-59
E-mail: *kordium@imbg.org.ua*

Education and Degrees

1950–1955	Graduate Student, Faculty of Biology, Taras Shevchenko National University of Kyiv, Kyiv, Ukraine
1955–1958	Postgraduate Student, Department of Microbiology, Taras Shevchenko National University of Kyiv, Kyiv, Ukraine
1960	Ph.D. (microbiology)
1972	Dr.Sci. (microbiology)
1991	Corresponding Member of NASU (medical genetics)
1993	Professor
2000	Full Member of NAMSU (medical genetics)

Professional Employment

1958–1963	Junior Research Scientist, D. K. Zabolotny Institute of Microbiology and Virology (IMV), NASU, Kyiv, Ukraine
1963–1968	Senior Research Scientist, IMV NASU, Kyiv, Ukraine
Since 1973	Head of the Department of Cell Regulatory Mechanisms, Institute of Molecular Biology and Genetics, NASU, Kyiv, Ukraine

Honours, Prizes, Awards

1977	Prize of Council of Ministers of the USSR
1979	State Prize of Ukraine in Science and Technology for a series of works on space biology
2003	Diploma of Verkhovna Rada of Ukraine
2008	Honoured Worker of Science and Technology of Ukraine
2012	The Order of Prince Yaroslav the Wise, V degree

Kordium V. A., Head of Department
Chernykh S. I., Chief Research Scientist, Dr.Sci.
Rymar S. Y., Senior Research Scientist, Ph.D.
Shpylova S. P., Senior Research Scientist, Ph.D.
Deryabina O. G., Senior Research Scientist, Ph.D.
Lykhacheva L. I., Research Scientist., Ph.D.
Kovalchuk M. V., Research Scientist, Ph.D.
Okunev O. V., Research Scientist, Ph.D.
Toporova O. K., Research Scientist
Gulko T. P., Junior Research Scientist
Irodov D. M., Junior Research Scientist
Dragulian M. B., Junior Research Scientist
Pokholenko Ia. O., Junior Research Scientist
Nikolaev Yu. S., Junior Research Scientist
Morgunov P. V., Leading Engineer
Shuvalova N. S., Leading Engineer
Vozniuk T. M., Leading Engineer
Soroka M. P., Leading Engineer
Petrunnikova A. V., Leading Engineer
Tomusiak G. V., Leading Engineer
Lysenko S. P., Leading Engineer
Gorbatiuk O. B., Leading Engineer
Gordienko L. S., Technician
Matkovska N. V., Technician
Procenko V. T., Technician

Research Area

The study on intercellular informational interactions

Current Research Activities and Recent Achievements

The development of gene therapy for diabetes type-1 and atherosclerosis

A series of recombinant vector DNAs containing the human full-size preproinsulin and apolipoprotein A1 genes in the integrative expression cassettes have been constructed in the Department. The mammalian cell lines that express the target human proteins were obtained. Vector DNA polyplexes based on modified polyethyleneimine containing glycoside ligands have been optimized for efficient and safe targeted gene transfer in mammalian liver cells. The consistently reproducible technique for obtaining experimental models of chemically induced diabetes in animals of four species (mice, rats, rabbits and pigs) has been perfected. The models of alimentary hypercholesterolemia and of lipid metabolism disorders under diabetes, induced by streptozotocin in rabbits, have been developed. Therapeutic efficacy of targeted vector DNAs has been demonstrated in long-term experiments with these animal models (Fig. 1): a) antihyperglycemic action of polyplexes containing human preproinsulin gene in the model of type 1 diabetes in mice, rats, rabbits and pigs; b) antiatherogenic effects of polyplexes containing human apolipoprotein A1 gene in the models of alimentary hypercholesterolemia and combined carbohydrate and lipid metabolism disorders in rabbits.

Study on human umbilical cord MSC isolation, cultivation, characterisation and usage

A technology of MSC isolation from human umbilical cord Wharton jelly with maximal preservation of their native characteristics has been developed. The necessity of individual approach for the cells obtaining from umbilical cord was confirmed. The optimal culturing conditions, in particular, considering an influence of gas mixture were determined. It has been shown that lowered oxygen concentration and nitrogen substitution with argon had positive effect on the umbilical cord MSC during their cultivation. The morphological characteristics as well as surface markers expression were studied. MSC from umbilical cord were shown to be heterogeneous at isolation (0 passage), but already at the first passage they had typical for MSC spindle-shaped morphology. They were CD73, CD90, CD105 positive and CD34, CD45 negative, which is characteristic of MSC. After the second ***ex vivo*** passage (Fig. 2), gradual change of the MSC properties occurred (cell morphology, surface markers expression, doubling time, etc.), as well as spontaneous differentiation to adipo- and chondrocytes began. Accordingly, only the cells of this or lower culture level passage can be used. Collagens I and

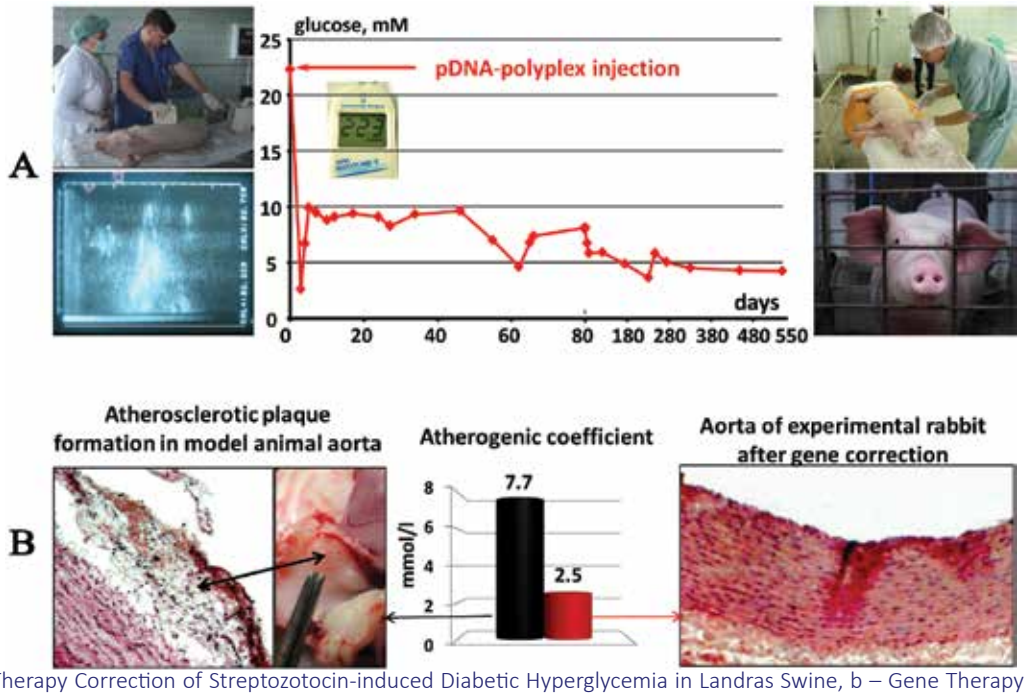


Fig. 1. a – Gene Therapy Correction of Streptozotocin-induced Diabetic Hyperglycemia in Landras Swine, b – Gene Therapy for Experimental Hypercholesterolemia in Rabbits

II types were extracted, and matrices for the cell cultivation were prepared.

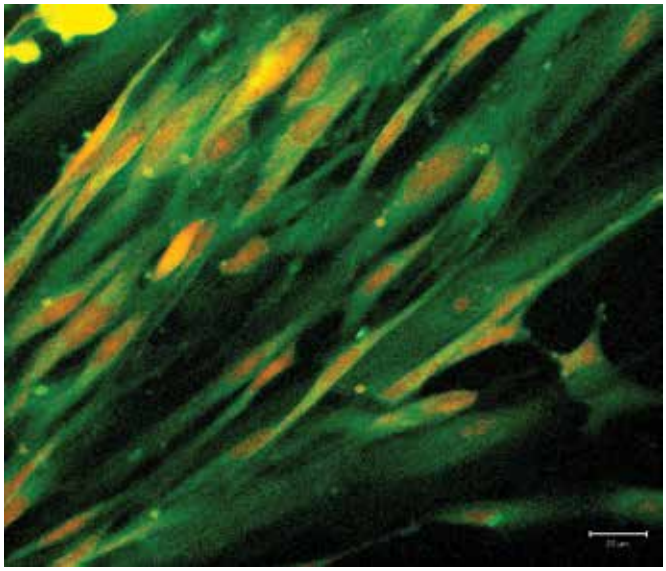


Fig. 2. MSC culture, 2 passage. Confocal microscopy, staining with ethidium bromide + FITC

In recent years, the use of transplanted cells producing active factors has been proven to be an emergent technology. However, the transplantation of allogenic and xenogenic cell material results in the immune rejection of cell transplants. Cell microencapsulation is a promising tool to prevent an attack of immune system even in case of xenogenic transplants. Microcapsules, prepared from semipermeable membranes, ensure transmission of target proteins, on the one hand, and defend the cells from attacks of immune system – on the other. It makes possible to avoid the use of long-term therapies of modulating and/or immunosuppressive agents, which have potentially severe side-effects. Usage of encapsulated cells, producing growth factors, cytokines, hormones and other therapeutic proteins, is at present a very promising way of delivery of therapeutic material into an organism.

The Department takes part in this field of research. The genetically engineered cells are a source of therapeutic proteins. Transgenic mammalian cell lines producing some important recombinant human cytokines (LIF, FGF2, IL10) have been obtained by us via a nonviral gene transfer technique. The recombinant protein secretion into the cultural medium was shown. When the cells producing cytokines were encapsulated in alginate microcapsules, the production of the recombinant cytokines was continuing and the cytokine molecules are secreted from the microcapsules into the cultural medium (Fig. 3). The therapeutic effects of the cytokines, produced by genetically modified eukaryotic cells, are planned to be tested on animal models when the microcapsules will be transplanted to animals suffering from some disordes caused by the lack of tested cytokines.

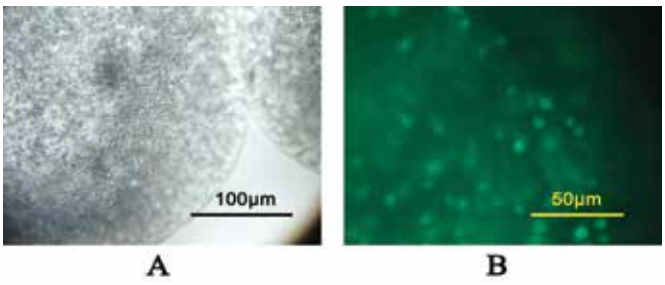


Fig. 3. CHO-K1 cells transfected by pC1eGFP in alginate microcapsules (a – light microscopy; b – fluorescent microscopy)

The study on influence of recombinant cytokines on structural and functional state of ischemic tissues

It has been demonstrated in the experimental model of chronic kidney ischemia in rabbits that the intraparenchymal administration of the FGF-2 in developed polymeric carrier, based on cross-linked heparin, 5 months after ligature application, decreases the initial sclerotic changes in stroma and vessels and protects from the development of irreversible sclerotic changes in the interstitium and atrophy of the elements of parenchyma in ischemic and contralateral kidney.

The data of angiography indicate that the architectonics of arterial bed of kidney of experimental animals with segmental ischemia was almost the same as of intact contralateral kidney after the injection of the preparation of FGF-2 studied (Fig. 4). The gene coding for human interleukin-10 has been cloned, the high-level expression of this cytokine in E.coli cells has been obtained, and the method for its downstream purification and obtaining in biologically active form has been elaborated in the Department. It has been shown that the intraparenchymal administration of the interleukin-10 into ischemic kidney tissue reduced the activity of the processes of lipid peroxidation and decreased the risk of ischemic kidney damage. The genes coding for human stromal-derived factor-1α (SDF-1α) and vascular endothelial growth factor have been cloned for further studies. The expression of these recombinant proteins in E.coli cells has been obtained, and the method for downstream purification and obtaining in biologically active form of SDF-1α has been elaborated.

Fig. 4. Angiogram of vessels of rabbit urinary system after 6 months the application of ligatures on the upper pole of left kidney. The place of the ligature application shown by arrow

National Grants

Projects of National Academy of Sciences of Ukraine:

- 2010–2014 N 35/13 Progect: "Fundamental foundations of multigene therapy for mass pathology with complications" (scientific supervisor – Kordium V. A.)
- 2010–2014 N 36/10 Progect: "Developing a fundumental basis for obtaining new generation immunoreagents" (scientific supervisor – Okunev O. V.)

Projects of State Agency on Science, Innovations and Informatization of Ukraine:

- 2013–2014 Project: "The Development of technology for the repairing injured liver function by MSC transplantation" (scientific supervisor – Rymar S. Y.)

Collaboration

with Ukrainian organizations:

- State Institute of Genetic and Regenerative Medicine, NAMSU (Kyiv)
- D. F. Chebotarev State Institute of Gerontology, NAMSU (Kyiv)
- State Institution "V. K. Gusak Institute of Urgent and Reconstructive Surgery of NAMS of Ukraine" (Donetsk)
- State Institution "Institute of Urology of NAMS of Ukraine" (Kyiv)
- State Institution "V. P. Komisarenko Institute of Endocrinology and Metabolism of NAMS of Ukraine" (Kyiv)
- Educational and Scientific Centre "Institute of Biology" Taras Shevchenko National University of Kyiv (Kyiv)
- State Institution "Institute of Pediatrics, Obstetrics and Gynecology of NAMS of Ukraine" (Kyiv)
- State Institution "Institute of Neurosurgery named after A. P. Romodanov of NAMS of Ukraine" (Kyiv)
- State Institution "Institute of Otolaryngology named after O. S. Kolomiychenko of NAMS of Ukraine" (Kyiv)
- State Institution "National Research Center for Radiation Medicine of NAMS of Ukraine" (Kyiv)
- State Institution "V. P. Filatov Institute of Eye Diseases and Tissue Therapy of NAMS of Ukraine" (Odessa)
- Institute of Veterinary Medicine, NAASU (Kyiv)
- O. V. Palladin Institute of Biochemistry, NASU (Kyiv)

with foreign organizations:

- Leipzig University (Leipzig, Germany)
- Centre for Stem Cells Sciences (Hyderabad, India)

Selected Publications

1. Maslova O, Kordium V, Deryabina O Umbilical Cord matrix cells – promising instrument for regenerative medicine. In: Loredana De Bartolo, Augustinus Bader, editors. Biomaterials for stem cell therapy: state of the art and vision for the future: CRC Press, Taylors&Francis Group, Boca Raton, London, New York, A science publishers book; 2013. p. 212–227.
2. Maslova OO, Shuvalova NS, Sukhorada OM, et al. Heterogeneity of umbilical cords as a source for MSC. ***Dataset Papers in Biology*** 2013, Article ID 370103.
3. Shpylova SP, Shuvalova NS, Deryabina OG, Kordium VA. Spontaneous formation of spheroids in human umbilical cord matrix cell cultures. ***Studia Biologica***. 2012; 6(2):79–86.
4. Maslova OO, Shuvalova NS, Sukhorada OM, et al. Alteration of morphofunctional characteristics of umbilical cord matrix mesenchymal cells during passaging. ***Problems of cryobiology***. 2012; 22(2):153–6.
5. Pokholenko IaO, Rachkova LT, Gulko TP, et al. The development of biodegradable scaffold from collagen type I and study of their biological properties ***in vitro*** and ***in vivo***. In: Achievements and problems of genetics, breeding and biotechnology. K.: Logos. 2012. p. 358–62.
6. Rymar SYu, Ruban TA, Irodov DM, Kordium VA. Expression and secretion of human recombinant LIF by genetically modified mammalian cells. ***Biopolym. Cell.*** 2011; 27(1):53–8.
7. Vozianov OF, Romanenko AM, Pirogov VO, et al. Novel systems for the restoration of blood flow in ischemic kidney. Ninth International Symposium on Frontiers in biomedical polymers FBPS. 2011:103–4.
8. Toporova OK, Gulko TP, Sukhorada OM, et al. Long-term correction of experimental diabetes in mice and pigs after nonviral insulin gene therapy. ***Human Gene Therapy.*** 2009; 20(4):397.
9. Novikova SN, Toporova OK, Sukhorada OM, et al. Experimental gene therapy for atherosclerosis. ***Problemu stareniya i dolgoletiya.*** 2008; 17(2):174–83.
10. Toporova OK, Kyrylenko SD, Irodov DM, Kordium VA. Plasmid vector for human preproinsulin gene delivery in mammalin cells. ***Biopolym. Cell.*** 2007; 23(2):100–7.

Laboratory of Microbial Ecology of Department of Cell Regulatory Mechanisms

Head
Nataliia O. Kozyrovska
Ph.D. (molecular biology),
Senior Research Scientist
Phone : +380 (44) 526-55-96
Fax: +380 (44) 526-07-59
E-mail: *kozyrna@ukr.net*

Education and Degrees

1971–1976 Graduate Student, Faculty of Biology, Taras Shevchenko National University of Kyiv, Kyiv, Ukraine, M.Sc. (biology, microbiology)
1984 Ph.D. (molecular biology)

Professional Employment

1976–1983 Engineer, Senior Engineer, Department of Regulatory Cell Mechanisms, Institute of Molecular Biology and Genetics (IMBG), NASU, Kyiv, Ukraine
1983–2010 Junior Research Scientist, Research Scientist, Senior Research Scientist, IMBG NASU, Kyiv, Ukraine
Since 2010 Head of the Laboratory of Microbial Ecology, IMBG NASU, Kyiv, Ukraine

Honours, Prizes, Awards

1989 DAAD (German Academic Exchange Service) Grant
1993 Royal Society Grant
2003 WIPO (World Intellectual Property Organization) Gold medal for an invention

Kozyrovska N. O., Head of Laboratory
Zaets I. E., Senior Research Scientist, Ph.D.
Moshynets O. V., Research Scientist, Ph.D.
Podolich O. V., Research Scientist, Ph.D.
Burlak O. P., Junior Research Scientist
Ovcharenko L. P., Ph.D. Student

Research Area

Scientific and biotechnological aspects of polymicrobial community study

Current Research Activities and Recent Achievements

Interaction of microorganisms with plants: the mechanism of plant protection against biotic and abiotic factors, involving endophytic microbial populations

The concept of plant protection under the assistance of communities of resident endophytic bacteria is elaborated. In addition to known plant defence mechanisms (basic and induced resistance), the reserve mechanism is revealed, which involves latent endophytic microorganisms. The effectiveness of this mechanism depends on the plant genotype-associated endophytic microbiome and its ability to resuscitate from the latent state and to respond to external factors. Biocontrol agents used for plant protection may serve as activators of the latent state. The reaction of plants on pathogens after priming by biocontrol agents depends on the endophytic microbiome structure and its quality. The concept may explain, why the same microbial preparations for plant protection act differently on different plant species and even varieties, and provides a tool for selection of plant varieties with beneficial endophytic microbiome composition.

Polymicrobial communities: communal interactions with an emphasis on a biofilm formation. Design of biodegradable composites based on nanocellulose for use in medical and aerospace industries

Kombucha polymicrobial community (a tea “fungus”) is known within two millennia, and for the first time, the full microbiome of one of the ecotype (Ukrainian) has been revealed by DNA barcoded pyrosequencing. Construction of

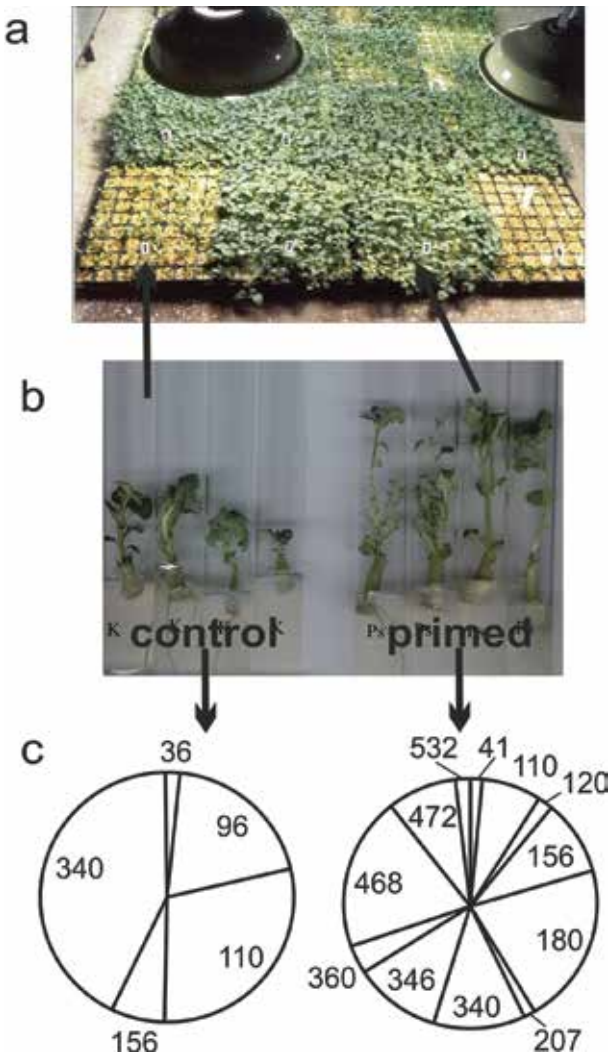


Fig. 1. a – Survival of potato plants under ***post vitro*** conditions; b – primed ***in vitro*** plants; c – increase of bacterial OTUs inside potato roots after priming with PGPB (on results of 16S rDNA PCR/TRFLP (***Hha I***)-analysis)

consortia, using different kombucha community members, for a high throughput synthesis of cellulose showed that the level of kombucha cellulose film synthesis depends on partners-duals in the community. Biodegradable antimicrobial composites based on nanocellulose were designed for a wide application.

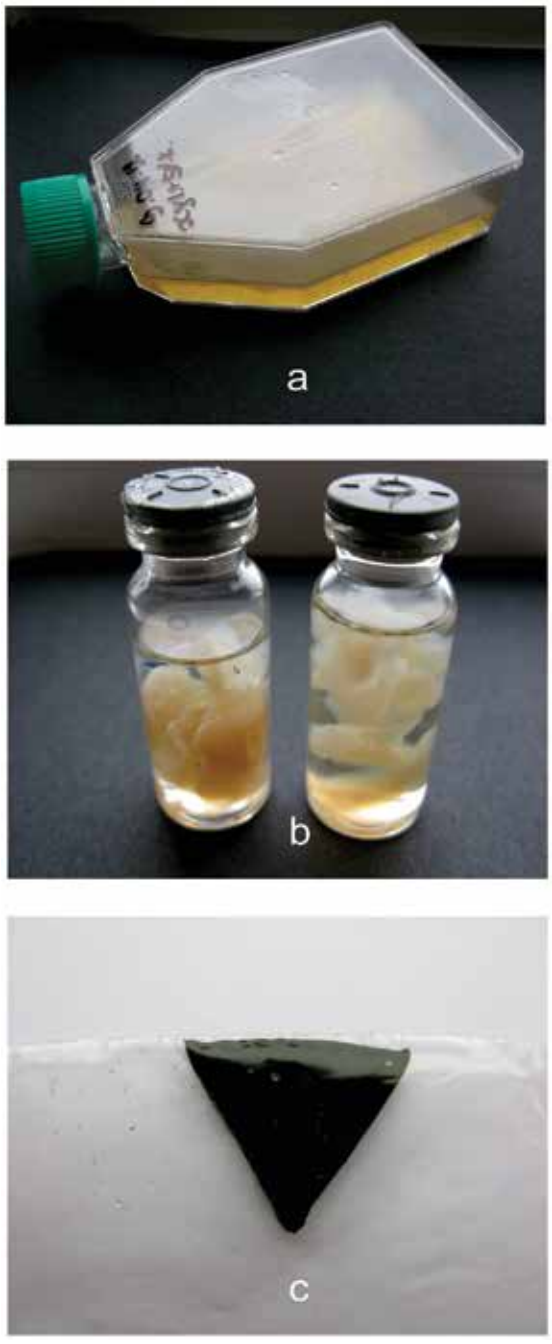


Fig. 2. Stages of new composite nanomaterials manufacture: growing biofilm (a), purification from bacterial cells (b), modification of pure cellulose (c) (joint materials of IMBG, IBOPCH NASU)

National Grants

Projects of National Academy of Sciences of Ukraine:

- 2012–2016 N 47 Project: "Participation in international project BIOMEX (NASU)"
- 2009 N 44 Project: "System biotechnology of potato protection and molecular tests of potato pathogens"

Projects of Ministry of Education and Science of Ukraine:

- 2009–2010 M/431 Ukrainian-German Project: "A study of model organisms for a use on a Lunar base"

International Grants

- 5th Framework Programme (FP5) Project: "The use of mycorrhizal fungi in phytoremediation projects"
- BMBF (German Federal Ministry of Education and Research) Project: "Biological and Mars Experiment (BIOMEX)"
- COST (European Cooperation in Science and Technology) Action FA1103 Project: "Endophytes in Biotechnology and Agriculture"
- STCU (Science and Technology Center in Ukraine) N16 Project: "Molecular interactions between bacteria under microgravity"

Collaboration

with Ukrainian organizations:

- Educational and Scientific Centre "Institute of Biology" of Taras Shevchenko National University of Kyiv (Kyiv)
- Institute of Bioorganic Chemistry and Petrochemistry, NASU (Kyiv)
- Institute of Physics, NASU (Kyiv)

with foreign organizations:

- Institute of Planetary Research, DLR (Berlin, Gemarny)
- University of Oulu (Oulu, Finland)

Selected Publications

1. Kozyrovska NO. Crosstalk between endophytes and the plant host within information-processing networks. ***Biopolym. Cell.*** 2013; 29(3):234–43.
2. Ardanov P, Sessitsch A, Häggman H, Kozyrovska N, Pirttilä AM. Methylobacterium-induced endophyte community changes correspond with protection of plants against pathogen attack. ***PLoS ONE.*** 2012; 7:e46802.
3. Kozyrovska N, Reva O, Goginyan V, de Vera J-P. Kombucha microbiome as a probiotic: a view from the perspective of post-genomics and synthetic ecology. ***Biopolym. Cell.*** 2012; 28(2):103–10.
4. Zaets I, Kozyrovska N, Heavy metal resistance in Plants: a putative role of endophytic Bacteria In: A. Zaidi et al. (eds.), Toxicity of heavy metals to legumes and bioremediation. Springer-Verlag, Wien 2012.
5. Zaetz I, Burlak O, Rogutskyy I. et al. Bioaugmentation strategy of growing plants for lunar bases. ***Adv. Space Res.*** 2011; 47: 1071–8.
6. Ardanov P, Ovcharenko L, Zaets I, Kozyrovska N, Pirttilä AM Endophytic bacteria enhancing growth and disease resistance of potato (***Solanum tuberosum*** L.). ***Biocontrol.*** 2011; 56 (1):43–9.
7. Burlak O, Lar O, Rogutskyy IS, et al. A bacterial consortium alleviating a low-dose gamma irradiation effect in kalanchoe plantlets. ***Space Sci. Technol.*** 2010; 1:32–40.
8. Podolich O, Laschevskyy V, Ovcharenko L, Kozyrovska N, Pirttilä AM. Methylobacterium sp. resides in unculturable state in potato tissues ***in vitro*** and becomes culturable after induction by Pseudomonas fluorescens IMGB163. ***J. Appl. Microbiol.*** 2009; 116: 728–32.

Laboratory of Modification of Biologically Active Substances of Department of Cell Regulatory Mechanisms

Head
Anatoliy I. Potopalsky
Ph.D. (medical science),
Docent
Phone: +380 (44) 526-11-39
Fax: +380 (44) 526-07-59
E-mail: *potopalsky@imbg.org.ua*
www.potopalsky.kiev.ua

Education and Degrees

1952–1956	Zhytomyr Medical School N 1, Paramedic-obstetrician, Zhytomyr, Ukraine
1957–1963	M.D., Ivano Frankivsk National Medical University, Ivano Frankivsk, Ukraine, doctor
1966	Ph.D., Ivano Frankivsk National Medical University, Ivano Frankivsk, Ukraine
1972	Docent, Danylo Halytsky Lviv National Medical University, Lviv, Ukraine

Professional Employment

1955–1957	Military Hospital, Medical point in Ushomyr MTS, Ukraine
1957–1963	Student Research Worker, Ivano Frankivsk National Medical University, Ivano Frankivsk, Ukraine
1963–1967	Post Graduate, Department of Pathophysiology, Ivano Frankivsk National Medical University, Ivano Frankivsk, Ukraine
1967–1970	Assistant of Department of Pathophysiology, Danylo Halytsky Lviv National Medical University, Lviv, Ukraine
1970–1977	Head of Laboratory, Department of Pathophysiology, Danylo Halytsky Lviv National Medical University, Lviv, Ukraine
1977–1978	Senior Research Scientist, Institute of Molecular Biology and Genetics (IMBG), NASU, Kyiv, Ukraine
Since 1992	Director, Institute of Health Promotion and Rebirth of People of Ukraine Ltd., Kyiv, Ukraine
Since 2004	Head of the Laboratory of Modification of the Structure of Biologically Active Substances, IMBG NASU, Kyiv, Ukraine

Honours, Prizes, Awards

1985	Awarded title “The Best Inventor of NASU”
1994	Biography included in the international edition of “500 Top Movers”, USA
1996	Man of the Year according to the American Biographical Institute, Member of the Ukrainian National Society of Inventors
2004	Anatoliy I. Potopalsky together with former colleagues V. Novytsky (Austria) and M. Oliyovska were nominated for Nobel Prize in medical chemistry for the development of antitumoral medications based on celandine alkaloids modification
2006	Awarded the honorary title “Honoured Inventor of Ukraine” (Decree of the President of Ukraine N 1004/2006 of 28 November 2006)

Potopalsky A. I., Head of Laboratory
Voloshchuk T. P., Senior Research Scientist, Ph.D.
Zaika L. A., Senior Research Scientist, Ph.D.
Bolsunova O. I., Research Scientist, Ph.D.
Kazan V. A., Research Scientist, Ph.D.
Yurkevich L. N., Research Scientist
Potopalska Yu. A., Research Scientist
Vorobyova I. I., Leading Engineer
Zadorozhnyi B. O., Leading Engineer
Nehrebetska E. M., Leading Engineer

Research Area

The development of methods for modification of biologically active substances and the study of the molecular aspects of their actions

Current Research Activities and Recent Achievements

The mechanisms of alkylation of amines, nucleic acids and their components by the ethyleneimine derivatives are being studied. The products of alkylation were purified and characterized, their biological activity being studied in different systems, and antitumoral, antiviral, and immunomodulating effects were found (Fig. 1). The anticancer drug Amitozyn has successfully undergone clinical trials and is recomended for Pharmaceutical Committee to oficial registration.

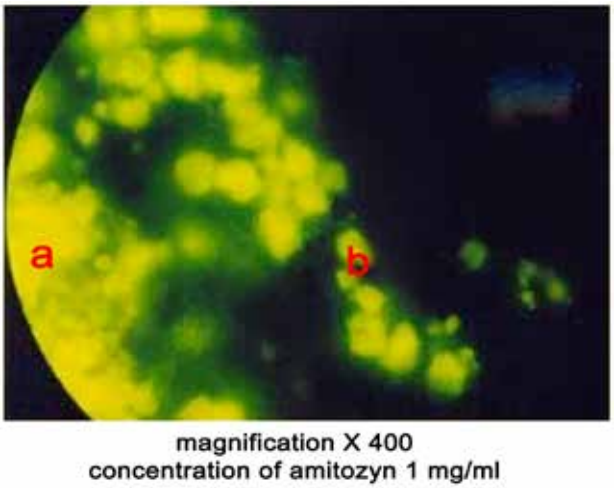


Fig. 1. Picture of luminescent microscopy of pancreas carcinoma in the conditions of amitozyn preparation's own fluorescence. a) fluorescence of cancer cells in 2 hours after the 0.25 mg/kg of amitozyn intravenous administration; b) infiltration of pancreas normal tissue by fluorescent cancer cells

Novel medications were obtained and the ways of their application in medicine, veterinary, and agriculture that influence biological processes were developed. The preparation Izatizon which has a wide range of antiviral, antitumoral and antibacterial effects, was registered in veterinary for treatment and prevention of viral diseases of birds and livestock, it was also recommended to cure people with viral diseases and tumors (Fig. 2). New medicinal Izatizon forms (e. g. Izatizoniy) are being developed and tested.

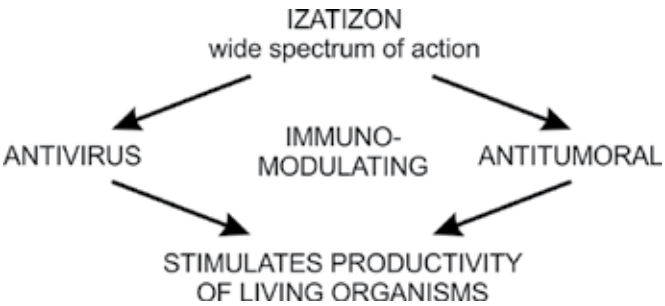


Fig. 2. Izatizon spectrum of action

The preparations of stimulators of plants growth are being developed on the basis of nucleic acids and their components. The genetic effects of alkyl DNAs were determined and new forms of rye, millet, and tomatoes with valuable features were obtained. Special kind of feed lupine with high protein content Industrialny (i. e. industrial) and a kind of pumpkin Kavbuz Zdorovjaga (i. e. watermelon/pumpkin, giant) were registered at the State sorts register of Ukraine (Fig. 3).

Experimental study of modified products of alkaloids, their analogues and derivatives with wide range of biological activity has being conducted. The results of these researches are used for improvement of human health and environment.

Unique plants are collected in "Peremoha" park, established by A. Potopalsky in Korosten region (Fig. 4).

Fig. 3. New plant varieties elaborated according to the new technology are resistant to harmful environmental factors and are registered in the State Register for the Plant Varieties of Ukraine, most of them have been still studied

Fig. 4. Kizyris – a hybrid of dogwool and barberry in "Peremoha" park established by A.Potopalsky in 1979 in Korosten region

National Grants

Projects of National Academy of Sciences of Ukraine:

- 2010–2014 N 114/10-H Project: "Creating of antitumor complex based on nanoparticles of amitozyn and platydiam drugs and its experimental and clinical study"

Collaboration

with Ukrainian organizations:

- Taras Shevchenko National University of Kyiv (Kyiv)
- National Cancer Institute, Ministry of Health of Ukraine (Kyiv)
- R. E. Kavetsky Institute of Experimental Pathology, Oncology and Radiobiology, NASU (Kyiv)
- V. Bakul Institute for Superhard Materials, NASU (Kyiv)
- F. D. Ovcharenko Institute of Biocolloidal Chemistry, NASU, (Kyiv)
- Institute of Physics, NASU (Kyiv)
- D. K. Zabolotny Institute of Microbiology and Virology, NASU (Kyiv)
- Ukrainian Research Institute of Traumatology and Orthopedics, Ministry of Public Health of Ukraine (Kyiv)
- Kyiv Institute for Nuclear Research, NASU, (Kyiv)
- State Institution "Institution L. V. Gromashevsky Institute of Epidemiology and Infectious Diseases NAMS of Ukraine" (Kyiv)

with foreign organizations:

- CRBM (Macromolecular Biochemistry Research Center) UMR 5237, (Montpellier, France)
- M. M. Shemyakin-Yu. A. Ovchinnikov Institute of Bioorganic Chemistry, RAS (Moscow, Russia)

Selected Publications

1. Herman B, Gudrun A, Potopalsky AI, Chroboczek J, Tcherniuk SO. Amitozyn Impairs Chromosome Segregation and Induces Apoptosis via Mitotic Checkpoint Activation. ***PLoS ONE.*** 2013; 8(3): e57461.
2. Voloshchuk TP, Adonin VI, Vorobiova II, Potopalsky AI. Structure of alkyl radicals upon alkylation by thiotepa. ***Ukrainica Bioorganica Acta 1.*** 2013:24–32.
3. Potopalsky AI, Zaika LA, Bolsunova OI. Molecular genetic biotechnologies – the way to the welfare of the people and increasing of agriculture profitability. ***Biopolym. Cell.*** 2013; 29(4):261–265.
4. Potopalsky AI, Yurkevich LN, Katsan VA. Influence of Izatison and Nanosilver Preparations on the Photosynthesis Pigments Level Content in Leaves, Growth Processes and Productivity of Oat Plants Cultivar Nezlamny. Proceedings of the International Interdisciplinary Scientific Conference "Biologically Active Substances and Materials: Fundamental and Applied Problems", May 27–June 1, 2013, Novy Svet, AR Crimea, Ukraine. 1:233-234.
5. Zaets I, Kramarev S, Kozyrovska N. Inoculation with a bacterial consortium alleviates the effect of cadmium overdose in soybean plants. ***Centr Eur J Biol.*** 2010; 5(4):481–90.
6. Zaika LA, Bolsunova OI, Potopalsky AI. Antiviral, antitumoral and immunomodulatory properties of therapeutic drug izatizon. – K.: Kolobih, 2010, 212 p.
7. Ovcharenko LP, Voznyuk TM, Zaetz IE, Potopalsky AI, Reva O, Kozyrovska NO. A mobile genetic element in Serratia marcescens, a causative agent of onion disease. ***Biopolym. Cell.*** 2010; 26(4):279–85.
8. Potopalskyy AI, Yurkevych LN, Katsan VM. Homeobox genes as possible targets of exogenous DNA effect in obtaining new forms of rye. Regularities of exogenous DNA effect in selection of short stem forms of diploid rye. Factors of experimental evolution of organisms. Kyiv: Logos, 2009.7. P. 55–60.
9. Potopalska YuA, Osynskyy SP, Susak YaM. Antitumour and modifying effects of preparation of alkaloids of Chelidonium majus, alkylated by thiophosphamide (experimental research). ***Oncology.*** 2007: 9 (3):219–21.

Department of Cell Signaling

Head
Valeriy V. Filonenko
Dr.Sci. (molecular biology), Professor
Phone: +380 (44) 522-61-00, 526-20-16
Fax: +380 (44) 522-61-00
E-mail: *filonenko@imbg.org.ua*

Education and Degrees

1980–1985	Graduate Student, Faculty of Biology, Taras Shevchenko National University of Kyiv, Kyiv, Ukraine, M.Sc. (genetics)
1986–1989	Postgraduate Student, Engelhardt Institute of Molecular Biology, Moscow, Russia
1991	Ph.D. (molecular and cell biology). Thesis: "Immunochemical analysis of high-molecular weight aminoacyl-tRNA synthatase complex"
2005	Dr.Sci. (molecular biology). Thesis: "Structural and functional analysis of ribosomal protein S6 kinases (S6K1 and S6K2)"
2006	Professor (molecular biology)

Professional Employment

1985–1991	Junior Research Scientist, Institute of Molecular Biology and Genetics (IMBG), NASU, Kyiv, Ukraine
1992–1995	Postdoctoral Fellow, University of Connecticut Health Center, Department of Biochemistry, Farmington, USA
1995–1997	Postdoctoral Associate, Miami University, Department of Biochemistry and Molecular Biology, Miami, USA
1997–2003	Senior Research Scientist, Laboratory of Cell Growth Regulation, IMBG NASU, Kyiv, Ukraine
Since 2003	Head of the Department of Cell Signaling, IMBG NASU, Kyiv, Ukraine

Membership

Since 1998	Member of FEBS (Federation of European Biochemical Societies)
Since 2004	Member of Ukrainian Society of Cell Biology
Since 2007	Editorial Board member of Journal "Biopolymers and Cell" (Ukraine)
Since 2011	Editorial Board member of Journal "Biotechnologia Acta" (Ukraine)

Filonenko V. V., Head of Department
Kiyamova R. G., Leading Research Scientist, Dr.Sci.
Garifulin O. M., Senior Research Scientist, Ph.D.
Khoruzhenko A. I., Senior Research Scientist, Ph.D.
Malanchuk O. M., Senior Research Scientist, Ph.D.
Ovcharenko G. V., Senior Research Scientist, Ph.D.
Palchevskyy S. S., Senior Research Scientist, Ph.D.
Savinska L. O., Senior Research Scientist, Ph.D.
Tykhonkova I. O., Senior Research Scientist, Ph.D.
Gudkova D. O., Research Scientist, Ph.D.
Cherednyk O. V., Junior Research Scientist
Skorokhod O. M., Junior Research Scientist
Gaman N. O., Ph.D. Student
Klipa O. M., Ph.D. Student
Kosach V. P., Ph.D. Student

Research Area

- PI3K/mTOR/S6K signaling in regulation of cell metabolism, growth, proliferation and survival under normal and pathological conditions
- Identification and characterization of novel biomarkers for cancer treatment and diagnostics

Current Research Activities and Recent Achievements

mTOR/S6K (mammalian target of rapamycin/ ribosomal protein S6 kinase) pathway is a main signaling pathway that integrates input from a major intracellular and extracellular cues such as growth factors, stress, energy status, oxygen and amino acids to control major processes, including protein and lipid synthesis and autophagy. (Fig. 1).

Ribosomal protein S6 kinases (S6K1 and S6K2) are principal regulators of cell size, growth and methabolism. Functional peculiarities of S6Ks and their splicing isoforms in normal tissues and malignant tumours, their expression profile and subcellular localisation are under investigation.

We provide evidence of existence of the mTOR splicing isoform, mTORβ, which lacks most of its protein-protein interaction modules, HEAT and FAT, but retains domains responsible for FRB, protein kinase activity, and regulation (RD and FATC) (Fig. 2). Importantly, mTORβ could form complexes ***in vivo*** with Raptor and Rictor, which are known companions of full-length mTOR (mTORα). Also, it readily phosphorylates characterized mTORβ substrates, S6K1, PKB/Akt, and 4EBP1, ***in vitro***. In contrast to mTORα, mTORβ has the potential to shorten considerably the G1 phase of the cell cycle and to stimulate

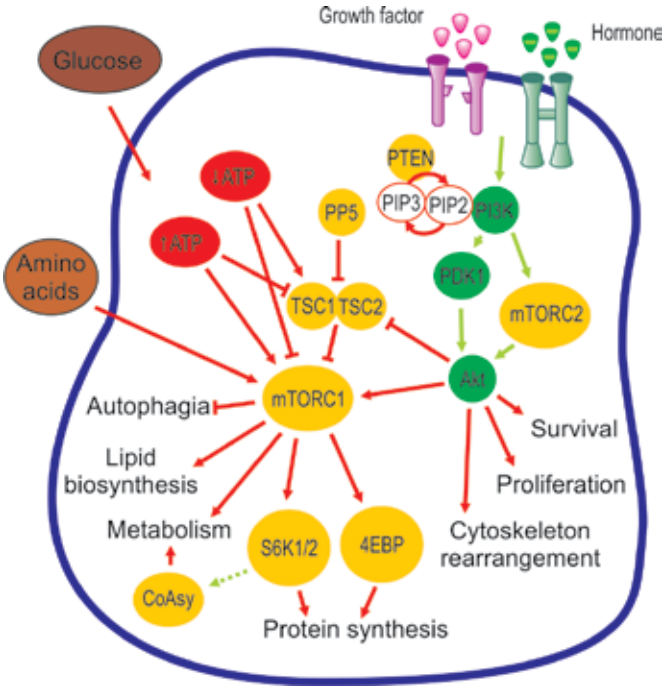


Fig. 1. The PI3K/mTOR/S6K signaling in regulation of cell functions

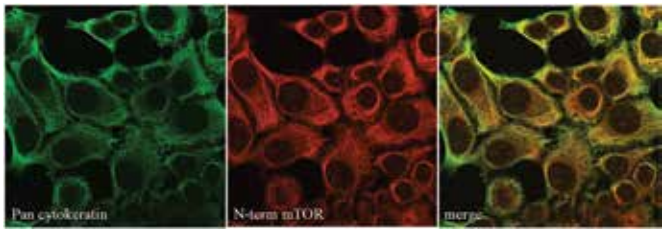


Fig. 2. Colocalization of mTOR and intermediate filaments in human breast adenocarcinoma cells MCF7. Immunofluorescent analysis with anti-mTOR and anti-Pan mAbs

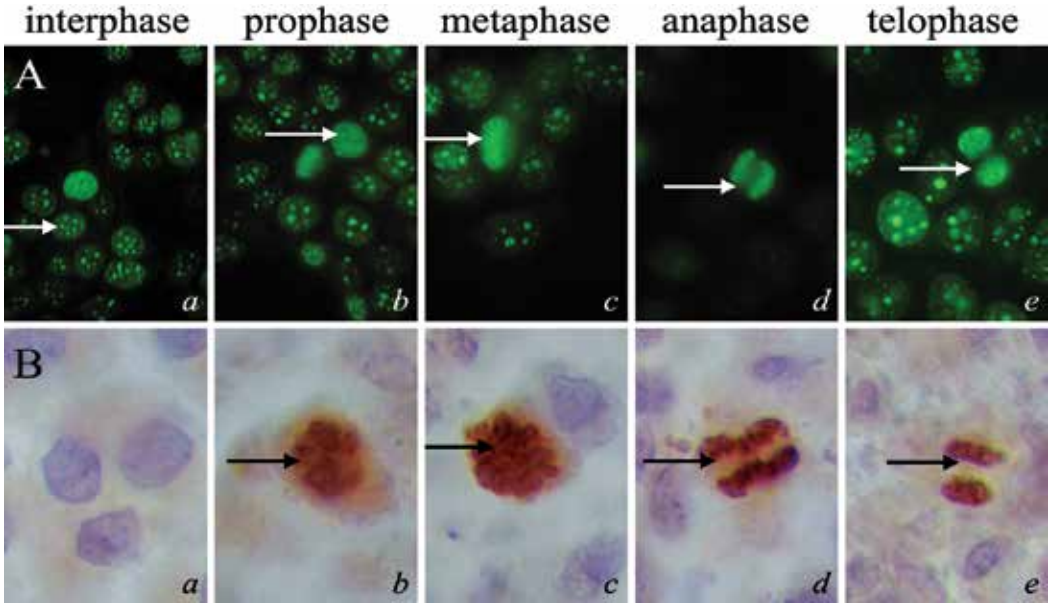


Fig. 3. A – Immunofluorescent detection of Ki-67 in cultured MCF-7 cells at different stages of cell cycle: a, interphase; b, prophase; c, metaphase; d, anaphase; e, telophase. Arrows indicate positive reaction for Ki-67 antigen in cells in interphase and at different phases of mitosis correspondently (Oc10x, Ob 40x). B – Immunohistochemical determination of Ki-67 content in proliferating human melanoma cells on paraffin sections. Arrows indicate positive reaction for Ki-67 antigen in melanocytes (hematoxylin, (Oc10x, Ob 100x)

cell proliferation. Significantly, overexpression of mTORβ transforms immortal cells and is tumorigenic in nude mice. Our studies suggest that the regulation of cell proliferation via the mTOR pathway could be mediated by mTORβ, which acts as a protooncogene and therefore could be a candidate for future anticancer drug discovery

The question about relationship between cancer and stroma cells requires additional comprehensive analysis. Earlier it was shown that fibroblasts are capable to inhibit the growth and proliferation of tumor cells in the early stages of oncogenesis, whereas in the later stages activated tumor-associated fibroblasts, demonstrate the ability to stimulate proliferation, invasion and angiogenesis. Three-dimensional culture is promising way of modeling the different stages of carcinogenesis ***in vitro***. This approach allows to reproduce some morphological and molecular characteristics of initial tissue more precisely than traditional monolayer culture. For investigation of tumor-stroma interaction in context of PI3K/mTOR/S6K signaling 3D culture model of human dermal fibroblasts and malignant cells was developed.

Identification of novel protein-partners of S6Ks, PTEN phosphatase and TSC1/TSC2 (tuberous sclerosis complex) complex by yeast-two hybrid technique revealed novel regulatory mechanisms and functional links within PI3K/mTOR/S6K-dependent signaling.

Recently we have identified PP5 as new binding partner for TSC2, a component of TSC1/2 complex and demonstrated that PP5 dephosphorylates specifically TSC2 at sites, associated with its activation via AMP kinase (AMPK) pathway. Taken together, these results suggest that PP5 exerts negative regulation on TSC1/2 function through dephosphorylation of AMPK-mediated sites and in turn positively regulates mTOR activity

Molecular cloning and characterization of CoA synthase (befunctional enzime that is responsible for the last two steps in CoA biosynthesis) interaction with S6K1 uncovered a potential link between mTOR/S6K signaling pathway and energy metabolism that requires CoA and its thioester derivatives, but its physiological relevance should to be further elucidated.

RCD8 (EDC4), Fyn and Csk kinases, phospholipase Cγ, NADPH oxidaseactivator 1 – p67phox, and structural membrane skeleton protein spectrin have been identified as CoAsy binding partners.

Analysis of regulatory mechanisms in CoA biosynthesis disclosed Shp2 protein tyrosine phosphatase as a positive regulator of CoA synthase. At the same time the main protein of Processing bodies (PB) RCD8, identified by mass-spec analysis as CoA synthase protein-partners, negatively regulates CoAsy activity.

Monoclonal antibodies specific to the components of signaling pathways (S6K1, S6K2, mTOR, Rictor, Raptor, mutant form of FGFR3) and oncomarkers (Ki-67, Napi2B, PRAME, NY-BR1) have been generated. (Fig.3)

Application of SEREX methodology (SErological analysis of Recombinant cDNA EXpression libraries) allowed to identify more than 100 autoantigens of colon, thyroid, melanoma and medullary breast carcinoma tumors. Among them Ki-67, catenin beta like1, α-catenin, HSP 105, ovarian cancer biomarker - sodium-dependent phosphate transporter NaPi2b, LGALS3BP, RAD50, FAM50A, RBPJ, PABPC4, LRRFIP1. Characterization of their gene expression profile in different type of malignancy, subcellular localization and immunogenicity in sera of cancer patients led to identification of potential molecular markers of human malignancy which can be used for both diagnosis and therapy of oncological diseases, and for the understanding of the molecular mechanisms of malignant transformation of cell, tumor progression and anti-tumor immune response (Fig.4).

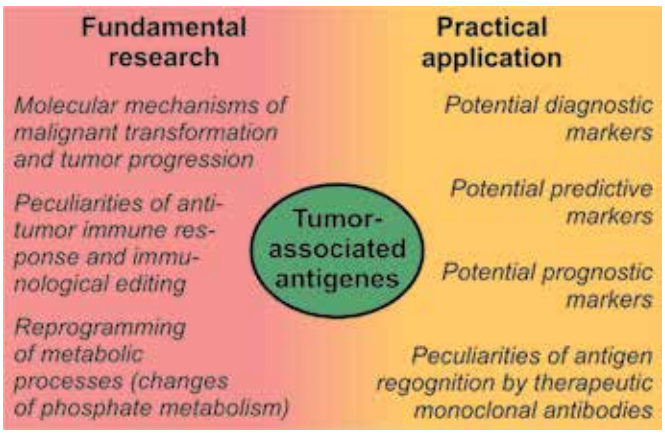


Fig. 4. The prospects of tumor-associated antigens application

National Grants

Projects of National Academy of Sciences of Ukraine:

- 2012–2016 N 2.2.4.21 Project: "Genotype-phenotype correlation in malignant tumors"
- 2010–2014 N 29/10 Project: "Generation and characterization of monoclonal antibodies specific to oncogenic, mutant forms of fibroblast growth factor FGFR3 for diagnostics and tumor therapy"
- 2006–2008 Bilateral cooperation program between of NASU and Siberian Branch of Russian Academy of Sciences Project: "Innovation technologies in cancer treatment". Partners – Institute of Chemical Biology and Fundamental Medicine, Institute of Cytology and Genetics, Novosibirsk Institute of Organic Chemistry

Projects of State Fund for Fundamental Researches of Ukraine:

- 2011–2012 Bilateral cooperation program between NASU and Russian Academy of Sciences N Ф40.4/061 Project: "Proteome analysis of autoantigenic repertoire of tumors with favorable prognosis associated with lymphocyte infiltration". Partner – Lomonosov Moscow State University
- 2011–2012 State Key Laboratory of Molecular and Cellular Biology N Ф46/457-2011 Project: "Macromolecules and their complexes in realization of genetic information"

International Grants

- 2011–2014 7th Framework Programme (FP7) FP7-INCO-2011-6, ERA-WIDE Project: "Strengthening cooperation in Molecular Biomedicine between EU and UKRAINE", COMBIOM (scientific supervisor – Prof. A. Elskaya)
- 2006–2008 INTAS (The International Association for the Promotion of Co-operation with Scientists from the New Independent States of the Former Soviet Union) Project: "Studies of mTor/S6K signaling pathway by proteome analysis and DNA microarrays". Partners – University College London (UK), Ludwig Institute for Cancer Research (USA), Biomedical Sciences Research Center "Alexander Fleming" (Greece)
- 2006–2007 INTAS Project: "PTEN – FAB4 interaction as a link to the regulation of lipid metabolism and adipogenesis"
- 2005–2008 Bilateral cooperation program between Ludwig Institute for Cancer Research- IMBG NASU
- 2004–2007 INTAS Project: "Identification and characterization human of tumour-associated antigens Partners – University College London (UK), Ludwig Institute for Cancer Research (USA)"
- 1999–2001 INTAS N 97-30890 Project: "Identification and characterization of tumor-associated antigens in thyroid cancer"
- NATO (North Atlantic Treaty Organization) N NUKR/982645 Project: "Generation of new biodetection tools for cancer research and diagnostics"
- 1998–2001 WELLCOME TRUST N 055427/Z/98 Project: "Identification and functional analysis of novel PI3-kinase binding partners"

Collaboration

with Ukrainian organizations:

- National Cancer Institute, Ministry of Health of Ukraine (Kyiv)
- R. E. Kavetsky Institute of Experimental Pathology, Oncology and Radiobiology, NASU (Kyiv)
- O. V. Palladin Institute of Biochemistry, NASU (Kyiv)
- Institute of Cell Biology, NASU (Lviv)
- National University Lviv Polytechnic (Lviv)
- State Institution "V. P. Filatov Institute of Eye Diseases and Tissue Therapy of NAMS of Ukraine" (Odessa)
- O. O. Chuiko Institute of Surface Chemistry, NASU (Kyiv)
- Ivan Franko National University of Lviv (Lviv)
- National Forestry University of Ukraine (Lviv)
- Kyiv City Bureau of Forensic Expertise (Kyiv)

with foreign organizations:

- Lomonosov Moscow State University (Moscow, Russia)
- Ludwig Institute for Cancer Research (New York, USA)
- University College London (London, UK)
- Heidelberg University Hospital (Heidelberg, Germany)
- Biomedical Sciences Research Center "Alexander Fleming" (Vari, Greece)

Selected Publications

1. Filonenko VV. PI3K/mTOR/S6K signaling pathway – new players and new functional links. ***Biopolym. Cell.*** 2013; 29(3): 207–214
2. Gudkova D, Panasyuk G, Nemazanyy I, et al. EDC4 interacts with and regulates the dephospho-CoA kinase activity of CoA synthase. ***FEBS Lett.*** 2012; 586(20):3590–5.
3. Savinska L, Skorokhod O, Klipa O, et al. Development of monoclonal antibodies specific to ribosomal protein S6 kinase 2. ***Hybridoma (Larchmt).*** 2012; 31(4):289–94.
4. Kostianets O, Antoniuk S, Filonenko V, Kiyamova R. Immunohistochemical analysis of medullary breast carcinoma autoantigens in different histological types of breast carcinomas. ***Diagn Pathol.*** 2012 Nov 26;7:161.
5. Kostianets O, Shyian M, Demidov S, et al. Serological analysis of SEREX-defined medullary breast carcinoma-associated antigens. ***Cancer Invest.*** 2012; 30(7):519–27.
6. Gryshkova V, Lituiev D, Savinska L et al. Generation of monoclonal antibodies against tumor-associated antigen MX35/sodium-dependent phosphate transporter NaPi2b. ***Hybridoma (Larchmt).*** 2011; 30(1):37–42.
7. Gorbenko O, Panayotou G, Zhyvoloup A, et al. Identification of novel PTEN-binding partners: PTEN interaction with fatty acid binding protein FABP4. ***Mol. Cell. Biochem.*** 2010; 337(1–2):299–305.
8. Breus O, Panasyuk G, Gout IT, et al. CoA Synthase is phosphorylated on tyrosines in mammalian cells, interacts with and is dephosphorylated by Shp2PTP. ***Mol. Cell. Biochem.*** 2010; 335(1-2):195–202.
9. Panasyuk G, Nemazanyy I, Zhyvoloup A, et al. mTORbeta splicing isoform promotes cell proliferation and tumorigenesis. ***J. Biol. Chem.*** 2009; 284(45):30807–14.
10. Panasyuk G, Nemazanyy I, Zhyvoloup A, et al. Nuclear export of S6K1 II is regulated by protein kinase CK2 phosphorylation at Ser-17. ***J. Biol. Chem.*** 2006; 281(42):31188–201.

Laboratory of Molecular Pharmacology of Department of Cell Signaling

Head
Zenovii Yu. Tkachuk
Ph.D. (molecular biology),
Senior Research Scientist
Phone: +380 (44) 526-20-16
Fax: +380 (44) 526-07-59
E-mail: *ztkachuk@bigmir.net*

Education and Degrees

1965–1970 Graduate Student, Faculty of Biology, Yurii Fedkovych Chernivtsi National University, Chernivtsi, Ukraine, M.Sc. (biochemistry)
1971–1973 Postgraduate Student, Department of Genetics of Microorganisms, D. K. Zabolotny Institute of Microbiology and Virology (IMV), NASU, Kyiv, Ukraine
1974 Ph.D. (genetics of microorganisms)

Professional Employment

1974–1977 Junior Research Scientist, Department of Genetics of Microorganisms, IMV NASU, Kyiv, Ukraine
1977–1983 Junior Research Scientist, Institute of Molecular Biology and Genetics (IMBG), NASU, Kyiv, Ukraine
1983–1987 Senior Research Scientist, IMBG NASU, Kyiv, Ukraine
1987–1998 Head of the Laboratory of Oligonucleotides Biochemistry, IMBG NASU, Kyiv, Ukraine
Since 2004 Head of the Laboratory of Molecular Pharmacology, IMBG NASU, Kyiv, Ukraine
1991–1992 Advisor to the Verhovna Rada of Ukraine
1992–1993 Advisor to the Prime-minister of Ukraine
1993–1994 Advisor to the President of Ukraine
1995–1996 Advisor to the Speaker of Ukraine
1996–1997 Advisor to the Prime-minister of Ukraine

Tkachuk Z. Yu., Head of Laboratory
Levchenko S. M., Junior Research Scientist, Ph.D.
Kozlov A. V., Junior Research Scientist
Tkachuk L. V., Junior Research Scientist
Semernikova L. I., Junior Research Scientist
Tkachuk V. V., Junior Research Scientist
Yakovenko T. I., Leading Engineer
Shapoval S. O., Engineer
Rybenchuk A. A., Ph.D. Student
Skorobogatov O. Yu., Ph.D. Student

Research Area

- Studying the mechanism of action of 2'-5'oligoadenylates and their role in the regulation of the innate immunity
- Creating new immunomodulatory and antiviral drugs from natural oligonucleotides

Current Research Activities and Recent Achievements

- We study the immunomodulatory effects and antiviral activity of oligoadenilates against a wide range of viruses of both DNA and RNA nature. We also investigate the effect of oligonucleotides on innate immunity genes expression at various viral diseases and cancer.

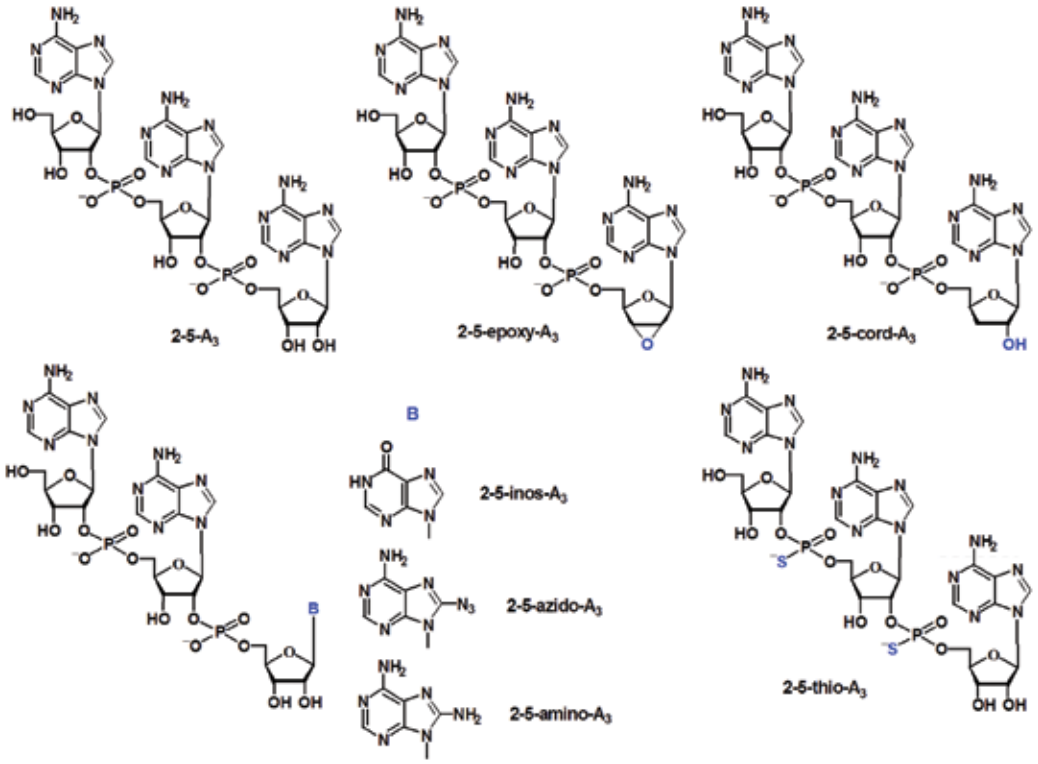


Fig. 1. Structures of 2'-5'- oligoadenylate and its analogues, that were synthesized by phosphotriester method

- We examine the polyvalent activity of oligoadenilates and their ability to bind signaling proteins, slightly altering their conformation and thus modulating their activity. These are primarily Ca^{2+} binding proteins, protein kinases and nucleases. The ability of oligonucleotides to change the secondary structure of both viral DNA and RNA, making them accessible for enzymatic cleavage is studied.
- The hypothesis which explains the mechanism of action of oligoadenylates and their involvement in the regulation of innate immunity has been proposed. Based on this hypothesis, a new imunomodulating drug Nucleinat and antiviral medicine Nuclex with a wide spectrum of action have been developed and implemented. Nuclex is effective against different viruses of both RNA and DNA nature.

Fig. 2. MALDI mass spectrum of interferon and 3'-5'oligoadenylate.
It was shown that all investigated oligoadenylates, regardless of their length and structural features, are capable of multiple interactions with α-interferon

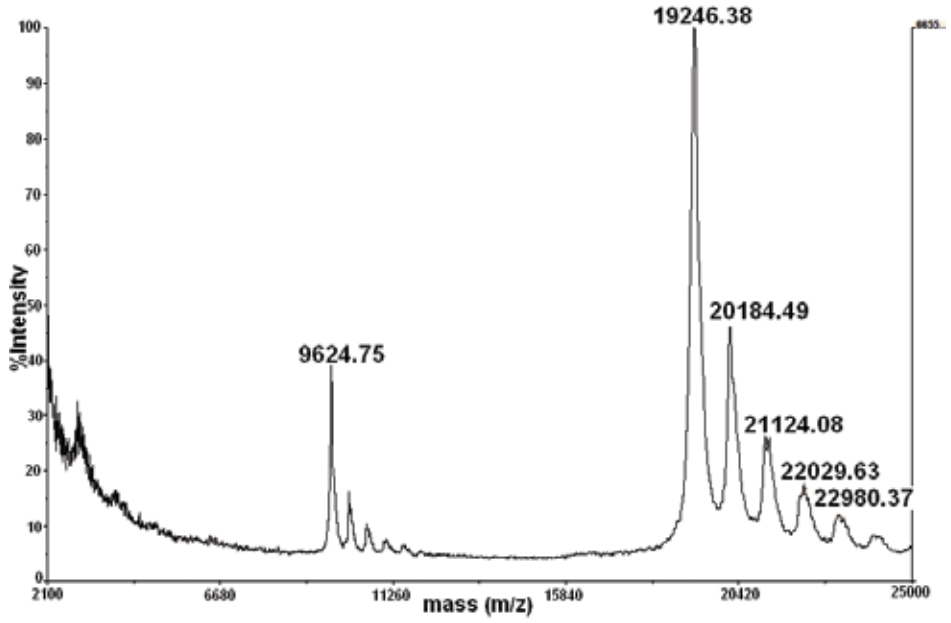


Fig. 3. Multy antiviral drug Nuclex.
Indications for use. As the drug in the anti-influenza and flu therapy. In complex therapy of the chronic virus hepatitis, urogenital herpes. *Order of the Ministry of Health of Ukraine 01.09.10 No. 752*

National Grants

Projects of National Academy of Sciences of Ukraine:

- 2013–2014 Project "Fundamentals of the development of anticancer and antiviral drugs" (scientific supervisors – Dubey I. Ya., Tkachuk Z. Yu.)
- 2009–2013 Project "To study the mechanism of 2', 5'-oligoadenylate interaction with calcium-binding proteins" (scientific supervisor – Tkachuk Z. Yu.)
- 2007–2010 Project "To study the mechanism of calmodulin activation of "core" 2'-5'-oligoadenylates and their analogues and the synthesis and study of biological activity of new ligands based on oligonucleotides" (scientific supervisor – Tkachuk Z. Yu.)
- 2004–2008 Project "To study the interaction of 2'-5'-oligoadenylate analogues with fosfodiesterase of cyclic nucleotides and to monitor new anti-inflammatory drugs ***in vitro*** and ***in vivo***" (scientific supervisors – Tkachuk Z. Yu., Dubey I. Ya.)

Collaboration

with Ukrainian organizations:

- Taras Shevchenko National University of Kyiv (Kyiv)
- Institute of Physics, NASU (Kyiv)
- O. V. Palladin Institute of Biochemistry, NASU (Kyiv)

with foreign organizations:

- Institute of Biochemistry and Biophysics, PAS (Warsaw, Poland)

Selected Publications

1. Tkachuk ZYu. 2'-5'-Oligoadenylates as a "tool" of innate immunity. ***Biopolym. Cell.*** 2013; 29(4):266–76.
2. Levchenko SM, Rebriev AV, Tkachuk VV, Dubey LV, Dubey IYa, Tkachuk ZYu. Studies on the interaction of oligoadenylates with proteins by MALDI-TOF mass spectrometry. ***Biopolym. Cell.*** 2013; 29(1):42–8.
3. Tkachuk Z. Multiantivirus compound, composition and method for treatment of virus disease. – United States Patent – 2013 –N 8,420,617 B2. Apr.16, P. 38.
4. Tkachuk ZYu, Sotska YaA, Frolov VM, Kruglova OA. Nuclex therapy for patients with chronic hepatitis C. ***Int. J. Immunological Studies.*** 2012; 1(4):349–64.
5. Frolov VM, Tkachuk ZYu, Kruglova OA. Application of immunomodulator Nucleinat in clinical practice ***Infections Diseases.*** 2012. 4:82–90.
6. Tkachuk ZYu, Dubey L, Tkachuk VV, et al. Studying the interaction of 2'-5'-oligoadenylate and their counterparts from proteins by fluorescence spectroscopy. ***Ukr.biochem.J.*** 2011; 83(1):45–53.
7. Tkachuk Z. Compound, compozision and method for treatment of inflammatory and inflammatory-related disorders. - United States Patent-2004- N US 6,737,271. May 18, P.38.

Laboratory of Molecular Mechanisms of Autoimmune Processes of Department of Cell Signaling

Head
Liudmila L. Sidorik
Ph.D. (molecular biology),
Senior Research Scientist
Phone: +380 (44) 526-55-89
Fax: +380 (44) 526-07-59
E-mail: *sidorik@imbg.org.ua*

Education and Degrees

1974–1979	Graduate Student, Faculty of Biology, Taras Shevchenko National University of Kyiv, Kyiv, Ukraine, M.Sc. (biophysics)
1990	Ph.D. (molecular biology)

Professional Employment

1979–1984	Engineer, Department of Structure and Functions of Nucleic Acids (DSFNA), Institute of Molecular Biology and Genetics (IMBG), NASU, Kyiv, Ukraine
1985–1989	Junior Research Scientist, DSFNA, IMBG NASU, Kyiv, Ukraine
1990	Senior Research Scientist, DSFNA, IMBG NASU, Kyiv, Ukraine
1991	Head of Immunochemistry Group, DSFNA, IMBG NASU, Kyiv, Ukraine
1992	Fellowship of INSERM (Institut National de la Santé et de la Recherche Médicale), Pasteur Institute, Paris, France (3 months)
1993	Fellowship of INSERM, Pasteur Institute, Paris, France (2 months)
Since 1995	Head of Lecture course in Molecular and Cellular Immunology, Faculty of Biology, Taras Shevchenko National University of Kyiv, Kyiv, Ukraine
Since 2002	Head of the Laboratory of Molecular Mechanisms of Autoimmune Processes, IMBG NASU, Kyiv, Ukraine

Sidorik L. L., Head of Laboratory
Kroupskaya I. V., Senior Research Scientist, Ph.D.
Rozhko O. T., Senior Research Scientist, Ph.D.
Bobyk V. I., Research Scientist, Ph.D.
Kapustian L. N., Research Scientist, Ph.D.
Yakovenko L. F., Research Scientist, Ph.D.

Chorny S. A., Research Scientist, Ph.D.
Vigontina O. G., Young Research Scientist
Markelova E. Yu., Young Research Scientist
Kukharenko O. E., Young Research Scientist
Matsuka V. Kh., Engineer

Research Area

Molecular chaperons as universal regulators of eukaryotic stress-induced signaling

Fig. 1. Probable binding configuration of Hsp60 with Akt1

Current Research Activities and Recent Achievements

The development of experimental animal models of inducible heart failure (various stages of inducible myocarditis and inducible DCM-like myocardial injury) – for primary screening of bioactivity, possible cardiotoxicity and/or immunogenicity of new pharmaceutic drugs and nanotechnologies.

Study on peculiarities of molecular chaperons Hsp60 and Hsp90 expression, function and localyzation and their regulatory role in apoptotic signaling of cardiomyocytes at heart failure progression.

Study on chaperonin Hsp60 proinflammation biological activity of patients with congestive heart failure and women with chronic infertility

Creation of bank of recombinant chaperons and specific

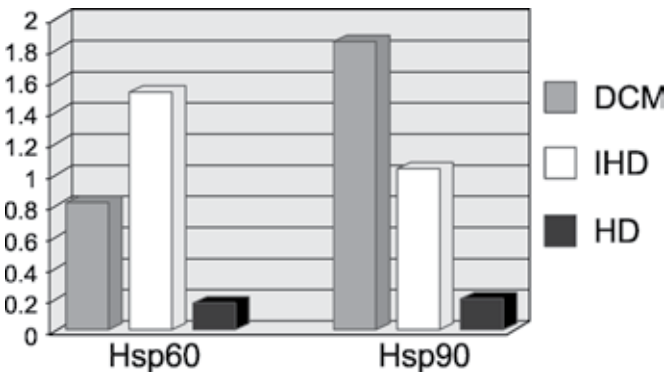


Fig.2. Anti-Hsp60 and anti-Hsp90 autoantibodies level determined by ELISA method in sera of patients affected by DCM, ischemic disease (IHD) and healthy donors (HD)

anti-chaperons antibodies for development of diagnostic tools for verification of heart failure different stages, prognosis of severe arterial hypertension progression

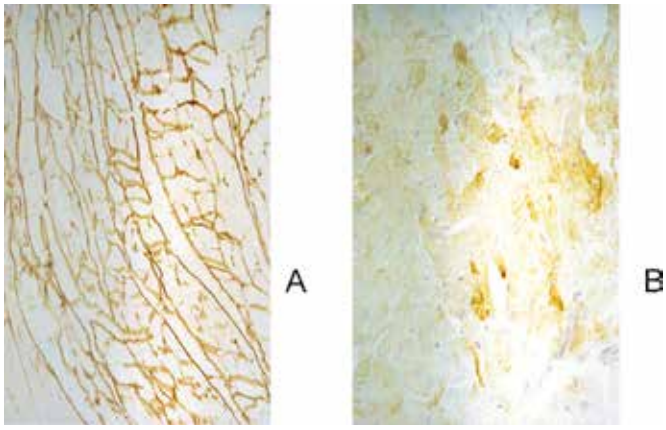


Fig.3. Hsp90 localization in left ventricular of DCM-affected (A) and normal (B) human myocardia detected by immunohystochemical method. Magnification x 100

National Grants

Projects of National Academy of Sciences of Ukraine:

- 2012–2016 N 2.2.4.20 Project: "Structure-functional peculiarities of Hsp90 interaction with targets in heart failure pathogenesis" (scientific supervisor – Sidorik L. L.)
- 2010–2014 N 102.10-H Project: "Evaluation of biocompatibility and biosecurity of metal nanoparticles ***in vitro*** and ***in vivo***, perspective as cargo targeting of cardiogeneic and antiapoptotic drugs" (scientific supervisors – Director of F. D. Ovcharenko Institute of Biocolloidal Chemistry, NASU, (Kyiv); Dr.Sci. (chem.), Prof. Ulberg Z. R.)
- 2007–2011 N 2.2.4.20 Project: "Study of peculiarities of molecular chaperon Hsp90 expression and function using experimental model of chronic stress"
- 2003–2006 N 2.2.4.20 Project: "Investigation of cytoplasmic and mitochondrial chaperons' function at dilated cardiomyopathy"

Projects of State Fund for Fundamental Researches

- 1997–1998 N 1.1.2/2225 Project: "The study of autoantibodies directed against protein biosynthesis components at systemic autoimmune diseases"
- 1993–1994 N 5/357 Project: "Immunochemical investigation of structure and function peculiarities of cytoplasmic rybonucleoproteines"
- 1991–1993 Project: "The study of heart and vessels injury' molecular and cellular mechanisms at cardio-vascular pathologies"

Projects of Ministry of Education and Science of Ukraine:

- 2010–2011 Ukraine-Poland scientific and technical cooperation N M/135-2009 Project: "Autoantibodies against Hsp60, Hsp90 and Sgt1 as new diagnostic tool in dilated cardiomyopathy"

International Grants

- 2013–2017 GDRI (International Research Networks) N UMR 8203 Project: "New pharmacological approach by siRNA-squalene for targeting junction oncogenes in thyroid and involvement of molecular chaperon (HSP 60 & 70) in thyroid cancer progression" (scientific supervisors – Professor Massaud Lilian, Institute Gustave-Roussy, Paris, France and Sidorik Lyudmila, IMBG NASU, Kyiv, Ukraine)

Collaboration

with Ukrainian organizations:

- National Scientific Center "M. D. Strazhesko Institute of Cardiology, NAMS of Ukraine" (Kyiv)
- M. M. Amosov National Institute of Cardiovascular Surgery, NAMSU (Kyiv)
- State Institution "Scientific-Practical Medical Center of Pediatric Cardiology and Cardiac Surgery" of the Health Ministry of Ukraine (Kyiv)
- R. E. Kavetsky Institute of Experimental Pathology, Oncology and Radiobiology, NASU (Kyiv)
- O. V. Palladin Institute of Biochemistry, NASU (Kyiv)
- Institute of Cell Biology, NASU (Lviv)
- Taras Shevchenko National University of Kyiv (Kyiv)
- Morphological Laboratory "BIONTEC" (Dnepropetrovsk)
- Bogomoletz Institute of Physiology, NASU (Kyiv)

with foreign organizations:

- A. N. Bach Institute of Biochemistry, RAS (Moscow, Russia)
- M. M. Shemyakin–Yu. A. Ovchinnikov Institute of Bioorganic Chemistry, RAS (Moscow, Russia)
- Kirensky Institute of Physics of Siberian Branch, RAS (Krasnoyarsk, Russia)
- International Institute of Molecular and Cell Biology (Warsaw, Poland)
- Nencki Institute of Experimental Biology, PAS (Warsaw, Poland)
- Institute Gustave-Roussy (Paris, France)

Selected Publications

1. Kapustian LL, Vigontina OA, Rozhko OT et al. Hsp90 and its co-chaperone, Sgt1, as autoantigens in dilated cardiomyopathy. ***Heart Vessels.*** 2013;28(1):114–9.
2. Bobyk VI, Kapustian LN, Morozova LM, et al. Estimation of autoimmune and DNA-damage influence of gold nanoparticles. ***Biotechnology.*** 2012; 5(2):115–21.
3. Kroupskaya I.V., Kapustian L.N., Tykhonkova I.O., Sidorik L.L. Identification of complex between molecular chaperon Hsp60 and p70S6K1 kinase in human cardiomyocytes. ***Biopolym. Cell.*** 2011; 27(1):36–9.
4. Rozhko OT, Kapustian LN, Bobyk VI, et al. Investigation of p70S6 kinase expression and localization at heart failure progression. ***Biopolym. Cell.*** 2010. 26(6):486–491.
5. Kondratyuk Y, Sidorik L, Bobyk V, Ryabenko D, Kornelyuk A. Autoantibodies against tyrosyl-tRNA synthetase at heart failure. ***Biopolym. Cell.*** 2010; 26(5):373–7.
6. Kroupskaya IV, Kapustian LN, Sidorik LL. Bioinformatic prediction of phosphorylated sites of integrin b1-coupled protein melusin. ***Biopolym. Cell.*** 2008; 24(6):503–7.
7. Bobyk VI, Ryabenko DV, Sergienko OV, et al. Development of unique experimental model of autoimmune myosine-induced injury of myocardium. ***Biopolym. Cell.*** 2007; 23(2):115–21.
8. Sidorik L, Kyyamova R, Bobyk V et al. Molecular chaperon HSP60 and cytochrome P450 2E1 co-expression in dilated cardiomyopathy. ***Cell Biology International.*** 2005; 29:51–5.

Department of Translation Mechanisms of Genetic Information

Head
Anna V. El'skaya
Dr.Sci. (molecular biology), Professor,
Full Member of National Academy of Sciences of Ukraine
Phone: +380 (44) 526-07-49
Fax: +380 (44) 526-07-59
E-mail: *anna.elskaya@yahoo.com*

Education and Degrees

1963	Graduate Student, Maxim Gorky Donetsk National Medical University, Donetsk, Ukraine, M.D.
1968	Ph.D. (molecular biology), O. V. Palladin Institute of Biochemistry (IBC), NASU, Kyiv, Ukraine
1976	Dr.Sci. (molecular biology), IBC NASU, Kyiv, Ukraine
1986	Full Professor, Taras Shevchenko National University of Kyiv, Kyiv, Ukraine
1988	Corresponding Member of NASU (molecular biology)
1992	Full Member of NASU (molecular biology)

Professional Employment

1963–1965	Senior Laboratory Assistant, Maxim Gorky Donetsk National Medical University, Donetsk, Ukraine
1965–1968	Postgraduate Student, O. V. Palladin Institute of Biochemistry (IBC) NASU, Kyiv, Ukraine
1968–1973	Junior Research Scientist, IBC NASU, Kyiv, Ukraine
1973–1978	Senior Research Scientist, Institute of Molecular Biology and Genetics (IMBG), NASU, Kyiv, Ukraine
1978–1996	Head of Department, IMBG NASU, Kyiv, Ukraine
1996–2003	Deputy Director, IMBG NASU, Kyiv, Ukraine
Since 2003	Director, IMBG NASU, Kyiv, Ukraine

Membership

Vice-President of Ukrainian Biochemical Society
Head of the Expert committee on biology of Ministry of Education and Science of Ukraine
Head of the Scientific Council of IMBG NASU
Head of NASU Scientific and Technical Program "Sensor systems for medico-ecological and industrial-technological requirement: metrological support and experimental operation"
Head of the Scientific Expert Group for the "Fundamentals of Molecular and Cellular Biotechnology" Program of NASU
Editor-in-Chief of Journal "Biopolymers and Cell" (Ukraine)
Editorial Board member of Journals: "Ukrainica Bioorganica Acta" (Ukraine), "Bulletin of Vavylov Society of Geneticists and Breeders of Ukraine" (Ukraine)
Editorial Council member of Journals: "Ukrainian Biochemical Journal" (Ukraine), "Biotechnologia Acta" (Ukraine)

Honours, Prizes, Awards

1976	O. V. Palladin Award of National Academy of Sciences of Ukraine
1982	Diploma of Presidium of Verkhovna Rada of Ukrainian SSR
1986	State Prize of Ukraine in Science and Technology
1989	Diploma of State Committee for Inventions and Discoveries of USSR
1998	Honoured Worker of Science and Technology of Ukraine
2004	Diploma of Verhovna Rada of Ukraine
2005	Gold Medal of the Ukrainian Federation of Scientists
2008	The Order of Princess Olga, III degree
2009	"European Quality Award" and Europe Business Assembly Diploma
2012	The Order of St. Andrew, III degree

Research Area

- The mechanisms of protein synthesis and its regulation in higher eukaryotes
- The development of novel analytical systems, bio- and chemosensors, on the basis of different transducers and biological material or synthetic biomimics

Laboratory of Biomolecular Electronics of Department of Translation Mechanisms of Genetic Information

Head
Alexei P. Soldatkin
Dr.Sci. (biotechnology), Professor,
Corresponding Member of National Academy of Sciences of Ukraine
Phone: +380 (44) 200-03-28
Fax: +380 (44) 526-07-59
E-mail: *a_soldatkin@imbg.org.ua*

Education and Degrees

1973–1978	Graduate Student, Faculty of Biology, Taras Shevchenko National University of Kyiv, Kyiv, Ukraine, M.Sc. (biochemistry)
1978–1985	Ph.D. (molecular biology). Thesis: "Dependence of poly (U) translation accuracy on tRNA pool", Institute of Molecular Biology and Genetics (IMBG), NASU, Kyiv, Ukraine
1999	Dr.Sci. (biotechnology). Thesis: "Development of scientific and technological basis for creation of electrochemical biosensors for medicine, biotechnology and environmental control", D. K. Zabolotny Institute of Microbiology and Virology (IMV), NASU, Kyiv, Ukraine
2004	Professor (biotechnology)
2012	Corresponding Member of NASU (novel biomedical technologies)

Professional Employment

1978–1994	Engineer-researcher, Junior Research Scientist, Research Scientist, and Senior Research Scientist, IMBG NASU, Kyiv, Ukraine
1993	Associated Research Scientist of CNRS (Centre National de la Recherche Scientifique (Red Position) at LPCI (Laboratoire de Physicochimie Industrielle), URA (Unité de Recherche Associée) CNRS 404, Ecole Centrale de Lyon, France
Since 1994	Head of the Laboratory of Biomolecular Electronics, IMBG NASU, Kyiv, Ukraine
1995–1997	Associated Professor at LPCI, URA (Unités Mixtes de Recherche) CNRS 404, Ecole Centrale de Lyon, France
1996–1997	Co-Director of NATO (North Atlantic Treaty Organization) Linkage Grant N ENVIR.LG 950913
1998–2000	Co-Director of NATO Linkage Grant N ENVIR.LG 97 2305
1998–2000	Co-Director of INTAS (The International Association for the Promotion of Co-operation with Scientists from the New Independent States of the Former Soviet Union) Grant N 96 1971
2000–2001	Associated Research Scientist of CNRS (Red Position) at IFoS (Laboratoire d'Ingénierie et de Fonctionnalisation des Surfaces), UMR 5621, Ecole Centrale de Lyon, France
2001–2003	Co-Director of NATO Collaborative Linkage Grant N LST.CLG 977826
2001–2004	Team Leader of INTAS Grant N 00-751
2003–2005	Co-Director of NATO Collaborative Linkage Grant N LST.CLG 980008
2004–2005	Co-Director of bilateral Grant N EXKDO91281 of CNRS-NASU Program
2006–2011	Coordinator of 2 STCU (Science and Technology Center in Ukraine) Grants and Team Leader of 1 STCU Grant

Honours, Prizes, Awards

1986	State Prize of Ukraine in Science and Technology (molecular biology)
1993	Award of the best oral communication at Eurosensors VII
1998–1999	Personal Grant for Senior Scientists from the International Science Foundation

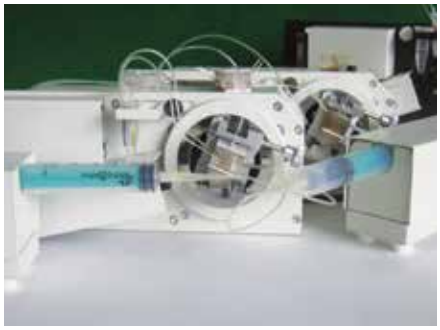
El'skaya A. V., Head of Department
Soldatkin A. P., Head of Laboratory
Dzyadevych S. V., Chief Research Scientist, Dr.Sci., Professor
Sergeeva T. A., Leading Research Scientist, Dr.Sci.
Korpan Ya. I., Leading Research Scientist, Ph.D.
Arkhypova V. M., Senior Research Scientist, Ph.D.
Biloivan O. A., Senior Research Scientist, Ph.D.
Rachkov O. E., Senior Research Scientist, Ph.D.
Soldatkin O. O., Senior Research Scientist, Ph.D.
Shkotova L. V., Senior Research Scientist, Ph.D.
Zinchenko O. A., Research Scientist, Ph.D.
Pyeshkova V. M., Research Scientist, Ph.D.
Marchenko S. V., Junior Research Scientist
Sayapina O. Ya., Junior Research Scientist, Ph.D.
Zhybak M. T., Ph.D. Student
Chan Deni, Ph.D. Student
Dudchenko O. Ye., Ph.D. Student
Matsishin N. J., Ph.D. Student

Research Area

Scientific and technological aspects of the development of bio- and chemosensor systems based on electrochemical and optical transducers

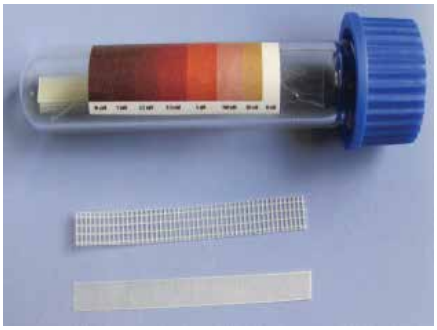
Current Research Activities and Recent Achievements

- Development and creation of micro/nano electrochemical bio- and chemosensors for the ***in vitro*** and ***in vivo*** determination of major metabolites, some neurotransmitters, alcohols, aldehydes and toxic substances
- Use of nanomaterials, nanotubes and zeolites to improve analytical characteristics of bio- and chemosensor devices
- Use of new genetically engineered proteins and synthetic recognition molecules to create sensors with given analytical characteristics
- Creation of synthetic analogues of biological receptors by molecular imprinting (molecularly imprinted polymers – MIP) and their introduction in sensor technology, solid phase extraction and chromatography
- Development of electrochemical and optical affine (immune- and DNA-) sensors
- Study on fundamentals of interaction of immobilized enzymes with substrates and inhibitors using electrochemical sensors



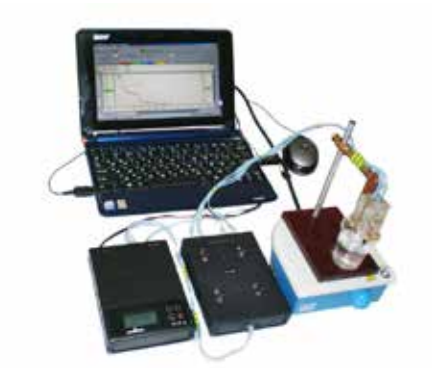
SPR-based system for identification of viruses, DNA- and for immune diagnostics

Conductometric enzyme system for determination of carbohydrates and aldehydes



Colorimetric sensor system for phenol determination based on nano-MIP-membranes

Potentiometric multisensor enzyme system for analysis of toxic substances



ISFET-based multisensor enzyme system for blood metabolites determination

Optical biosensor based on nano-MIP-membranes for determination of aflatoxin B1

National Grants

Projects of National Academy of Sciences of Ukraine:

- 2010–2012 N 3/1 Project: "Portable analyzer of alkaloids in crops and foods based on electrochemical biosensor. Creation of bioselective element and its adjustment to analyzer operation" (scientific supervisor – Anna V. El'skaya)
- 2010–2012 N 5/1 Project: "Portable analyzer based on amperometric enzyme biosensors for quality control of beverages in winemaking. Development of amperometric enzyme biosensor for determination of glucose, lactate and glycerol" (scientific supervisor – Sergiy V. Dzyadevych)
- 2010–2012 N 8/1 Project: "ISFET-based multisensor for identification of major blood metabolites. Development of biosensor elements for determination of glucose, urea and creatinine, exploration of their work" (scientific supervisor – Alexei P. Soldatkin)
- 2010–2012 N 21/1 Project: "Development and research of sensor systems based on polymers-biomimics with catalytic properties for phenol determination. Elaboration of portable sensor systems for phenol determination" (scientific supervisor – Tatiana A. Sergeeva)
- 2010–2012 N 4/2 Project: "Multibiosensor for determination of overall toxicity of solutions and some toxic substances. Development of methods of immobilization of enzymes and investigation of simultaneous operation of the latter in multisensor" (supervisor – Valentina M. Arkhipova)
- 2010–2012 N 6/2 Project: "Design and fabrication of experimental prototypes of electrochemical biosensors for the formaldehyde analysis in foods, pharmaceuticals and environment. Development of formaldehyde analyzer based on conductometric planar thin-film electrodes" (scientific supervisor – Yaroslav I. Korpan)
- 2010–2012 N 7/2 Project: "Biosensor conductometric system for saccharides analysis in food industry. Methods of immobilization of enzyme and multienzyme complexes and investigation of their work" (scientific supervisor – Sergiy V. Dzyadevych)
- 2010–2012 N 28/2 Project: "Sensor based on the effect of localized surface plasmon resonance in arrays of gold nanostructures for investigation of biomolecular processes, molecular spectroscopy of organic compounds and precision measurement of the refractive index. Investigation of biomolecular processes by sensor based on the effect of localized surface plasmon resonance" (scientific supervisor – Olexander E. Rachkov)
- 2010–2014 Project: "Development of multiparametrical devices for express detection and monitoring of chemical and biological liquid compounds. Elaboration of methods of enzyme immobilization onto the surface of multitransducers" (scientific supervisor – Sergiy V. Dzyadevych)
- 2010–2014 N 24/12 Project: "Optical sensor systems based on nanostructured molecularly imprinted polymer membranes for environmental monitoring and medical diagnostics" (scientific supervisor – Tatiana A. Sergeeva)
- 2010–2014 N 25/12 Project: "Development of bioselective membranes based on carbon nanomaterials functionalized by biomolecules for creation of analytical microdevices of new generation" (scientific supervisors – Olga A. Biloivan and Yaroslav I. Korpan)
- 2010–2014 N 5.34 Project: "Creation and exploration of new nanobiomaterials based on recombinant single-chain antibodies and nanostructured substrates for nanobiosensor immune diagnostics" (scientific supervisor – Alexei P. Soldatkin)
- 2010–2014 N 99/10-N Project: "Study on interaction of nucleic acids with nanocrystalline semiconductors to create new bionanostructured materials capable of recognition of biologically important markers of hereditary diseases" (scientific supervisor – Alexei P. Soldatkin)

International Grants

- 2013–2016 7th Framework Programme (FP7) N 318053 Project: "Micro/nanosensors for early cancer warning system – diagnostic and prognostic information" (scientific supervisor – Yaroslav I. Korpan)
- 2012–2015 7th Framework Programme (FP7) N 318524 Project: "Integrated nanodevices" (scientific supervisor – Sergiy V. Dzyadevych)
- 2012–2015 NATO Scientific Programmes N CBP.NUKR. SFPP 984173 Project: "New electrochemical nanosensors for determination of toxic ions" (scientific supervisor – Yaroslav I. Korpan)
- 2011–2012 NATO Scientific Programmes N CBP.NUKR.CLG 984221 Project: "Development of biosensors for determination of botulinum neurotoxin and their adaptability to products examination against biological terrorist attacks" (scientific supervisor – Sergiy V. Dzyadevych)

Collaboration

with Ukrainian organizations:

- Taras Shevchenko National University of Kyiv (Kyiv)
- Institute of Cell Biology, NASU (Lviv)
- V. E. Lashkaryov Institute of Semiconductor Physics, NASU (Kyiv)
- O. V. Palladin Institute of Biochemistry, NASU (Kyiv)
- Institute of Electrodynamics, NASU (Kyiv)
- F. D. Ovcharenko Institute of Biocolloidal Chemistry, NASU (Kyiv)
- Institute of Macromolecular Chemistry, NASU (Kyiv)
- National Institute of Vine and Wine "Magarach", NAASU (Yalta)
- Medved's Institute of Ecohygiene and Toxicology, Ministry of Health of Ukraine (Kyiv)
- State Institution "V. P. Komisarenko Institute of Endocrinology and Metabolism of NAMS of Ukraine" (Kyiv)
- Institute for Potato Research of National Academy of Agricultural Sciences of Ukraine (NAASU) (PO Nemishaeve, Borodianka district, Kyiv region)
- V. M. Glushkov Institute of Cybernetics, NASU (Kyiv)
- State Institution "Institute of Nephrology of NAMS of Ukraine" (Kyiv)
- Frantsevich Institute for Problems of Materials Science, NASU (Kyiv)

with foreign organizations:

- Université Claude Bernard Lyon 1 (Lyon, France)
- Lyon Research Institute of Catalysis and Environment (Lyon, France)
- Jean Monnet University (Lyon, France)
- University of Barcelona, Institute of Nanoscience and Nanotechnology (Barselona, Spain)
- University of Rovira and Virgili (Tarragona, Spain)
- McGill University (Quebec, Canada)
- Polytechnic School of Montreal, Department of Engineering Physics (Montréal, Canada)
- Texas University, (USA)
- Clemson University (South Carolina, USA)
- Cranfield University, Cranfield Health (Cranfield, UK)
- Clarkson University, Department of Chemistry & Biomolecular Science (New York, USA)
- Middle East Technical University (Ankara, Turkey)
- Sogang University (Seoul, Korea)
- Institute of Technology Tallaght (Tallaght, Ireland)
- University of Bucharest (Bucharest, Romania)
- University of Coimbra (Coimbra, Portugal)
- Linköping University, Biosensors & Bioelectronics Centre (Linköping, Sweden)
- University Joseph Fourier (Grenoble, France)
- University of the Western Cape (Bellville, South Africa)
- National Research Centre (Cairo, Egypt)
- Nabeul Engineering Preparatory Institute (Nabeul, Tunisia)
- Hassan II University – Mohammedia (Mohammedia, Morocco)
- Fakir Mohan University, Department of Biotechnology (Balasore, India)
- "Tudomány és Technológia Transzfer Kft" Company (Budapest, Hungary)
- "Ecobioservices" Company (Florence, Italy)
- "Electronical Engineering" Company (Casablanca, Morocco)

Selected Publications

1. Soldatkin OO., Kucherenko IS., Shelyakina MK, et al. Electroanalys. Application of different zeolites for improvement of the characteristics of a pH-FETs biosensor based on immobilized urease. ***Electroanalysis.*** 2013; 25(2):468–74.
2. Zinchenko OA, Marchenko SV, Sergeyeva TA, et al. Application of creatinine-sensitive biosensor for hemodialysis control. ***Biosens Bioelectron.*** 2012; 35(1):466–9.
3. Rachkov A, Patskovsky S, Soldatkin A, Meunier M. Surface plasmon resonance detection of oligonucleotide sequences of the rpoB genes of Mycobacterium tuberculosis. ***Talanta.*** 2011; 85(4):2094–9.
4. Rogaleva N., Korpan Y., Biloivan O. Glucose biosensor based on screen-printed electrodes and glucose oxidase layer modified by MWCNT-NH2. ***Sensor Letters.*** 2011; 9(6):2356–9.
5. Korpan Y., Soldatkin O., Sosovska O et al. Formaldehyde-sensitive conductometric sensors based on commercial and recombinant formaldehyde dehydrogenase. ***Microchimica Acta.*** 2010; 170:337–44.
6. Sergeyeva TA, Slinchenko OA, Gorbach LA, et al. Catalytic molecularly imprinted polymer membranes: Development of the biomimetic sensor for phenols detection. ***Anal Chim Acta.*** 2010; 659(1–2):274–9.
7. Arkhipova VN, Dzyadevych SV, Jaffrezic-Renault N, Martelet C, Soldatkin AP. Biosensors for assay of glycoalkaloids in potato tubers ***Prikl Biokhim Mikrobiol.*** 2008; 44(3):347–52.
8. Dzyadevych SV, Arkhypova VN, Soldatkin AP, El'skaya AV, Martelet C, Jaffrezic-Renault N. Conductometric enzyme biosensors. In: Marks R.S., Lowe C.R., Culen D.C., Weetall H.H., Karube I., editors. Handbook of Biosensors and Biochips: Wiley-Interscience; 2007. p. 379–94.
9. Soldatkin AP, Dzyadevych SV, El'skaya AV, Martelet C, Jaffrezic-Renault N. Pathways for improving potentiometric and conductometric enzymatic biosensors In: Grimes CA, Dickey EC, Pishko MV, editors. Encyclopedia of Sensors. California, USA: American Scientific Publishers; 2006. p. 331–48.
10. Dzyadevych SV, Soldatkin AP. Scientific and technological basics of development of miniaturized electrochemical biosensors Ed. Elska G. Kyiv: Naukova dumka, 2006. 255 p.

Laboratory of Protein Biosynthesis of Department of Translation Mechanisms of Genetic Information

Head
Boris S. Negrutskii
Dr.Sci. (molecular biology), Professor,
Phone: +380 (44) 200-03-37
Fax: +380 (44) 526-07-59
E-mail: *negrutskii@imbg.org.ua*

Education and Degrees

1974–1979	Graduate Student, Donetsk National University, Donetsk, Ukraine, M.Sc. (biochemistry)
1979–1983	Postgraduate Student, Department of Translational Mechanisms of Genetic Information (DTMGI), Institute of Molecular Biology and Genetics (IMBG), NASU, Kyiv, Ukraine
1987	Ph.D. (molecular biology), IMBG NASU, Kyiv, Ukraine
1999	Dr.Sci. (molecular biology), IMBG NASU, Kyiv, Ukraine

Professional Employment

1983–2000	Engineer, Junior Research Scientist, Research Scientist, Senior Research Scientist, Leader Research Scientist, DTMGI, IMBG NASU, Kyiv, Ukraine
Since 2000	Head of the Laboratory of Protein Biosynthesis, DTMGI, IMBG NASU, Kyiv, Ukraine

El'skaya A. V., Head of Department
Negrutskii B. S., Head of Laboratory
Shalak V. F., Senior Research Scientist, Ph.D.
Porubljova L. V., Senior Research Scientist, Ph.D.
Kovalenko M. I., Senior Research Scientist, Ph.D.
Lukash T. O., Research Scientist, Ph.D.
Novosylna O. V., Junior Research Scientist
Verem'eva M. V., Junior Research Scientist
Vislovukh A. A., Junior Research Scientist
Vlasenko D. O., Leading Engineer
Trosyuk T. V., Ph.D. Student
Koroljov O. S., Ph.D. Student

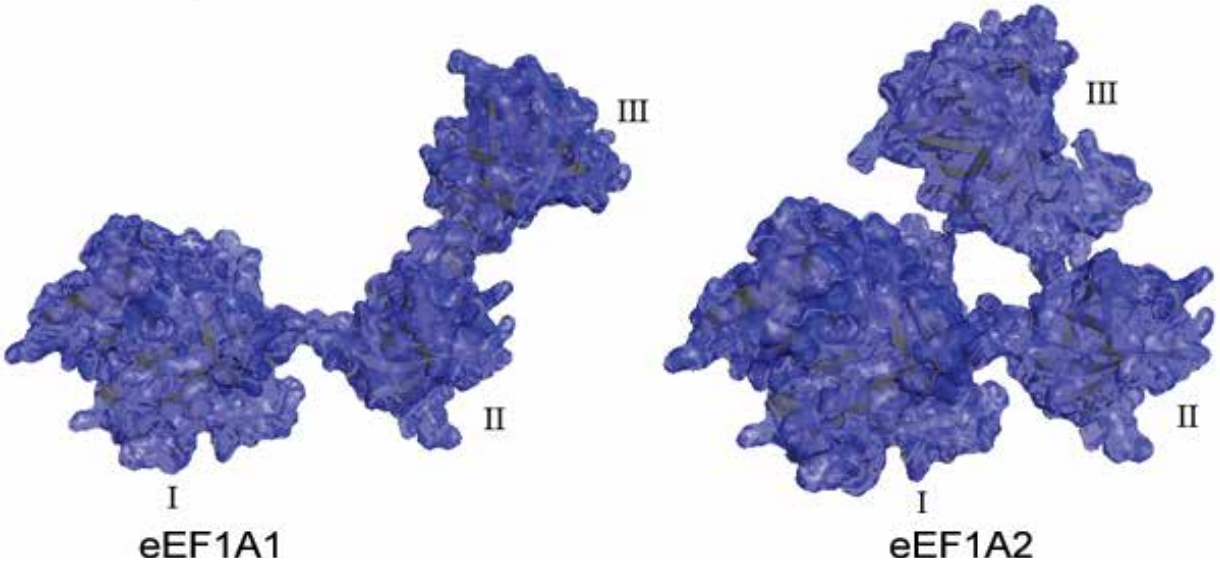
Research Area

We investigate the mechanisms of dynamic compartmentalization of the protein synthesis machinery in mammals, molecular composition and cancer-related features of the translation elongation factor 1 (eEF1) complex, spatial structure, expression, post-translational modifications and functions of the normal and proto-oncogenic isoforms of translation elongation factor 1A (eEF1A)

Current Research Activities and Recent Achievements

- The concept of vectorial transfer of tRNA during translation elongation process in mammalian cells has been established. Molecular mechanisms of tRNA channeling have been uncovered
- Spatial structures of A1 and proto-oncogenic A2 isoforms of mammalian eEF1 have been shown to be different despite 97 % homology of their amino acid sequences.

Spatial models of eEF1A1 and eEF1A2 isoforms



Differential interaction of the isoforms with protein partners has been demonstrated which might be important for oncogenecity of A2

- X-ray structure of the proto-oncogenic A2 isoform has been obtained, in collaboration with Department of Protein Synthesis Enzymology, and some peculiariries in the mechanism of GTP/GDP exchange have been reveiled
- Mechanism of overexpression of A2 in tumors has been shown to be related to special microRNAs whose role has been predicted theoretically and proved experimentally
- The components of macromolecular eEF1 complex have been shown to function independently from the complex in human cancer cells and tissues where the subunits may apparently fulfill a non-translational role

National Grants

- Several grants from National Academy of Sciences of Ukraine, State Fund of Fundamental Research and the Ministry of Education and Science of Ukraine have been obtained. Recently, the laboratory works in frame of State Key Laboratory of Molecular and Cell Biology

International Grants

- 2012–2014 Project PICS (Projet International de Coopération Scientifique) "Translation apparatus in cytosol: role in mitochondrial translation and antioxidant homeostasis"
- 2012–2013 Project 5507 STCU (Science and Technology Center in Ukraine) "The A2 isoform of translation elongation factor 1 as a potential oncomarker" supported
- 2011–2014 7th Framework Programme (FP7) FP7-INCO-2011-6, ERA-WIDE Project: "Strengthening cooperation in Molecular Biomedicine between EU and UKRAINE", COMBIOM (scientific supervisor – Prof. A. Elskaya)
- 2010–2011 Project UKR10/A10 "Structural and biological studies of the eukaryotic elongation factors (eEF) 1B", supported by BMBF (Bundesministerium für Bildung und Forschung), Germany
- 2009–2012 Program of European science projects GDRI grant "Earlier steps in the development of oncological, autoimmune and neurodegenerative diseases"
- 2009–2011 Program of collaboration between Academy of Sciences of Poland and Ukraine. Project "Investigation of post-translational modifications of the components of human translation machinery during carcinogenesis"
- 2009–2011 PICS (Projet International de Coopération Scientifique) grant "Structural and Functional organization of the translation apparatus in the cytoplasm of human cells"
- 2008–2009 Program of collaboration between NASU and Russian Academy of Sciences. Project "Structural and functional study of the two tissue-specific forms of eukaryotic elongation factor eEF1A"
- 2006–2008 Wellcome Trust N 074742/Z04/Z "Two-faced Janus: mammalian translation elongation factor 1A and its isoforms"
- 2006–2008 INTAS Project 05-7750 "Multisubunit translation elongation factor 1 in health and carcinogenesis"
- 2005–2007 Program of collaboration between Academy of Sciences of Czech Republic and Ukraine, Project "Thermodynamical analysis of the structure of the elongation factors domains in prokaryotes and eukaryotes"

Collaboration

with Ukrainian organizations:

- R. E. Kavetsky Institute of Experimental Pathology, Oncology and Radiobiology, NASU (Kyiv)

with foreign organizations:

- Laboratory of Enzymology and Structural Biochemistry, CNRS (Gif-sur-Yvette, France)
- Laboratory of Epigenetics of Cancer, CNRS (Gif-sur-Yvette, France)
- University of Liverpool (Liverpool, UK)
- Institute of Protein, RAS (Puschino, Russia)

Selected Publications

1. Vislovukh A, Kratassiouk G, Porto E, Gralievska N, Beldiman C, Pinna G, El'skaya A, Harel-Bellan A, Negrutskii B, Groisman I. Proto-oncogenic isoform A2 of eukaryotic translation elongation factor eEF1 is a target of miR-663 and miR-744. ***Br J Cancer.*** 2013 Jun 11;108(11):2304–11.
2. Negrutskii B, Vlasenko D, El'skaya A. From global phosphoproteomics to individual proteins: the case of translation elongation factor eEF1A. ***Expert Rev. Proteomics.*** 2012; 9(1):71–83.
3. Yaremchuk A, Shalak VF, Novosylna OV, et al. Purification, crystallization and preliminary X-ray crystallographic analysis of mammalian translation n elongation factor eEF1A2. ***Acta Cryst.*** 2012; F68:295–7.
4. Havrylenko S, Legouis R, Negrutskii B, Mirande M. Caenorhabditis elegans evolves a new architecture for the multi-aminoacyl-tRNA synthetase complex. ***J. Biol. Chem.*** 2011; 286:28476–87.
5. Veremieva M, Khoruzhenko A, Zaicev S, Negrutskii B, El'skaya A. Unbalanced expression of the translation complex eEF1 subunits in human cardioesophageal carcinoma. ***Eur. J. Clin. Invest.*** 2011; 41:269–76.
6. Kaminska M, Havrylenko S, Decottignies P, Le Maréchal P, Negrutskii B, Mirande M. Dynamic organization of aminoacyl-trna synthetase complexes in the cytoplasm of human cells. ***J. Biol. Chem.*** 2009; 284: 13746–54.
7. Kaminska M, Havrylenko S, Decottignies P, et al. Dissection of the structural organization of the aminoacyl-tRNA synthetase complex. ***J. Biol. Chem.*** 2009. 284:6053–60.
8. Budkevich TV, El'skaya AV, Nierhaus KH. Features of 80S mammalian ribosome and its subunits. ***Nucleic Acids Res.*** 2009. 36:4736–44.
9. Panasyuk G, Nemazanyy I, Filonenko V, Negrutskii B, El'skaya AV. A2 isoform of mammalian translation factor eEF1A displays increased tyrosine phosphorylation and ability to interact with different signalling molecules. ***Int. J. Biochem. Cell Biol.*** 2008; 40:63–71.
10. Negrutskii BS, El'skaya AV. Eukaryotic translation elongation factor 1 alpha: structure, expression, functions, and possible role in aminoacyl-tRNA channeling. ***Prog. Nucleic Acid Res. Mol. Biol.*** 1998; 60:47–78.

Laboratory of Systems Biology of Department of Translation Mechanisms of Genetic Information

Head
Maria Yu. Obolens'ka
Dr.Sci. (molecular biology), Professor
Phone: +380 (44) 526-11-39
Fax: +380 (44) 526-07-59
E-mail: *m.obolenska@gmail.com*

Education and Degrees

1958–1964 Graduate Student, Bogomolets National Medical University, Kyiv, Ukraine
1964–1967 Postgraduate Student, Department of Molecular Biology, D. F. Chebotarev State Institute of Gerontology, NAMSU, Kyiv, Ukraine
1968 Ph.D. (biochemistry)
1999 Dr.Sci. (molecular biology)

Professional Employment

1964–1975 Junior Research Scientist, Department of Molecular Biology, D. F. Chebotarev State Institute of Gerontology, NAMSU, Kyiv, Ukraine
1975–1980 Research Scientist, Department of Molecular Mechanisms of Protein Biosynthesis, Institute of Molecular Biology and Genetics (IMBG), NASU, Kyiv, Ukraine
1980–1991 Senior Research Scientist, Department of Molecular Mechanisms of Protein Biosynthesis, IMBG NASU, Kyiv, Ukraine
1991–1994 Research Scientist, Institute of Molecular and Cell Biology, Albert-Ludwig University, Freiburg i. Br., Germany
1994–1999 Senior Research Scientist, group leader, Department of Translational Mechanisms of Genetic Information (DTMGI), Laboratory of Protein Biosynthesis, IMBG NASU, Kyiv, Ukraine
2000–2009 Leading Research Scientist, DTMGI, Laboratory of Protein Biosynthesis, IMBG NASU, Kyiv, Ukraine
Since 2009 Head of the Laboratory of Systems Biology, DTMGI, IMBG NASU, Kyiv, Ukraine

Honours, Prizes, Awards

1998–1999 Personal Grant from Jozef Mianowski Fund, Poland (2 months)
Personal Grant from UICC (Global Cancer Control), ICRET (International Cancer Technology Transfer Fellowships) N580, 2001 for the work in National Cancer Institute, NIH (National Institutes of Health), Bethesda, USA (3 months)

El'skaya A. V., Head of Department
Obolenska M. Yu., Head of Laboratory
Tokovenko B. T., Senior Research Scientist, Ph.D.
Fedorenko O. A., Senior Research Scientist, Ph.D.
Martsenyuk O. P., Research Scientist, Ph.D.
Rodrigues R. R., Engineer
Chabanova M. V., Technician
Kuklin A. V., Ph.D. Student
Draguschenko O. O., Ph.D. Student
Korneeva K. L., Ph.D. Student
Frolova A. O., Ph.D. Student
Dotsenko V., Ph.D. Student

Research Area

- Systems Biology. Bioinformatics: Whole genome search for target genes of transcription factors; Reconstruction of gene regulatory networks. Theoretical predictions and experimental corroborations.
- Gene expression and its regulation in eukaryotic cells.

Current Research Activities and Recent Achievements

Systems analysis of non-canonical functions of interferon alpha

The regulation of gene expression at the transcriptional level relies upon the effects of the transcription factors (TF) bound to specific regulatory elements. Experimental identification of TF binding sites within single-gene promoters is effort- and time-consuming with no prior information. We have elaborated a genome-wide finder of regulatory elements in promoters of protein coding genes available at *http://biomed.org.ua/COTRASIF/*. The application of this tool to the search for potential target genes of prior response to interferon alpha (IFNα) has revealed several previously "unknown" genes referring to the central nervous and compliment systems. Experimental verification of theoretically anticipated genes is in the focus of our current investigations. The modern systematic approach to capture the behavior of cellular genome is to develop the mathematical model of gene regulatory network (GRN) where the nodes are the genes and the edges represent interactions between genes via mRNAs and proteins. The reconstruction is based on the data of gene expression profiling by microarray or next generation sequencing and ever developing methods of bioinformatics. To get the GRN in rat hepatocytes treated with IFNα we conducted microarray experiment and elaborated Ensemble method for the GRN reconstruction (see source code and data repository at *https://github.com/sysbio-vo/*).

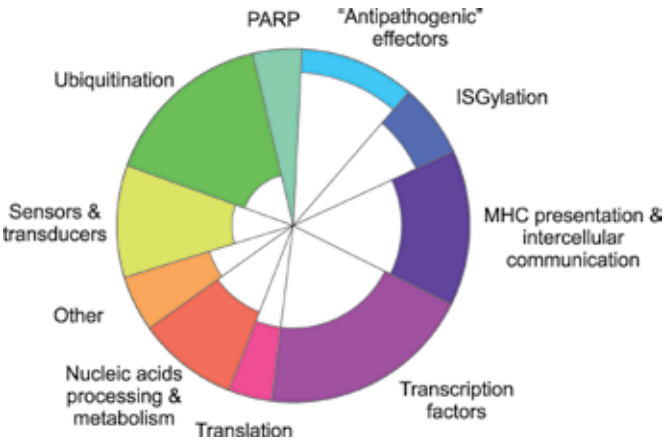


Fig. 1. Time-dependent response of differentially expressed genes in rat hepatocytes to IFNα. The square of the big sectors (colored plus white parts) is proportional to the number of differentially expressed genes after 6 h of hepatocytes treatment with IFNα and the square of the inner unshaded sectors – to the number of genes after 3 h treatment

Gene expression during transition of liver cells from quiescence to proliferation induced by partial hepatectomy in rats

The liver conscientiously and successfully combines the role of "biochemical laboratory" with the role of a major organ of innate immunity. The hepatic cells constantly eliminate the antigens derived from gastrointestinal tract, aging and transformed cells and reveal self-tolerance to their continuous presence. Extensive damage of liver parenchyma, transplantation, when the transplanted organ is too small to cope with metabolic demands or classical 70 % partial hepatectomy (PH) reverse the tolerance and induce an innate immunity response manifested by complement activation, cytokine production, expansion of natural killer cells, activated signaling from several Toll-like receptors and inhibitory signaling from signal transducing and activator factor 3 preventing liver failure. We have suggested a definite role of interferon alpha (IFNα) in triggering liver restoration. Our recent studies have proved this idea revealing transient up-regulation of IFNα mRNA and IFNα-specific antiviral activity during 1 – 6 h post-PH preceding the presynthetic period of hepatocytes cell cycle. The activation of intracellular IFNα signaling after PH corroborated our results (Chen and others 2010). The current activity is focused on the study of expression of target genes of IFNα at the beginning of liver restoration.

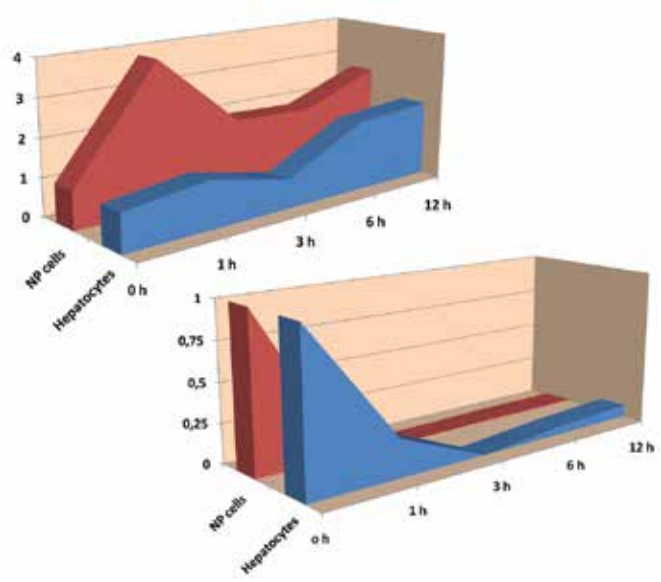


Fig. 2. Fold change of IFNα specific mRNA content in hepatocytes and nonparenchymal cells after partial hepatectomy (A) and laparatomy (B)

Folate-related metabolism of one-carbon units in human placenta

Folate-related one-carbon unit metabolism (FOCM) is a basic metabolic network tightly connected with essential cell functions – proliferation, differentiation, maintenance of redox status, all processes of methylation, etc. The experimental study of each chain of the system with various alterations of its multiple components is a laborious and expensive task though the general behavior of the system is greatly required by clinicians. The function of FOCM is tissue-specific and primarily dependent on activities of its highly polymorphic enzymes, vitamins B, folic acid and amino acids supply. The marker of FOCM is a level of homocysteine which is up-regulated during cardiovascular diseases, pregnancy pathologies, and mental disorders. We created stoichiometric mathematical model of FOCM in human placenta, taking into account the tissue-specific characteristics of corresponding genes expression, simulated the pathological situations typical for obstetrics pathologies and analyzed the whole network behavior. The results of analysis have revealed: firstly, the reliability of the model for predictions of network behavior as some of predicted characteristics correspond to experimentally obtained ones in the most studied clinical pathologies; secondly, the obtained predictions of the network behavior in slightly investigated situations will serve as a road map for the further studies and introduction of results into clinical practice.

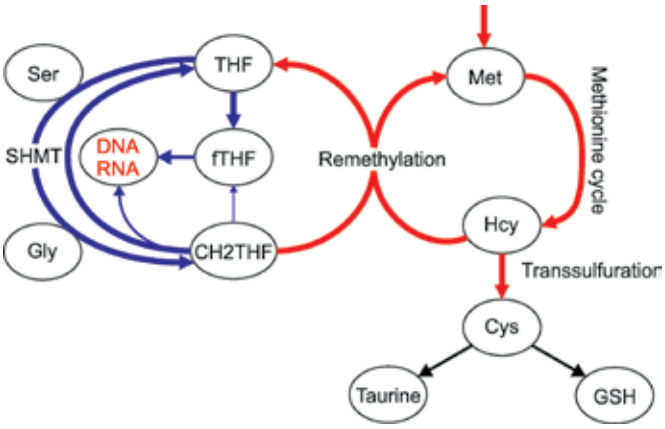


Fig. 3. Changes of metabolic fluxes in folate-related metabolism at twofold overload of human placenta with homocysteine
Folate and methionine cycles are represented at the figure. The decrease of metabolic fluxes is marked with blue color and increase – with red color. The more thick are the arrows the more pronounced is the increase of the flux and more thin are the arrows the more pronounced is the decrease of the flux

National Grants

Projects of National Academy of Sciences of Ukraine:

- 2012 N 69-53 Project: "Development of Ensembl method with high rate of parallelization for gene regulatory modeling in GRID environment"
- 2011 N Г16–46 Project: "Design of new highly parallelized GRID-methods of gene regulatory networks modeling for systems analysis of liver response to interferon alpha"
- 2010 N Г16–46 Project: "Elaboration of new methods of GRID calculations with high rate of parallelization for systems analysis of liver regeneration by gene regulatory modeling on the basis of large-scale study of gene expression"

Grants of Ministry of Education and Science of Ukraine

- 2013 Grant for talented youth from President of Ukraine "Estimation of risk factors for preecalmpsa development and the markers for early diagnosis"
- 2006 Grant for talented youth from President of Ukraine "Biomarkers for prevention of pregnancy's complications"

International Grants

- 2008–2009 N M/28-2008 Grant from scientific and technological cooperation Ukraine – Slovakia "Folate-and detoxication activity in human placenta from environmentally exposed pregnancies"
- 2008–2009 INTAS (The International Association for the Promotion of Co-operation with Scientists from the New Independent States of the Former Soviet Union) Grant for young scientists N 06-1000014-5961 "Folate-related one-carbon unit metabolism in human placenta from environmentally exposed pregnancies"
- 2007–2009 STCU (Science and Technology Center in Ukraine) N 4381 Project: "New technologies in the study of interferon alpha functional activity"
- 2006–2009 UNESCO (United Nations Educational, Scientific and Cultural Organization) Short-term Grants (M.Perepelyuk, 2006; B.Tokovenko, 2007; A.Slonchak, 2008; A.Kuklin, 2009)
- 2006–2007 Grant from scientific and technological cooperation Ukraine – Slovakia N 152-2006 "Polluted environment and genotoxic damage of human placenta"
- 2006–2007 Grant from International Federation of Scientists in the area Medicine "Interferon alpha and its role in liver cells transition from quiescence to proliferation"
- 2001 UICC, ICRET N 580 Project: "DNA adducts in placentas of environmentally exposed pregnancies"
- Grant form Polish Ministry of science and education N 40115732/3043 "Regulation of GSTP1 expression in human placenta from environmentally exposed pregnancies"

Collaboration

with Ukrainian organizations:

- State Institution "L. V. Gromashevsky Institute of Epidemiology and Infectious Diseases of NAMS of Ukraine" (Kyiv)
- Bogomoletz Institute of Physiology, NASU (Kyiv)

with foreign organizations:

- University of Warsaw, Institute of Informatics (Warsaw, Poland)
- Institute of Cell Biology, Histology and Embryology, Medical University of Graz (Graz, Austria)

Selected Publications

1. Dragushchenko O, Markadeiev M, Obolenska MY. Gene Mbl1 is a target of interferon alpha. ***FEBS Journal.*** 2013; 280 (Suppl. 1): 80–81.
2. Frolova AO. Overview of methods of reverse engineering of gene regulatory networks: Boolean and Bayesian networks. ***Biopolym. Cell.*** 2012; 28(3): 163–170.
3. Rodriguez RR, Lushchyk IS, Obolenska MYu.Stoichiometric model of folate-dependent metabolism of one-carbon units in human placenta. ***Ukr Biokhim Zh.*** 2012 Jul-Aug; 84(4):20–31.
4. Slonchak AM, Chwieduk A, Rzeszowska-Wolny J, Obolenskaya MYu Regulation of Glutathione S-transferase expression in melanoma cells. In: Yohei Tanaka, editor. Breakthroughs in Melanoma Research. Vienna, Austria: InTech; 2011. p. 145–156.
5. Mislanova C, Martsenyuk O, Huppertz B, Obolenskaya M. Placental markers of folate-related metabolism in preeclampsia. ***Reproduction.*** 2011; 142(3):467–76.
6. Obolenskaya M.Yu., Rodriguez R.R., Martsenyuk O.P. Folate-related processes in human placenta: gene expression, aminothiols, proliferation and apoptosis. ***Ukr Biokhim Zh.*** 2011, 83(1):6–17.
7. Obolenskaya MY, Teplyuk NM, Divi RL, Human placental glutathione S-transferase activity and polycyclic aromatic hydrocarbon DNA adducts as biomarkers for environmental oxidative stress in placentas from pregnant women living in radioactivity- and chemically-polluted regions. ***Toxicol Lett.*** 2010; 196(2):80–6.
8. Dragushchenko O. O., Tokovenko B. T., Obolenskaya M. Yu. Primary analysis of results of whole genome search for genes of response to the effect of interferon alpha. ***Ukr Biokhim Zh.*** 2010; 82(1):82–9.
9. Tokovenko B, Golda R, Protas O, Obolenskaya M., El'skaya A. COTRASIF: conservation-aided transcription-factor-binding site finder. ***Nucleic Acids Res.*** 2009; 37(7):e49.
10. Porubliova LV, Rebriev AV, Gromovoy TYu, Minya IY, Obolenskaya MYu. MALDI-TOF mass-spectrometry in investigation of high-molecular biological compounds. ***Ukr Biokhim Zh.*** 2009; 81(3):46–56.

Department of Molecular Genetics

Head
Gennadiy D. Telegeev
Dr.Sci. (molecular biology),
Senior Research Scientist
Phone: +380 (44) 526-07-29
Fax: +380 (44) 526-07-59
E-mail: *g.d.telegeev@imbg.org.ua*

Education and Degrees

1968–1974	Graduate Student, Bogomolets National Medical University, Kyiv, Ukraine
1978–1982	Ph.D. Student, Department of Gene Engineering, Institute of Molecular Biology and Genetics (IMBG), NASU, Kyiv, Ukraine
1990	Ph.D. (molecular biology)
2013	Dr.Sci. (molecular biology)

Professional Employment

1977–1984	Engineer, Department of Gene Engineering, IMBG NASU, Kyiv, Ukraine
1984–1992	Junior Research Scientist, Department of Gene Engineering, IMBG NASU, Kyiv, Ukraine
1992–1998	Research Scientist, Department of Gene Engineering, IMBG NASU, Kyiv, Ukraine
1998–2008	Senior Research Scientist, Department of Molecular Genetics, IMBG NASU, Kyiv, Ukraine
Since 2008	Head of the Department of Molecular Genetics, IMBG NASU, Kyiv, Ukraine

Telegeev G. D., Head of Department
Maliuta S. S., Dr.Sci., Professor, Corresponding Member of NASU
Shvachko L. P., Senior Research Scientist, Ph.D.
Alkhimova O. G., Senior Research Scientist, Ph.D.
Dybkov M. V., Research Scientist, Ph.D.
Lysetska T. Yu., Research Scientist, Ph.D.
Cherepenko O. Y., Senior Research Scientist, Ph.D.
Kravchuk I. V., Junior Research Scientist
Malyuta O. V., Junior Research Scientist
Polischuk L. O., Junior Research Scientist
Tyutyunnikova A. P., Junior Research Scientist
Antonenko.S. V., Ph.D. Student
Gurianov D. S., Ph.D. Student

Research Area

- Investigation of factors and molecular mechanisms of malignant transformation in human
- Development of technology of targeted drug delivery to eukaryotic cells

Current Research Activities and Recent Achievements

Study on molecular pathogenesis of chronic myelogenous leukemia (CML) and role of Bcr domains in this pathology.

Elaboration of the test-system for Ph-positive leukemias diagnostics and detection of Abl mutations in patients with resistance to imatinib.

Formulating novel role of PH domain as protein-protein and protein-lipid anchor, study on proteins that interact with it as well as changes in methylation status of the promotor regions of certain genes in cancer.

Development of nanovectors on the basis of branched dextran-polyacrilamide and dispersed silicium for targeted drug delivery to cells with phagocyte activity as a step for therapy of monocytic leukemias and histiocytic neoplasms.

Studies on CXCR4 expression in cancer progenitor cells and development of nanotechnology-based therapy and imaging for prostate cancer using CXCR4-targeted metal nanoparticles.

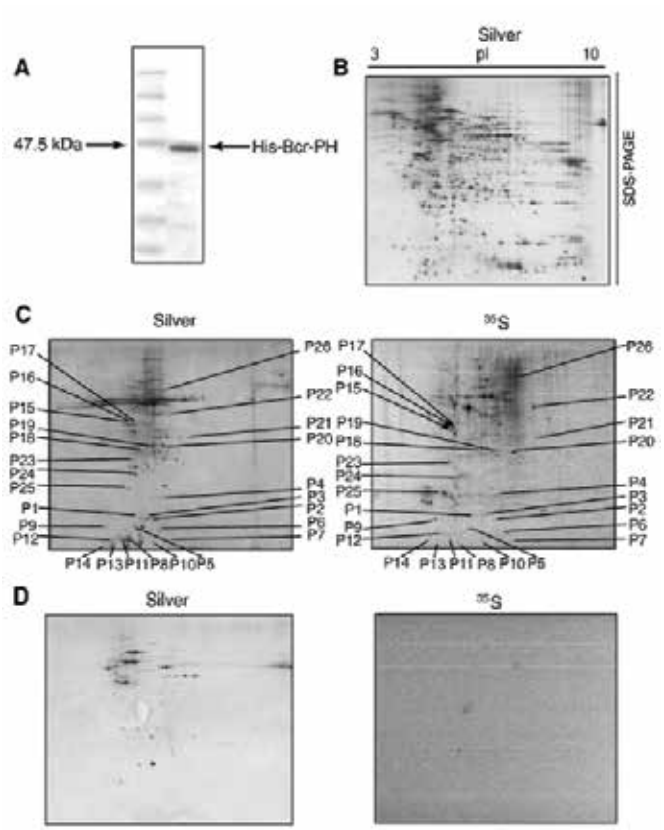


Fig 1. Proteomic analysis of proteins that interact with the PH domain of Bcr-Abl(A) SDS-PAGE analysis of purification of PH domain of Bcr-Abl with histidine tag (amino acid residues 674-869). Visualization was carried out using the dye Coomassie brilliant blue B) Two-dimensional gel electrophoresis of total cellular proteins from the K562 cell culture. PH gradient separation in the first dimension and SDS-PAGE direction are shown on the top and on the right side of the gel, respectively. Images of two-dimensional gels of proteins that were co-precipitated with PH domain containing histidine tag (C)). Two-dimensional gel electrophoresis of total cellular proteins containing His tag or with His tag alone (D). Silver staining (left side panel) and 35S-labeled proteins (right side panel)

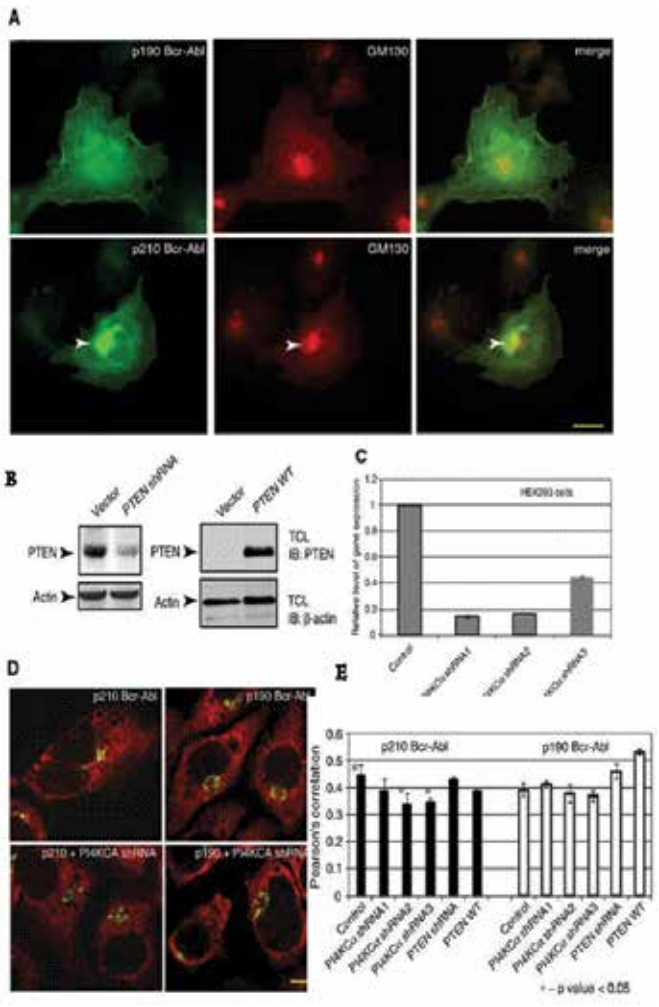


Fig 2. Interaction of p210 Bcr-Abl with the Golgi complex. (A) Cos-1 cells transfected with p190Bcr-Abl and p210Bcr-Abl. Immunofluorescent staining: Bcr-Abl-anti-Abl antibody AlexaFluor488-labeled secondary antibodies, Detection of Golgi apparatus was performed by using monoclonal antibodies against GM130, secondary antibodies – TRITC-conjugated murine antibodies. Dash – 20 mkm. The arrow shows the Golgi apparatus B) Assessment of inhibition of PTEN protein by specific sh RNA (specific anti-PTEN antibodies were used for the detection) C) Evaluating the effectiveness of inhibition of sh RNA specific to PI4K using real-time PCR. D) Effect of sh RNA specific to PI4K on localization of p210 Bcr-Abl and p190Bcr-Abl in HEK293 cells. D) Pearson correlation, overlapping p210 Bcr-Abl and p190Bcr-Abl with GM 130

National Grants

Projects of National Academy of Sciences of Ukraine:

- 2013 Innovative Project: "The development and introduction into medical practice of highly specific molecular genetic diagnostic markers for malignant tumors of the genitourinary system"
- 2012 Innovative Project: "The development and introduction into clinical practice the complex immunocytochemical and molecular genetic technologies for diagnosis of acute leukemia"
- 2010–2014 N 42/10 Project: "The study of molecular genetic changes in myeloproliferative diseases and their use in clinical diagnostics"

Projects of State Fund for Fundamental Researches:

- 2010–2014 N 5.17.2.35 Project: "Development of nanotechnology from silica and branched dextran-polyacrylamide polymers to deliver drugs into cells with phagocytic activity as a step towards targeted therapies of monocytic leukemias and histiocytic tumors"

Collaboration

with Ukrainian organizations:

- National Cancer Institute, Ministry of Health of Ukraine (Kyiv)
- Kyiv Regional Oncological Dispensary (Kyiv)
- Taras Shevchenko National University of Kyiv (Kyiv)
- O. O. Chuiko Institute of Surface Chemistry, NASU (Kyiv)
- R .E. Kavetsky Institute of Experimental Pathology, Oncology and Radiobiology, NASU (Kyiv)
- Kyiv Institute for Nuclear Research, NASU (Kyiv)

with foreign organizations:

- Institute of Biochemistry and Biophysics, PAS (Warsaw, Poland)
- OncoRay – National Center for Radiation Research in Oncology (Dresden, Germany)

Selected Publications

1. Cojoc M, Peitzsch C, Trautmann F, Polishchuk L, Telegeev GD, Dubrovska A. Emerging targets in cancer management: role of the CXCL12/CXCR4 axis. ***Onco Targets Ther.*** 2013; 6:1347–61.
2. Dubrovska A, Elliott J, Salamone RJ, Telegeev GD, et al. CXCR4 expression in prostate cancer progenitor cells. ***PLoS One.*** 2012;7(2):e31226.
3. Miroshnichenko D, Dubrovska A, Maliuta S, Telegeev G, Aspenstrom P. Novel role of pleckstrin homology domain of the BCR-ABL protein: Analysis of protein-protein and protein-lipid interactions. ***Exp Cell Res.*** 2010;316(4):530–42.
4. Telegeev GD, Dubrovska AN, Nadgorna VA, et al. Immunocytochemical study of Bcr and Bcr-Abl localization in K562 cells. ***Exp Oncol.*** 2010;32(2):81–3.
5. Polishchuk LA, Telegeeva PG, Stakhovsky AE, Telegeev GD, Stakhovsky EA. New specific molecular diagnostic markers for Uro-oncology. ***Laboratory Diagnostics.*** 2010;54(4):46–51.
6. Dybkov MV, Gartovska IR, Maliuta SS, Telegeev GD. Detection of V617F mutation of gene jak2 at patients with chronic myeloproliferative neoplasms. ***Biopolym. Cell.*** 2010; 26(3):14–7.
7. Shvachko LP. DNA hypomethylation as Achilles' heel of tumorigenesis: a working hypothesis. ***Cell Biol Int.*** 2009; 33(8):904–10.
8. Rachkov A, Holodova Yu, Ushenin Yu, Miroshnichenko D, Telegeev G, Soldatkin A. Development of bioselective element of Spr spectrometer for monitoring of oligonucleotide interactions and comparison with thermodynamic calculations. ***Sensor Letters.*** 2009;7(15):957–61.
9. Shvachko LP. Alterations of constitutive pericentromeric heterochromatin in lymphocytes of cancer patients and lymphocytes exposed to 5-azacytidine is associated with DNA-hypomethylation. ***Exp Oncol.*** 2008;30(3):230–4.
10. Telegeev GD, Dubrovska AN, Dybkov MV, Maliuta SS. Influence of BCR/ABL fusion proteins on the course of Ph leukemias. ***Acta Biochim Pol.*** 2004;51(3):845–9.

Department of Human Genetics

Head
Lyubov L. Lukash
Dr.Sci. (molecular genetics), Professor
Phone: +380 (44) 526-55-97
Fax: +380 (44) 526-07-59
E-mail: *lukash@imbg.org.ua*
www.lukash.org.ua

Education and Degrees

1967–1972	Graduate Student, Sumy State Pedagogical University named after A. S. Makarenko, Sumy, Ukraine, M.Sc. (biology and chemistry)
1972–1975	Ph.D. Student, Institute of Molecular Biology and Genetics (IMBG), NASU, Kyiv, Ukraine
1980	Ph.D. (genetics)
1990	Scientific degree of Senior Research Scientist (genetics)
1999	Dr.Sci. (molecular genetics)
2010	Professor (molecular genetics)

Professional Employment

1972	Laboratory Assistant, Department of Botany, Sumy State Pedagogical University named after A. S. Makarenko, Sumy, Ukraine
1976–1980	Engineer, IMBG NASU, Kyiv, Ukraine
1980	Leading Engineer, IMBG NASU, Kyiv, Ukraine
1980–1982	Junior Research Scientist, IMBG NASU, Kyiv, Ukraine
1982–1986	Senior Research Scientist, IMBG NASU, Kyiv, Ukraine
1986–1990	Leading Research Scientist, IMBG NASU, Kyiv, Ukraine
Since 1990	Head of the Department of Human Genetics, IMBG NASU, Kyiv, Ukraine

Honours, Prizes, Awards

1982	Medal “In memory of the 1500 anniversary of the city of Kyiv”
1998	Diploma of honour of Ministry of Education and Science of Ukraine
2003	Diploma of honour and valuable gift from mayor of Kyiv
2006	Gershenson Award of National Academy of Sciences of Ukraine
2010	Diploma of honour of Vavilov Society of geneticists and breeders of Ukraine
2010	Award of the National Academy of Sciences of Ukraine “For professional achievements”

Lukash L. L., Head of Department
Karpova I. S., Leading Research Scientist, Dr.Sci.
Lylo V. V., Senior Research Scientist, Ph.D.
Piven O. O., Senior Research Scientist, Ph.D.
Pidpala O. V., Senior Research Scientist, Ph.D.
Iatsyshyna A. P., Senior Research Scientist, Ph.D.
Ruban T. P., Research Scientist
Sukhorada O. M., Research Scientist
Kochubey T. O., Junior Research Scientist
Kotsarenko K. V., Junior Research Scientist
Macewicz L. L., Junior Research Scientist
Vavilina I. V., Leading Engineer
Kolomiets Y. M., Leading Engineer
Samoilenko I. A., Leading Engineer
Yurieva O. F., Technician
Seema L. V., Technician
Kuchma M. D., Ph.D. Student
Kushniruk V. O., Ph.D. Student
Nidoyeva Z. M., Ph.D. Student
Papuga S. I., Ph.D. Student
Shabliy V. A., Ph.D. Student
Palchevskaya O. L., Ph.D. Student

Research Area

- Research of the biological mutagenesis and role of reparative systems in the correction of genetical damages in cells of pro- and eukaryotic origin
- Development of biotechnologies using human stem cells

Current Research Activities and Recent Achievements

The influence of exogenous biological factors on mutation process

In was found that exogenous viruses, DNAs and some mitogenic proteins are able to influence on the spontaneous mutation process and mutagenesis induced by alkylating compounds in mammalian cells ***in vitro***. More detailed investigations were performed to study the possibility of mutation process regulation by impact on DNA repair some mitogen proteins and inhibitors. It was shown jointly with American scientists that a modified base O^6-benzylguanine significantly strengthened the mutagenic effect induced by nitrosoguanidine, by reducing enzymatic activity of O^6-methylguanine-DNA methyltransferase (MGMT) which plays one of the key roles in cancer cells resistance to alkylating chemotherapeutic drugs (Fig. 1). Currently, together with the Department of Biomedical Chemistry of IMBG NASU, a new generation of MGMT inhibitors are being developed.

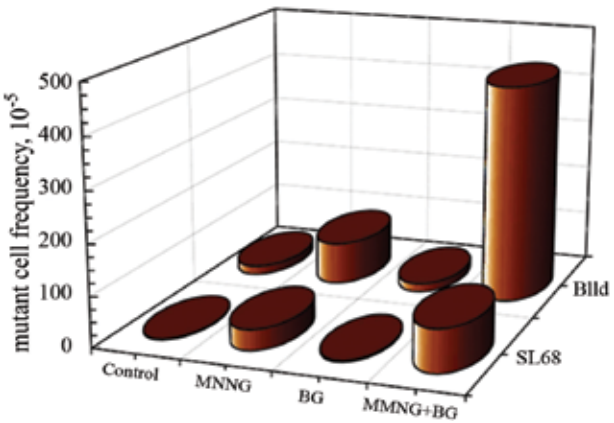


Fig. 1. Enhancing of MNNG mutagenic effect in the presence of O^6-benzylguanine in cells with different repair systems activity

The regulation of the expression of the gene for repair enzyme MGMT

We have shown that exogenous cytokines LIF, SCF, IL-3, EMAP II and IFN-a2b (a substrate of preparation "Laferobion") are able to influence on the ***MGMT*** gene expression at the protein level. EMAP-II showed an ability to modulate the level of ***MGMT*** gene expression in populations of human cells ***in vitro*** differently depending on the experimental conditions. Cytokines LIF, SCF, IL-3 and "Laferobion" usually were causing downregulation of ***MGMT*** gene expression in studied human cells. We detected unknown ~50kDa protein which is induced by stress factors as MGMT and recognized by monoclonal anti-MGMT antibodies (clone MT23.3, "Novus Biologicals", USA). A search for new regulatory elements within the promoter of the mouse and human ***MGMT*** gene was performed to learn the complex molecular mechanisms of regulation of this gene

expression at the transcriptional level, what perhaps will explain the variation in its expression. Among the detected regulatory promoter sites are those that potentially interact with inducible and tissue-specific transcription factors and alter the level of gene expression in response to various factors. Based on the obtained results we offered the hypothesis about the possiblility of the *MGMT* gene regulation by various biologically active agents, which are commonly used in supporting therapy of cancer (Fig. 2).

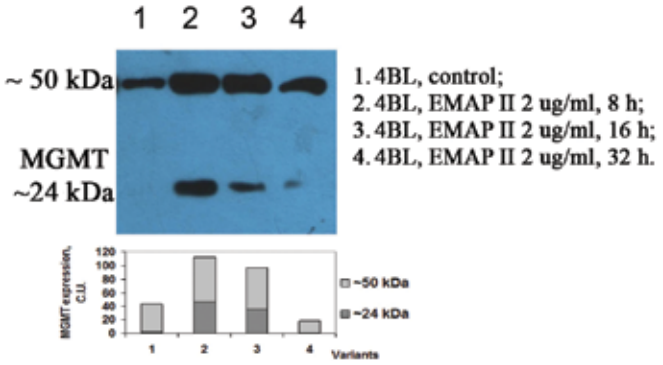


Fig. 2. Regulation of *MGMT* gene expression on protein level by biologically active compounds in human cells

Investigation of the disruptions of signaling and structural functions of adherent junctions proteins as potential mechanism for some heart pathologies development

With using conditional knock-out and transgenic animal models we have shown that the structural role of heart adherent junctions is crucial for early cardiogenesis of mammals: loss of N-cadherin in the embryonic heart leaded to the disruption of its development and to embryonic lethality. Cardiospecific deletion of one allele of *b-catenin* gene resulted in the delay of development of the adult heart, increased expression of the set of embryonic genes (ANP, BNP, b-MHC) and decreased activity of WNT-b-signaling pathway in mutant animals compared with control ones; at the same time morphological reconstructions of adult myocardium were not detected (Fig. 3).

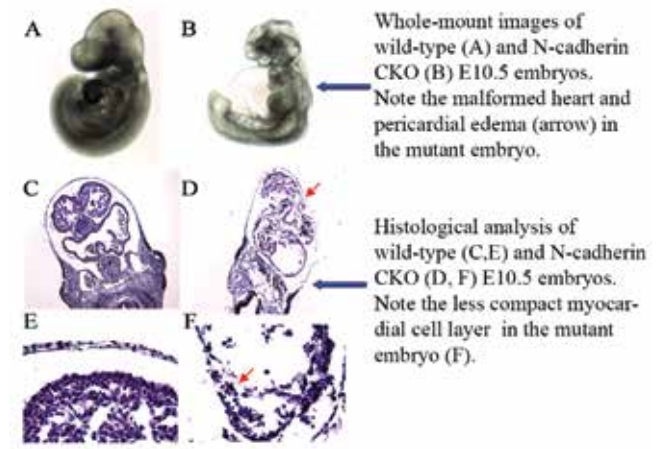


Fig. 3. Cardiac-specific deletion of N-cadherin gene leads to cardiomyocyte adhesion defect and embryonic lethality

The technologies of obtaining, cultivation and differentiation of human stem cells with the purposes of further application in cell therapy

We processed the approaches to obtaining lines of undifferentiated mammalian cells and directing them into differentiation by using the original method of medium conditioning and specific cytokines and growth factors. A several immortalized cell lines were obtained, which originated from human and mouse stem and progenitor cells: line 4BL derived from peripheral blood of adult donor, line SK1 – from skin of adult patient; lines G1, G4, G6 and G7 – from embryonic primordial mouse gonads. Cell line 4BL was used for creating skin equivalents, which were successfully tested in clinic on a limited cohort of patients with burn disease. Currently, together with the Institute of Cell Therapy we are developing the technologies of obtaining multipotent mesenchymal stromal cells (MMSK) and hematopoietic progenitor cells from native and cryopreserved human placenta (Fig. 4).

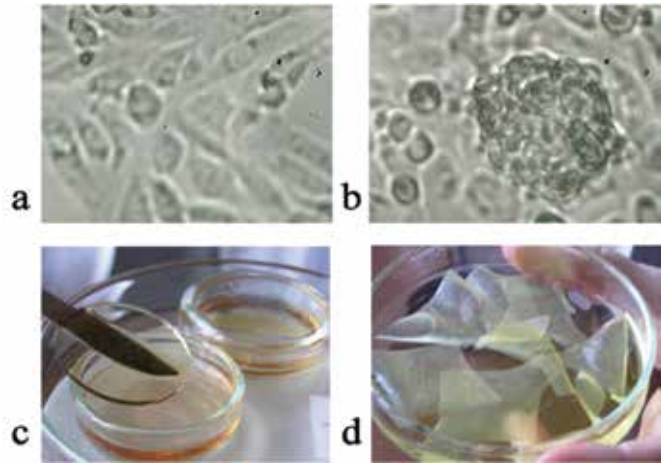


Fig. 4. 4BL cells growth features. Cells can growth as monolayer (a) and with forming of compact colonies (b). For production of dermal skin equivalents for thermal burns treatment cells were cultivated on synthetic (c) and natural (d) membranes

Approaches to improvement of biosystems stability to environmental factors and occupational hazards

We were the first to investigate the effects of some proteins of different origin especially lectins as factors modulating the mutation and repair processes with using pro- and eukaryotic systems. The influence of several lectins of plant and animal origin on the induction of primary DNA damage and gene mutations caused by mutagens with different mechanisms of action (salts of heavy metals and alkylating compounds) was revealed in cell populations and individual mammalian cells *in vitro*. Gene-protector properties of *Sambucus nigra* bark lectin and antimutagenic properties of the same lectin and lectin from perch roe were detected and characterized (Fig. 5).

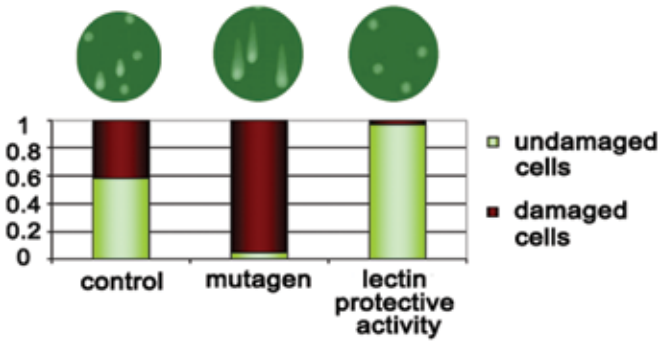


Fig. 5. Modulation of $NiCl_2$-induced DNA damage by black elderberry bark lectin. The comet assay was used

Creation of a model of mutation process and prototype of software for working with databases

The analysis of experimental data of mutation process manifestation in cell populations treated by different biological factors was performed. The dependence of a mutation process on heterogeneity of populations, energy ensuring, reparative capabilities was shown. In collaboration with the Institute of Cybernetics of V. M. Glushkov NAS of Ukraine the computational modeling of mutagenesis dynamics was carried out, based on obtained facts and hypothesis. As a result, the possibility to predict the effects of mutagenesis in time have occurred, based on empirically derived characteristics of populations; as well as to establish the data bank, reducing time and financial costs on conducting investigations. The software for the calculation of experimental data was also developed. (Fig. 6).

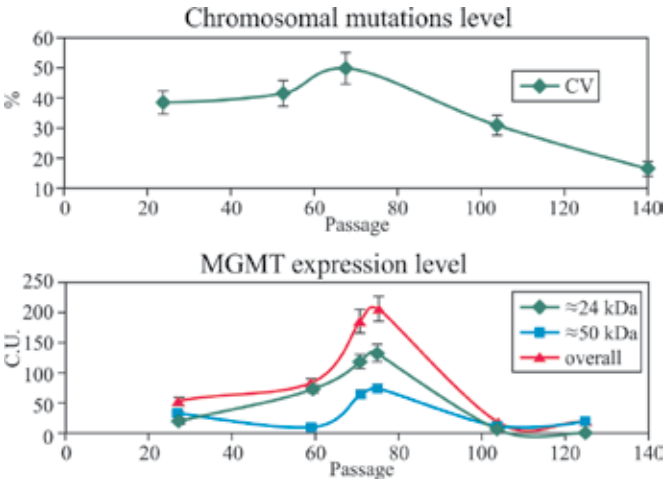


Fig. 6. Co-modeling of mutagenesis processes and repair enzyme expression at consecutive stages of G1 murine cell line *in vitro* formation. CV – coefficient of variation for chromosome number distribution, index of chromosomal instability level

National Grants

Projects of National Academy of Sciences of Ukraine:

- 2012–2016 N 2.2.4.21 Project: "Relation of genotype-phenotype in malignant tumors. Modeling of optimal schemes of supporting therapy during the treatment of cancer with alkylating agents" (scientific supervisor – Lukash L. L.)
- 2010–2014 N 40/2011 Project: "Development of fundamental basis of stem cell therapy of heart pathologies" (scientific supervisor – Lukash L. L.)

International Grants

- 2011–2014 7th Framework Programme (FP7) FP7-INCO-2011-6, ERA-WIDE Project: "Strengthening cooperation in Molecular Biomedicine between EU and UKRAINE", COMBIOM (scientific supervisor – Prof. A. Elskaya; supervisor of a subsection of the project – Lukash L. L.)
- 2008–2012 RECOOP HST (Regional Cooperation for Health, Science and Technology) Consortium. Lukash L. L. was permanent representative of IMBG NASU in RECOOP HST Consortium.

Collaboration

with Ukrainian organizations:

- P. L. Shupyk Natinal Medical Academy of Postgraduate Education (Kyiv)
- Institute of Cell Therapy (Kyiv)
- M. M. Amosov National Institute of Cardiovascular Surgery, NAMSU (Kyiv)
- State Institution "Institute of Neurosurgery named after A. P. Romodanov of NAMS of Ukraine" (Kyiv)
- National Technical University of Ukraine "Kyiv Polytechnic Institute" (Kyiv)
- Bogomoletz Institute of Physiology, NASU (Kyiv)
- Zabolotny Insititue of Microbiology and Virology, NASU (Kyiv)

with foreign organizations:

- International Institute of Molecular and Cell Biology (Warsaw, Poland)
- Michigan State University (East Lansing, USA)
- Pennsylvania State University (University Park, USA)
- Institute of Toxicology, University Medical Center (Mainz, Germany)
- Max Planck Institute for Heart and Lung Research (Bad Noyhem, Germany)

Selected Publications

1. Lukash LL. Regulation of mutagenesis by exogenous biological factors in the eukaryotic cell systems. ***Biopolym. Cell.*** 2013; 29(4):283–94.
2. Kotsarenko KV, Lylo VV, Macewicz LL, Babenko LA, Kornelyuk AI, Ruban TA, Lukash LL. Change of the *MGMT* gene expression under influence of exogenous cytokines in human cells *in vitro*. ***Cytol. Genet.*** 2013;47(4):9–15.
3. Iatsyshyna AP. Current approaches to improve the anticancer chemotherapy with alkylating agents: state of the problem in world and Ukraine. ***Biopolym. Cell.*** 2012;28(2):83–92.
4. Shabliy VA, Kuchma MD, Kirik VM, Onishchenko AN, Lukash LL, Lobyntseva GS. Cryopreservation of human placental tissue as a source of hematopoietic progenitor cells and multipotent mesenchymal stromal cells. ***Cell transplantation and tissue engineering.*** 2012;7(1):54–62.
5. Piven OO, Kostetskii IE, Macewicz LL, Kolomiets YM, Radice GL, Lukash LL. Requirement for N-cadherin-catenin complex in heart development. ***Exp Biol Med (Maywood).*** 2011;236(7):816–22.
6. Lukash LL. Cell therapy of heart pathologies. ***Biotechnology.*** 2008;1(1):40–45.
7. Pidpala OV, Iatsyshyna AP, Lukash LL. Mobile genetical elements of human genome: distribution and functional role. ***Cytol. Genet.*** 2008;42(6):69–81.
8. Karpova IS, Korets'ka NV, Pal'chykovs'ka LH, Nehruts'ka VV. Lectins from *Sambucus nigra* L inflorescences: isolation and investigation of biological activity using procaryotic test-systems. ***Ukr Biokhim Zh.*** 2007;79(5):145–52.
9. Macewicz LL, Suchorada OM, Lukash LL. Influence of *Sambucus nigra* bark lectin on cell DNA under different *in vitro* conditions. ***Cell Biol Int.*** 2005;29(1):29–32.
10. Lukash LL, Boldt J, Pegg AE, Dolan ME, Maher VM, McCormick JJ. Effect of O^6-alkylguanine-DNA alkyltransferase on the frequency and spectrum of mutations induced by N-methyl-N'-nitro-N-nitrosoguanidine in the *HPRT* gene of diploid human fibroblasts. ***Mutat Res.*** 1991;250(1-2):397–409.

Department of Molecular Oncogenetics

Head
Volodymyr I. Kashuba
Dr.Sci. (molecular biology),
Senior Research Scientist
Phone: +380 (44) 526-07-09
Fax: +380 (44) 526-07-59
E-mail: *v.i.kashuba@imbg.org.ua*

Education and Degrees

1977–1983	Graduate Student, Faculty of Chemistry, Taras Shevchenko National University of Kyiv, Kyiv, Ukraine, M.Sc. (biochemistry)
1991	Ph.D. (molecular biology)
2009	Dr.Sci. (molecular biology)

Professional Employment

1983–1989	Engineer, Department of Biosynthesis of Nucleic Acids, Institute of Molecular Biology and Genetics (IMBG), NASU, Kyiv, Ukraine
1989–1991	Junior Research Scientist, IMBG NASU, Kyiv, Ukraine
1991–2009	Research Scientist, IMBG NASU, Kyiv, Ukraine
2009–2011	Senior Research Scientist, IMBG NASU, Kyiv, Ukraine
Since 2011	Head of the Department of Molecular Oncogenetics, IMBG NASU, Kyiv, Ukraine

Membership

Since 1995	Member of European Association for Cancer Research (EACR)
Since 2010	Member of Ukrainian Society of Geneticists and Breeders

Kashuba V. I., Head of Department
Strokovskaya L. I., Chief Research Scientist, Dr.Sci.
Zinchenko V. A., Research Scientist, Dr.Sci.
Vagyn Yu. V., Senior Research Scientist, Dr.Sci.
Gordiyuk V. V., Senior Research Scientist, Ph.D.
Kikhno I. M., Senior Research Scientist, Ph.D.
Chaschin M. O., Senior Research Scientist, Ph.D.
Gerashchenko A. V., Senior Research Scientist, Ph.D.
Vagina I. M., Senior Research Scientist, Ph.D.
Zayets V. M., Senior Research Scientist, Ph.D.
Anopriyenko O. V., Research Scientist, Ph.D.
Maksymchuk O. V., Research Scientist, Ph.D.
Morozova L. M., Research Scientist, Ph.D.
Bobrovska M. T., Research Scientist, Ph.D.
Chaschina L. I., Junior Research Scientist
Kondratov A. G., Junior Research Scientist
Shyrina T. V., Junior Research Scientist
Panasenko G. V., Junior Research Scientist.
Rudenko Y. Y., Junior Research Scientist
Zacharuk O. A., Junior Research Scientist.
Rudenko A. V., Leading Engineer
Kitam V. O., Leading Engineer
Goncharova L. O., Leading Engineer
Rushchak V. V., Leading Engineer
Rosokhatska I. V., Engineer
Glagka I. Y., Engineer
Gajdayenko T. M., Technician
Khrebtiyevska L. D., Technician
Grechana L. O., Technician
Bortnichuk G. V., Technician

The Department was established on the basis of the Department of Biochemical Genetics (Prof. A. P. Solomko)

Research Area

Identification of genetic and epigenetic changes in malignant epithelial tumors

Current Research Activities and Recent Achievements

Identification of molecular-genetic markers for early detection and prognosis of epithelial tumors

We analyze different types of epithelial tumors (breast, kidney, cervical, colon, ovarian and lung) with Not-I microarray technology. We have found loci/genes with changes in high percents of samples. Further cluster analysis permits to select genes candidates for discrimination different cancer stages. Not-I microarray technology allows the development of marker panels for the detection of differences between types of cancer and discrimination of stages, for early detection, presence or absence of metastases and the tumor aggressiveness.

On the basis of the case study the panel of 19 markers was created for detection of lung carcinoma, differentiation between adenocarcinoma and squamous lung carcinoma with or without methastases. For ovary carcinoma the panels of 11 markers were created for early detection, discrimination of benign tumors and cancer, and discrimination of I + II stages and III + IV stages. We considered a new approach to search for epithelial cancer epigenetic markers. The results are perspective for use in practical medicine.

The baculovirus expression system for obtaining recombinant proteins

We investigate the potential of the baculovirus Autographa californica multiple nucleopolyhedrovirus (AcMNPV) as a safe

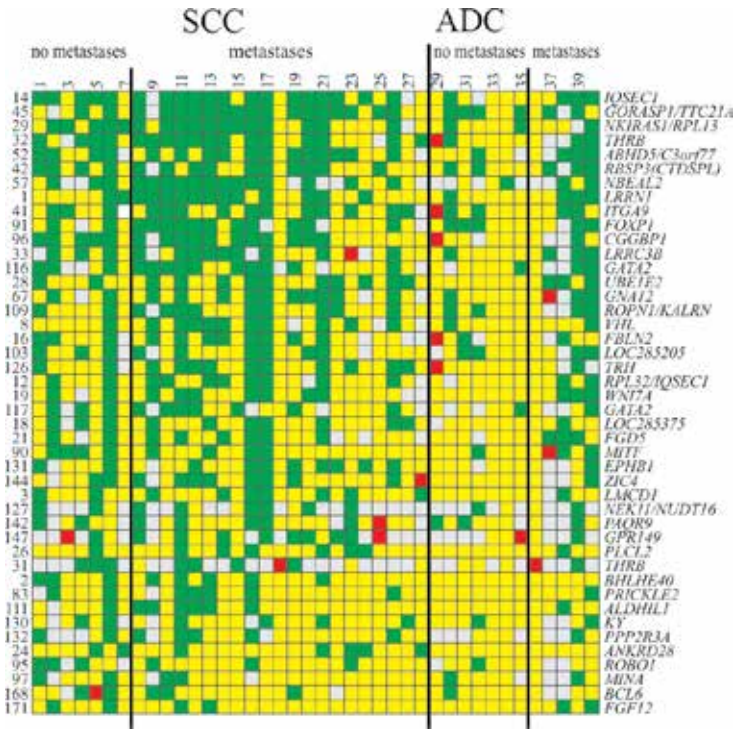


Fig. 1. Hybridization pattern of DNA from NSCLC samples (SCC and ADC) on NotI-microarrays. Horizontally – 40 NSCLC samples. Vertically – 44 NotI sites arranged by methylation/deletion frequency (from 58 % to 15 %)

alternative vehicle in different strategies of cancer therapy. On mouse models we examine baculoviruses ability for targeting cancer cells or transducing hypothetical "vector cells" that in turn target tumors. For this we assessed the efficiency of different constructed recombinant baculovirus vectors (with the GFP reporter gene and a number of therapeutic cytokine genes under the control of strong mammalian promoters) in transduction of different mouse normal and tumor cell lines. It was shown that coculture of melanoma cells with fetal fibroblasts, transduced with the recombinant baculovirus vector expressing mouse therapeutic β-interferon, leads to inhibition of malignant cell growth (Fig.2) and coinjection of melanoma cells and transduced fibroblasts causes tumor growth inhibition and increase in life-span of experimental animal.

We also use baculovirus expression system for production and study of a number of protein tumor-suppressors.

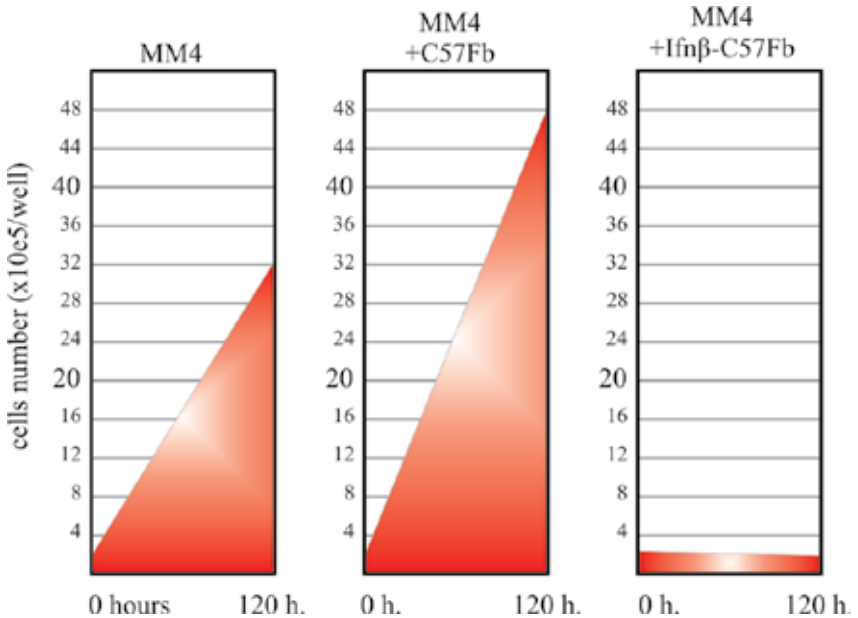


Fig. 2. The growth inhibition of tumor mouse melanoma cells (MM4) during coinjection with murine fetal fibroblasts (C57Fb), transduced with the recombinant baculovirus vector expressing mouse β-interferon (Ifnβ).

National Grants

Projects of National Academy of Sciences of Ukraine:

- 2010–2014 N 22/12 Project: "Functional bionanomaterials for medical diagnostics of oncological diseases" (scientific supervisor – Kashuba V. I.)
- 2010–2014 N 41/12 Project: "Identification of molecular-genetic markers for diagnostics of the epithelial malignant tumors" (scientific supervisor – KashubaV. I.)
- 2010–2014 N 33/12 Project: "Recombinant baculovirus vectors efficacy research and construction for gene and vaccine therapy" (scientific supervisor – Strokovskaya L. I.)

Projects of State Fund for Fundamental Researches:

- 2011–2012 N F/40 Project: "Molecular mechanisms of D-glucorunil C5-epimerase inactivation in cancerogenesis" (scientific supervisor – Kashuba V. I.)
- 2006 N 18/012 Project: "Identification and characterization of genes, which are specific for renal and ovarian cancer" (scientific supervisor – Kashuba V. I.)

Projects of State Agency on Science, Innovations and Informatization of Ukraine:

- 2012 N SP/487 Project: "Creation and introduction to exploitation of the laboratory module for a micro-arrays design and application" (scientific supervisor – Kashuba V. I.)

International Grants

- 2004–2006 INTAS (The International Association for the Promotion of Co-operation with Scientists from the New Independent States of the Former Soviet Union) N 03-51-4983 Project: "Not I microarrays for identification of new cancer-causing genes"

Collaboration

with Ukrainian organizations:

- R. E. Kavetsky Institute of Experimental Pathology, Oncology and Radiobiology, NASU (Kyiv)
- V. E. Lashkaryov Institute of Semiconductor Physics, NASU (Kyiv)

Selected Publications

1. Rudenko EE, Gerashchenko GV, Lapska YY, et al. Genetic and epigenetic changes of GPX1and GPX3 in human clear- cell renal carcinoma. ***Biopolym. Cell.*** 2013; 29(5):395–401.
2. Law EW, Cheung AK, Kashuba VI, et al. Anti-angiogenic and tumor-suppressive roles of candidate tumor-suppressor gene, Fibulin-2, in nasopharyngeal carcinoma. ***Oncogene.*** 2012; 31(6): 728–38.
3. Kashuba V, Dmitriev AA, Krasnov GS, et al. NotI Microarrays: Novel Epigenetic Markers for Early Detection and Prognosis of High Grade Serous Ovarian Cancer. ***Int J Mol Sci.*** 2012; 13(10): 13352–77.
4. Kondratov AG, Kvasha SM, Stoliar LA, et al. Alterations of the WNT7A gene in clear cell renal cell carcinomas. ***PLoS One.*** 2012; 7(10):e47012.
5. Kondratov AG, Stoliar LA, Kvasha SM, et al. Methylation pattern of the putative tumor-suppressor gene LRRC3B promoter in clear cell renal cell carcinomas. ***Mol Med Report.*** 2012;5(2):509–12.
6. Haraldson K, Kashuba VI, Dmitriev AA, et al. LRRC3B gene is frequently epigenetically inactivated in several epithelial malignancies and inhibits cell growth and replication. ***Biochimie.*** 2012; 94(5):1151–7.
7. Prudnikova TY, Mostovich LA, Kashuba VI, Ernberg I, Zabarovsky ER, Grigorieva EV. miRNA-218 contributes to the regulation of D-glucuronyl C5-epimerase expression in normal and tumor breast tissues. ***Epigenetics.*** 2012; 7(10):1109–14.
8. Dmitriev AA, Kashuba VI, Haraldson K, et al. Genetic and epigenetic analysis of non-small cell lung cancer with NotI-microarrays. ***Epigenetics.*** 2012; 7(5):502–13.
9. Solomko AP, Zaharuk OA, Chaschina LI, Strokovskaya LI. Baculovirus vectors in experimental gene- and vaccine therapy. ***Biopolym. Cell.*** 2011; 27(3):167–80.
10. Kashuba VI, Li J, Wang F, Senchenko VN, et al. RBSP3 (HYA22) is a tumor suppressor gene implicated in major epithelial malignancies. ***Proc Natl Acad Sci USA.*** 2004; 101(14):4906–11.

Department of Biosynthesis of Nucleic Acids

Head
Vadym M. Kavsan
Dr.Sci. (molecular biology), Professor,
Corresponding Member of National Academy of Sciences of Ukraine
Phone: +380 (44) 526-34-98
Fax: +380 (44) 526-07-59
E-mail: *kavsan@imbg.org.ua*

Education and Degrees

1960–1964	Graduate Student, Bogomolets National Medical University, Kyiv, Ukraine, M.D.
1965–1969	Postgraduate Student, D. K. Zabolotny Institute of Microbiology and Virology (IMV), NASU, Kyiv, Ukraine
1969	Ph.D. (biochemistry)
1985	Dr.Sci. (molecular biology)
1991	Professor (molecular biology)
1995	Corresponding Member of NASU

Professional Employment

1969–1981	Junior Research Scientist, IMV NASU, Kyiv, Ukraine
1981–1983	Head of the Laboratory of Biosynthesis of Nucleic Acids, Institute of Molecular Biology and Genetics (IMBG), NASU, Kyiv, Ukraine
Since 1983	Head of the Department of Biosynthesis of Nucleic Acids, IMBG NASU, Kyiv, Ukraine

Membership

American Association for the Advancement of Science (AAAS)
European Association for Cancer Research (EACR)
European Association of Neurooncology (EANO)
Human Genome Organization (HUGO)
International Brain Research Organization (IBRO)
Promotions Committee, University of Canterbury, Christchurch, New Zealand
Editorial Board of the Journal “Biopolymers and Cell” (Ukraine)
Editorial Board of the Journal “Cytology and Genetics” (Ukraine)

Honours, Prizes, Awards

1979	State Prize of Ukraine in Science and Technology
1994	Award of the Union Internationale Contre le Cancer (UICC)
1998	Rank of G. Soros Professor and Personal Grant from International Soros Science Education Program (ISSEP)

Kavsan V. M., Head of Department
Dmitrenko V. V., Leading Research Scientist, Dr.Sci.
Skripkina I.Ya., Senior Research Scientist, Ph.D.
Balynska O. V., Junior Research Scientist, Ph.D.
Avdieiev S. S., Junior Research Scientist
Areshkov P. O., Junior Research Scientist
Boyko O. I., Junior Research Scientist
Bukreieva T. V., Junior Research Scientist
Iershov A. V., Junior Research Scientist
Stepanenko O. A., Ph.D. Student
Chausovskiy T. I., Leading Engineer
Dudar V. I., Technician
Beltyukova L. V., Technician
Nizyuk Z. I., Technician

Research Area

- Investigation of the mechanisms of malignant tumors initiation and progression in order to create the general therapeutic approaches to cancer treatment
- Clarification of the role of potential oncoproteins interactions and tumor suppressor proteins in RAS/MAPK and PI3K/AKT signaling cascades, involvement of these interactions in the malignant transformation of brain cells, proliferative and invasive properties by tumor cells and search for specific inhibitors of these signaling pathways

Current Research Activities and Recent Achievements

Hundreds of genes expression changes have been revealed in tumors of glial and meningial origin by modern methods of expression genetics. Opposite changes of several genes expression suppose different mechanisms of these tumors development and can be used as molecular biomarkers. 129 genes with 5-fold changed expression were found in glioblastoma, the most aggressive human brain tumor. 44 of them were overexpressed genes, which participate in angiogenesis, immunity, ECM, cell signaling pathways, and related to the IGF-system. IGF1 is a key peptide in many tumors but its gene was not found as overexpressed in glioblastoma. It was shown that ***CHI3L1*** gene with considerably increased expression could participate instead of ***IGF1*** in the development of glial tumors.

The new human cell line stably producing CHI3L1 was constructed and found that these cells had an accelerated growth rate and could undergo anchorage-independent growth in soft agar that is one of the most consistent indicators of oncogenic transformation (Fig. 1). ***293_CHI3L1*** cells had activated PI3K and MAPK pathways; phosphorylated AKT was localized in cytoplasm, while ERK1/2 were localized in both cytoplasm and nuclei where they could activate different transcription factors with certain biological outcome. The formation of tumors in rats by 293 cells expressing ***CHI3L1***, evidenced that ***CHI3L1*** is an oncogene which is involved in tumorigenesis. It was the first animal model of human brain tumor which could be used for studying of various biological properties of brain tumors in the immunocompetent animals (Fig. 2).

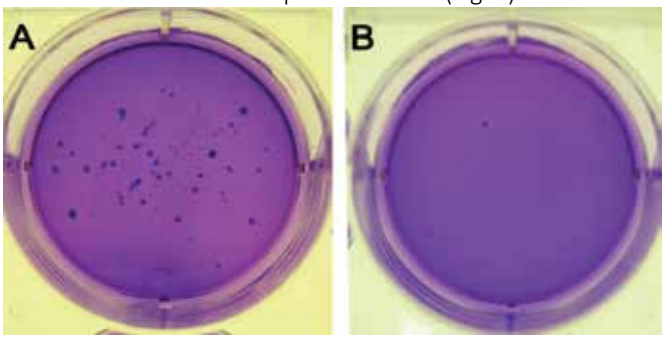


Fig. 1. Cells with overexpressed ***CHI3L1*** oncogene formed significantly more colonies in soft agar which is a sign of malignant transformation. A – 293 cells stable transfected by a pcDNA3.1_***CHI3L1*** plasmid which expresses ***CHI3L1*** gene. B – 293 cells stable transfected by "empty" pcDNA3.1 plasmid vector.

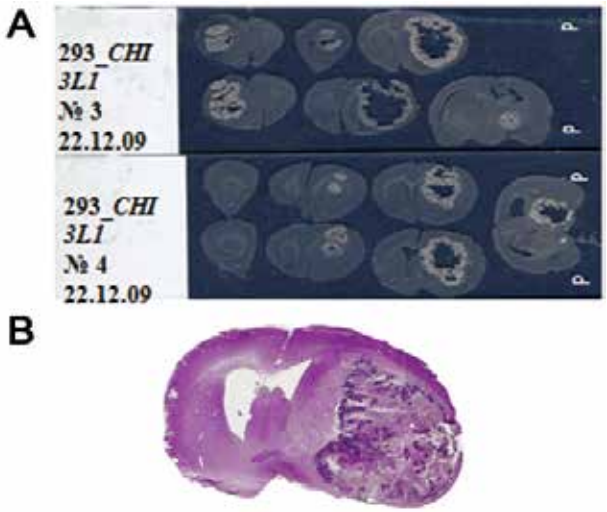


Fig. 2. Malignant tumors in the rat brain after stereotactic intracerebral implantation of ***293_CHI3L1*** transformed cells. A – ***293_CHI3L1*** cells were implanted under ketamine anesthesia in kaudoptamen using Narishige stereotactic device, according to the coordinates of Swanson's Brain Atlas. B – General view of tumor paraffin section, initiated by ***293_CHI3L1*** cells. Hematoxylin-eosin staining

It was found that ***CHI3L1*** gene promotes chromosomal instability. Constitutive expression of ***CHI3L1*** leads to qualitative and quantitative chromosomal abnormalities, contributes to the malignant phenotype by accelerating cell proliferation, and also increasing the genetic heterogeneity of cell populations (Fig. 3).

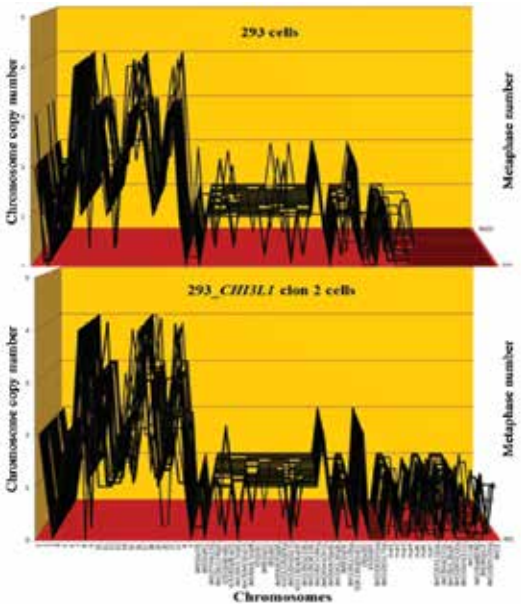


Fig. 3. Constitutive expression of the oncogene ***CHI3L1*** promotes chromosomal instability in cells. Karyographs of the cell lines 293 and ***293_CHI3L1 clone*** 2. X axis designates the chromosomes, axis Y – chromosomes copy number, axis Z – quantity of karyotyped cells (20 cells). Karyographs demonstrate variability and clonality of chromosomal changes within cell lines

CHI3L1 gene knockdown by ***CHI3L1*** siRNA transfection gave noticeable CHI3L1 protein blockade (80-90 %) with significantly reduced. pERK1/2 and the colony-forming ability of ***293_CHI3L1*** cells in soft agar (Fig. 4). The obtained results demonstrate that activity of ***CHI3L1*** mediated by pathways involved ERK1/2 and AKT has a growth-promoting role during tumorigenesis and indicate that efforts to inhibit its activity should be considered during cancer therapy.

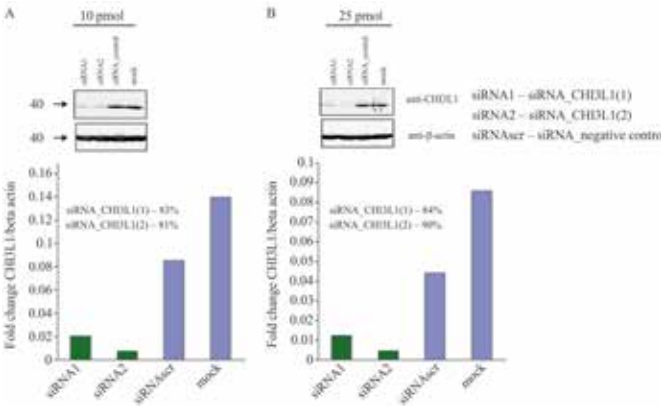


Fig.4. Western blot analysis displayed ***CHI3L1*** gene knockdown in ***293_CHI3L1*** cells

Along with superexpressed genes, it was found 85 genes relating to the potential tumor suppressor genes. The results show that ***CHI3L2*** is an antagonist to ***CHI3L1*** and if ***CHI3L1*** is a real oncogene that may play an important role in tumorigenesis, ***CHI3L2*** is anti-oncogene. A spatial model of CHI3L2 protein was constructed and it was revealed the main structural features that distinguish it from the homologous one but functionally opposite CHI3L1 protein (Fig. 5). Heparin-binding site of CHI3L1 has been identified using site-directed mutagenesis and it has been shown that it might be responsible for the oncogenic properties of ***CHI3L1***.

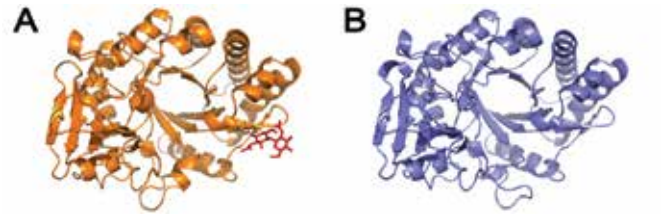


Fig. 5. Three-dimensional structure of CHI3L2 protein obtained by a modeling on the base of homology with CHI3L1 protein. A – CHI3L1 protein. B – CHI3L2 protein.

The antiproliferative properties of two distinct classes of molecules, namely bradykinin (BK) antagonists and azolidinones, were shown in three different ***in vitro*** models of malignant transformation: 293 cells, stably transfected by ***CHI3L1*** oncogene (***293_CHI3L1***), human glioblastoma cells U373 and mantle cell lymphoma (MCL) cells Granta, JeKo, Mino, and UPN1 (Fig. 6). For drugs delivery into the brain tumors are used the nanocojugates of Polycefin on the basis of polymaleic acid which can penetrate across the blood-brain barrier.

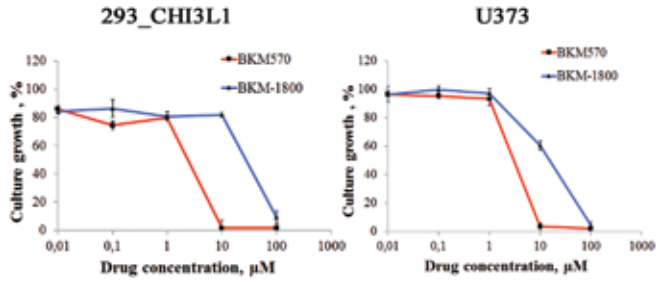


Fig. 6. Inhibition of ***293_CHI3L1*** and U373 cells growth by bradykinin antagonists

Artificial intellect approach was used for diagnostics of glial brain tumors by self-organized Kohonen's map (SOM). Obtained data clearly show the clusterization of glioblastoma and normal brain samples (Fig. 7).

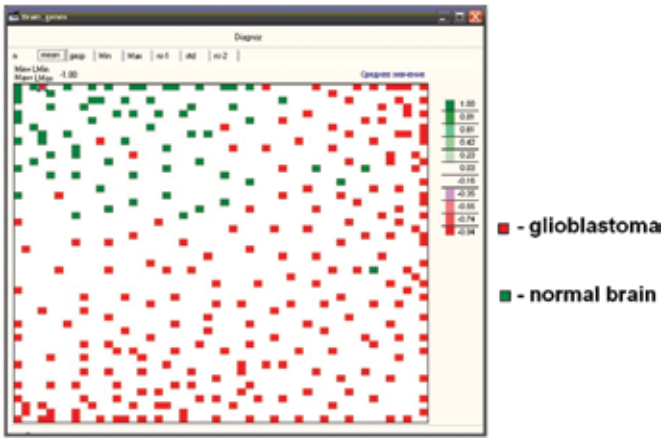


Fig. 7. Classification of brain tumors using artificial neural network. Distribution of glioblastoma and normal brain samples using Kohonen map

International Grants

- 2011–2014 FP7-INCO-2011-6, ERA-WIDE Project "Strengthening cooperation in Molecular Biomedicine between EU and UKRAINE", COMBIOM (scientific supervisor – Kavsan V. M.)
- 2011–2013 STCU Project, 5446 "Nanoconjugates of natural biopolymers with antisense oligonucleotides and antibody for inhibition of glial tumors" (scientific supervisor – Kavsan V. M.)

National Grants

Projects of National Academy of Sciences of Ukraine:

- 2013–2017 Project "From Molecular to Cellular Events in Human Pathologies" (scientific co-supervisor – Kavsan V. M.)
- 2012–2013 Project "Identification of transcriptome changes and the search of genes for intellectual classification of human brain tumors" (scientific supervisor – Dmitrenko V. V.)
- 2010–2014 Project "New molecular genetic markers for gene expression signatures of brain tumors and their interaction with signaling pathways" (scientific supervisor – Kavsan V. M.)
- 2010–2014 Project "Creation of system for brain tumors growth inhibition based on nanoconjugates of antysense oligonucleotides and antibodies against to oncoproteins, with natural biopolymers" (scientific supervisor – Kavsan V. M.)

Grants of State Fund for Fundamental Researches

- 2013–2014 Project "Characterization of new biomarkers of human glial tumors" (scientific supervisor – Kavsan V. M.)
- 2013–2014 Project "Identification of perspective molecular markers for monitoring of human neurodegenerative and oncological diseases" (scientific co-supervisor – Kavsan V. M.)
- 2011–2014 Project "Molecular mechanisms of cell signaling in normal and pathological conditions: the focus on ion channels" (SKL Molecular and Cell Biology, scientific co-supervisor – Kavsan V. M.)

Grant of State Committee of Ukraine for Science, Innovation and Information:

- 2014–2015 Project "Identification and characterization of new biomarkers of human glial tumors" (scientific supervisor – Kavsan V. M.)

Collaboration

with Ukrainian organizations:

- State Institution "Institute of Neurosurgery named after A. P. Romodanov of NAMS of Ukraine" (Kyiv)
- R. E. Kavetsky Institute of Experimental Pathology, Oncology and Radiobiology, NASU (Kyiv)
- Danylo Halytsky Lviv National Medical University (Lviv)

with foreign organizations:

- Belarusian State University (Minsk, Belarus)
- Serbsky State Scientific Center for Social and Forensic Psychiatry (Moscow, Russia)
- Institute of Chemical Biology and Fundamental Medicine, SB RAS (Novosibirsk, Russia)
- University of Colorado Denver (Denver, USA)
- Cedars-Sinai Medical Center (Los Angeles, USA)
- Institute Gustave-Roussy (Paris, France)
- Service de Neurologie Mazarin, INSERM U 711 (Paris, France)

Selected Publications

1. Stepanenko AA, Vassetzky YS, Kavsan VM. Antagonistic functional duality of cancer genes. ***Gene***. 2013; 529: 199-207.
2. Stepanenko AA, Kavsan VM. Cancer genes and chromosome instability. Oncogene and Cancer – ***From Bench to Clinic, InTech Publisher***, 2013; 151-182.
3. Stepanenko AA, Kavsan VM. Evolutionary karyotypic theory of cancer versus conventional cancer gene mutation theory. ***Biopolym. Cell.*** 2012; 28(4): 267–280.
4. Baklaushev VP, Kavsan VM, Balynska OV, Yusubalieva GM, Abakumov VA, Chekhonin VP. New experimental model of brain tumors in brains of adult immunocompetent rats. ***Brit. J. Med. & Med. Res.*** 2012; 2 (2): 206-215.
5. Areshkov PO, Avdieiev SS, Balynska OV, LeRoith D, Kavsan VM. Two closely related human members of chitinase-like family, CHI3L1 and CHI3L2, activate ERK1/2 in 293 and U372 cells but have the different influence on cell proliferation. ***Int. J. Biol. Sci.*** 2012 ; 8: 39-48.
6. Kavsan VM, Baklaushev VP, Balynska OV, et al. Gene encoding chitinase 3-like 1 protein (CHI3L1) is a putative oncogene. ***Int. J. Biomed. Sci.*** 2011; 7: 230-237.
7. Kavsan VM, Iershov AV, Balynska OV. Immortalized cells and one oncogene in malignant transformation: old insights on new explanation. ***BMC Cell Biol.*** 2011; 12:23.
8. Iershov A, Odynets K, Kornelyuk A, Kavsan V. Homology modeling of 3D structure of human chitinase-like CHI3L2 protein. ***Central Eur. J. Biol.*** 2010; 5(4): 407-420.
9. Moureau C, Moynier M, Kavsan VM, Montagnier L, Bahraoui E. Specificity of anti-Nef antibodies produced in mice immunized with DNA encoding the HIV-1 ***nef*** gene product. ***Vaccine.*** 2000; 18: 333-341.
10. Palamarchuk AY, Kavsan VM, Sussenbach JS, Holthuizen PE. The chum salmon IGF-II gene promoter is activated by hepatocyte nuclear factor 3ß. ***FEBS Lett.*** 1999; 446: 251-255.

Department of Cell Population Genetics

Head
Viktor A. Kunakh
Dr.Sci. (genetics), Professor,
Corresponding Member of National Academy of Sciences of Ukraine
Phone: +380 (44) 526-07-98
Fax: +380 (44) 526-07-59
E-mail: *kunakh@imbg.org.ua*

Education and Degrees

1969	Graduated with honors, Faculty of Biology, Taras Shevchenko National University of Kyiv, Kyiv, Ukraine, M.Sc. (genetics)
1975	Ph.D. (genetics)
1989	Dr.Sci. (genetics)
1993	Professor (genetics)
1997	Corresponding Member of NASU

Professional Employment

1966–1969	Senior Laboratory Assistant, M. G. Kholodny Institute of Botany, NASU, Kyiv, Ukraine
1971–1978	Junior Research Scientist, Department of Cytogenetics and Polyploidy, Institute of Molecular Biology and Genetics (IMBG), NASU, Kyiv, Ukraine
1978–1983	Senior Research Scientist, IMBG NASU, Kyiv, Ukraine
1983–1989	Head of the Laboratory of Cell Population Genetics, IMBG NASU, Kyiv, Ukraine
Since 1989	Head of the Department of Cell Population Genetics, IMBG NASU, Kyiv, Ukraine

Membership

Since 2003	Editor-in-Chief of Academic and Applied Research Journal “The Bulletin of Vavylov Society of Geneticists and Breeders of Ukraine”
Since 2007	President of Vavylov Society of Geneticists and Breeders of Ukraine and Editorial Board member of Journal “Cytology and Genetics” (Ukraine)

Honours, Prizes, Awards

2003	Yuriev Award of National Academy of Sciences of Ukraine
2005	Ukrainian State Award in the Field of Science and Technologies
2007	Kholodnyi Award of National Academy of Sciences of Ukraine

Kunakh V. A., Head of Department
Andreev I. O., Senior Research Scientist, Ph.D.
Miriuta N. Yu., Senior Research Scientist, Ph.D.
Pererva T. P., Senior Research Scientist, Ph.D.
Spiridonova K. V., Senior Research Scientist, Ph.D.
Melnyk V. M., Senior Research Scientist, Ph.D.
Poronnik O. O., Senior Research Scientist, Ph.D.
Bublyk O. M., Research Scientist, Ph.D.
Parnikoza I. Yu., Research Scientist, Ph.D.
Twardovska M. O., Research Scientist, Ph.D.
Konvaliuk I. I., Junior Research Scientist, Ph.D.
Mozhylevska L. P., Research Scientist
Adonin V. I., Junior Research Scientist
Myriuta G. Yu., Junior Research Scientist

Research Area

Studies on plant genome variability in nature and in cell populations ***in vitro*** as a basis for adaptation to changing growth conditions

Current Research Activities and Recent Achievements

Studies on the causes and mechanisms of structural and functional genome variability in cell populations *in vitro* and in nature, as well as search for ways of this variability regulation aimed to develop molecular genetic, physiological, and biochemical principles of plant biotechnology

It has been theoretically and experimentally proved that cultured ***in vitro*** plant cells populations represent a novel experimentally generated biological system, characterized by remarkable properties.

The plant cell adaptation to the ***in vitro*** growth conditions was found to be a multistep event that can be divided into three periods depending on the nature of adaptation, type, direction and intensity of cell selection: primary population of the isolated cells, strain formation and established strain. Cell populations of established strains were found to exhibit

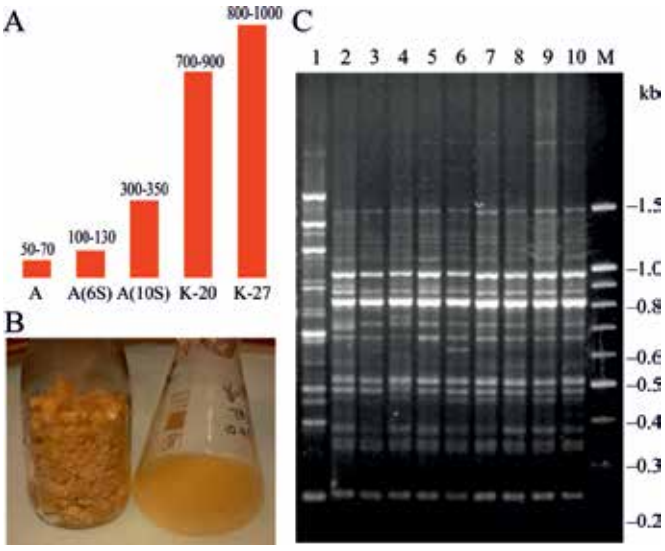


Fig. 1. Ajmaline super-synthesis in long-term stable ***Rauwolfia serpentina in vitro*** cultures.
A – Ajmaline production in phytohormone-independent ***R. serpentina*** cell lines of related origin (mg/mL). B – General view of callus and cell suspension ***R. serpentina*** culture. C – PCR-analysis of ***R. serpentina*** plant and cell lines: 1 – plant; 2-6 – 1990-91 years' samples of R-31, A, M, K-20 and K-27 cell lines; 7-10 – 2004 year's samples of K-27, growing for more than 10 years on different media.

physiological and genetic homeostasis due to the stabilizing selection.

For the first time the possibility for long-term (over 30 years of study) stable ***in vitro*** super-synthesis of bioactive substances in ***Rauwolfia serpentina*** and ***Panax ginseng*** cell lines was demonstrated thus opening a new vista to develop industrial technologies for production of valuable herbal pharmaceuticals for medicine. As demonstrated by the example of ***Panax ginseng***, poliployidization of cell cultures may result in increased biomass yield but the highest secondary metabolites accumulation is typical for the cultures comparable by ploidy level to intact plants.

Dynamics of cell systems ***in vitro*** has been described using the phenomenology equation. Networks of the appropriate oscillator interactions have been constructed for highly productive tissue culture strains of medicinal plants under various maintenance conditions.

The plant individual development was shown to be accompanied by the changes in the pattern of high-molecular weight nuclear DNA cleavage indicating structural and functional reorganization of DNA within chromatin. The difference in the size of chromatin loop domains consisted of the different DNA repeats was found in rye, as well as their enhanced cleavage in non-proliferating cells indicating the increased availability of matrix-associated regions to nucleases.

Studies on genetic polymorphism and genome plasticity in plants under extreme environmental conditions

Comprehensive studies involving cytogenetics, molecular genetics, biotechnology, biometrics, physiological approaches have been initiated to elucidate the features of variability and selection events in natural plant populations and plant cell populations ***in vitro*** as a basis for adaptation to growth conditions. Preliminary genetic analysis of ***Deschampsia antarctica*** using different types of DNA markers revealed difference in the level of genetic diversity between samples from two regions of Maritime Antarctic spaced apart from one another in the latitudinal direction. Population-genetic analysis using the DNA markers showed relatively high levels of genetic diversity and species specific features of genetic structure in yellow gentian (***Gentiana lutea***) and dwarf iris (***Iris pumila***), which probably resulted from individual evolutionary history of the populations.

Search for and development of new molecular genetic and cytological markers to assess the genetic diversity of rare plant species

To substantiate and enhance the efficiency of conservation measures the search is carried out for new molecular genetic and cytogenetic markers that would allow us to assess the genetic diversity of some rare plant species of the Ukraine. Primary screening allowed us to select polymorphic PCR primers specific to different genomic sequences. Molecular genetic analysis of yellow gentian (***Gentiana lutea***) and dwarf iris (***Iris pumila***) plants from a number of model populations from Ukraine showed the possibility of using selected PCR markers for assessment of genetic diversity as well as for analysis of the features of its distribution within and between populations.

Studies on the antimutagenic and anticancer properties of herbal remedies and development of approaches for their primary screening

Bacterial test system based on the wild strain of ***E.coli*** and its bacteriophage MS2-induced mutants has been developed. The former serves as an indicator of toxic properties of the tested substance, and the latter represents a specific test-culture simulating a tumor cell. Comparison of the data obtained for higher organisms and for the test system shows its adequate response to the substances already recognized for their anticancer properties. The developed test system is now used for primary screening and investigation of antibacterial and antimutagenic activities of extracts from natural plants and cultured tissues.

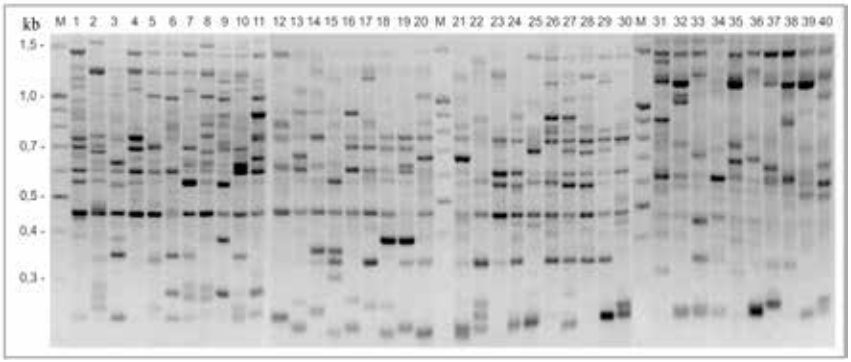


Fig. 2. Polymorphic ISSR-PCR profiles (primer UBC #840) of ***I. pumila*** plants from different locations of Mykolaiyvska and Poltavska obl.: 1–11 – vil. Migiia; 12–20 – vil. Aliaudy; 21–30 – vil. Kolarovo; 31–40 – vil. Andriivka. M – "100 bp Ladder" molecular weight marker.

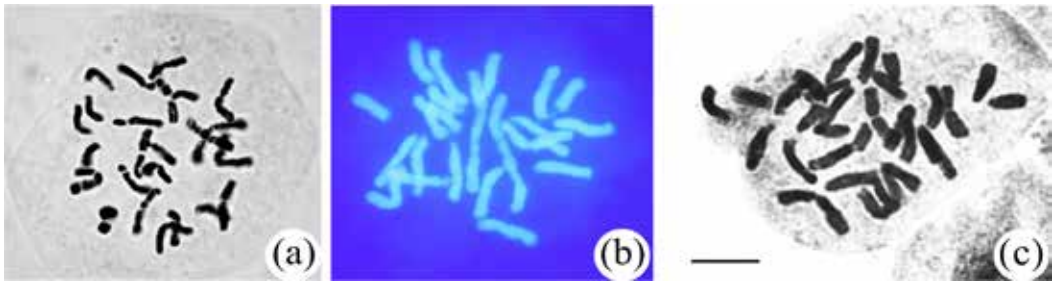


Fig. 3. Metaphase plates of ***Deschampsia antarctica*** (a) and ***Iris pumila*** (b,c) stained with acetoorsein (a,b) and DAPI (c)

National Grants

Projects of National Academy of Sciences of Ukraine:

- 2012–2016 Project: "Structural and functional genomics for the studies on some issues related to function of viruses, bacteria and higher eukaryotes"
- 2012–2014 National Academy of Sciences of Ukraine and Polish Academy of Sciences Joint Research Project: "Study on ecological and genetic mechanisms of plants adaptation to extreme environments"
- 2010–2014 N 39/12 Project: "Comparative genomics for gene pool diagnostics in some endangered species of Ukrainian flora"

Project of National Antarctic Scientific Center, State Agency on Science, Innovations and Informatization of Ukraine

- 2010–2012 N H12/2012 Project: "Development of bio-indication system for assessment of climate change in Maritime Antarctica by the parameters of terrestrial ecosystems dynamics"

Projects of State Fund of Fundamental Research:

- 2013–2014 F53/108-2013 Joint Project of the State Fund for Fundamental Research (DFFD) and the Russian Foundation for Basic Research (RFBR): "Biological and soil processes in unique tundras of Western Antarctic: biogeography, biogeochemistry and ecology of isolated geosytems in temporal and spatial scale"

Collaboration

with Ukrainian organizations:

- Taras Shevchenko National University of Kyiv (Kyiv)
- Ivan Franko National University of Lviv (Lviv)
- National University of "Kyiv-Mohyla Academy" (Kyiv)
- Ternopil National Pedagogical University named after Volodymyr Hnatiuk (Ternopil)
- Yurii Fedkovych Chernivtsi National University (Chernivtsi)
- M. G. Kholodny Institute of Botany, NASU (Kyiv)
- Institute of Ecology of the Carpathians, NASU (Lviv)
- National Scientific Centre "Institute of Agriculture of the National Academy of Agricultural Sciences" (Chabany)
- M. M. Grishko National Botanical Garden, NASU (Kyiv)
- National Antarctic Scientific Center of Ukraine, State Agency on Science, Innovations and Informatization of Ukraine (Kyiv)

with foreign organizations:

- Saratov Chernyshevsky State University (Saratov, Russia)
- Saint Petersburg State University (Saint Petersburg, Russia)
- Institute of Nature Conservation, PAS (Krakow, Poland)
- John Paul II Catholic University of Lublin (Lublin, Poland)
- University of Gdansk (Gdansk, Poland)
- W. Szafer Institute of Botany, PAS (Kraków, Poland)
- Lehigh University (Bethlehem, USA)
- Agricultural Research Service, United States Department of Agriculture (USA)

Selected Publications

1. Bublyk OM, Andreev IO, Kalendar RN, Spiridonova KV, Kunakh VA. Efficiency of different PCR-based marker systems for assessment of *Iris pumila* genetic diversity. ***Biologia.*** 2013; 68 (4): 613-20.
2. Kunakh VA. Evolution of cell populations *in vitro*: peculiarities, driving forces, mechanisms and consequences. ***Biopolym. Cell.*** 2013; 29(4): 295-31.
3. Bublyk OM, Andreev IO, Spiridonova KV, Kunakh VA. Genetic variability in regenerated plants of *Ungernia victoris*. ***Biologia Plantarum.*** 2012; 56(2):395–400.
4. Miryuta NYu, Kunakh VA. Dynamics of cell population systems *in vitro*. III. Hypothesis of cell differential process self-control and it's phenomenology realization by the example of *Rauwolfia serpentina* Benth. tissues culture ***"Biotechnology" J.*** 2012; 5(3):40–52.
5. Parnikoza IYu, Loro P, Miryuta NYu. Kunakh VA, Kozeretska IA. The influence of some environmental factors on cytological and biometric parameters and chlorophyll content of *Deschampsia antarctica* Desv in maritime Antarctic. ***Cytol. Genet.*** 2011. 45(3):170–6.
6. Konvalyuk II, Hrytsak LR, Mel'nyk VM, Drobyk NM, Kunakh VA. Obtaining and characterization of isolated root culture from plants of genus *Gentiana*. ***"Biotechnology" J.*** 2011; 4(3): 29–35.
7. Volkov RA, Kozeretska IA, Kyryachenko SS, et al. Molecular evolution and variability of ITS1–ITS2 in populations of *Deschampsia antarctica* from two regions of the maritime Antarctic. ***Polar Science.*** 2010; 4(3):469–78.
8. Pererva TP, Miryuta AYu, Moysa LN, Mozhylevskaya LP, Kunakh VA. Interaction of plant extracts of *Ungernia victoris*, *Rhodiola rosea* and *Polyscias filicifolia* with a bacterial cell. ***Cytol. Genet.*** 2010; 44(4):221–226.
9. Kunakh VA, Mozhylevskaya LP, Potapchuk EA, Musyka VI, Kolonina IV. Obtaining culture of *Ungernia victoris* tissues and its specificities in growing on nutrient media of various composition. ***Biotechnology.*** 2007; 1:14–21.
10. Kunakh V. Biotechnology of Medicinal Plants. Genetic and Physiologically–Biochemical basis. K.: Logos; 2005.

Department of Protein Synthesis Enzymology

Head
Mykhaylo A. Tukalo
Dr.Sci. (molecular biology), Professor,
Corresponding Member of National Academy of Sciences of Ukraine,
Deputy Director in Scientific Work
Phone: +380 (44) 200-03-35
Fax +380 (44) 526-07-59
E-mail: *mtukalo@imbg.org.ua*

Education and Degrees

1968–1973	Graduate Student, Taras Shevchenko National University of Kyiv, Kyiv, Ukraine, M.Sc. (biochemistry)
1981	Ph.D. (molecular biology)
1989	Dr.Sci. (molecular biology)
2005	Professor, Taras Shevchenko National University of Kyiv
2009	Corresponding Member of NASU

Professional Employment

1973	Research Assistant, Institute of Molecular Biology and Genetics (IMBG), NASU, Kyiv, Ukraine (molecular biology)
1974–1977	Visiting Scientist at the Novosibirsk Institute of Bioorganic Chemistry, Novosibirsk, Russia
1977–1982	Junior Research Scientist, Group leader, IMBG NASU, Kyiv, Ukraine
1982–1986	Senior Research Scientist, Group leader, IMBG NASU, Kyiv, Ukraine
1986–1990	Leading Research Scientist, Group leader, IMBG NASU, Kyiv, Ukraine
Since 1990	Head of the Department of Protein Synthesis Enzymology, IMBG NASU, Kyiv, Ukraine
1994–2002	Staff Scientist at the European Molecular Biology Laboratory, Grenoble Outstation, France
Since 2006	Deputy Director in Scientific Work, IMBG NASU, Kyiv, Ukraine

Honours, Prizes, Awards

1982	Medal “In memory of the 1500 anniversary of the city of Kyiv”
1986	State Prize of Ukraine in Science and Technology for contribution to molecular biology through research on the regulation of protein biosynthesis.
1995–2000	Howard Hughes Medical Institute International Research Grant INTAS Collaborative Grant
2011	Diploma of Verhovna Rada of Ukraine
2011	Gershenson Award of National Academy of Sciences of Ukraine

Tukalo M. A., Head of Department
Gudzera O. I., Senior Research Scientist, Ph.D.
Yaremchuk G. D., Senior Research Scientist, Ph.D.
Kovalenko O. P., Senior Research Scientist, Ph.D.
Kriklyvyi I. A., Research Scientist
Boyarshin S. K., Junior Research Scientist
Paperna A. E., Engineer
Rayevskiy A. V., Engineer
Pomanenko T. O., Technician

Research Area

Study on the molecular basis of decoding genetic information, translation quality control and RNA-protein recognition

Current Research Activities and Recent Achievements

Structural and functional study on aminoacyl-tRNA synthetases

The research of the last years was directed at the identification of the structural bases of the decoding of genetic information. The current area is the specific recognition of aminoacyl-tRNA synthetases (aaRSs) for their cognate amino acid and tRNA, mechanisms of catalysis and editing. Using biochemical methods, site-directed mutagenesis and X-ray crystallography, a work was carried out on different prokaryotic (including important pathogenic bacteria ***Enterococcus faecalis, Mycobacterium tuberculosis*** and ***Streptococcus pneumoniae***), eukaryotic and archaeal systems. In collaboration with Dr. S. Cusack (the European Molecular Biological Laboratory) the 3-dimensional structures of several aaRSs and their complexes with various combinations of substrata, including the tRNA complexes, are being studied. The synthesis of specific products by aaRSs has been shown to be accompanied by the conformational changes both in the active centre of enzyme and beyond. The data obtained allowed the understanding of the mechanism of amino acids activation and the molecular mechanism of the recognition of homologous tRNA and their aminoacylation by these enzymes.

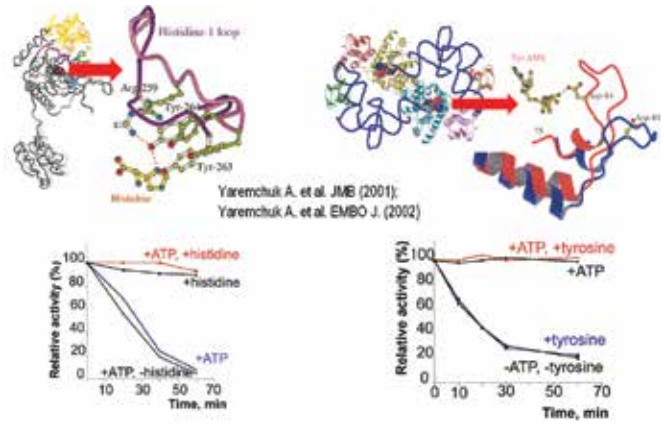


Fig. 1. Conformational changes occuring when a histidine binds in the active site of HisRSTT (the left) or tyrosyl-adenylate analogue binds in the active site of TyrRSTT (the right)

Recognition of tRNAs with a long variable arm by aminoacyl-tRNA synthetases

In prokaryotic cells three tRNA species, $tRNA^{Ser}$, $tRNA^{Tyr}$ and $tRNA^{Leu}$, possess a long variable arm of 11–20 nucleotides (a type 2 tRNAs) rather than the usual 4 or 6 (a type 1 tRNAs). We studied the molecular basis for recognition and discrimination of type 2 tRNAs by ***Thermus thermophilus s***eryl-,

tyrosyl- and leucyl- tRNA synthetases (SerRS, TyrRS and LeuRS) using X-ray crystallography and chemical probing of tRNA in solution. The determination of a complex of SerRs and $tRNA^{Ser}$ provided the first information on the structure of a tRNA with a long variable arm and elucidated the details of how enzyme interacts with tRNA. As a result of solving the structure of TyrRS an unusual for these enzymes type recognition of tRNA has been demonstrated for the first time. Tyrosyl-tRNA synthetase belongs to the first structural class, but its type of recognition is specific for the class 2 aaRSs, where tRNA interacts with an enzyme from the side of a long variable arm. Finally, after the structure of a complex of the leucyl-tRNA synthetase with $tRNA^{Leu}$ was determined, a full picture of the interaction of the synthetases with tRNA, which has a long variable arm, has been obtained. The distinctions, revealed in the tertiary structures of $tRNA^{Ser}$, $tRNA^{Tyr}$ and $tRNA^{Leu}$, using the methods of X-ray structure analysis and chemical modification, allowed us to understand the importance of their role in the recognition and discrimination by homologous aaRSs.

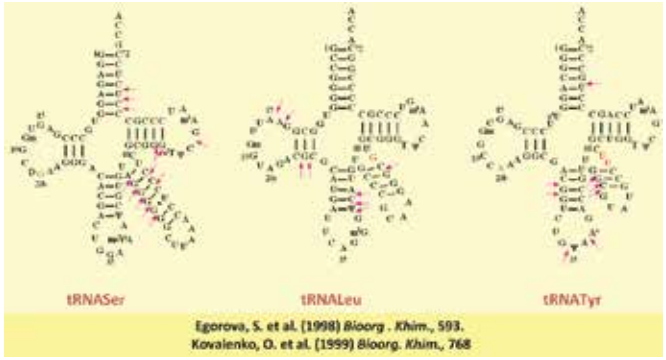


Fig. 2. Cloverleaf structures of *T. thermophilus* $tRNA^{Tyr}$, $tRNA^{Ser}$ and $tRNA^{Leu}$ with position of phosphates protected by cognate synthetase from alkylation with ethylnitrosourea

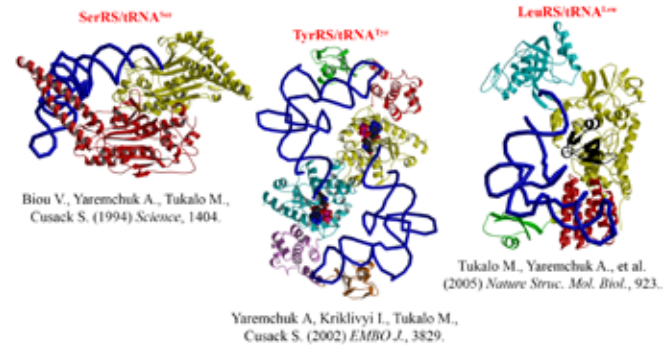


Fig. 3. Recognition of tRNAs with a long variable arm by cognate aminoacyl-tRNA synthetases

The molecular basis for editing errors by aminoacyl-tRNA syntetases

The affinity difference is not enough for the aminoacyl-tRNA synthetases to discriminate strictly between similar amino acids. When a tRNA is acylated with the wrong amino acid this would lead to an error in the incorporation of genetically coded amino acids into protein. To overcome this problem, several aaRSs have developed the ability to hydrolyze the mischarged tRNA in an extra editing domain. We are studying the molecular mechanisms of editing by synthetases from two different classes: *Thermus thermophilus* leucyl-tRNA synthetase (LeuRSTT) from class I and *Enterococcus fecalis* prolyl-tRNA synthetase (ProRSEF) from class II. To understand the mechanisms of editing reaction for enzymes with absolutely different architecture of editing domains, we have used a number of approaches, including molecular modeling, quantum-mechanical calculations, site-directed mutagenesis and enzyme modification of tRNA. Our intensive alanine scanning mutagenesis of LeuRSTT and ProRSEF editing sites has failed to identify catalytic residues for hydrolysis within the active site. On the other hand, modification of $tRNA^{Pro}$ at the 2'-OH of A76 and $tRNA^{Leu}$ at the 3'-OH of A76 by replacing each of them with a hydrogen or fluorine, revealed an essential function of these groups in hydrolysis. On the basis of obtained experimental results and our QM/MM calculations we suggest a tRNA-assisted mechanism of post-transfer editing by LeuRS and ProRS in which 2'- or 3'-OH group of the substrate plays a key role.

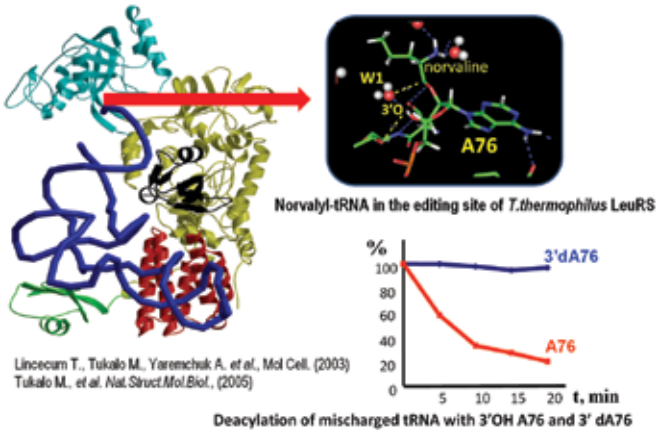


Fig. 4. tRNA-assisted mechanism of post-transfer editing by leucyl-tRNA synthetase

Development of novel classes of antibiotics

We are using the differences between human and prokaryotic prolyl-, tyrosyl- and leucyl-tRNA synthetases for the development of the inhibitors as potential drugs against *Mycobacterium tuberculosis, Enterococcus faecalis* and *Streptococcus pneumonia*. The search strategy for antibacterial compounds is based on the combination of X-ray structural analysis of the target protein, computer modelling of the interaction of low-molecular ligands with the target protein and synthetic procedures of combinatorial chemistry.

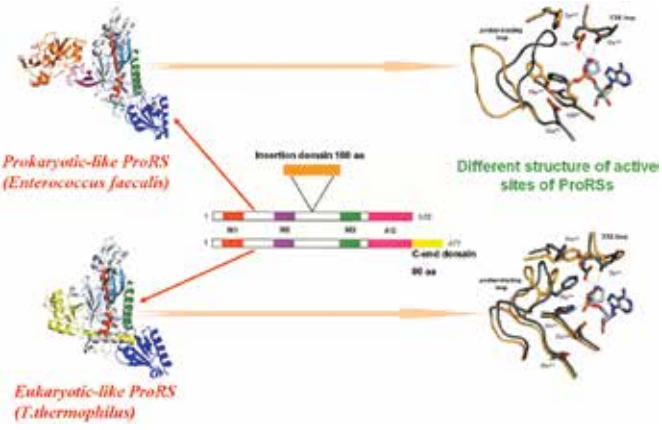


Fig. 5. Exploitation of structural differences of human and pathogenic bacterial prolyl-tRNA synthetases for the identification of novel inhibitors as potential anti-pathogen drugs

National Grants

Projects of National Academy of Sciences of Ukraine:

- 2012–2016 Progect: "Target-directed search for a new antibacterial, antiviral and antitumor agents" (scientific supervisor – M. Tukalo)
- 2010–2014 N 30/10 Progect: "Development of target-specific technologies for searching of the aminoacyl-tRNA synthetases inhibitors with selective action against causative agents of human infection diseases" (scientific supervisor – M. Tukalo)

Projects of State Agency on Science, Innovations and Informatization of Ukraine:

- 2012–2015 N 059/514 Project: "Development of the methodologies target-directed, rational search for new anti-TB drugs" (scientific supervisor – M. Tukalo)

International Grants

- 2013–2016 GDRI (International Research Networks) Project: "From molecular to cellular events in human pathologies" (scientific supervisors – Prof. P. Curmi and Prof. O. Lavrik)
- 2011–2014 7th Framework Programme (FP7) FP7-INCO-2011-6, ERA-WIDE Project: "Strengthening co-operation in Molecular Biomedicine between EU and UKRAINE", COMBIOM (scientific supervisor – Prof. A. Elskaya)
- 2011–2012 STCU (Science and Technology Center in Ukraine) Research Grants
- 2007–2009 STCU Research Grants
- 1992–1995 NATO (North Atlantic Treaty Organization) Collaborative Research Grant

Collaboration

with Ukrainian organizations:

- Taras Shevchenko National University of Kyiv (Kyiv)
- Bogomoletz Institute of Physiology, NASU (Kyiv)

with foreign organizations:

- European Molecular Biology Laboratory (Grenoble, France)
- Institute Gustave-Roussy (Paris, France)
- Laboratory of Enzymology and Structural Biochemistry, CNRS (Gif-sur-Yvette, France)
- International Institute of Molecular and Cell Biology (Warsaw, Poland)
- Institute of Chemical Biology and Fundamental Medicine, SB RAS (Novosibirsk, Russia)

Selected Publications

1. Yaremchuk AD, Kovalenko OP, Gudzera OI, Tukalo MA. Molecular cloning, sequencing and expression in Escherichia coli cells *Thermus thermophilus* leucyl-tRNA synthetase ***Biopolym. Cell.*** 2011; 27(6): 436–41.
2. Rock FL, Mao W, Yaremchuk A, et al. An antifungal agent inhibits an aminoacyl-tRNA synthetase by trapping tRNA in the editing site. ***Science.*** 2007;316(5832):1759–61.
3. Tukalo M, Yaremchuk A, Fukunaga R, Yokoyama S, Cusack S. The crystal structure of leucyl-tRNA synthetase complexed with tRNALeu in the post-transfer-editing conformation. ***Nat Struct Mol Biol.*** 2005;12(10):923–30.
4. Lincecum TL Jr, Tukalo M, Yaremchuk A, et al. Structural and mechanistic basis of pre- and posttransfer editing by leucyl-tRNA synthetase. ***Mol Cell.*** 2003;11(4):951–63.
5. Yaremchuk A, Kriklivyi I, Tukalo M, Cusack S. Class I tyrosyl-tRNA synthetase has a class II mode of cognate tRNA recognition. ***EMBO J.*** 2002;21(14):3829–40.
6. Yaremchuk A, Cusack S, Tukalo M. Crystal structure of a eukaryote/archaeon-like protyl-tRNA synthetase and its complex with tRNAPro(CGG). ***EMBO J.*** 2000; 19(17): 4745–58.
7. Cusack S, Yaremchuk A, Tukalo M. The 2 A crystal structure of leucyl-tRNA synthetase and its complex with a leucyl-adenylate analogue. ***EMBO J.*** 2000;19(10):2351–61.
8. Cusack S, Yaremchuk A, Tukalo M. The crystal structure of the ternary complex of *T.thermophilus* seryl-tRNA synthetase with tRNA(Ser) and a seryl-adenylate analogue reveals a conformational switch in the active site. ***EMBO J.*** 1996; 15(11):2834–42.
9. Biou V, Yaremchuk A, Tukalo M, Cusack S. The 2.9 A crystal structure of *T. thermophilus* seryl-tRNA synthetase complexed with tRNA(Ser). ***Science.*** 1994;263(5152):1404–10.
10. Belrhali H, Yaremchuk A, Tukalo M, et al. Crystal structures at 2.5 angstrom resolution of seryl-tRNA synthetase complexed with two analogs of seryl adenylate. ***Science.*** 1994; 263(5152): 1432–6.

Laboratory of Technology Transfer, Innovation and Intellectual Property of Department of Protein Synthesis Enzymology

Head
Iryna I. Khomenko
Phone: +380 (44) 526-07-39, 235-56-66
Fax: +380 (44) 526-07-59
E-mail: *i.i.khomenko@imbg.org.ua*, *patentxom@ukr.net*

Education and Degrees

1994–1995	Accountant, Pryluky branch of O.N.C. of Ministry of Statistics of Ukraine
1995–2001	Engineer-Mechanic, National Technical University of Ukraine “Kyiv Polytechnic Institute”
1999–2001	Marketing Specialist, National Technical University of Ukraine “Kyiv Polytechnic Institute”
2000	Specialist on Realty, Business, Property Expert Evaluation, Training Center of “EXPERT-L”, State Property Fund of Ukraine
2001	Course: “Introduction to Intellectual Property”, World Intellectual Property Organization (WIPO)
2003–2004	Intellectual Property Expert, Inter-branch Institute for Professional Development, National Technical University “Kharkiv Polytechnic Institute”
2010	Patent Agent, State Department of Intellectual Property, Ministry of Education and Science of Ukraine

Professional Employment

1995–1996	Second Accountant, “Almagest Ltd” firm, Kyiv, Ukraine
1996	Accountant-cashier, “Prigov and Partners” Patent Agency, Kyiv, Ukraine
1996–2003	Patent Engineer, “Vepol” Patent Agency, Kyiv, Ukraine
2003–2007	Head of the Laboratory of Technology Transfer, Innovation and Intellectual Property, Institute of Molecular Biology and Genetics, NASU, Kyiv, Ukraine
Since 2007	Head of the Department of Industrial Property Researches, Center of Intellectual Property and Technology Transfer, NASU, Kyiv, Ukraine
Since 2007	Research Scientist, Laboratory of Technology Transfer, Innovation and Intellectual Property, IMBG NASU, Kyiv, Ukraine

Staff:

Khomenko I. I., Head of Laboratory
Soldatkina I. A., Research Scientist, Ph.D.
Shukhman A. B. , Leading Engineer

Laboratory of Technology Transfer, Innovation and Intellectual Property is engaged in obtaining and protecting the rights for the objects of intellectual property, created at the Institute of Molecular Biology and Genetics of NASU. During the years since the Institute was founded, the achievements of the scientists resulted in/were crowned with two discoveries, certified by the State Committee of Discoveries and Inventions of the USSR.

The notable scientists, Academicians of NASU, made these discoveries.

- Certificate for invention N 340 "Property of exogenous DNA (desoxyribonucleic acids) to induce selective mutations of genes" by S. M. Gershenzon.
- Certificate for invention N 367 "Property of specific proteins producent cells to change the synthesis of transport RNA in course of differentiation" by G. Kh. Matsuka, A. V. El'skaya.
- The inventions were made in the following fields:
- Genetic engineering and novel biotechnologies.
- Cells – producents of biologically active compounds, drugs and others.
- Synthetic compounds – antiviral, antitumoral, immunomodulating and other therapeutic agents.
- Biosensors.
- Varieties/Lines and technologies for agro industrial complex.

For forty years the scientists of the IMBG NASU have received more the 250 provisional patents (inventor's certificates, patents of Ukraine, international applications, submitted according to the Patent Cooperation Treaty). Also, a number of innovations, proposed to upsurge scientific research efficiency, have been registered.

During the last few years, according to the Patent Cooperation Treaty (PCT), the Institute has submitted several international applications, in particular, "Synthesis, pharmaceutical composition and method of application of (2'–5') oligoadenylate analogues", by Z. Yu. Tkachuk, E. Kvasyuk, G. Kh. Matsuka, I. Michaylopulo; Microsensor for detection of D-amino-acids" Cespuglio Raymond, Scuvailo Oleg, Soldatkin Alexey. "Biological preparation for plant growing and protection "Kleps" (patent N 4418A) by N. O. Kozyrovska, V. V. Negrutska. They were prize-winners of "Discovery 2002" contest, and as women-inventors were awarded the medal of the International Organization of Intellectual Property. Biological preparation Kleps is being used in the agricultural complex in Ukraine, it insures a rise in grain, vegetables and industrial crops up to 10–20 %.

Institute is conducting marketing on the issues of implementing scientific developments. For several years institute under licencing agreement granted the right to use invention "Biological preparation for plant growing and protection "Kleps" (Patent of Ukraine N 44189, authors: N. O. Kozyrovska, V. V. Negrutska).

Department of Molecular and Quantum Biophysics

Head
Dmytro M. Hovorun
Dr.Sci. (molecular biology), Professor,
Corresponding Member of National Academy of Sciences of Ukraine,
Deputy Director in Scientific Work
Phone: +380 (44) 526-11-09, 526-20-14
Fax: +380 (44) 526-07-59
E-mail: *dhovorun@imbg.org.ua*

Education and Degrees

1967–1972	Graduate Student, Faculty of Radiophysics, Taras Shevchenko National University of Kyiv, Kyiv, Ukraine M.Sc. (nonlinear optics)
1987	Ph.D. (optics). Thesis: “Manifestation of infra- and intermolecular interactions in vibrational spectra of some liquids”
2000	Dr.Sci. Thesis: “Physico-chemical mechanisms of biomolecular recognition”
2004	Professor (biophysics)
2006	Corresponding Member of NASU

Professional Employment

1972–1976	Junior Research Scientist, Faculty of Radiophysics, Taras Shevchenko National University of Kyiv, Kyiv, Ukraine
1976–1986	Research Scientist, Faculty of Radiophysics, Taras Shevchenko National University of Kyiv, Kyiv, Ukraine
1987–1995	Senior Research Scientist, Department of Molecular Biophysics, Institute of Molecular Biology and Genetics (IMBG), NASU, Kyiv, Ukraine
Since 1995	Head of the Molecular Biophysics Department, IMBG NASU, Kyiv, Ukraine
1998, 2001	Professor-researcher, Department of Chemistry, Jackson State University, Jackson, MS, USA
Since 1999	Professor of the National University of “Kyiv-Mohyla Academy”, Chair of Physics and Mathematics, Kyiv, Ukraine
Since 2003	Professor of Taras Shevchenko National University of Kyiv, Chair of Medical Radiophysics, Kyiv, Ukraine
Since 2003	Deputy Director in Scientific Work, IMBG NASU, Kyiv, Ukraine

Membership

Member of FEBS (Federation of European Biochemical Societies)
Member of Ukrainian Biochemical Society
Member of Ukrainian Biophysical Society
Member of Ukrainian Society of Molecular Biology
Associate Editor of Journal “Biopolymers and Cell”
Editorial Board member of Journal “Physics of the Alive” (Ukraine)
Editorial Board member of Journal “Ukrainica Bioorganica Acta” (Ukraine)

Honours, Prizes, Awards

1994–1995	Soros International Science Foundation Grant
2003	Diploma of Verhovna Rada of Ukraine
2008	State Prize of Ukraine in Science and Technology
2008	Gershenson Award of National Academy of Sciences of Ukraine
2012	Honoured Worker of Science and Technology of Ukraine

Hovorun D. M., Head of Department
Samijlenko S. P., Leading Research Scientist, Ph.D.
Zarudna M. I., Senior Research Scientist, Ph.D.
Kolomiets I. M., Senior Research Scientist, Ph.D.
Potyahaylo A. L., Senior Research Scientist, Ph.D.
Brovarets' O. O., Senior Research Scientist, Ph.D.
Palchykovska L. G., Senior Research Scientist, Ph.D.
Martynenko O. I., Senior Research Scientist, Ph.D.
Platonov M. O., Research Scientist, Ph.D.
Stepanyugin A. V., Junior Research Scientist, Ph.D.
Bukaty O. M., Junior Research Scientist, Ph.D.
Kyrylenko T. K., Junior Research Scientist, Ph.D.
Litovchenko N. V., Technician
Kuznetsova L. M., Technician

Research Area

Search for universal physical and chemical fundamentals of specific interactions between components of nucleoprotein complexes and elucidation of a role of prototropic tautomerism of nucleic acid bases and proton transfer in elementary processes of protein-nucleic acid recognition and interactions between bases in nucleic acids

Current Research Activities and Recent Achievements

- Using the methods of molecular spectroscopy (IR, UV, Raman, NMR) and quantum-chemical calculations at different levels of theory, the shifts in tautomeric equilibrium of nucleotide bases influenced by hydrogen bonding or interaction with ligands of peptidic nature and coordination with alkali cations are being investigated (Fig. 1, 2). Changes in the tautomeric state of nucleotide bases, expected under the influence of heterogeneous environment in cells, may be regarded as one of possible mechanisms responsible for structural-dynamic

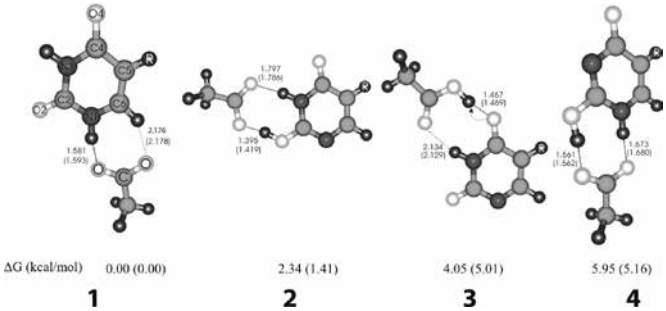


Fig. 1. Ura (Thy) tautomer double complexes with CH_3COO^-. ΔG: Gibbs energy values of the complexes. Dotted lines show H-bonds, with their lengths presented in Å; the arrow means proton transfer.

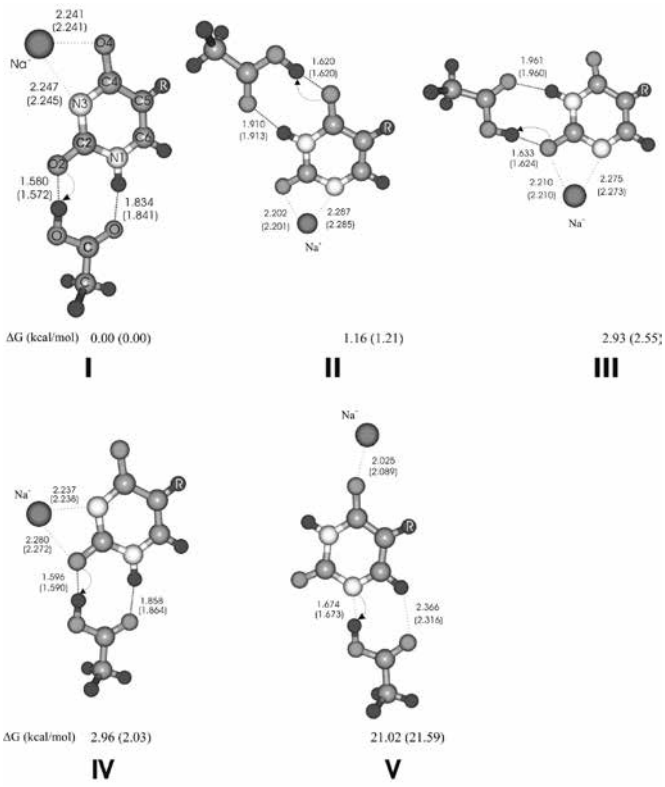


Fig. 2. Triple complexes of Ura (Thy) tautomers with CH_3COO^- and Na^+. ΔG: Gibbs energy values of the triple complexes. The bold dotted lines show H-bonds, with their lengths presented in Å; the arrows mean proton transfer.

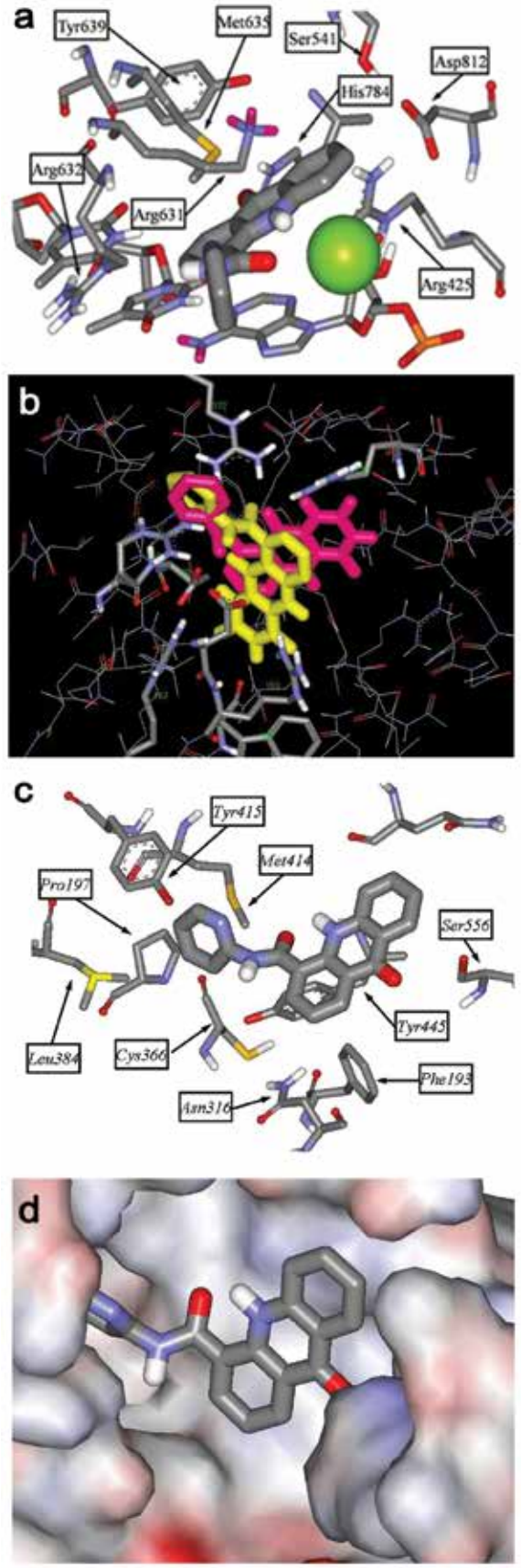


Fig. 3. Inhibition by Acridone derivatives activity of (a) T7 RNA polymerase, (b) influenza virus neuraminidase, (c, d) HCV NS3 Helicase

transformations in protein-nucleic acid complexes. Theoretical and experimental investigations of the tautomeric state of nucleotide bases in model complexes of protein-nucleic recognition provide grounds to the concept of a significant role of the high-energy tautomers in biochemical processes .

- The specific features of the spatial organisation of signal elements in cellular and viral RNAs, namely, their secondary and tertiary structures, are being studied using modern methods of electrophoresis, protonic buffer capacity, molecular modelling and bioinformatics.
- A new line of investigation in the Department is directed to design, synthesis and study of biologically active heterocyclic compounds – antibacterial, antiviral and antitumor agents, which are inhibitors of the DNA and RNA polymerases and topoisomerases I and II. For screening inhibitors of the DNA and RNA polymerases there were applied effective and universal models: PCR and transcriptional complex of the phage T7 RNA polymerase. The cross-analysis procedure of the database of potential biological targets for low-molecular ligands is being used both to determine pharmacological profile of compounds and to search for the highest possible number of their targets. (Fig. 3)
- In the Department there was invented a new method of the special spectroscopic technique ATR IR – attenuated total reflection of infrared light, covered by the patent of Ukraine. This technique can be used to obtain high-quality IR spectra of fine films of nucleic acids and their complexes.
- Based on quantum chemical calculation, the CH…O/N intermolecular hydrogen bonds in biologically significant canonical and modified pairs of DNA were investigated; there were proposed new structural mechanisms of spontaneous errors of insertion and the DNA replication errors, which are grounded on the Watson-Crick tautomeric hypothesis (Fig. 4).

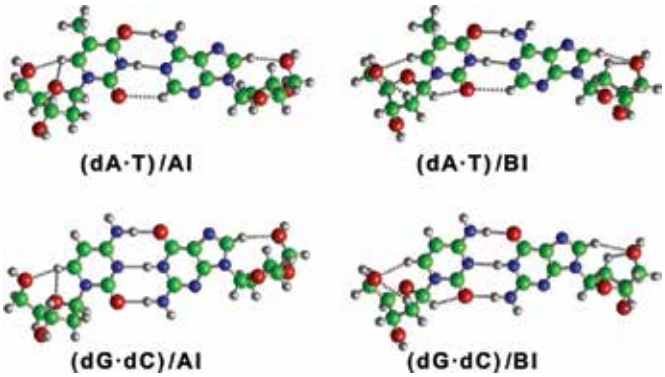


Fig. 4: Hydrogen bonds in Watson-crick nucleoside pairs, corresponding to the AI and BI forms of DNA.

- In the frame of fundamental problems in the up-to- date phytobiology, the mechanisms of plants' response to abiotic factors are being studied at the level of a genome reaction. Monitoring the global dynamics of the plant genome activity under the influence of chemical agents is being implemented by the DNA : RNA ratio lurking. This allows us to isolate molecules of genomic DNA of various functional activities with the purpose of studying their adequate structural changes.

National Grants

Projects of National Academy of Sciences of Ukraine:

- 2012–2016 Project: "Structural and functional genomics in the study of disorders in functioning viruses, bacteria and higher eukaryotes. CESSHIV-1 database as an instrument of investigating the secondary structure of control elements of human immunodeficiency virus" (scientific supervisor – D. M. Hovorun)
- 2011 Grant of NASU for Young Scientists: "Conformational analysis of nucleic acid constituents as a key to understanding their biological activity" (scientific supervisor – Ye. P. Yurenko)
- 2008–2009 NASU-STCU (National Academy of Sciences of Ukraine and Science and Technology Center in Ukraine) Project: "The RNA secondary structure role in HIV-1 replication: study by molecular genetics, phylogeny, and bioinformatics"
- 2008 N 10 Project: "Phylogenetic study of structural variants of signaling elements in 5' UTR of the HIV-1 genome"
- 2007–2011 N 2.2.4.20 Project: "Investigation of the control elements structure in genome RNA of human immunodeficiency virus"
- 2007–2009 Project: "Amides of triazinyl-propane carbonic acid – efficient inhibitors of human mycoses and mycotoxicoses: toxic and pharmacological studies and search for medical forms" (scientific supervisor – L. G. Palchykovska)
- 2005–2007 Project: "Highly efficient inhibitors in fighting agents of human mycoses and mycotoxicoses on the basis of substituted amides of triazinyl-propane carbonic acid" (scientific supervisor – L. G.Palchykovska)

Projects of Ministry of Education and Science of Ukraine:

- 2009–2010 The French-Ukrainian joint action program in the field of scientific and technological cooperation "Dnipro" CNRS, N M/111–2009 Project: "Investigation of tautomeric and conformational states of nucleotide bases and their nucleosides in model complexes of protein-nucleic acid recognition" (scientific supervisor – D. M. Hovorun)

Projects of State Fund for Fundamental Researches

- During last decades we have received several SFFR grants, last of them:
- 2011–2012 Project: "Conformational variability of 2'-deoxyribonucleosides and 2'-ribonucleosides: quantum-chemical studies" (scientific supervisor – D. M. Hovorun)

International Grants

- Research Partnership Program of STCU and EU N 4302 Project. Laboratory of Lymphotropic Viruses, D. I. Ivanovsky Institute of Virology of Russian Academy of Medical Sciences (scientific supervisor – D. M. Hovorun)

Selected publications

1. Brovarets' OO, Yurenko YP, Hovorun DM. Intermolecular CH···O/N H-bonds in the biologically important pairs of natural nucleobases: a thorough quantum-chemical study. ***J Biomol Struct Dyn.*** 2013 Jun 03.
2. Brovarets' OO, Yurenko YP, Dubey IY, Hovorun DM. Can DNA-binding proteins of replisome tautomerize nucleotide bases? Ab initio model study. ***J Biomol Struct Dyn.*** 2012;29(6):597–605.
3. Zarudnaya MI, Potyahaylo AL, Kolomiets IM, Hovorun DM. Structural model of the complete poly(A) region of HIV-1 pre-mRNA. ***J Biomol Struct Dyn.*** 2013;31(10):1044–1056.
4. Yurenko YP, Zhurakivsky RO, Samijlenko SP, Hovorun DM. Intramolecular CH···O hydrogen bonds in the AI and BI DNA-like conformers of canonical nucleosides and their Watson-Crick pairs. Quantum chemical and AIM analysis. ***J Biomol Struct Dyn.*** 2011;29(1):51–65.
5. Furmanchuk A, Isayev O, Gorb L, Shishkin OV, Hovorun DM, Leszczynski J. Novel view on the mechanism of water-assisted proton transfer in the DNA bases: bulk water hydration. ***Phys Chem Chem Phys.*** 2011;13(10):4311–7.
6. Samijlenko SP, Yurenko YP, Stepanyugin AV, Hovorun DM. Tautomeric equilibrium of uracil and thymine in model protein-nucleic acid contacts. Spectroscopic and quantum chemical approach. ***J Phys Chem B.*** 2010;114(3):1454–61.
7. Danilov VI, van Mourik T, Kurita N, Wakabayashi H, Tsukamoto T, Hovorun DM. On the mechanism of the mutagenic action of 5-bromouracil: a DFT study of uracil and 5-bromouracil in a water cluster. ***J Phys Chem A.*** 2009;113(11):2233–5.
8. De Logu A, Palchykovska LH, Kostina VH, et al. Novel N-aryl- and N-heteryl phenazine-1-carboxamides as potential agents for the treatment of infections sustained by drug-resistant and multidrug-resistant Mycobacterium tuberculosis. ***Int J Antimicrob Agents.*** 2009;33(3):223–9.
9. Stankiewicz-Drogon A, Palchykovska LG, Kostina VG, Alexeeva IV, Shved AD, Boguszewska-Chachulska AM. New acridone-4-carboxylic acid derivatives as potential inhibitors of hepatitis C virus infection. ***Bioorg. Med. Chem.*** 2008; 6(19):8846–8852.
10. Zarudnaya MI, Kolomiets IM, Potyahaylo AL, Hovorun DM. Downstream elements of mammalian pre-mRNA polyadenylation signals: primary, secondary and higher-order structures. ***Nucleic Acids Res.*** 2003;31(5):1375–86.

Laboratory of Computational Structural Biology of Department of Molecular and Quantum Biophysics

Head
Leonid G. Gorb
Dr.Sci. (chemistry),
Senior Research Scientist
Phone: +380 (44) 526-11-09
Fax: +380 (44) 526-07-59
E-mail: *leonid.gorb@gmail.com*

Education and Degrees

1971–1976	Graduate Student, Faculty of Chemistry, Oles Honchar Dnipropetrovsk National University, Dnipropetrovsk, Ukraine, M.Sc. (chemistry)
1980–1983	Postgraduate Student, Zelinsky Institute of Organic Chemistry of Russian Academy of Sciences, Moscow, Russia
1983	Ph.D. (physical and organic chemistry)
2009	Dr.Sci. (chemistry)

Professional Employment

1976–1980	Research Assistant, State Enterprise "Ukrainian State Research Institute Plastic Masses", Donetsk, Ukraine
1984–1997	Head of the Quantum-Chemistry Group, A. V. Dumansky Institute of Colloid and Water Chemistry, NASU, Kyiv, Ukraine
1994–1996	Associate Professor, National University of "Kyiv-Mohyla Academy", Kyiv, Ukraine
2001–2005	Research Associate, Jackson State University, Mississippi, USA
Since 2005	Head of the Laboratory of Computational Structural Biology, Institute of Molecular Biology and Genetics (IMBG), NASU, Kyiv, Ukraine

Membership

1999	Member of American Chemical Society
2005	Member of the Organizing Committee of the International Symposiums "Methods and Applications of Computational Chemistry"
Referee	Journal of Physical Chemistry
	Journal of Biomolecular Structure and Dynamics
	Journal of Biomolecular Structure and Dynamics
	Journal of Molecular Structure (Theochem)
	International Journal of Molecular Science
	Structural Chemistry
	Journal of Physical Organic Chemistry
	Journal of Molecular Modeling
	Europian Journal of Soil Science
	Chemical Physical Letters
	Physical Chemistry and Chemical Physics

Honours, Prizes, Awards

1991–1994	The Fellowship of the Centre National de la Recherche Scientifique (France) for the Participation in the Project "Modelling of the Chemical Reactivity on the Border of Water – Solid Interface"
1993	Award of the USSR branch of World Association of Theoretical Organic Chemists for the work: "Quantum-Mechanical and Statistical Theory of Solutions"
2009	Gershenson Award of National Academy of Sciences of Ukraine for the work "Quantum-Chemical Nature of Spontaneous Point Mutations in DNA"

Gorb L. G., Head of Laboratory
Danilov V. I., Leading Research Scientist, Ph.D.

Zhurakivskiy R. A., Senior Research Scientist, Ph.D.
Sheremetyeva O. O., Technician

Research areas

An application of the methods of computational biology to the predictions of the properties of DNA and its components

Current research activities

- Application of the state of the art methods of quantum chemistry to study tautomerization mechanisms of DNA bases
- Application of docking and molecular dynamics methods (both classical and *ab initio*) to study physical and chemical properties of nucleoside-tri-phosphates and their correct and incorrect interaction with active sites of DNA-polymerase

National Grants

Projects of State Fund for Fundamental Researches

- 2011 N F40/52–2011 Project "Theoretical studies of biologically relevant molecular systems in the framework of continuous environment model, taking into account its heterogeneity" (scientific supervisor – L. G. Horb)

Selected publications

1. Isayev O, Crespo-Hernández CE, Gorb L, Hill FC, Leszczynski J. ***In silico*** structure-function analysis of E. cloacae nitroreductase. ***Proteins.*** 2012;80(12):2728–41.
2. Ford-Green J, Isayev O, Gorb L, Perkins EJ, Leszczynski J. Evaluation of natural and nitramine binding energies to 3-D models of the S1S2 domains in the N-methyl-D-aspartate receptor. ***J Mol Model.*** 2012;18(4):1273–84.
3. Sviatenko L, Gorb L, Hovorun D, Leszczynski J. Interaction of 2'-deoxyadenosine with cis-2-butene-1,4-dial: computational approach to analysis of multistep chemical reactions. ***J Phys Chem A.*** 2012;116(9):2333–42.
4. Shishkin OV, Dopieralski P, Omelchenko IV, Gorb L, Latajka Z, Leszczynski J. Dynamical Nonplanarity of Benzene. Evidences from the Car–Parrinello Molecular Dynamics Study. ***J. Phys. Chem. Lett.*** 2011;2(22):2881–4.
5. Petrova T, Tarabara I, Palchikov V, et al. Ethanolysis of N-substituted norbornane epoxyimides: discovery of diverse pathways depending on substituent's character. ***Org Biomol Chem.*** 2010;8(9):2142–57.
6. Furmanchuk A, Isayev O, Shishkin OV, Gorb L, Leszczynski J. Hydration of nucleic acid bases: a Car-Parrinello molecular dynamics approach. ***Phys Chem Chem Phys.*** 2010; 12(14):3363–75.
7. Kosenkov D, Kholod Y, Gorb L, et al. ***Ab initio*** kinetic simulation of gas-phase experiments: tautomerization of cytosine and guanine. ***J Phys Chem B.*** 2009;113(17):6140–50.
8. Kosenkov D, Kholod YA, Gorb L, et al. Effect of a pH change on the conformational stability of the modified nucleotide queuosine monophosphate. ***J Phys Chem A.*** 2009;113(33):9386–95.
9. Palamarchuk GV, Shishkin OV, Gorb L, Leszczynski J. Dependence of deformability of geometries and characteristics of intramolecular hydrogen bonds in canonical 2'-deoxyribonucleotides on DNA conformations. ***J Biomol Struct Dyn.*** 2009; 26(5):653–62.
10. Gorb L, Podolyan Y, Dziekonski P, et. al. Double-proton transfer in adenine-thymine and guanine-cytosine base pairs. A post-Hartree-Fock ***ab initio*** study. ***J Am Chem Soc.*** 2004; 126(32):10119–29.

Department of Functional Genomics

Head
Alla V. Rynditch
Dr.Sci. (molecular biology), Professor,
Corresponding Member of National Academy of Sciences of Ukraine
Phone: +380 (44) 526 96 18
Fax: +380 (44) 526 07 59
E-mail: *rynditch@imbg.org.ua*

Education and Degrees

1971	Ph.D. (biochemistry) Thesis: "Properties of DNA from nuclear polyhedrosis virus of silkworm", O. V. Palladin Institute of Biochemistry, NASU, Kyiv, Ukraine
1990	Dr.Sci. (molecular biology). Thesis: "Structure and expression of Rous sarcoma virus in the cells of unrelative hosts". Institute of Molecular Biology and Genetics (IMBG), NASU, Kyiv, Ukraine
1995	Professor (molecular biology), IMBG NASU
1995	Corresponding Member of NASU

Professional Employment

1963–1964	Senior assistant, D. K. Zabolotny Institute of Microbiology and Virology (IMV), NASU, Kyiv, Ukraine
1964-1966	Trainee Researcher, IMV NASU, Kyiv, Ukraine
1966–1968	Junior Research Scientist, IMV NASU, Kyiv, Ukraine
1968–1977	Junior Research Scientist, IMBG NASU, Kyiv, Ukraine
1977–1986	Senior Research Scientist, IMBG NASU, Kyiv, Ukraine
1986–1989	Leading Research Scientist, IMBG NASU, Kyiv, Ukraine
1989–1992	Head of the Laboratory of Molecular Oncogenetics, IMBG NASU, Kyiv, Ukraine
Since 1992	Head of the Department of Functional Genomics IMBG NASU, Kyiv, Ukraine

Membership

Since 1989	Member of European Association for Cancer Research (EACR)
Since 1991	Member of Human Genome Organisation (HUGO)
Since 1994	Member of Committee of EACR
Since 2005	Editorial Board member of Journal "Gene" (The Netherlands)
Since 2009	Editorial Board member of Journal "Biopolymers and Cell" (Ukraine)

Honours, Prizes, Awards

2004	Gershenson Award of National Academy of Sciences of Ukraine

Rynditch A. V., Head of Department
Tsyba L. O., Leading Research Scientist, Ph.D.
Skrypkina I. Ya., Senior Research Scientist, Ph.D.
Nikolaienko O. V., Senior Research Scientist, Ph.D.
Dergai M. V., Senior Research Scientist, Ph.D.
Kropyvko S. V., Research Scientist, Ph.D.
Gryaznova T. A., Junior Research Scientist
Novokhatska O. V., Junior Research Scientist
Gerasymchuk D. O., Junior Research Scientist
Morderer D. Ye, Junior Research Scientist
Dergai O. V., Junior Research Scientist
Gubar O. S., Junior Research Scientist
Foienko I. M., Leading Engineer
Chain L. O., technician
Bazan T. A., technician

Research Area

- The role of adaptor/scaffold proteins in the formation and regulation of multiprotein complexes during endocytosis, signal transduction, actin polymerization, viral infections and neuronal functioning
- Regulation of gene expression at the level of alternative splicing
- Identification and characterization of cancer–related genes

Current Research Activities and Recent Achievements

Identification of novel functional interactions of intersectin (ITSN) family of adaptor/scaffold proteins

Scaffolding proteins of ITSN family are crucial for the initiation stage of clathrin-mediated endocytosis. Moreover, they regulate actin cytoskeleton rearrangements, cell signalling and survival. Abnormalities of expression of ITSN1 gene, which is located on chromosome 21, are associated with

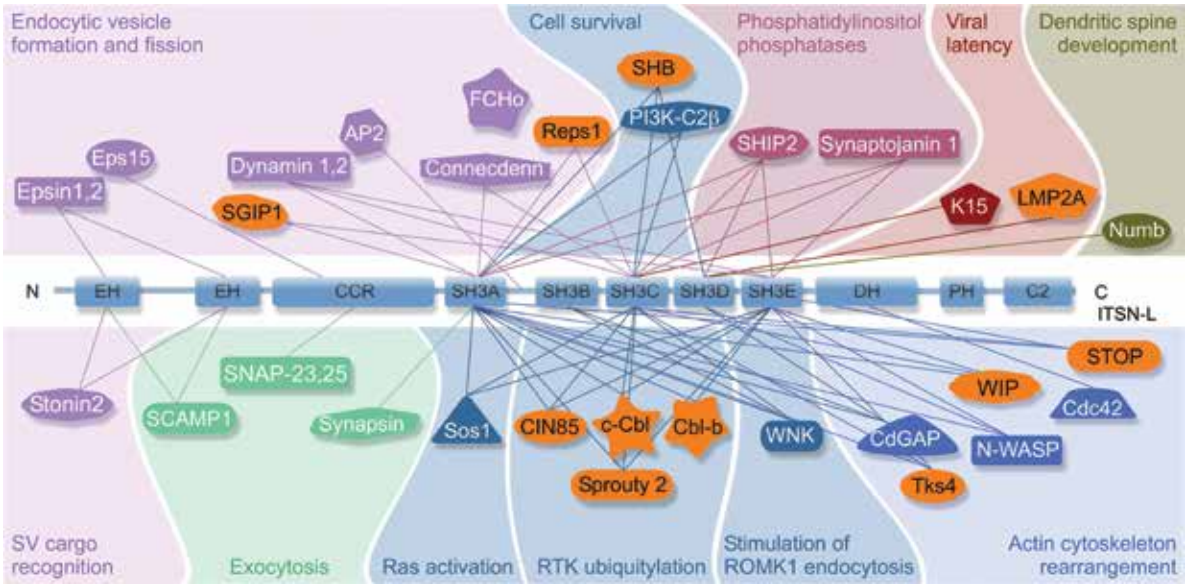


Fig. 1. Schematic representation of the proteins that interact with ITSNs

the endocytic anomalies reported in patients with Down syndrome and Alzheimer's disease. Our studies are focused on identification of novel ITSN interacting proteins and their functional significance, as well as determination of the mechanisms of posttranslational regulation of ITSN family. We have identified 11 novel protein partners of ITSN1 and ITSN2 implicated in endocytosis, cell signal transduction, actin cytoskeleton rearrangement and maintenance of virus latency. We have shown that latent membrane protein 2A (LMP2A) of Epstein–Barr virus forms a complex with ITSN1 and regulates its phosphorylation. ITSN2 was found to undergo tyrosine phosphorylation in a growth factor-dependent manner. Using Xenopus animal model we have demonstrated the role of ITSN2 in the coordinated changes of actin cytoskeleton during early embryonic development.

The role of alternative splicing in the modulation of functions of ITSN1

We identified six novel splicing events of ITSN1 transcripts that do not introduce premature termination codon. Different combinations of these splicing events could generate 28 isoforms of ITSN1. The isoforms differ in their domain organization, interaction with protein partners, localization in different tissues and stages of development. The role of alternative splicing was clearly demonstrated in case of ITSN1 microexon 20 splicing that provides a mechanism for tissue-specific control of protein–protein interactions in neurons. Using mutational analysis we found that neuron-specific insertion of a microexon 20 leads to regulation of the SH3A domain specificity due to the shifting of negatively charged amino acids towards the interaction interface. Neuron-specific isoform of the SH3A domain binds with significantly higher affinity endocytic proteins dynamin 1 and synaptojanin 1, as well as GTPase-activating protein CdGAP, while the ubiquitously expressed isoform preferentially interacts with signalling proteins Sos1 and Cbl. We also detected the shortest ITSN1 isoform with an alternative C-terminus encoded by exon 22a. We demonstrated intramolecular binding within ITSN1-22a that negatively regulates its association with the ubiquitin ligase Cbl.

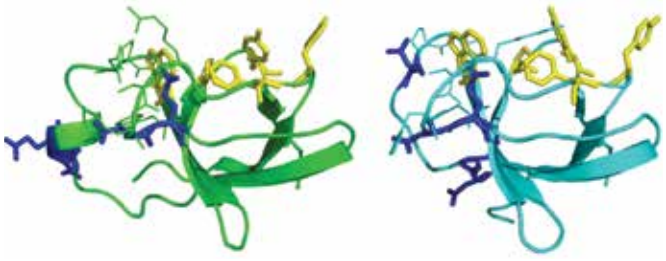


Fig. 2. 3D models of the ubiquitously expressed and neuron-specific form of the SH3A domain. Side chains of the conserved hydrophobic residues are depicted in yellow, negatively charged amino acids are in red.

Investigation of the role of ITSN1 in the synaptic transmission and plasticity

We identified a stable tubule-only polypeptide (STOP) as an ITSN1-binding protein using affinity chromatography followed by MALDI-TOF mass spectrometry. STOP and ITSN1 were shown to form a complex ***in vivo*** and to partially co-localize in rat primary hippocampal neurons. STOP is a microtubule-stabilizing protein that is required for several forms of synaptic plasticity in the hippocampus. Identification of this interaction raises the possibility of ITSN1 participation in this process. Elucidation of the functional significance of ITSN1-STOP interaction in neurons is in progress.

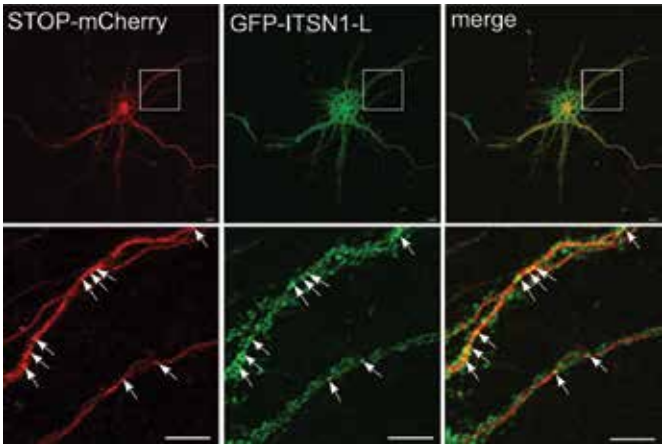


Fig. 3. Primary hippocampal neurons (14–21 DIV) were plated on coverslips and co-transfected by plasmid constructs encoding STOP-mCherry and GFP-ITSN1-L. The cells were fixed 48 h post-transfection. Images were obtained on Carl Zeiss LSM 510 META confocal microscope White arrows indicate structures positive for both proteins. Scale bars=5 µm.

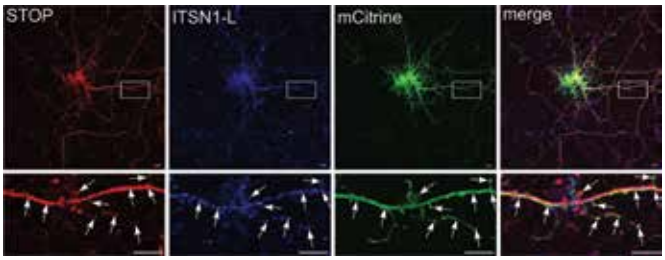


Fig. 4. Primary hippocampal neurons (14–21 DIV) were plated on coverslips and transfected with pmCitrine-N1. The cells were fixed in formaldehyde 48 h post-transfection, blocked in 2 % BSA and sequentially stained with anti-ITSN1 and anti-STOP antibodies, which were visualized by anti-rabbit Alexa 405 and anti-mouse Texas Red conjugated IgG, respectively. Scale bars=5 µm.

National Grants

Projects of National Academy of Sciences of Ukraine:

- 2012–2016 N 2.2.4.23 Project: "The role of protein-protein interactions in normal physiology and pathological processes" (scientific supervisor – Alla Rynditch)
- 2012–2013 NASU and RFBR (Russian Foundation for Basic Research) N P1/2012 Project: "Identification and characterization of eukaryotic adaptor proteins which interact with transcriptional and chromatin remodeling complexes" (scientific supervisor – Alla Rynditch)
- 2010–2014 N 20/12 Project: "Production of nanoconjugates for high sensitive detection of biomarkers of early stages of neurodegenerative and oncological diseases in plasma" (scientific supervisor – Alla Rynditch)
- 2010–2014 N 37/12 Project: "Functional characterization of novel prognostic breast cancer marker ITSN2" of NASU (scientific supervisor – Alla Rynditch)
- 2010–2014 N 113/12-H Project: "Development of high sensitive test system for Alzheimer's disease neuronal markers detection in blood plasma using nanoconjugates" of NASU (scientific supervisor – Alla Rynditch)

Projects of State Fund for Fundamental Researches:

- 2011–2013 State Key Laboratory of Molecular and Cell Biology N46/457 Project "Molecular mechanisms of cell signalling in normal and pathological conditions: the focus on ion channels"
- 2010–2013 N Ф33.4/001 Project: "Identification of perspective molecular biomarkers for monitoring neurodegenerative and oncological diseases of human" (scientific supervisor – M. A. Tukalo)

International Grants

- 2011–2014 7th Framework Programme (FP7) FP7-INCO-2011-6, ERA-WIDE Project: "Strengthening cooperation in Molecular Biomedicine between EU and UKRAINE", COMBIOM (scientific supervisor – Prof. A. Elskaya)

Collaboration

with Ukrainian organizations:

- O. V. Palladin Institute of Biochemistry, NASU (Kyiv)
- Bogomoletz Institute of Physiology, NASU (Kyiv)
- National University Lviv Polytechnic (Lviv)
- National Cancer Institute, Ministry of Health of Ukraine (Kyiv)
- State Institution "Institute of Urology of NAMS of Ukraine" (Kyiv)

with foreign organizations:

- Institute of Gene Biology, RAS (Moscow, Russia)
- Karolinska Institute (Stockholm, Sweden)
- Institute Jacques-Monod, CNRS (Paris, France)
- Institute Gustave-Roussy (Paris, France)
- Institute of Cellular and Integrative Neurosciences, CNRS (Strasbourg, France)
- International Institute of Molecular and Cell Biology (Warsaw, Poland)

Selected Publications:

1. Dergai O, Dergai M, Skrypkina I, et al. The LMP2A protein of Epstein-Barr virus regulates phosphorylation of ITSN1 and Shb adaptors by tyrosine kinases. ***Cell Signal.*** 2013; 25(1): 33–40.
2. Morderer D, Nikolaienko O, Skrypkina I, et al. Endocytic adaptor protein intersectin 1 forms a complex with microtubule stabilizer STOP in neurons. ***Gene.*** 2012; 505(2):360–4.
3. Novokhatska O, Dergai M, Houssin N, Tsyba L, Moreau J, Rynditch A. Intersectin 2 nucleotide exchange factor regulates Cdc42 activity during Xenopus early development. ***Biochem Biophys Res Commun.*** 2011; 408(4):663–8.
4. Dergai M, Skrypkina I, Dergai O, et al. Identification and characterization of a novel mammalian isoform of the endocytic adaptor ITSN1. ***Gene.*** 2011; 485(2):120–9.
5. Tsyba L, Nikolaienko O, Dergai O, et al. Intersectin multidomain adaptor proteins: regulation of functional diversity. ***Gene.*** 2011; 473(2):67–75.
6. Kropyvko S, Gerasymchuk D, Skrypkina I, et al. Structural diversity and differential expression of novel human intersectin 1 isoforms. ***Mol Biol Rep.*** 2010; 37(6):2789–96.
7. Nikolaienko O, Skrypkina I, Tsyba L, et al. Intersectin 1 forms a complex with adaptor protein Ruk/CIN85 ***in vivo*** independently of epidermal growth factor stimulation. ***Cell Signal.*** 2009; 21(5):753–9.
8. Tsyba L, Gryaznova T, Dergai O, et al. Alternative splicing affecting the SH3A domain controls the binding properties of intersectin 1 in neurons. ***Biochem Biophys Res Commun.*** 2008; 372(4):929–34.
9. Kvasha S, Gordiyuk V, Kondratov A, et al. Hypermethylation of the 5'CpG island of the FHIT gene in clear cell renal carcinomas. ***Cancer Lett.*** 2008; 265(2):250–7.
10. Razin SV, Iarovaia OV, Sjakste N, et al. Chromatin domains and regulation of transcription. ***J Mol Biol.*** 2007; 369(3): 597–607.

Department of Synthetic Bioregulators

Head
Igor Ya. Dubey
Dr.Sci. (bioorganic chemistry),
Senior Research Scientist
Phone: +380 (44) 526-07-09, 526-55-98
Fax: +380 (44) 526-07-59
E-mail: *dubey@imbg.org.ua*

Education and Degrees

1979–1984	Graduate Student, Department of Chemistry, Taras Shevchenko National University of Kyiv, Kyiv, Ukraine, M.Sc. (organic chemistry of natural compounds)
1984–1987	Postgraduate Student, Laboratory of Genetic Engineering, M. M. Shemyakin Institute of Bioorganic Chemistry, Moscow, Russia
1990	Ph.D. (bioorganic chemistry)
2009	Dr.Sci. (bioorganic chemistry)

Professional Employment

1987–1990	Junior Research Scientist, Laboratory of Nucleic Acids Chemistry (LNAC), Institute of Bioorganic Chemistry and Petrochemistry (IBCP), NASU, Kyiv, Ukraine
1990–1992	Research Scientist, LNAC, IBCP NASU, Kyiv, Ukraine
1992–1998	Senior Research Scientist, LNAC, IBCP NASU, Kyiv, Ukraine
1998–2009	Leading Research Scientist, Department of the Structure and Function of Nucleic Acids, IMBG NASU, Kyiv, Ukraine
Since 2009	Head of the Department of Synthetic Bioregulators, IMBG NASU, Kyiv, Ukraine

Membership

Since 2002	Member of International Society of Nucleosides, Nucleotides and Nucleic Acids
Since 2005	Editorial Board member of Journal “Ukrainica Bioorganica Acta” (Ukraine)
Since 2009	Member of the American Chemical Society
Since 2010	Editorial Board member of Journal “Biopolymers and Cell” (Ukraine)

Honours, Prizes, Awards

1992, 1993	Personal grants from the Soros International Science Foundation
1993	Honorary Diploma from the NASU
2001	State Prize of Ukraine in Science and Technology

Dubey I. Ya., Head of Departmernt
Alexeeva I. V., Leading Research Scientist, Ph.D.
Ilchenko M. M., Senior Research Scientist, Ph.D.
Kostenko O. M., Research Scientist, Ph.D.
Kostina V. G., Research Scientist, Ph.D.
Kryvorotenko D. V., Research Scientist, Ph.D.
Negrutska V. V., Research Scientist, Ph.D.
Dubey L. V., Junior Research Scientist
Kuziv Ya. B., Leading Engineer
Lysenko N. A., Leading Engineer
Davydenko G. Z., Technician

Research Area

- Design, synthesis and study of biologically active heterocyclic compounds
- Specific ligands of quadruplex DNA
- Chemistry and biological properties of nucleosides, nucleotides and oligonucleotides, their analogs and conjugates
- Polymers for biomedical applications and solid phase synthesis

Current Research Activities and Recent Achievements

Design of low-molecular ligands of G-quadruplexes and study on their interaction with quadruplex DNA. Telomerase inhibitors

Design, synthesis and structure optimization of heterocyclic ligands of G-quadruplex DNA (G4) is being performed. The enzymatic test system TRAP (Telomeric Repeat Amplification Protocol) has been introduced to analyze the effect of new compounds on telomerase activity *in vitro*. A number of compounds (porphyrins, cyanines, phenazine derivatives) have been found to efficiently inhibit telomerase at micromolar concentrations. Enzyme inhibition by these compounds is based on their binding to G-quadruplex structures of telomeric DNA (Fig. 1).

Spectral-fluorescent studies of the interaction of some inhibitors (first of all, porphyrin derivatives) with quadruplex DNA allowed determining their binding modes that include intercalation and external binding, as well as aggregation.

Simple G-quadruplex models, G-quartets and octets, have been developed that allowed computer modelling of ligand–quadruplex interactions using semi-empirical and non-empirical quantum chemistry approaches. An optimized model of full 22-mer DNA quadruplex Tel22 (PDB 1KF1) has been introduced to determine the geometries and energies of G4 complexes with low-molecular ligands. In addition to semi-empirical methods, a hybrid QM/MM approach ONIOM2 has been successfully applied for molecular modelling of this complex system (Fig. 2).

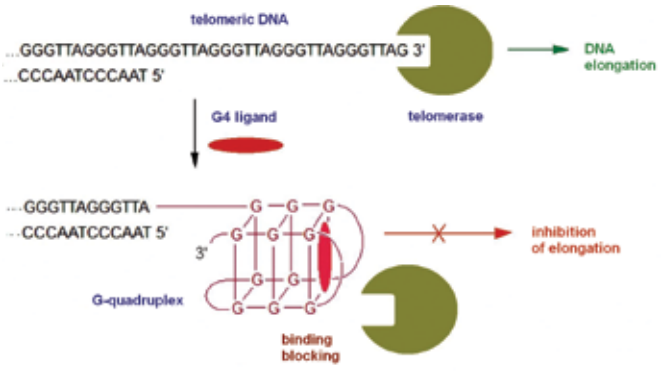


Fig. 1. Scheme of telomerase inhibition by specific ligands of quadruplex DNA

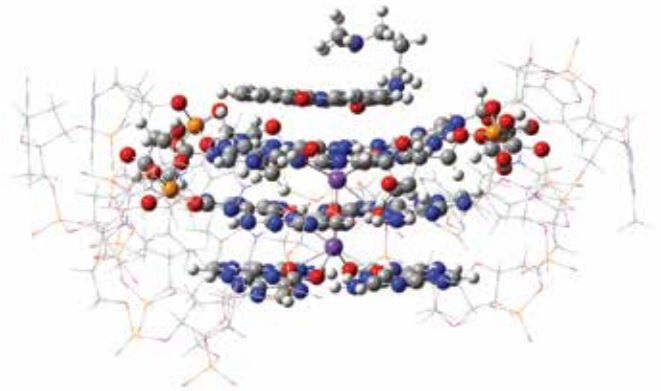


Fig. 2. Interaction of Tel22 DNA quadruplex with acridone derivative (ONIOM2 model; high layer atoms are presented as spheres)

Inhibitors of topoisomerase I based on condensed heterocyclic systems

A series of potential topoisomerase I inhibitors have been synthesized and tested in enzymatic DNA relaxation system *in vitro*. New compounds include benzimidazole and phenazine derivatives and amino-substituted cyanines. A number of compounds were found to completely inhibit the enzyme at 1-2 μM concentration. Investigation of their interaction with DNA and topoisomerase complex using biophysical and electrophoretic methods allowed identifying inhibitors that bind efficiently to DNA, as well as compounds interacting with enzyme or enzymatic complex. Some cyanines form highly fluorescent complexes with DNA and RNA and thus are suitable for sensitive visualization and quantification of picogram quantities of nucleic acids in electrophoretic gels (Fig. 3).

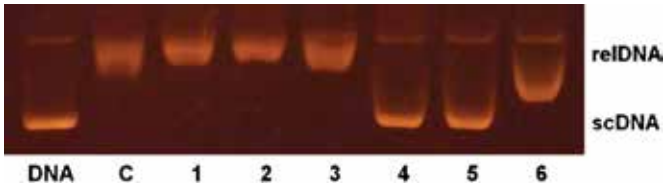


Fig. 3. Agarose gel analysis of relaxation of supercoiled pTZ19R plasmid DNA by *E. coli* topoisomerase I in the presence of compounds 1-6 (10 μM). C – control reaction (DNA+TopoI in the absence of inhibitors), relDNA and scDNA – relaxed and supercoiled DNA, respectively. Compounds 4, 5 efficiently inhibit enzymatic reaction

Modification, conjugation, labeling and immobilization of biomolecules

Novel aminespecific dioxaborine polymethine dye was successfully applied for the fluorescent labeling of proteins, both in the solution and in electrophoretic gels. Conjugation of this stable dye to proteins does not require any activation and results in ca. 80 fold emission increase that makes it a convenient label for protein staining in the gel (Fig. 4). We have developed efficient methods for the preparation of oligonucleotide conjugates with imidazo[4,5 b]phenazine dye. Spectroscopic studies of complexes formed by these conjugates with complementary oligonucleotides have demonstrated that the dye chromophore intercalates into the DNA duplex to stabilize it (Fig. 5,a). A series of new 3 hetarylcoumarin based reagents were prepared for the fluorescent labeling of oligonucleotides and other biomolecules.

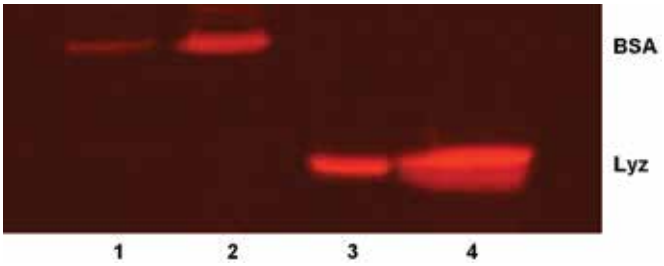


Fig. 4. PAGE analysis of proteins labeled with amine-reactive dioxaborine fluorescent dye. 1, 2 – bovine serum albumin (1 and 5 μg); 3, 4 – lysozyme (1 and 5 μg)

Polymer supports for affinity chromatography, drug delivery and solid phase synthesis

A number of new silica-based supports for solid phase oligonucleeotide synthesis containing efficient linker groups were proposed. Polymeric carriers for the delivery of various therapeutic oligonucleotides and proteins including e.g. interferons have been developed which are mainly based on functionalized and cross-linked polysaccharide matrices (dextran, hyaluronic acid, heparin etc) or polyethylene glycol. We have introduced a new simple method for the preparation of amine-modified polysaccharide hydrogels based on periodate oxidation of sugar residues followed by a partial cross-linking of the formed aldehyde groups with aliphatic diamines. Dextran hydrogel nanoconjugates containing covalently attached telomerase inhibitor, TMP3 porphyrin (drug content 10-20 μM/g), have been obtained. A number of organic and inorganic affinity sorbents with immobilized proteins, antibodies and low-molecular ligands were developed for biotechnology and molecular biology research (Fig. 5,b).

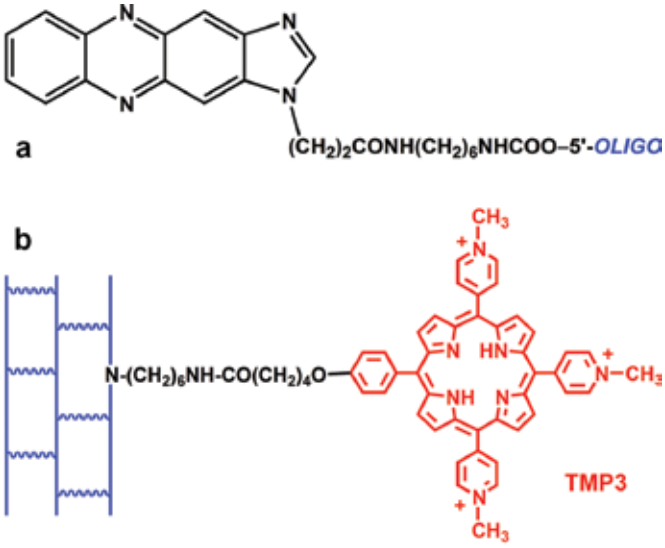


Fig. 5. The structure of bioconjugates: a – imidazophenazine-oligonucleotide; b – cross-linked dextran modified with telomerase inhibitor TMP3

National Grants

Projects of National Academy of Sciences of Ukraine

- 2012–2015 N 30–12 Project: "Design, synthesis and biological testing of new heterocyclic inhibitors of topoisomerase I as potential antitumor agents" (scientific supervisor – I. Ya. Dubey)
- 2010–2014 N 5.16.3.36 Project: "Nanoconjugates of novel antitumor agents based on the specific ligands of quadruplex DNA – inhibitors of telomerase" (scientific supervisor – I. Ya. Dubey)
- 2010–2014 N 43/10 Project: "New generation antitumor drugs based on heterocyclic telomerase inhibitors, specific ligands of quadruplex DNA" (scientific supervisor – I. Ya. Dubey)

Projects of State Fund for Fundamental Researches

- 2011–2012 N F40.4/078 Project: "Clathrochelates of transition metals as inhibitors of some enzymes of nucleic acids biosynthesis system and prospective antitumor and antiviral pharmaceuticals" (scientific supervisor – I. Ya. Dubey)

Collaboration

with Ukrainian organizations

- Institute of Organic Chemistry, NASU (Kyiv)
- Institute of Bioorganic Chemistry and Petrochemistry, NASU (Kyiv)
- B. Verkin Institute for Low Temperature Physics and Engineering, NASU (Kharkiv)
- R. E. Kavetsky Institute of Experimental Pathology, Oncology and Radiobiology, NASU (Kyiv)
- D. K. Zabolotny Institute of Microbiology and Virology, NASU (Kyiv)
- State Institution "L. V. Gromashevsky Institute of Epidemiology and Infectious Diseases of NAMS of Ukraine" (Kyiv)
- O. V. Palladin Institute of Biochemistry, NASU (Kyiv)
- V. M. Glushkov Institute of Cybernetics, NASU (Kyiv)
- Taras Shevchenko National University of Kyiv (Kyiv)

with foreign organizations

- Laboratory of Coordination Chemistry of CNRS (Toulouse, France)
- A. N. Nesmeyanov Institute of Organoelement Compounds, RAS (Moscow, Russia)
- Cranfield University, Cranfield Health (Cranfield, UK)
- Mississippi Center for Supercomputing Research (Jackson, USA)
- National Institute of Allergy and Infectious Diseases, National Institutes of Health (Bethesda, USA)

Selected publications

1. Lebed EG, Belov AS, Dolganov AV, Vologzhanina AV, et al. First clathrochelate iron and cobalt(II) tris-dioximates with reactive apical substituents. ***Inorg. Chem. Commun.*** 2013; 30:53–57.
2. Ryazanova O, Dubey L, Dubey I, Zozulya V. Spectroscopic study on the effect of imidazophenazine tethered to 5'-end of pentadecathymidilate on stability of poly(dA)·(dT)15 duplex. ***J Fluoresc.*** 2012; 22(6):1431–9.
3. Gerasov A, Shandura M, Kovtun Y, Losytskyy M, Negrutska V, Dubey I. Fluorescent labeling of proteins with amine-specific 1,3,2-(2H)-dioxaborine polymethine dye. ***Anal Biochem.*** 2012; 420(2):115–20.
4. Zozulya VN, Ryazanova OA, Voloshin IM, Dubey LV, Dubey IYa. Spectroscopic studies on binding of porphyrin-phenazine conjugate to intramolecular G-quadruplex formed by 22-mer oligonucleotide. ***Int Rev Biophys Chem.*** 2011; 2(4):1129.
5. Tkachuk ZYu, Dubey LV, Tkachuk VV, et al. Studying the interaction of 2'-5'-oligoadenylates and their analogues with proteins by fluorescence spectroscopy. ***Ukr. Biokhim. Zh.*** 2011; 83(1):45–53.
6. Palchykovska LG, Alexeeva IV, Negrutska VV, et al. ***In vitro*** transcription inhibition by 2-arylidene derivatives of thiazolo[3,2-a] benzimidazol-3(2H)-one. ***Biopolym. Cell.*** 2010; 26(6):508–11.
7. Piletsky SA, Piletska OV, Turner APF, Dubey I, Dubey L. Polymeric binding materials US Patent Application N20090082480, 26.03.2009.
8. De Logu A, Palchykovska LH, Kostina VH, et al. Novel N-aryl- and N-heteryl phenazine-1-carboxamides as potential agents for the treatment of infections sustained by drug-resistant and multidrug-resistant Mycobacterium tuberculosis. ***Int J Antimicrob Agents.*** 2009; 33(3):223–9.
9. Ryazanova O, Voloshin I, Dubey I, Dubey L, Zozulya V. Fluorescent studies on cooperative binding of cationic pheophorbide-a derivative to polyphosphate. ***Ann N Y Acad Sci.*** 2008;1130:293–9.
10. Stankiewicz-Drogon A, Palchykovska LG, Kostina VG, Alexeeva IV, Shved AD, Boguszewska-Chachulska AM. New acridone-4-carboxylic acid derivatives as potential inhibitors of hepatitis C virus infection. ***Bioorg Med Chem.*** 2008; 16(19):8846–52.

Department of Protein Engineering and Bioinformatics

Head
Olexander I. Kornelyuk
Dr.Sci. (molecular biology), Professor,
Corresponding Member of National Academy of Sciences of Ukraine
Phone: +380 (44) 526-55-89
Fax: +380 (44) 526-07-59
E-mail: *kornelyuk@imbg.org.ua*
Web: *proted.imbg.org.ua*, *moldyngrid.org*, *edu.imbg.org.ua*

Education and Degrees

1967–1972	Graduate Student, Faculty of Radiophysics, V. N. Karazin Kharkiv National University, Kharkiv, Ukraine, M.Sc. (biophysics)
1981	Ph.D. (molecular biology), Institute of Molecular Biology and Genetics (IMBG), NASU, Kyiv, Ukraine
1995	Dr.Sci. (molecular biology), IMBG NASU, Kyiv, Ukraine
1999	Professor (molecular biology)
2006	Corresponding Member of NASU

Professional Employment

1972–1975	Engineer, Junior Research Scientist, B. Verkin Institute for Low Temperature Physics and Engineering, NASU, Kharkiv, Ukraine
1975–1978	Postgraduate Student, IMBG NASU, Kyiv, Ukraine
1978–1987	Junior Research Scientist, Senior Research Scientist, Department of Structure and Functions of Nucleic Acid, IMBG NASU, Kyiv, Ukraine
1982–2004	Professor, Department of Molecular Biology, Faculty of Biology, Taras Shevchenko National University of Kyiv, Kyiv, Ukraine
1987–2000	Deputy Head of the Department, Group Leader, Department of Structure and Function of Nucleic Acids, IMBG NASU, Kyiv, Ukraine
Since 2001	Head of the Department of Protein Engineering, IMBG NASU, Kyiv, Ukraine
Since 2008	Professor, Head of the Division of Molecular Biology, Biophysics and Biotechnology, Institute of High Technologies, Taras Shevchenko National University of Kyiv, Kyiv, Ukraine

Membership

	Member of the Ukrainian Biochemical Society
	Member of the Ukrainian Biophysical Society
	Member of Scientific Council of the IMBG NASU
Since 1996	Member of the New York Academy of Sciences

Honours, Prizes, Awards

2003	Diploma of Honour and valuable gift from Mayor of Kyiv
2006	Diploma of Honour from Ministry of Education and Science of Ukraine
2008	State Prize of Ukraine in Science and Technology
2010	Diploma of the Verkhovna Rada of Ukraine
2012	Diploma of the best lecturer of the Institute of High Technologies of Taras Shevchenko National University of Kyiv

Kornelyuk O.I. Head of Department
Dragan A.I., Senior Research Scientist, Ph.D.
Kordysh M.O., Research Scientist, Ph.D.
Malyna A.E., Junior Research Scientist
Babenko L.A., Junior Research Scientist
Savytskyi O.V., Junior Research Scientist
Odynets K.O., Junior Research Scientist
Lozhko D.M., Junior Research Scientist
Mykuliak V.V., Leading Engineer
Andriychuck L.O., Ph.D. Student
Chysta S.V., Ph.D. Student

Research Area

- Molecular mechanisms of aminoacyl-tRNA synthetases and the functional role of protein dynamics
- Computational modeling of protein structure
- Molecular dynamics simulations of proteins and protein-nucleic acid complexes
- Grid technologies in molecular biology

Current Research Activities and Recent Achievements

Molecular dynamics simulations of proteins

Molecular dynamics simulation (MD) is a very important approach of structural bioinformatics due to the possibility of modeling of proteins and their complexes in solution. However, MD simulations are computationally very expensive and usually require a high processing power and huge storage space for trajectories. Grid computing is a very promising approach in order to encounter the limits of computational power of long MD simulations. Recently, in our department an all-atom model of full-length Hs tyrosyl-tRNA synthetase (TyrRS) was developed [1]. Long 100 ns MD simulations in grid of HsTyrRS (Fig. 1A). Domain binding interfaces also revealed

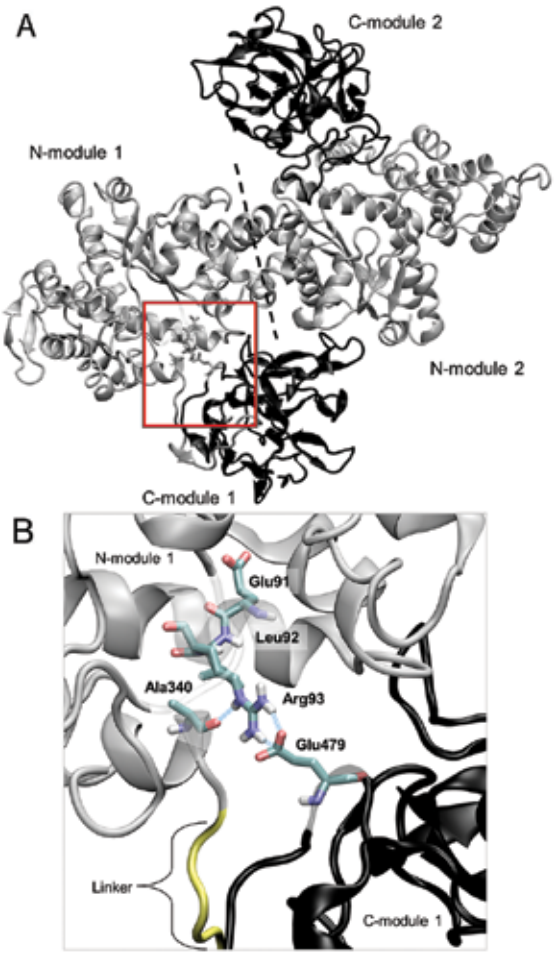


Fig. 1. Asymmetric structure and domain binding interfaces of human tyrosyl-tRNA synthetase after 100 ns molecular dynamics simulation (A). Typical configuration of the hydrogen bonds between the ELR cytokine motif of N-module and the C-module at simulation time of 96 ns (B)

the formation of H-bonds between ELR cytokine motif in TyrRS and its protection by C-module (Fig. 1B) [1].

Virtual laboratory MolDynGrid

MolDynGrid virtual laboratory (*http://moldyngrid.org*) was established for interdisciplinary studies in computational structural biology and bioinformatics (Fig. 2). The main objective of MolDynGrid project was to provide an effective infrastructure for automation of MD simulatons and trajectory analysis in Grid environment. Since 2013 Virtual Organization ***moldyngrid*** is a part of European Grid infrastructure and utilize LRZ Linux cluster resources in Germany (Fig. 2).

Fig. 2. Virtual Laboratory MolDynGrid as a part of Ukrainian National Grid-infrastructure (UNG) was established for interdisciplinary research in computational structural biology and bioinformatics. MolDynGrid usually utilizes computing elements (CE) of 8 clusters and storage elements (SE) of 2 clusters that correspond to ~2500 CPUs and ~100 TBytes of disk space, respectively.

MD simulations of HsTyrRS mutants associated with Charcot-Marie-Tooth disease

Several missence mutations G41R, E196K and 153-156delVKQV in were identified in families with CMT disease. MD simulations of CMT ***Hs***TyrRS mutants were performed in 100 ns time interval using MolDynGrid virtual laboratory services. A local β-sheet formation was observed in Rossmann fold insertion region in all 3 mutants (Fig. 3). Dispersion of CMT mutations in ***Hs***TyrRS could be understood in terms of long-range structural effects on dimer interface.

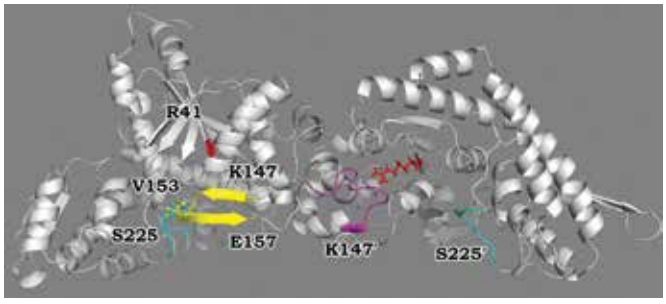


Fig. 3. Local β-sheet formation in K147-E157 region for 20-100 ns MD simulation time interval of in G41R mutant of H.sapiens TyrRS at Charcot-Marie-Tooth disease.

Solution structure of EMAP II cytokine

Solution structure of a novel EMAP II cytokine was determined by multidimentional NMR spectroscopy in collaboration with Institute of Biochemistry and Biophysics in Warsaw (Fig. 4). Solution structure of EMAP II cytokine revealed more exposed cytokine motif at N-terminal β-strand and highly flexible RNA binding surface.

Nanocomposite antitumor complexes of of EMAP II cytokine

Fundamentals of a new technology of antitumor of EMAP II cytokine production were developed in our department. EMAP II cytokine revealed antitumor activity on the growth of carcinoma of human prostate (Patent of Ukraine #33215). A novel nanocomposite complexes of EMAP II cytokine were proposed as novel anticancer drug (Patent of Ukraine #64374).

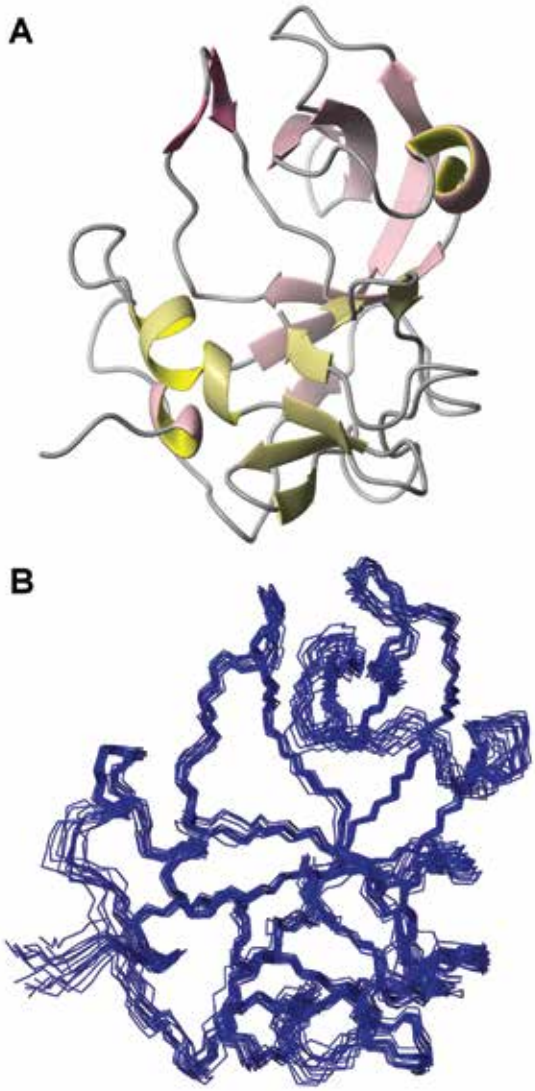


Fig. 4. Solution 3D structure of human EMAP II cytokine as determined by multidimentional NMR spectroscopy (A). Backbone view of ensemble of 20 low energy structures (B).

National Grants

Projects of the National Academy of Sciences of Ukraine:

- 2013–2015 N 49/2013 Project: "Development of intelligent supercomputer systems of SKIT family, ensuring their effective functioning and development of information technology, advanced mathematics, hardware and software to solve complex and complicated scientific problems (Intelligence)" (scientific supervisor – Kornelyuk O. I.)
- 2010–2014 N 34/2013 Project: "Fundamentals of a new technology of antitumor cytokine EMAP II production and its mutant forms with enhanced antiangiogenic effect" (scientific supervisor – Kornelyuk O. I.)
- 2009–2013 N 15/2013 Project: "Design and implementation of computer services for the analysis of molecular dynamics of proteins in the virtual laboratory MolDynGrid and its integration into the European grid infrastructure" (scientific supervisor – Kornelyuk O. I.)

Collaboration

with Ukrainian organizations:

- Taras Shevchenko National University of Kyiv (Kyiv)
- State Institution "V. P. Komisarenko Institute of Endocrinology and Metabolism of NAMS of Ukraine" (Kyiv)
- O. V. Palladin Institute of Biochemistry, NASU (Kyiv)
- National Technical University of Ukraine "Kyiv Polytechnic Institute" (Kyiv)

with foreign organizations:

- International Institute of Molecular and Cell Biology (Warsaw, Poland)
- Warsaw University, Chemistry Department (Warsaw, Poland)
- Institute of Biochemistry and Biophysics, PAS (Warsaw, Poland)
- Slovenian NMR Centre, National Institute of Chemistry (Ljubljana, Slovenia)

Selected Publications:

1. Savytskyi OV, Yesylevskyy SO, Kornelyuk AI. Asymmetric structure and domain binding interfaces of human tyrosyl-tRNA synthetase studied by molecular dynamics simulations. ***J Mol Recognit.*** 2013;26(2):113–20.
2. Lozhko D, Stanek J, Kazimierczuk K, et al. (1)H, (13)C, and (15)N chemical shifts assignments for human endothelial monocyte-activating polypeptide EMAP II. ***Biomol NMR Assign.*** 2013;7(1):25–9.
3. A method of modeling antitumor effect on prostate adenocarcinoma, Patent of Ukraine, № 70342 from 11.06.2012.
4. Reznikov AG, Chaykovskaya LV, Polyakova LI, Kornelyuk AI, Grygorenko VN. Cooperative antitumor effect of endothelial-monocyte activating polypeptide II and flutamide on human prostate cancer xenografts. ***Exp Oncol.*** 2011;33(4):231–4.
5. Yesylevskyy SO, Savytskyi OV, Odynets KA, Kornelyuk AI. Interdomain compactization in human tyrosyl-tRNA synthetase studied by the hierarchical rotations technique. ***Biophys Chem.*** 2011;154(2-3):90–8.
6. Nanocomposite anticancer drug, Patent of Ukraine № 64374 from 14.11.2011.
7. Salnikov A, Sliusar I, Sudakov O, Savytskyi O, Kornelyuk A. Virtual laboratory MolDynGrid as a part of scientific infrastructure for biomolecular simulations. ***International Journal of Computing.*** 2010;9(4):295–301.
8. Application of cytokine-like polypeptide EMAP-II as a tool that shows antitumor activity on the growth of carcinoma of the human prostate, Patent of Ukraine № 33215 from 19.02.2008.
9. Kordysh M, Kornelyuk A. Conformational flexibility of cytokine-like C-module of tyrosyl-tRNA synthetase monitored by Trp144 intrinsic fluorescence. ***J Fluoresc.*** 2006;16(5):705–11.
10. Kovalskyy D, Dubyna V, Mark AE, Kornelyuk A. A molecular dynamics study of the structural stability of HIV-1 protease under physiological conditions: the role of Na+ ions in stabilizing the active site. ***Proteins.*** 2005;58(2):450–8.

Department of Human Genomics

Head
Ludmyla A. Livshits
Dr.Sci (molecular genetics),
Professor
Phone: +380 (44) 526-07-69
Fax: +380 (44) 526-07-69
E-mail: *livshits@imbg.org.ua*

Education and Degrees

1969–1975	Graduate Student, Faculty of Biology, Taras Shevchenko National University of Kyiv, Kyiv, Ukraine
1991	Ph.D. (molecular biology), Institute of Molecular Biology and Genetics (IMBG), NASU, Kyiv, Ukraine
2001	Dr.Sci. (molecular genetics), IMBG NASU, Kyiv, Ukraine
2004	Full Professor

Professional Employment

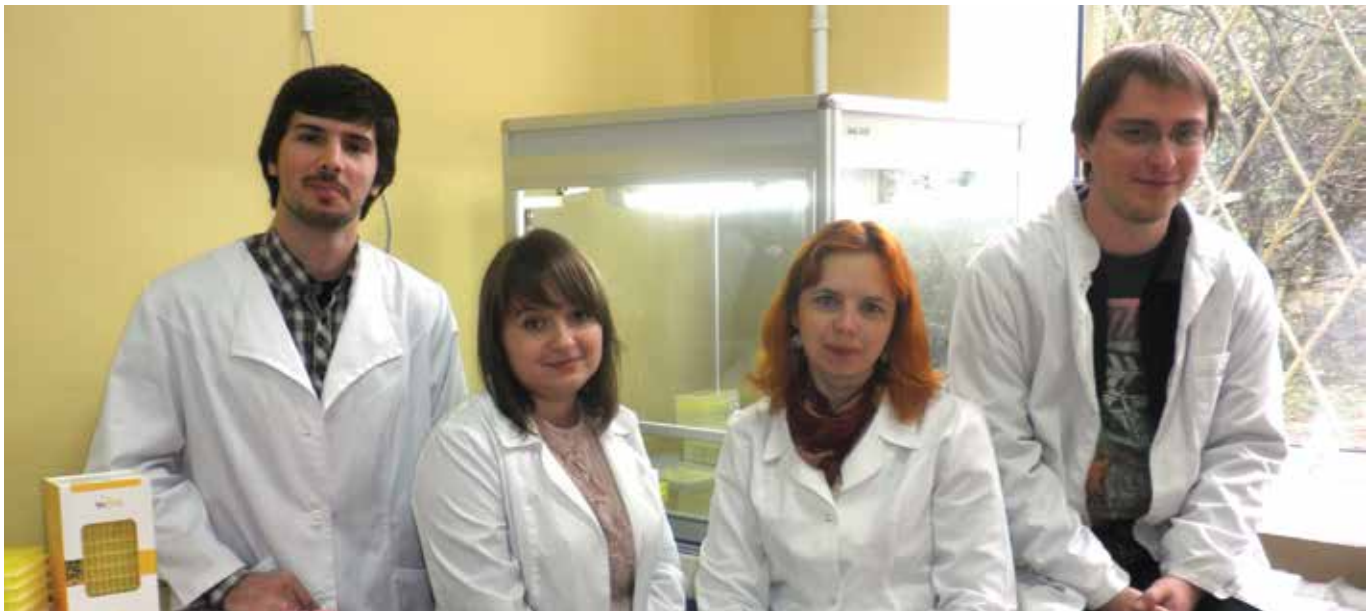
1973–2002	Researcher-assistant, Post-doc researcher, IMBG NASU, Kyiv, Ukraine
Since 2002	Head of the Department of Human Genomics, IMBG NASU, Kyiv, Ukraine

Membership

Since 2006	Editorial Board member of Journal “Biopolymers and Cell” (Ukraine)
Since 2006	Editorial Board member of Journal “Cytology and Genetics” (Ukraine)
Since 2006	Editorial Board member of Journal “Medical Aspects of Women Health” (Ukraine)
Since 2011	Editorial Board member “World Journal of Medical Genetics” (China)

Honours, Prizes, Awards

2006	Gershenson Award of National Academy of Sciences of Ukraine
2011	Diploma of the Verkhovna Rada of Ukraine



Livshits L. A., Head of Department
Kravchenko S. A., Senior Research Scientist, Ph.D.
Nechyporenko M. V., Research Scientist, Ph.D.
Pampukha V. M., Research Scientist, Ph.D.
Livshyts G. B., Research Scientist, Ph.D.
Hryshchenko N. V., Research Scientist, Ph.D.

Fesai O. A., Junior Research Scientist
Chernushyn S. Yu., Leading Engineer
Sodol R. I., Technician
Kucherenko A. M., Ph.D. Student
Gulkovskiy R. V., Ph.D. Student

Research Area

- Investigation of spectrum, origin, distribution and pathogenic effect of mutations and rearrangements in coding and non coding regions of human genome
- Development of test systems for hereditary diseases DNA diagnostics

Current Research Activities and Recent Achievements

Results have been obtained for spectrum, origin and mutation distribution, that cause rare monogenic diseases: cystic fibrosis, phenylketonuria, spinal muscular atrophy, Duchenne and Becker muscular dystrophy, haemophilia A, Charcot–Marie–Tooth type 1A, Huntington's disease, Martin-Bell syndrome, hemochromatosis, corneal dystrophy, syndromic intellectual disability. Molecular-genetic mechanisms of hereditary diseases pathogenesis are under investigation, as well as the genotype–phenotype association with these disease. Test system prototypes for the DNA diagnostics of following hereditary diseases: cystic fibrosis, phenylketonuria, spinal muscular atrophy, Martin-Bell syndrome, hemochromatosis, Charcot–Marie–Tooth type 1A and adrenogenital syndrome are being developed.

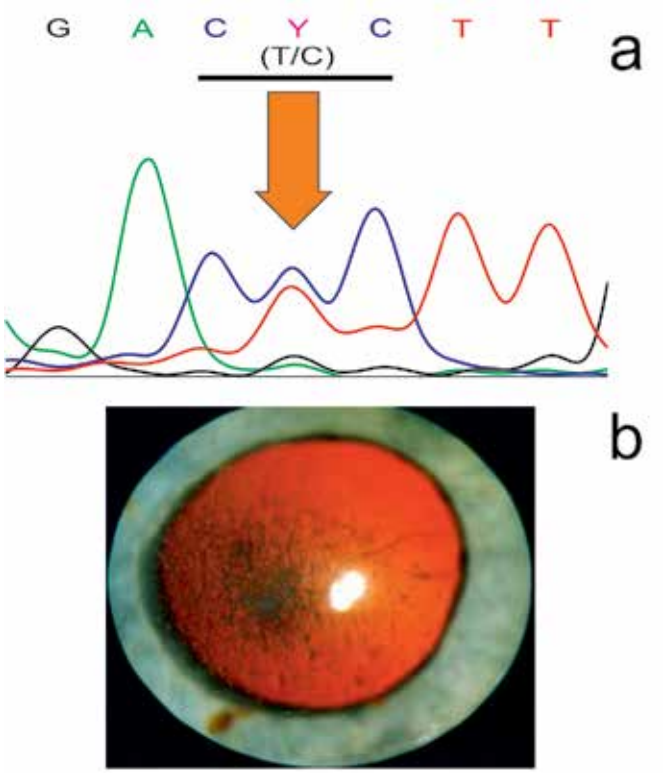


Fig. 1. Novel L558P mutation of the ***TGFBI*** gene (a) and new clinical phenotype of hereditary corneal dystrophy were identified (b)

Association of human genome DNA polymorphism with complex disorders such as ischemic stroke and reproductive health disorders (men and women infertility, pregnancy loss) is being studied. The genes encoding detoxication system, blood coagulation, folate cycle, vasoconstriction-dilation proteins, as well as sex hormones receptors and cytokines genes are studied as factors of hereditary susceptibility. Association between allelic variants of FSHR, ESR1, GSTP1 and FMR1 genes and diminished ovarian reserve, AR gene with spermatogenesis disorders was shown. It has been established that certain allelic variants of eNOS, ACE, F2, F7, MTHFR genes in combination with environmental conditions are factors of hereditary susceptibility for ischemic stroke events.

Study of human microsatellites loci as markers for genetic population structure and biological history analysis:

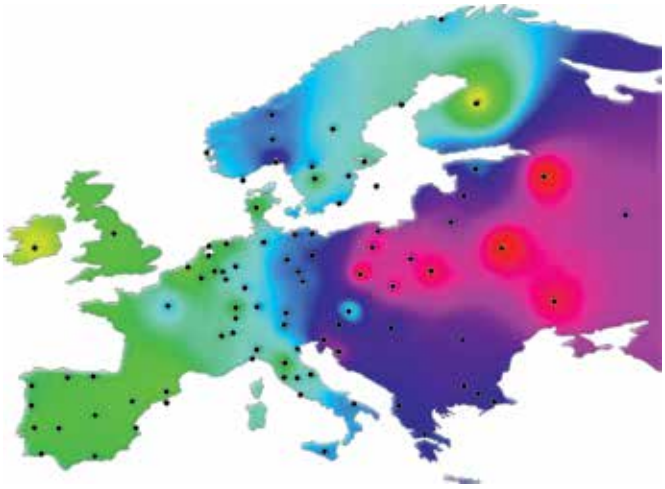


Fig. 2. Y-STR-haplotype comparative analysis between European populations

National Grants

Projects of National Academy of Sciences of Ukraine:

- 2012–2016 N 2.2.4.20 Project: "The development of pharmacogenetic approaches to assesse the peculiarities of hepatitis C and its treatment effectiveness" (scientific supervisor – Hovorun D. M.)
- 2011–2015 N 2.2.4.13 Project: "Allelic polymorphism of genes involved in monogenic and complex disorders" (scientific supervisor – Livshits L. A.)
- 2010–2014 N 29/10 Project: "Creating a prototype of test systems for DNA analysis of genome rearrangements that cause monogenic hereditary diseases and hereditary predisposition to the development of the most socially important human diseases" (scientific supervisor – Livshits L. A.)
- 2008–2009 N 22/08ДФ 15.04.2008 and N 22/09ДФ 06.04.2009 Bilateral Russian-Ukrainian research Project: "Stroke – a comparative study of molecular genetic risk factors in Russian and Ukranian populations" (scientific supervisor – Livshits L. A.)

International Grants

- 2011–2013 RM Y-STR consortium, Department of Forensic Molecular Biology, Erasmus MC University Medical Center Rotterdam, Netherlands Project: "Rapidly mutating Y-chromosomal STRs collaborative project" (scientific supervisor – Livshits L. A.)
- 2009–2012 7th Framework Programme (FP7) FP7-HEALTH, SICA, N 223692 Project: "Improving Diagnoses of Mental Retardation in Children in Eastern Europe and Central Asia through Genetic Characterisation and Bioinformatics/ Statistics", CHERISH (scientific supervisor – Livshits L. A.)

Collaboration:

with Ukrainian organizations:

- State Institution "Institute of Pediatrics, Obstetrics and Gynecology of NAMS of Ukraine" (Kyiv)
- State Institution "V. P. Komisarenko Institute of Endocrinology and Metabolism of NAMS of Ukraine" (Kyiv)
- State Institution "V. P. Filatov Institute of Eye Diseases and Tissue Therapy of NAMS of Ukraine" (Odessa)
- D. F. Chebotarev State Institute of Gerontology, NAMSU (Kyiv)
- Institute of Hereditary Pathology, NAMSU (Lviv)
- Clinic "Isida-IVF" (Kyiv)
- LTD "Sana-Med" (Kharkiv)
- Institute of Genetics of Human Reproduction (Kyiv)
- Charitable Fund "Children with spinal muscular atrophy" (Kharkiv)
- Crimean Republican Specialized Medical-Genetic Center (Symferopol)
- Khmelnitsky Regional Perinatal Centre (Khmelnitsky)
- Donetsk Regional Specialized Center of Medical Genetics and Prenatal Diagnosis (Donetsk)
- Donetsk Regional Centre of Maternity and Childhood Care (Donetsk)
- National Pirigov Memorial Medical University (Vinnitsa)

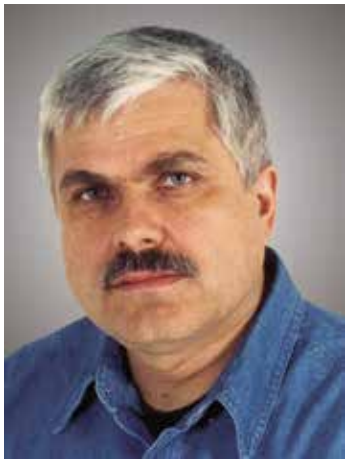
with foreign organizations:

- Cyprus Institute of Neurology and Genetics (Nicosia, Cyprus)
- University of Tartu (Tartu, Estonia)
- Vilnius University (Vilnius, Lithuania)
- University of Bologna (Bologna, Italy)
- Catholic University of Leuven, Center for Human Genetics (Leuven, Belgium)
- European Consortium for the Study of polymorphism DNA Y-chromosome (EU)
- Latvian Biomedical Research and Study Centre (Riga, Latvia)
- Erasmus Medical Centrum (Rotterdam, Netherlands)
- Technical University of Dresden. Institute of Clinical Genetics (Dresden, Germany)
- Institute of Molecular Genetics, RAS (Moscow, Russia)
- Federal State Budget Institution "V. I. Kulakov Research Center for Obstetrics, Gynecology and Perinatology" Ministry of Healthcare and Social Development of RF (Moscow, Russia)
- Institute of Chemical Biology and Fundamental Medicine, SB RAS (Novosibirsk, Russia)
- Research Institute of Medical Genetics, SB RAMS (Tomsk, Russia)

Selected Publications:

1. Livshyts G, Podlesnaja S, Kravchenko S, Livshits L. Association of PvuII polymorphism in ESR1 gene with impaired ovarian reserve in patients from Ukraine. ***Reprod Biol.*** 2013; 13(1): 96–9.
2. Hryshchenko NV, Bychkova GM, Livshyts GB, et al. Clinical Genealogical and Molecular Genetic Study of Patients with Mental Retardation. ***Cytol. Genet.*** 2012; 46(1):47–53.
3. Livshyts G, Podlesnaja S, Kravchenko S, Sudoma I, Livshits L. A distribution of two SNPs in exon 10 of the FSHR gene among the women with a diminished ovarian reserve in Ukraine. ***J Assist Reprod Genet.*** 2009; 26(1):29–34.
4. Pampukha VM, Kravchenko SA, Tereshchenko FA, Livshits LA, Drozhyna GI. Novel L558P mutation of the TGFBI gene found in Ukrainian families with atypical corneal dystrophy. ***Ophthalmologica.*** 2009; 223(3):207–14.
5. Tighe O, Dunican D, O'Neill C, Genetic diversity within the R408W phenylketonuria mutation lineages in Europe. ***Hum Mutat.*** 2003; 21(4):387–93.
6. Kravchenko SA, Slominskii PA, Bets LA, et al. Polymorphism of STR loci of the Y chromosome in three populations of eastern slavs from Belarus, Russia and Ukraine. ***Rus. J. Genetics.*** 2002; 38(1):80–6.
7. Livshits LA, Malyarchuk SG, Kravchenko SA, et al. Children of chernobyl cleanup workers do not show elevated rates of mutations in minisatellite alleles. ***Radiat Res.*** 2001; 155(1 Pt 1):74–80.
8. Rosser ZH, Zerjal T, Hurles ME, et al. Y-chromosomal diversity in Europe is clinal and influenced primarily by geography, rather than by language. ***Am J Hum Genet.*** 2000; 67(6):1526–43.
9. Dörk T, Macek M Jr, Mekus F, et al. Characterization of a novel 21-kb deletion, CFTRdele2,3 (21 kb), in the CFTR gene: a cystic fibrosis mutation of Slavic origin common in Central and East Europe. ***Hum Genet.*** 2000; 106(3):259–68.
10. Livshits LA, Kravchenko SA. Cystic Fibrosis in Ukraine: age, origin and tracing of the delta F508 mutation. ***Gene Geogr.*** 1996; 10(3):219–27.

Department of Medicinal Chemistry



Head
Sergiy M. Yarmoluk
Dr.Sci (bioorganic chemistry),
Professor
Phone: +380 (44) 522-24-58
Fax: +380 (44) 522-24-58
E-mail: *yarmolyuksm@gmail.com*

Education and Degrees

	Graduate Student, Taras Shevchenko National University of Kyiv, M.Sc. (chemistry of organic compounds)
1985–1989	Postgraduate Student, Novosibirsk Institute of Bioorganic Chemistry, Siberian Branch of Russian Academy of Sciences, Novosibirsk, Russia
1989	Ph.D. (chemistry)
2005	Dr.Sci. (chemistry), Institute of Molecular Biology and Genetics (IMBG), NASU, Kyiv, Ukraine
2006	Professor (bioorganic chemistry)

Professional Employment

1979–1983	Engineer, IMBG NASU
1983–1984	Senior Engineer, IMBG NASU
1984–1985	Senior Engineer, Institute of Bioorganic Chemistry, NASU, Kyiv, Ukraine
1985–1987	Senior Engineer, IMBG NASU
1987–1993	Junior Research Scientist, IMBG NASU
1993–1995	Research Scientist, IMBG NASU
1995–2002	Senior Research Scientist, IMBG NASU
2002–2003	Leading Research Scientist, IMBG NASU
Since 2003	Head of the Department of Medicinal Chemistry, IMBG NASU

Membership

Since 2004	Deputy Editor of Journal “Ukrainica Bioorganica Acta” (Ukraine)
	Editorial Board member of Journal “Biopolymers and Cell” (Ukraine)
Since 2008	Editorial Board member of Journal “Biotechnic and Histochemistry” (Sweden)

Honours, Prizes, Awards

2003	Diploma of Honour and valuable gift from Mayor of Kyiv
2005	Diploma of Honour from the Ministry of Education and Science of Ukraine
2012	National Prize of Autonomous Republic of Crimea

Yarmoluk S., Head of Department
Kovalska V., Senior Research Scientist, Ph.D.
Bdzhola V., Senior Research Scientist, Ph.D.
Kukharenko F., Senior Research Scientist, Ph.D.
Lukashov D., Senior Research Scientist, Ph.D.
Balanda F., Senior Research Scientist, Ph.D.
Losytskyy M., Research Scientist, Ph.D.
Fesun I., Research Scientist, Ph.D.
Borovikov O., Research Scientist, Ph.D.
Savitsky P., Research Scientist, Ph.D.
Briukhovetska N., Research Scientist, Ph.D.
Kharchenko V., Research Scientist
Sapelkin V., Junior Research Scientist
Prykhod'ko A., Junior Research Scientist
Tarnavsky S., Junior Research Scientist
Gryshchenko A., Junior Research Scientist
Ostrynska O., Junior Research Scientist
Volynets G., Junior Research Scientist, Ph.D.
Synyugin A., Junior Research Scientist
Chekanov M., Junior Research Scientist
Leshchenko V., Leading Engineer
Matiushok V., Leading Engineer
Kotey I., Leading Engineer
Borisenko I., Leading Engineer
Medyk P., Leading Engineer
Kachaput N., Leading Engineer
Chepurna P., Leading Engineer
Chubukov A., 1st Category Engineer
Prykhod'ko K., 2nd Category Engineer
Asyutina I., Engineer
Inshin D., Engineer
Shevchenko O., Engineer
Pacenko L., Technician
Gushel O., Technician

Research Area

- Computer-aided drug design
- Development of fluorescent probes for protein and nucleic acid detection

Current Research Activities and Recent Achievements

Development of low-molecular inhibitors of protein kinase CK2

In order to discover enzyme inhibitors we have performed screening program, using both ***in silico*** and ***in vitro*** approaches. AutoDock and DOCK software were used to conduct receptor-ligand flexible docking. The virtual screening experiments were carried out targeting the ATP binding site of protein kinase by searching compound library of about 100,000 compounds. Several hundreds ligands have been selected and taken for the kinase assay study. ***In vitro*** experiments allowed us to identify a number of novel classes of CK2 inhibitors – derivatives of (thieno[2,3-d]pyrimidin-4-ylthio)carboxylic acid, 3-carboxyquinoline and 4,5,6,7-tetrahalogeno-1,3-isoindolinedione. Guided by both molecular modeling and SAR analysis chemical optimization of the identified hit compounds allowed us significantly improve their activity and obtain nanomolar and selective CK2 inhibitors. The most active compound inhibiting CK2 belongs to flavonols (IC_{50}=9 nM). This inhibitor was called FLC21 (Fig. 1).

In silico design of ASK1 inhibitors

We have identified and characterized two classes of ASK1 inhibitors – 3H-naphtho[1,2,3-de]quinoline-2,7-diones and 2-thioxo-thiazolidin-4-ones. Structure-activity relationships of their derivatives have been studied and binding modes of these chemical classes have been predicted. The most perspective inhibitors were called NQDI-1 (IC50=3 μM) and PFTA-1 (IC50=650 nM) (Fig. 2). In our preliminary selectivity studies these compounds exhibited specific inhibitory activity towards ASK1. Compounds NQDI-1 and PFTA-1 demonstrated some cytoprotective effect in HEK293 during apoptosis induced by CHI3L2.

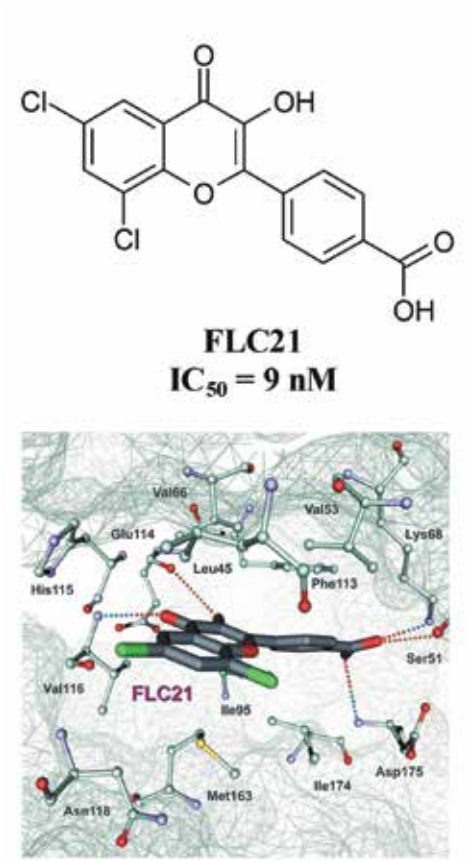


Fig. 1. Chemical structure of the inhibitor FLC21 and its binding mode with the active site of protein kinase CK2

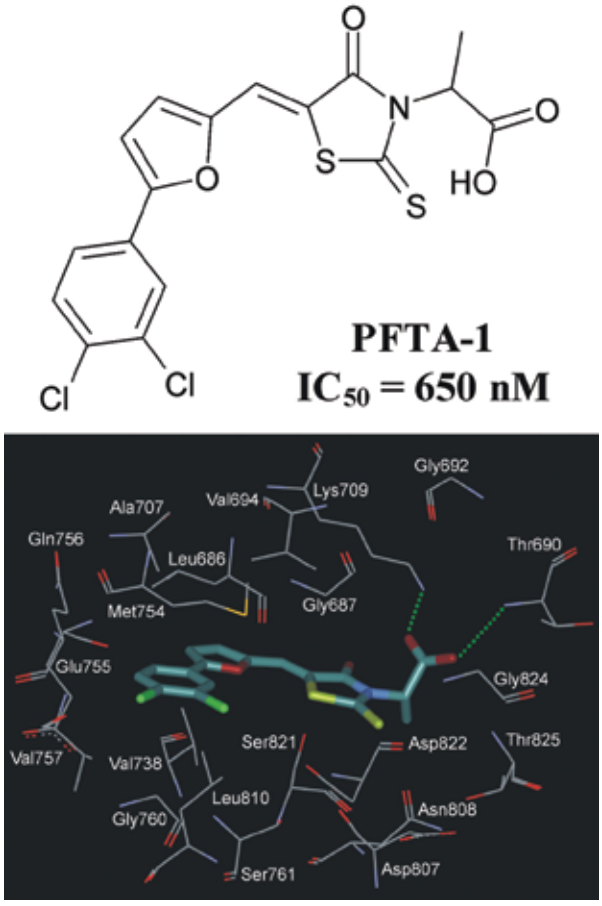


Fig. 2. Chemical structure of the inhibitor PFTA-1 and its binding mode with the active site of protein kinase ASK1

The search for inhibitors of protein kinase FGFR1

Using virtual screening experiments and *in vitro* tests we have found several classes of FGFR1 inhibitors: flavones, phenylbenzisoxazoles and aminopyrimidines. Then, we have performed ligand-oriented virtual screening and identified highly active inhibitors from the classes of oxindoles and quinazolines.

The development of new, efficient methods in the field of receptor-oriented high-throughput virtual screening

We have discovered and parameterized novel method for generating inexpensive and electrostatically reasonable atomic charges of organic compounds. This method is based on the principle of electronegativity relaxation of the Kirchhoff charge model. The new Kirchhoff charges were implemented into a virtual screening engine. To increase accuracy of ligand-receptor interaction energy evaluation the Kirchhoff charges calculation model was used for creating a new force field YFF. This force field is obtained by joining Van-der-Waals and bonded part of well-known MMFF94 with our charge calculation scheme.

Design of fluorescent probes for biomedical applications

We proposed cyanine dyes for detection of protein aggregation and for studies of globular protein conformational changes. Squaraine dyes have been proposed as efficient noncovalent fluorescent labels for albumins. Series of sensitive fluorescent probes for nonspecific detection of proteins in gels (Lucy506, Lucy569 and Lucy565) were developed by our scientists for Sigma-Aldrich Inc. In collaboration with Sigma-Aldrich we successfully developed novel high-sensitive fluorescent dye Nancy-520 for DNA visualization in gels. The dyes Cyan2 and Cyan40 can provide a highly sensitive method for detection and quantification of non-canonical DNA structures in genome and could be used for the search and development of agents that specifically bind with mentioned DNA motifs and inhibit their functioning (Fig. 3).

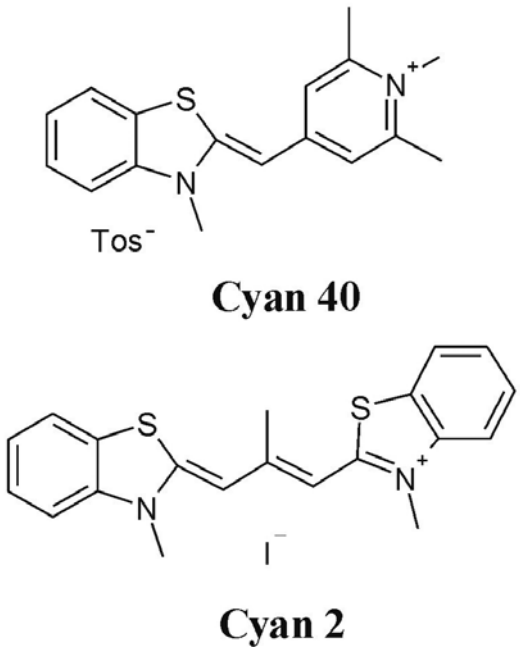


Fig. 3. Chemical structures of FGFR1 inhibitors

National Grants

Projects of National Academy of Sciences of Ukraine

- 2010–2014 N 30/12 Project: "Development of technologies of target-oriented search for inhibitors of aminoacyl-tRNA-synthetases with selective action against causative agents of human infective diseases" (scientific supervisor – Tukalo M. A.)

International Grants

- 2011–2013 STCU (Science and Technology Center in Ukraine) N 5508 Project: "Development of macrocyclic metallocomplexes – inhibitors of formation of amyloid fibril in neurodegenerative diseases" (scientific supervisor – Yarmoluk S. M.)
- 2010–2012 STCU N 5218 Project: "Rational search for inhibitors of aminoacyl-tRNA-synthetases with selective action against causative agent of tuberculosis" (scientific supervisor – Tukalo M. A.)
- 2011–2012 STCU N 5281 Project: "Development of fluorescent dyes for detection of oligomeric amyloid intermediates in neurodegenerative diseases" (scientific supervisor – Yarmoluk S. M.)

Collaboration

with Ukrainian organizations:

- Institute of Organic Chemistry, NASU, Colour and Structure of Organic Compounds Department (Kyiv)
- Institute of Bioorganic Chemistry and Petrochemistry, NASU (Kyiv)
- Institute for Scintillation Materials, NASU (Kharkiv)
- Vernadsky Institute of General and Inorganic Chemistry, NASU (Kyiv)

with foreign organizations:

- University Trás-os-Montes and Alto Douro (Vila Real, Portugal)
- University of Twente, Biophysical Engineering Group (Enschede, Netherlands)
- University of Southern Denmark (Denmark)
- University of Cologne (Cologne, Germany)
- Institute of Clinical Pharmacology, Hannover Medical School (Hannover, Germany)

Selected Publications:

1. Volynets G, Bdzhola V, Golub A, et al. Rational design of apoptosis signal-regulating kinase 1 inhibitors: discovering novel structural scaffold. ***Eur J Med Chem.*** 2013; 61:104–115.
2. Kovalska V, Losytskyy M, Chernii V, et al. Studies of anti-fibrillogenic activity of phthalocyanines of zirconium containing out-of-plane ligands. ***Bioorg Med Chem.*** 2012; 20(1):330–4.
3. Kovalska VB, Losytskyy MY, Tolmachev OI, et al. Tri- and penta-methine cyanine dyes for fluorescent detection of α-synuclein oligomeric aggregates. ***J Fluoresc.*** 2012; 22(6):1441–8.
4. Yakovenko OY, Li YY, Oliferenko AA, Vashchenko GM, Bdzhola VG, Jones SJ. Ab initio parameterization of YFF1, a universal force field for drug-design applications. ***J Mol Model.*** 2012;18(2):663–73.
5. Golub AG, Gurukumar KR, Basu A, et al. Discovery of new scaffolds for rational design of HCV NS5B polymerase inhibitors. ***Eur J Med Chem.*** 2012;58:258–64.
6. Volynets GP, Chekanov MO, Synyugin AR, et al. Identification of 3H-naphtho[1,2,3-de]quinoline-2,7-diones as inhibitors of apoptosis signal-regulating kinase 1 (ASK1). ***J Med Chem.*** 2011;54(8):2680–6.
7. Golub AG, Bdzhola VG, Briukhovetska NV, et al. Synthesis and biological evaluation of substituted (thieno[2,3-d]pyrimidin-4-ylthio)carboxylic acids as inhibitors of human protein kinase CK2. ***Eur J Med Chem.*** 2011;46(3):870–6.
8. Golub AG, Bdzhola VG, Briukhovetska NV, et al. Synthesis and biological evaluation of substituted (thieno[2,3-d]pyrimidin-4-ylthio)carboxylic acids as inhibitors of human protein kinase CK2. ***Eur J Med Chem.*** 2011;46(3):870–6.
9. Kramerov AA, Golub AG, Bdzhola VG, et al. Treatment of cultured human astrocytes and vascular endothelial cells with protein kinase CK2 inhibitors induces early changes in cell shape and cytoskeleton. ***Mol Cell Biochem.*** 2011;349(1–2):125–37.
10. Volkova KD, Kovalska VB, Losytskyy MYu, et al. Aza-substituted squaraines for the fluorescent detection of albumine. ***Dyes Pigments.*** 2011; 90(1):41–7.

Biotechnologies developed in Institute of Molecular Biology and Genetics of NASU

The identification of tumour-associated antigens for the development of modern immunological approaches of cancer diagnostics and treatment

Valeriy V. Filonenko, Dr.Sci., Professor

The identification of novel tumour-associated antigens (TAA) is a prerequisite for the creation of modern anti–tumour vaccines and specific antibodies against TAA.

While using SEREX methodology (serological identification of antigens by recombinant expression cloning) more than 60 tumour-associated antigens of melanoma, colon cancer, cancer of thyroid gland and breast cancer have been identified. The listed antigens could be used in future for both diagnosis and development of novel approaches in cancer treatment.

Up-to-date a number of mouse monoclonal antibodies have been generated against TAA and signaling molecules that undergo alteration at carcinogenesis. These are antibodies to S6K1, S6K2, TSC1, TSC2, Ki67, PTEN, mTOR, CK2, FGFR1, FGFR3. These antibodies could be used for detailed diagnosis and prognosis of oncological pathologies by immunohystochemical and serological approaches.

Large-scale search for biomarkers of epithelial tumors. The creation of different diagnostic and prognostic tools for cancer research

Alla V. Rynditch, Dr.Sci., Professor, Corresponding Member of NASU

Changes of circulating cell-free DNA levels in serum or plasma are associated with tumor burden and malignant progression. Moreover, cell-free DNA harbors genetic and epigenetic alterations specific to tumor DNA which opens the opportunity to detect tumor-specific signatures including the methylation of genes in patients serum. We evaluate the significance of cell-free DNA as a tumor marker by comparison of cell-free DNA concentration in cancer patients and healthy donors and hypermethylation determination of cancer associated genes in plasma.

We also investigate the expression and function of possible predictive marker for breast cancer – intersectin 2 (ITSN2). Intersectin 2 has been proposed to be used in diagnostic tests for prediction of disease outcome after breast cancer surgery and CMF-based chemotherapy. We analyze expression profiles of ITSN2 alternatively spliced isoforms in different groups of breast cancer patients and investigate the complex protein-interaction network of adaptor protein ITSN2. The results obtained during this project are expected to be helpful for the understanding of tumor progression mechanisms and will make a contribution to the approval of intersectin 2 as one of breast cancer predictive markers which could find clinical application.

From high-throughput analysis to creation of marker panel for diagnostics of different epithelial tumors

Volodymyr I. Kashuba, Dr.Sci., Senior Research Scientist

In Department of Molecular Oncogenetics the microarrays module was created that consists of tools for the designing and application of DNA microarrays. In collaborative work with Karolinska Institutet (Stockholm, Sweden) was developed NotI-microarray technology that allows performing global searching for genetic and epigenetic alterations of genes from chromosome 3 in epithelial tumors. The main advantages are simultaneous detection of genetic (deletions or amplifications) and epigenetic (methylation and demethylation) alterations. In current work we expanded an application of NotI-microarray from single chromosome to whole genome scanning of hot regions – genes which demonstrate altered expression in epithelial tumors (kidney, prostate, colon etc.). We use the dual-scan procedure which includes cross-platform analysis of gene expression with subsequent location of NotI-sites through human genome. It allows us to isolate genes which are used to design NotI-microchip for profiling hot regions in epithelial tumors. Subsequent application of selected set of genes is the creation of panel for detection of epithelial tumors by means identifying nucleic markers in body fluids.

The development of complex molecular diagnostics of chronic myelogenous and acute lymphoblastic leukemias using PCR and specific polyclonal antibodies

Stanislav S. Maliuta, Dr.Sci., Professor, Corresponding Member of NASU;
Gennadiy D. Telegeev, Dr.Sci., Senior Research Scientist

The method was tested on more than 200 patients from different regions of Ukraine after the corresponding assignment from The Institute of Hematology and Transfusiology of the Ministry of Public Health of Ukraine and from regional hematological departments. Entire correlation with other diagnostic tests and high sensivity (10^{-4}–10^{-5} of malignant cells) were obtained. This method gives the possibility to detect the type of translocation as well as to exclude false results completely. It is very important to estimate prognosis and therapy protocols.

Identification of transcryptome changes and detection of signatures for human brain tumor classification and diagnostics

Vadym M. Kavsan, Dr.Sci., Professor, Corresponding Member of NASU

Identification of changes in gene expression, potentially valuable for diagnostics and prognostics of glial tumors based

on hybridization analysis of DNA microarrays and serial analysis of gene expression (SAGE) using various statistical methods including artificial neural network. The selected genes, valuable for prognosis, will allow identifying gene expression signatures, suitable for molecular typing of glial tumors and prognostic evaluation of this devastating disease.

Nanoconjugates of natural biopolymers with antisense oligonucleotides for inhibition of glial tumors

Vadym M. Kavsan, Dr.Sci., Professor, Corresponding Member of NASU

The developing of new polyfunctional nanoconjugates for specific targeting the increased production of specific proteins associated with proliferative and angiogenic properties of tumor cells. Specific short interfering RNA (siRNA) or antisense morpholino oligonucleotides to ***CHI3L1*** and ***VEGF*** mRNAs, as well as bradykinin antagonists or azolidinone derivatives and known anticancer chemotherapeutic drug temozolomide in different combinations will be attached to polymer matrix, polymaleic acid (PMLA). Drug-releasing unit contains the antibody against transferrin receptor (TfR) to specifically target tumor cells and disulfide bonds, which are stable in the bloodstream and endosomes/lysosomes but are naturally cleaved by cytoplasmic glutathione.

Plasma cell-free DNA as diagnostic and prognostic tools for renal, colon cancers and metastatic uvenal melanoma

Inessa Ya. Skrypkina, Ph. D., Senior Research Scientist

The possible use of plasma cell-free DNA as an important source for detection of methylation status of sets of tumor-suppressor genes, tumor-specific mutations and levels of cell-free DNA concentration for determination early stages of oncological diseases are under investigation. Methodolodies of efficient isolation of cell-free DNA from plasma, and evaluation of its concentration by quantitative PCR assay, determination of methylation status of CpG islands of selected genes associated with development of renal and colon cancers as well as detection of mutations specific for metastatic uvenal melanoma by PCR combined with sequencing of the fragments specific for several genes associated with this disease are used for creation of cell-free DNA-based test systems. The advantages of such systems are: high sensitivity and specificity due to the usage of large number of tumor marker genes, the possibility to use the system for early diagnostics of cancer, noninvasive sampling methodology, no need in expensive equipment.

The establishment and operation of a laboratory module for microarray fabrication and application

Volodymyr I. Kashuba, Dr.Sci., Senior Research Scientist

- Diagnostics of different pathologies, especially, malignant tumors
- Early diagnostics of tumors of different localization sites
- Prognosis of the course of cancer disease and the response on therapy
- Diagnostic of pathogenic microorganisms.

Test systems for gene diagnostics of severe hereditary diseases and hereditary susceptibility to mass pathologies

Ludmila A. Livshits, Dr.Sci., Professor

The elaboration of diagnostic methods and individual components of the kits for DNA analysis of mutant genes that cause the development of the most widespread monogenic hereditary diseases in Ukraine (cystic fibrosis, phenylketonuria, spinal muscular atrophy, Duchenne muscular dystrophy, Martin-Bell syndrome (fragile X), haemophilia A, Huntington's disease, hereditary hemochromatosis, Charcot-Marie-Tooth neuropathy (CMT), hereditary corneal dystrophies, Stargardt's macular dystrophy), hereditary susceptibility to mass pathologies (cardiovascular, reproductive, inflammatory, endocrine) and genetic forms of men (azoospermia, oligospermia) and women (premature ovarian failure) infertility is being held. These diagnostic kits can be used for genetic testing, that is held during prenatal diagnostic, presymptomatic diagnostic, specification of the diagnosis, selective and mass screening for heterozygous carriers in the high risk groups and in the general population. The results of the genetic testing are the necessary requirements for prevention and precise treatment for the improvement of the demographic setting in Ukraine.

The list of the institutions, where the elaborated methods of the DNA-analysis for the clinical diagnostics of patients with cystic fibrosis, phenylketonuria, Martin-Bell syndrome (fragile X), hereditary hemochromatosis and secondary pathologies connected with it, Huntington's disease, Charcot-Marie-Tooth neuropathy, hereditary corneal dystrophies, genetical forms of men and women infertility, were used in: State Institution "Institute of Pediatrics, Obstetrics and Gynecology of NAMS of Ukraine" (Kyiv); State Institution "National Research Center for Radiation Medicine of NAMS of Ukraine" (Kyiv); State Institution "Institute of Neurosurgery named after A. P. Romodanov of NAMS of Ukraine" (Kyiv); State Institution "V. P. Filatov Institute of Eye Diseases and Tissue Therapy of NAMS of Ukraine" (Odessa); State Institution "Institute of Occupational Medicine of NAMS of Ukraine"(Kyiv); Institute of Hereditary Pathology, NAMSU (Lviv); Crimean Republican Specialized Medical-Genetic Center (Symferopol); Ukrainian Center of Diagnostics and Treatment of Cystic Fibrosis (Odesa); Interregional medical genetic centers in: Kyiv, Donetsk, Kharkiv, Odesa, Kryvyi Rig; Regional medical genetic consultations: Ternopilska, Rivnenska, Poltavska, Khmelnytska, Vinnytska, Volynska, Ivano-Frankivska, Chernigivska, Zakarpatska, Luganska; Clinic "Isida-IVF" (Kyiv).

Test system prototypes have been developed for the DNA diagnostics of following hereditary monogenic diseases: cystic fibrosis, phenylketonuria, spinal muscular atrophy, Martin-Bell syndrome and hemochromatosis.

We obtained the patent for utility model N64654 Method for DNA diagnostics of DF508 mutation in cystic fibrosis transmembrane regulator protein gene (CFTR) / O. O. Soloviov, S. A. Kravchenko, L. A. Livshits, owner IMBG NASU- № u 2011 05507, publ. 10.11.2011, Bulletin № 21.

The structural–based drug discovery against pathogenic bacteria

Mykhaylo A. Tukalo, Dr.Sci., Professor, Corresponding Member of NASU

We are using the differences between human and prokaryotic enzymes for the development of selective inhibitors as potential drugs against Mycobacterium tuberculosis, Enterococcus faecalis and Streptococcus pneumonia. The search strategy for antibacterial compounds is based on the combination of X-ray structural analysis of the target protein, computer modeling of the interaction of low-molecular ligands with the target protein and synthetic procedures of combinatorial chemistry.

Using flexible docking technique, the virtual screening of 100000 compounds from in-house collection (at the Department of Medicinal Chemistry) was carried out, and after ***in vitro*** and ***in vivo*** biological screening several inhibitors of ***M.tuberculosis*** leucyl-tRNA synthetase with anti-TB activity were selected.

The production of a novel antiangiogenic cytokine cendomap – C-module of tyrosyl-tRNA synthetase

Olexander I. Kornelyuk, Dr.Sci., Professor, Corresponding Member of NASU

A novel biotechnological product – cendomap cytokine has been obtained and tested ***in vitro***. The bacterial system for the expression and purification of cendomap cytokine permits to acquire a recombinant protein at preparative scale of about 10 mg from 1 liter of bacterial culture. Cendomap cytokine may be widely used as a mediator of procoagulant and antiangiogenic action, an inductor of apoptosis and, in perspective, as a putative antitumour medication for clinical oncology.

Development of a new multiplex PCR-based test for quick screening of staphylococci and methicillin-resistance in hospital patients with sepsis

Olena V. Moshynets, Ph.D., Research Scientist

Sepsis and its after effects are currently significant problems in hospital medicine. Sepsis is a potentially deadly medical condition characterized by a whole-body inflammatory state (so-called systemic inflammatory response syndrome) caused by severe infection. The early identification of sepsis and its effective treatment are especially important in some groups of patients, including new-borns, cancer and intensive care patients. Successful treatment depends on the early detection of the etiological agent of the sepsis as well as of any antibiotic resistances. Bacteria belonging to ***Staphylococcus*** spp. are the most important Gram-positive causative agents of sepsis and are responsible for ~ 50 % of sepsis and pyoinflammatory diseases in Ukraine. Up to 70 % of Ukrainian staphylococci are also methicillin resistant which is determined by the ***mec***-containing cassette SCCmec encoding the ***mecA*** β-lactam resistance gene. For this reason, a rapid screening assay is vitally needed in Ukraine for both the early identification of staphylococci and methicillin-resistance. Two PCR-based assays for ***Staphylococcus*** spp. and four for methicillin-resistance identification were tested using forty ***Staphylococcus*** spp. isolates obtained from patients of the Ukrainian Research Institute of Traumatology and Orthopedics, Ministry of Health of Ukraine (Kyiv). Based on the results of this work, a new "in house" multiplex PCR test for the direct simultaneous identification of ***Staphylococcus*** spp. and methicillin resistance was developed.

The molecular modeling and drug design: development of protein kinase inhibitors

Sergiy M. Yarmoluk, Dr.Sci,.Professor

Nowadays, drug development starts from identification of biological macromolecule target (DNA, or, in most cases, enzyme) responsible for certain disorder. By altering target activity with drug-like organic compounds it is possible to prevent or treat target-associated disorder(s). Among human proteins, protein kinase family has one of the greatest medico-biologic meanings.

Protein kinases constitute at least 2 % of the human genome and represent one of the most fundamental intracellular signaling mechanisms. Imbalances in kinase activity are a major factor in many disease states, especially those involving inflammatory and proliferative responses. Hence, protein kinases are attractive targets for drug research.

The goal of proposed project is the development of protein kinase inhibitors.

The approach used to develop protein kinase inhibitors is based on combined application of computer modeling techniques, directed organic synthesis and biological ***in vitro*** screening. The main points of the project are:

- Virtual screening of combinatorial libraries for hit compounds using docking and molecular dynamics simulation techniques, homology modeling (if required)
- Chemical synthesis of promising compounds
- ***In vitro*** testing of synthesized compounds and QSAR
- Lead compound identification
- Lead optimization

We have been developing the inhibitors of Casein Kinase 2 (CK 2) for about a year. At the time we have founded 3 lead compounds with IC_{50} up to 10^{-7} M and now perform their chemical optimization.

Telomerase inhibitors based on specific ligands of quadruplex DNA

Igor Ya. Dubey, Dr.Sci., Senior Research Scientist

Telomeric DNA and telomerase are currently considered promising targets for cancer therapy. Telomeres are guanine-rich DNA sequences located at the ends of the chromosomes that can adopt a specific quadruplex structures based on the stacks of G-quartets. Tumor cells express high levels of telomerase enzyme responsible of maintaining telomere length, whereas normal cells are devoid of telomerase activity. Small molecules that specifically bind to quadruplex structures

of telomeric DNA can inhibit telomerase in cancer cells and thus demonstrate antitumor properties.

We have prepared a series of novel cationic porphyrin derivatives, their metal complexes and conjugates as efficient G-quadruplex binders. Some of these compounds have been shown to inhibit telomerase activity ***in vitro*** at micro- and even nanomolar concentrations (TRAP assay). Metal complexes of cationic porphyrins conjugates with intercalating agents demonstrated antiproliferative activity in tumor cell culture with IC_{50} values in the range 6-11 μM comparable to those of doxorubicin and vincristine.

Antimycobacterial agents

Anatoly D. Shved, Dr.Sci., Senior Research Scientist

Sharp increase in human morbidity and mortality caused by tuberculosis becomes a worldwide problem. It is mainly associated with ***Mycobacterium tuberculosis*** strains which are resistant to one or more common therapeutic agents.

We have synthesized the library of new aryl and hetaryl amides of phenazine-1-carboxylic acid as potential antimycobacterial agents capable to inhibit RNA synthesis ***in vitro***. Their biological activity has been investigated in collaboration with Italian research team led by Prof. A. De Logu. A range of synthesized compounds have inhibited the growth of ***M.tuberculosis*** strains ***in vitro*** at concentrations equal or even lower than those for well-known antituberculosis drugs isoniazid, rifampicin and ethambutol. Moreover, some derivatives have shown high activity against clinical isolates with multiple drug resistance.

The baculovirus expression system for obtaining recombinant proteins

Olexander P. Solomko, Dr.Sci,.Professor

The system for an expression of recombinant proteins on the basis of a virus of nuclear polyhedrosis ***Malacosoma neustria*** (Mane) and cultures of insect cells was designed in the department of biochemical genetics. The designed system is the first baculovirus system of an expression of recombinant proteins in Ukraine. At present the similar systems find wide application in the world for obtaining recombinant proteins, including for effective antiviral vaccines. The laboratory procedure of obtaining biologically active recombinant human Prolactin with our system and commercial system was designed in cooperation with the Institute of biological chemistry and biophysics (Poland). The method is covered by the patent of Poland. Human Prolactin is a multifunctional hormon, which participates in many physiological processes. Recombinant Prolactin is necessary for effective tests – systems for detection of some pathologies (ischemia, renal failure, brain tumour). The protein can be used in therapy.

New anticancer and antiviral medications

Anatoliy I. Potopalsky, Ph.D., Docent

Medications amitozyn and izatizon with antiviral, antitumor and immunoregulating activity have been elaborated.

Amitozyn manifests antitumoral action and antimetastasis activity, but in comparison with existing medications it does not depress the hematosis processes, also it does not cause allergic reactions and has low toxicity. Amitozyn has undergone clinical tests in the system of the Ministry of Health of Ukraine. Izatizon has been approved in veterinary institutions and is studied in medicine. By using elaborated medications the technologies of diagnostics, prevention and treatment of plants agrobacterial cancer, non-vaccine prevention and treatment of mass virus diseases, increase in productivity of plants, mushrooms, useful insects (such as bees, silkworms, and oak silkworms), fish, poultry and animals have been worked out.

Based on the new biotechnology of the accelerated obtaining of new plant forms and varieties using nucleic acids preparations, such sorts as the feed lupine “Industrialny”, pumpkin “Kavbuz Zdorovyaga”, purple echinacea “Poliska Krasunya”, rye “Drevlyanske”, potato “Dzvin”, tomato “Ukrainski” were obtained and registered in the State Register for the Plant Varieties of Ukraine. The elaborations give the significant social and economic effect.

Biotechnology of the plant secondary metabolites production

Stanislav S. Maliuta, Dr.Sci., Professor, Corresponding Member of NASU

An efficient method for the increase of Glycyrrhizin (Gl) and flavonoids production from Ri-plasmids transformed licorice ***Glycyrrhiza sp.*** cells and hairy roots was developed. An endophyte mycorrhizal fungus was isolated from intact roots of the medical plant ***Potentila alba L.*** as a potential elicitor to stimulate the total biosynthesis of the secondary metabolites in transformed licorice cells and roots by 1.5 fold.

Glycyrrhizin (triterpen saponin) production in the biotechnological way is very perspective as a source of the natural sweetener for the diabetes patients, and its aglycone Glycyrrhizic acid has shown the inhibiting II-β-dehydrohynase (hepaprotective effect in liver and kindneys tissues ***in vitro*** as well as ***in vivo***). Flavonoids, 18-dehydroglycyrrhizic acid and Glycyrrhizinic acid have shown antioxidation effect. It is their anti-inflammatory effect by which one can explain their positive therapeutic effect on lungs and liver irradiated impact pathology, and note the anti-sclerotic, anti-inflammatory, anti-cancer, and anti-ulcer activity of licorice metabolites.

The application of lectins from medicinal plants for biomedical research

Iryna S. Karpova, Dr.Sci., Senior Research Scientist

The lectins are a large group of carbohydrate-binding proteins, which can specifically recognize receptors exposed on cellular membranes in all types of living organisms. In humans endogenic lectins play their role in fertilization, immune response, antiviral and antibacterial protection, clearance, apoptosis etc. Plant exogenic lectins have been widely used as a tool in the investigation of animal membranes which differ

in their surface sugars: in case of immuno-haematological and endocrine diseases, developing infection or neoplastic process and other pathological changes. In the United States some lectins are commercially used for purging of bone marrow for transplantations in leukemia patients. An original technology of medicinal plant lectins isolation and purification has been developed. The new approach to receptor diagnostics of different pathologies (such as acute radiation sickness and thyroid gland diseases) using a panel of lectins isolated from medicinal plants in reaction of haemagglutination with data processing has been proposed. The method is based on the unique properties of lectins to indicate the deviations in membrane structure. The endogenous misbalance of lectins occurs in a pathological state and the lectino-test as its indicator has been proposed. The application of herbal lectins in diagnostics and individual approaches to therapy is being developed. Contemporary research is devoted to further studying of peculiarities of medicinal plants lectins: their adhesive, immunomodulating and antitumour activity, and possible usage for stem cell identification and separation.

Unique cell strains of rare medicinal plants have been generated that produce bioactive compounds important for medicine and pharmacology

Victor A. Kunakh, Dr.Sci., Professor, Corresponding Member of NASU;
Oksana O. Poronnik, Ph.D.;
Ludmila P. Mozhylevska; Volodimyr I. Adonin

Technology for production of Rauwolfia serpentina cultured cells with high content of ajmaline, that is used as a basic compound for antiarrhythmic and antihypertensive drugs. The technology for production of biomass with ajmaline content of about 1.0 % was tested under the industrial conditions.

Technology for biomass production and micropropagation of Ungernia victoris, perennial plant, endemic of Pamir that is used as a source of alkaloids galantamine and licoryne. Preparations based on galantamine are used for treatment of myasthenia progressive muscle dystrophy (myopathia), radiculitis. Licoryne derivatives are used to treat the chronic and acute inflammations of respiratory system, and bronchial asthma.

Technology for Panax ginseng cell biomass production for use in the manufacturing of medicines, nutritional supplements and cosmetics. Techniques have been developed for regulation of ginsenosides biosynthesis as well as their quantitative and qualitative composition in callus biomass.

Technology for production of Echium plantagineum cultured cells biomass with high content of shikonin, which is used as a color additive, medical remedy with antitumor, antibacterial, anti-inflammation, wound healing and antiviral activities, and a compound of cosmetics with medicinal properties.

A new test system “Escherichia coli – bacteriophage λ” have been developed to study the mutagenic and antimutagenic properties of biologically active compounds (V. A. Kunakh, T. P. Pererva, H. Yu. Miriuta, L. P. Mozhylevska)

Nanocellulose-based composites

Anatoliy I. Potopalsky, Ph.D., Docent ;
Nataliia O. Kozyrovska, Ph.D., Senior Research Scientist

Antimicrobial biodegradable composites based on nanocellulose and antimicrobials (isatison; polyhexamethylenguanidine chloride, PHMG-Cl) for use in medical practice have been designed. New composite of nanocellulose with multipurpose drug izatizon might be effective for a treatment of wound surfaces, ulcers and burns, melanoma, as well as against herpes and other viral infections of the skin. The PHMG-Cl prevents the biofilm formation by microorganisms and could be further exploited as a wound dressing for healing and the regeneration of a scarless skin.

A concept of low-cost technology of growing and utilizing pioneer plants in a lunar garden

Nataliia O. Kozyrovska, Ph.D., Senior Research Scientist

On the base of the model system ***Tagetes patula L.*** **–** anorthosite (analog of lunar soil) – a consortium of microorganisms, a concept of low-cost technology of growing and utilizing pioneer plants in a lunar garden has been developed for the first time. The putative scenario anticipates using a local material – regolith – and a consortium of rationally assembled microorganisms (biomobilizing plant-essential elements, plant growth promoting, plant protection from abiotic stressors, etc.).

Test-system for detection of potato viruses VPX, VPY, VPM, and viroid by RT-PCR

Nataliia O. Kozyrovska, Ph.D., Senior Research Scientist

Specific for conditions of Ukraine phytoviruses VPX, VPY, VPM and viroid have been isolated on the basis of potato disease symptoms and proved by ELISA and TEM. A set of the test system consists of primers pairs specific to the gene, encoding virus capsid protein, designed for either phytovirus, and positive controls, fragments of capsid protein, gene have been cloned in plasmid. The set for phytoviruses detection was tested at the Institute for Potato Research of the National Academy of Agricultural Sciences, NAASU (t. Nemishaeve, Kyiv region).

Bacterial inoculant KLEPS®

Nataliia O. Kozyrovska, Ph.D., Senior Research Scientist

The first bacterial inoculant KLEPS®, which provides the plant with biological nitrogen, growth promoters and enhances its defense system, has been designed and registered in Ukraine. The inoculant is recommended for pre-treatment of seeds of cereal and vegetable crops. KLEPS® increases yield by 10–40 %, forms an extensive root system that provides early flowering and ripening crops, reduces the incidence of cultures. Application of KLEPS® reduces the use of mineral nitrogen fertilizers and pesticides by 70 % and allows protection of the environment.

Express method of the *Klebsiella oxytoca* authentication by PCR

Nataliia O. Kozyrovska, Ph.D., Senior Research Scientist

Unique sequence of the ***pehX*** gene we cloned from industrial strain of bacterium ***K. oxytoca*** IMBG26 enabled us to develop a method of the bacterium identification by polymerase chain reaction. Rapid, sensitive and specific test is recommended for discrimination of ***K. oxytoca*** between similar types of bacteria of the genus ***Klebsiella***, as well as for the environmental monitoring of ***K. oxytoca***.

Technology of the use of bacterial inoculants for adaptation of potato *in vitro* to *post vitro* conditions and protection of plants from pathogens in the commercial production of potatoes

Nataliia O. Kozyrovska, Ph.D., Senior Research Scientist

The principles of the use of biological products that contain beneficial bacteria for plant protection from pathogens in the process of adaptation of potato ***in vitro*** plants to ***post vitro*** conditions have been elaborated.

Technology of bacteria-assisted phytostabilization of heavy metals

Nataliia O. Kozyrovska, Ph.D., Senior Research Scientist

To implement the plant-microbe system to a variety of polluted environments for a remediation, a flexible and hardy plant-bacteria system is designed. A rationally assembled bacterial consortium for a multipurpose application at different level of heavy metal (HM) pollution in the soil is proven in the field model and natural environments. In the case of aerogenic HM pollution (transport and industrial off-gases) bacteria promote growing clean crops. On the other hand, the consortium provides environmentally appropriate technology for HM phytostabilization on moderate and extremely polluted lands near industrial enterprises and mines.

Gene and Cell Therapy

Vitalii A. Kordium, Dr.Sci., Professor,
Corresponding Member of NASU,
Full Member of NAMSU

The main directions of the department activity are the study of fundamental basis of aged and sick organism renewal, the development and usage of gene and cell technologies for damaged cells and hereditary material replacement, as well as biotechnological obtaining o therapeutic recombinant proteins.

Approaches to the obtaining of mesenchymal stem cells from Wharton jelly for further clinical usage were developed. MSC were characterized morphologically, by surface and inner markers, ability to differentiate in first 6 passages. It has been shown that practically all the characteristics change after the 3rd passage in cell culture confirming that only 1-2 passages answer the requirements for the clinical use.

Scientific approaches for gene therapy technologies of multifactor diseases have been developed. They are based on the introduction of recombinant genetic material into an organism with the aim of pathologies correction. Effective non viral systems for target therapeutic genes delivery to the cells and organs were created. The systems for the targeted therapeutic genes delivery into specific cells and tissues that will ensure high-level transgene expression in organism are developed. Positive results of gene therapy for pathologies, namely artificially induced insulin – dependent diabetes mellitus and atherosclerosis – were obtained on laboratory animals.

Today, the most promising way to deliver in organism different cells, which are the source of therapeutic agents (hormones, growth factors, cytokines), is the encapsulation of such cells in semipermeable microcapsules or another devices. In the scope of department research the approaches to the delivery of genetically engineered cells that produce several cytokines (LIF, FGF-2, IL-10) are developed.

Significant success was achieved in genetic engineering biotechnology. The scientists of the department developed the unique method of recombinant proteins obtaining in ***E. coli*** with the use of λ phage. This method has no world analogues, it provides for target product obtaining in high concentration in active soluble form directly in culture medium. Its effectiveness for obtaining proteins of both pro- and eukaryotic origin was shown. Industrial technologies for such products as ß-galactosidase, human α-2a and α-2b interferon, human growth hormone, etc. obtaining were developed according to this method. Preparation of recombinant human α-2a interferon, under the trademark “Laferon” is being produced in Ukraine for more than 10 years, and is successfully used in medical practice.

Today the problem of ischemia of renal parenchyma is an important issue for diagnostics and development of further therapeutic treatment of patient with renal pathology. The experimental data obtained revealed that the injection of complex of bFGF with our developed carrier (that increases its half-life in tissues) led to the enhancement of blood perfusion in ischemic kidney under condition of chronic ischemia and protects contralateral kidney from the development of irreversible sclerotic changes.

Theoretical basis of damaged hereditary material substitution due to exchange of genetic material between cells, including stem cells, is developed. Now it is under experimental examination.

Development of technology for repairing injured liver function by MSC transplantation

Svetlana Yu. Rymar, Ph.D., Senior Research Scientist

Liver disease is one of the leading death causes (4th rank) in Ukraine. In the world Ukraine occupies 9th rank in the liver disease mortality. Currently orthotopic liver transplantation represents the only therapeutic option for patients with advanced liver diseases and hepatic failure. Now the cell therapy has been proposed as an alternative way to treat liver injury. Chronic liver injury induces liver fibrosis resulted in cirrhosis terminated with hepatocellular carcinoma. In this investigation the process of liver injury causes by CCl4 to

laboratory rats. The characteristics of cirrhosis development in rats are similar to human cirrhosis. Human cord MSC isolated and cultivated in our department may be used for the transplantation. Based on the liver injury dynamics data, a detailed protocol of human cord MSC transplantation will be developed. The protocol will result in an effective rescue experimental liver failure and contributes to a liver regeneration and offers a potentially alternative therapy for treatment of liver diseases.

The development of skin equivalents on the base of human stem cells cultivated on special carriers *in vitro* for treatment of massive burns

Lyubov L. Lukash, Dr.Sci., Professor

The biotechnology of skin equivalents obtaining with the usage of adult human mesenchymal stem cells has been developed (patent of Ukraine UA N 82583). Particularly the database of characterized cell lines originated from samples of embryonic and adult human tissues and compositions of cultural mediums, carriers and hydrogel substrates applied at the production and optimization of skin transplantants is in progress. There is also in progress of creating a cellular bank, which will be connected with Euro Skin Bank as a central provider of biomaterials for treatment of burns in the USA and Europe, and the international organization Bone Marrow Donor Worldwide which supplies the transplantations of bone marrow. The joint activity with the Center of Thermal Burns and Plastic Surgery of the Ukrainian Ministry of Health has been initiated on the introduction of the developed by the Institute skin equivalents, based on human fibroblasts, into medical practice.

The development and creation of electrochemical and optical biosensors for medicine

Anna V. El'skaya, Dr.Sci., Professor, Full Member of NASU; Alexei P. Soldatkin, Dr.Sci., Professor, Corresponding Member of NASU

- Development of potentiometric mono- and multibiosensors specific to glucose, urea and creatinine for the medical diagnostics and monitoring of hemodialysis
- Development of amperometric microbiosensors for *in vivo* determination of main metabolites (glucose, lactate, ATP) and monitoring of some neurotransmitters (acetyl choline, choline, glutamate and D-serine) in brain of mammals
- Development of immuno- and DNA-sensors based on surface plasmon resonance for revealing some mutations and pathogenic microorganisms.

The development and creation of analytical devices based on electrochemical mono- and multibiosensors for environment monitoring

Anna V. El'skaya, Dr.Sci., Professor, Full Member of NASU; Tatiana A. Sergeeva, Dr.Sci.; Yaroslav I. Korpan, Ph.D.

- Development of potentio- and conductometric enzyme mono- and multibiosensors for direct and inhibitor analyses of single toxicants and their mixtures (herbicides, pesticides, steroidal glycoalcaloids, formaldehyde, heavy metal ions, etc.)
- Development of technology of production of synthetic analogues of biological receptors (polymers-biomimics) and creation on their basis of a number of electrochemical sensors (conductometric, capacitive and amperometric) for determination of herbicides of triazine type.

The development and creation of electrochemical biosensors for biotechnological processes and foodstuff control

Alexei P. Soldatkin, Dr.Sci., Professor, Corresponding Member of NASU; Sergiy Dzyadevych, Dr.Sci., Professor

- Development of amperometric biosensors and sensors arrays for determination of glucose, glycerol, ethyl and lactate in wine samples
- Development of potentio- and conductometric biosensors for penicillin determination
- Development of the potentiometric enzyme sensor based on inhibitor analysis for determination of nature neurotoxic substances – glycoalcaloids – in potato, tomatoes and other foodstuff of solanaceous type
- Development of conductometric biosensors and sensors arrays for determination of carbohydrates in food industry.

State Key Laboratory of Molecular and Cellular Biology

Research and Education Center
"Macromolecules and their complexes in realization of genetic information"

State Agency on Science, Innovation and Informatization of Ukraine,
State Fund for Fundamental Research of Ukraine

Multidisciplinary project has been proposed to complete a research program of the first Ukrainian State Key Laboratory of Molecular and Cellular Biology (SKL), established by the State Agency on Science, Innovation and Informatization on the basis of two leading research institutions in biosciences: Bogomoletz Institute of Physiology of NASU and Institute of Molecular Biology and Genetics of NASU.

All-Ukrainian competition of the applications to the State Key Laboratory was supervised by the highly qualified international jury – International Expert Council (IEC). After evaluation, only 3 out of 24 project proposals have been chosen for funding by the majority of the IEC members. One of them was the proposal of the Institute of Molecular Biology and Genetics of NASU: "Macromolecules and their complexes in realization of genetic information".

The idea of the project consists in the consolidation of the combined efforts of researchers specialising in molecular biology, biophysics, genetics, and bioinformatics, which are aimed at elucidating molecular mechanisms of the realization of genetic information through macromolecular interactions, formation of multienzyme complexes and regulatory networks in diverse cellular processes in health and disease. The following fundamental tasks are addressed in the project: physicochemical principles governing DNA replication fidelity, editing function of aminoacyl-tRNA synthetases in the control of translation accuracy, specific macromolecular complexes in mammalian protein biosynthesis, control of neuronal functions by macromolecular interactions, epigenetic regulation of gene expression.

Research teams of SKL, established as a Research and Education Centre "State Key Laboratory of Molecular and Cellular Biology", also focus on providing teaching facilities for undergraduate and postgraduate students, specialising in the field of biosciences.

In 2011-2013 a number of world-class results in life sciences were obtained, a few of which stand to mention:

1. A broad research of different types of lung, ovarian, renal cancer, some malignant blood diseases and brain tumors both at the level of specific genes and at the level of large-scale changes in human genome as a whole, was conducted. The correlation between genetic apparatus disorders and clinical signs of some malignant diseases was found and may serve as a basis for further designing of diagnostic and prognostic test-systems and elaboration of new medical preparations.

2. For the first time ever the crystals of one of the main factors of the system, responsible for editing genetic information and protein biosynthesis, main components of the living matter, were obtained. Further analysis of its spatial structure and interaction with other components of the system will shed light on fundamental mechanisms of both normal functioning of protein-synthesizing system and its disorders at severe pathologies.

3. Errors in editing genetic information may cause death of organism cells and its early aging. The scientists of SKL obtained priority data on the mechanisms, ensuring translation accuracy (protein biosynthesis) at the level of structural and functional organization of key molecules. For this reason the crystalline structure of some of them was first discovered.

4. New mechanisms of spontaneous point mutations, the initial cause of hereditary diseases, were discovered.

The first Ukrainian State Key Laboratory of Molecular and Cellular Biology will keep gaining new fundamental knowledge and establishing the basis for the development of novel diagnostics and therapeutic approaches.

International Expert Council of the State Key Laboratory of Molecular and Cellular Biology

Dr. Ivan Gout, University College London, London, UK
Dr. Valeriy Kukhar, National Academy of Sciences of Ukraine
Dr. Jacek Kuznicki, International Institute of Molecular and Cell Biology, Warsaw, Poland
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Dr. Valentin Vlasov, Russian Academy of Sciences, Novosibirsk, Russia
Dr. Marat Yusupov, Institute of Genetics and Molecular and Cellular Biology, Illkirch, France

“Strengthening Cooperation in Molecular Biomedicine between EU and Ukraine” (COMBIOM)

(2011–2014)

www.combiom-fp7.org

In 2011 the Institute of Molecular Biology and Genetics of NASU won in strong competition the EU grant of the 7 Framework Programme for Research and Technological Development “Strengthening Cooperation in Molecular Biomedicine between EU and Ukraine” (COMBIOM).

The main aim of this project is to enhance scientific collaboration between European and Ukrainian scientists in biomedicine area in the frame of the 7th EU Framework Program.

Ukraine is one of the largest and closest EU neighbours with high potential for scientific and technological development. The main policy drivers for S&T cooperation with Ukraine are:

- EC-Ukraine S&T Cooperation Agreement signed on 04 July 2002 (recently negotiation on the S&T chapter of the New Enhanced Agreement was concluded)
- EU-Ukraine Action Plan with the General Objective: to share the EU’s stability, security and prosperity with Ukraine, and Specific Objective: Ukrainian fuller integration into the broader European Research Area (ERA)
- European neighbourhood strategy (implementation of the EU-Ukraine ENP Action Plan endorsed by the EU-Ukraine Cooperation Council on 21 February 2005 - input in the economic and scientific policy of Ukraine more elements of the EU best practices).

Health is the topic of mutual interest in the EU’s 7th FP work programmes, moreover, it is a major theme of the Cooperation program of FP7, and the EU has earmarked a total of € 6.1 billion for funding this theme over the duration of FP7. The Specific FP7 program on Cooperation supports all types of research activities carried out by different research bodies in transnational cooperation and aims to gain or consolidate leadership in key scientific and technology areas. Priority is given among others to the “Biotechnology, generic tools and technologies for human health – producing knowledge that will be applied in the area of health and medicine”. True European leadership at the emerging frontiers of biomedical sciences could be achieved more effectively with participation of the most prominent scientists from the ENP countries. Research on medical aspects of molecular biology and genomics – molecular biomedicine – is a very sophisticated field of science, which obviously requires the multinational efforts. Cancer and neurodegenerative diseases have no borders and no Shengen space and only grouping together scientists from different countries working in different subfields may help to fight these diseases more successfully. Moreover, exchange of best practices and expertise between the MS and ENP is likely to contribute to a greater understanding of these issues. Closer collaboration between Ukraine, Poland and France will be a way to counteract the brain-drain phenomenon from less to more advantaged European countries.

This project is devoted to the development of the operational network of EU and Ukrainian scientists based on the different approaches to solve the problem of deciphering the molecular mechanisms of cancer and neurodegenerative diseases, with the special emphasis on the possible links between these two pathologies. For instance, according to a large population-based epidemiological study published online in Neurology 2009, Dec 23 people with Alzheimer disease may be less likely to develop cancer and people with cancer may have a lower risk of AD. This is in line with earlier report stating the similar relationship between another neurodegenerative disease – Parkinson’s and cancer (Neurology 2007, Oct 9).

The Institute of Molecular Biology and Genetics (IMBG), the project coordinator, is one of the leading research institutions in molecular biomedicine, oncogenomics and gene technologies in Ukraine. It can carry out even higher quality investigations aimed at searching for effective diagnostics and therapy of oncological and neurodegenerative diseases, which could be implemented for all European citizens.

A number of IMBG NASU laboratories working in the field of molecular cancer exemplify research activities of the highest quality supported by such well-reputation funding agencies as Wellcome Trust, INTAS, NATO, CRDF, CNRS etc. (about 30 international research grants per year). For example, between 1990 and 2003 IMBG NASU scientists took part in the international Human Genome Project and now they participate in FP7 research project on human genomics, in FP7 East-NMR programme, and in IRSES project dealing with analytical biotechnologies. The scientists of IMBG NASU publish in the top scientific journals such as: Science, Nature Structural & Molecular Biology, Trends in Biotechnology, Biochemistry, Human Genetics, Human Mutation, Proteins, Nucleic Acid Research, Molecular and Cellular Biology, Journal of Biological Chemistry, EMBO Journal, European Journal of Biochemistry, Journal of Molecular Biology.

The project EU partners are: Institute of Cancerology Gustave-Roussy (IGR, France, *www.igr.fr*) and the International Institute of Molecular and Cell Biology (the IIMCB, Poland, *www.iimcb.gov.pl*). Both of these outstanding European research institutions have large long-term experience in the

international collaboration as well as at coordination of their scientific interests with the research priorities of ERA.

We believe that thanks to the participation in COMBIOM project and the twinning with the EU partners, the IMBG NASU scientists will be able to widen their capacities in international cooperation, particularly – the involvement into FP7 and future FPs, especially in the field of molecular biomedicine, where they have the most prospective results for citizens health care. Thus, the first objective is to enhance the involvement of IMBG NASU researchers into ERA in frames of EU-Ukraine mutual interests, especially in biomedical research, and to create a core consortium for future FP7 collaborative projects.

IMBG NASU has good long-term bilateral relations with more than 30 well-known research centres in 9 European countries, for example, CNRS (France) and Polish Academy of Science institutions. However, it is not easy for IMBG NASU scientists to participate in sustainable European consortia or to find a coordinator for a new consortium, which we could propose on the basis of our existing bilateral European partnerships. These are the main problems in the way of increasing participation of Ukrainian scientists in FP7 and future FPs. Implementation of the ERA-WIDE project, where IMBG NASU will play a role of a coordinator would allow us:

- To learn by experience the role and functions of the coordinator of FP7 projects.
- To build capacities for further enhanced participation in FP7 as a partner in collaborative projects' consortia
- To participate effectively in preparing a new collaborative research FP7 project and creating research projects consortium with European partners.

Thus, the second objective of this project is to increase cooperation capacities of IMBG NASU as a promising partner in EU research programmes.

On the other hand, being a high level research institution IMBG NASU may serve as an interface aiming to prove the achievements and high potential of Ukrainian biomedical research to ERA and to accommodate it to European research priorities. This is the third objective of the COMBIOM project. Presenting the IMBG NASU research potential for European scientific community and building the extended multilateral collaboration with the European high quality research centres in France and Poland will serve for further reinforcement and facilitation of involvement of Ukrainian biomedical science into ERA.

Prof. A. El'skaya
Full Member of NASU, COMBIOM Project Coordinator

Ya. Mishchuk
COMBIOM Project Manager

Department of Scientific and Technical Information

Head
Olga V. Korzh
Phone: +380 (44) 526-11-29
Fax +380 (44) 526-07-59
E-mail: *inform@imbg.org.ua*

Department of Scientific and Technical Information was founded in 1973.

The Department's activities are focused on the following tasks:

- Scientific and technical information, regulatory and normative documentation supply
- State registration of the IMBG NASU research projects
- Dissemination of the information on IMBG NASU activities and propositions for collaboration with local and foreign scientific, business and non-governmental organizations
- Distribution of the information flows inside and outside the institute
- Organization of conferences, seminars, exhibitions, forums, meetings, etc.
- IMBG NASU web site support.

Scientific Library

Head
Olga O. Luk'yanenko
Phone: +380 (44) 526-07-39
Fax: +380 (44) 526-07-59
E-mail: *library@imbg.org.ua*

The library was founded in 1969.

It counts about 83 000 volumes of home and foreign books and journals, more than 14 000 units of foreign periodical editions on microfishes.

The fund of the library covers different fields of natural sciences – genetics, molecular biology, biochemistry, biophysics, organic chemistry, medical and agricultural sciences. There are a number of dictionaries and reference books. The literature is classified in the alphabetical and systematic catalogues. The work of the library is aimed at efficient assistance in the professional and informational needs of the scientists. Weekly expositions of the recent acquisitions, subject–matter selection of the literature and bibliographical consultations are realised by the library. The staff of the library attends readers of scientific institutions and receives the literature from many libraries by Interlibrary Loan System.

“Biopolymers and Cell” Journal

Editor-in-Chief
Anna V. El’skaya (Ukraine)
Associate Editors
Dmytro M. Hovorun (Ukraine)
Yegor S. Vassetzky (France)
Phone / fax: +380 (44) 526-07-89
E-mail: *biopolym.cell@gmail.com*
www.biopolymers.org.ua

“Biopolymers and Cell” is a scientific journal issued by the National Academy of Sciences of Ukraine, Institute of Molecular Biology and Genetics. It was established in 1985 (ISSN 0233-7657), online version since 2006 (ISSN 1993-6842). Previous titles were Биополимеры и клетка (1985–2009), Біополімери і клітина (2001–2009). In 2009 journal was reregistered as Biopolymers and Cell (Biopolym. Cell).

“Biopolymers and Cell” covers a wide scope of problems related to the structure biopolymers and their functioning in different organisms at different conditions.

Unpublished previously and completed experimental works presented as articles, reviews, minireviews, short communications, book reviews and and special issues are dedicated to international scientific events.

The format of Biopolym. Cell corresponds to the international standards.

Biopolymers and Cell is issued bimonthly and contains the following sections:

- Structure and Function of Biopolymers
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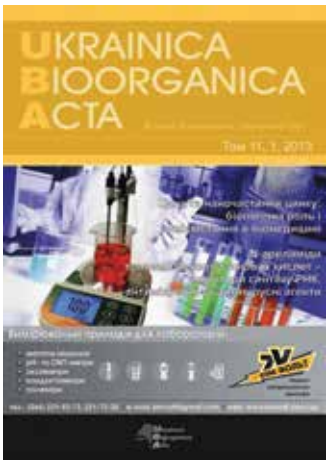

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Associate Editor
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Phone / Fax: +380 (44) 522-24-58
E-mail: *bioorganica@ukr.net*
www.bioorganica.org.ua

“Ukrainica Bioorganica Acta” journal presents scientific investigations from all branches of bioorganic chemistry. Scientific topics of the journal include synthesis and study of biologically important organic compounds, investigation of the natural bioregulators, proteins, nucleic acids, lipids and carbohydrates. Both natural compounds and their synthetic analogues are considered. Significant attention is pointed to the bioconjugate problems. The journal may be of interest for specialists in bioorganic, organic and medical chemistry, biochemistry, pharmacology and biotechnology.

We hope that this novel project will work for the noble aim of the representing of Ukrainian bioorganic school achievements, assist our bioorganic chemistry scientists’ integration into European scientific association.

Electronic version of the edition (*www.bioorganica.org.ua*) is included in the Directory of Open Access Journals (DOAJ, *www.doaj.org*).

The journal appears twice a year, the accepted languages are Ukrainian and English.

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Yuriy M. Syvolap (South Plant Biotechnology Center, NAASU, Kyiv)
Phone: +380 (44) 526-07-98
Fax: +380 (44) 526-07-59
E-mail: *kunakh@imbg.org.ua*
www.utgis.org.ua

Journal covers a theory, state and problems, methods and results of researches in the field of genetics, breeding and modern biotechnology, and influence of these sciences on development of related areas of biology, medical and agricultural sciences. The journal publishes original research reports, review articles on cell and molecular basis of inheritance and variation, problems and methods for regulation of genetic variation and realization of genetic information, the latest developments in the field of theoretical basis of breeding and its practical achievements, etc. Journal focuses on novel directions and methods of genetic, breeding and biotechnological investigations, informs on congresses and conferences on the above issues, and also presents reviews and information on scientific publications. Journal is included to the list of professional scientific editions of High Attestation Commission of Ukraine in the field of biological and agricultural sciences.

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Telegeev Gennadiy D., Dr.Sci. (mol. biol.), Senior Research Scientist
Yarmoluk Sergiy M., Dr.Sci. (bioorg. chem.), Professor

The Alphabetic Directory of Scientific Council

Bobyk V. I. .....+380 (44) 526-55-89.....*vasiliybobik@gmail.com*
El'skaya A. V. .....+380 (44) 526-07-49.....*anna.elskaya@yahoo.com*
Dzyadevich S. V. .....+380 (44) 200-03-28.....*dzyad@yahoo.com*
Dubey I. Ya. .....+380 (44) 526-07-09, 526-55-98.....*dubey@imbg.org.ua*
Filonenko V. V. .....+380 (44) 526-20-16, 522-61-00.....*filonenko@imbg.org.ua*
Hovorun D. M. .....+380 (44) 526-20-14, 526-11-09.....*dhovorun@imbg.org.ua*
Kavsan V. M. .....+380 (44) 526-34-98.....*kavsan@imbg.org.ua*
Kashuba V. I. .....+380 (44) 526-07-09.....*v.i.kashuba@imbg.org.ua*
Kharchenko V. M. .....+380 (44) 526-11-59.....*kharchenko@imbg.org.ua*
Kordium V. A. .....+380 (44) 526-55-96.....*kordium@imbg.org.ua*
Kornelyuk O. I. .....+380 (44) 526-55-89.....*kornelyuk@imbg.org.ua*
Korpan Y. I. .....+380 (44) 200-03-28, 522-28-24.....*yaroslavkorpan@yahoo.com*
Kunakh V. A. .....+380 (44) 526-07-98.....*kunakh@imbg.org.ua*
Livshits L. A. .....+380 (44) 526-07-69.....*livshits@imbg.org.ua*
Lukash L. L. .....+380 (44) 200-03-36, 526-55-97.....*lukash@imbg.org.ua*
Maliuta S. S. .....+380 (44) 526-07-29.....*maliuta@imbg.org.ua*
Mishchuk Ya. R. .....+380 (44) 526-11-29.....*mishchuk@imbg.org.ua*
Negrutskii B. S. .....+380 (44) 200-03-37.....*negrutskii@imbg.org.ua*
Rynditch A. V. .....+380 (44) 526-96-18, 200-03-27.....*rynditch@imbg.org.ua*
Sergeeva T. A. .....+380 (44) 200-03-41.....*t_sergeyeva@yahoo.com*
Skorohod O. M. .....+380 (44) 526-20-16.....*rmd@imbg.org.ua*
Soldatkin O. P. .....+380 (44) 200-03-28.....*a_soldatkin@imbg.org.ua*
Strokovska L. I. .....+380 (44) 526-07-09.....*lstrokovskaya@yahoo.com*
Telegeev G. D. .....+380 (44) 526-07-29.....*g.d.telegeev@imbg.org.ua*
Tukalo M. A. .....+380 (44) 200-03-35.....*mtukalo@imbg.org.ua*
Yarmoluk S. M. .....+380 (44) 522-24-58.....*yarmoluksm@gmail.com*

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