**LABORATORY OF RADIATION BIOLOGY**

**Theme: 1077**

**Project: “Research on the biological effects of heavy charged particles with different energies”**

**Period: 2015-2023**

**Year of last approval: 2020**

**PART A: Achievements**

1.   Contributions of the JINR group:

LRB: preparation and irradiation of biological objects; dosimetry; research on different cell cultures; DNA damage research with fluorescent microscopy, immunocytogenetic and immunohistochemical techniques; molecular genetics methods; classic cytogenetic methods, fluorescent *in situ* hybridization analysis; animal experiments; development of vivarium; behavioral test systems; pathomorphological analysis; mathematical models, data analysis, systematization and interpretation; computer simulations (using “Govorun” supercomputer at LIT); radiation safety research; upgrade and development of radiobiological irradiation stations; nuclear planetary science instruments; student education programs on radiobiology (BSc, MSc, PhD at Dubna State University).

List of JINR radiation sources used:

LRB: X-ray irradiator;

DLNP: medical proton beam, gamma-ray irradiator (Rokus-M);

FLNR: heavy ion beam at U400M cyclotron, “Genome” facility;

VBLHEP: heavy ion beams from Nuclotron;

FLNP: neutron source for nuclear planetary science test stand.

All experiments within project are performed by the LRB team at JINR facilities with participation of other institutions. Minor parts of research (gene sequencing, single molecule microscopy data analysis, etc) are performed by other project member institutions with participation of JINR team.

LRB is a member of the International Biophysics Collaboration, LRB director (A.N. Bugay) is a member of Executive committee (2019-present).

2.   Publications:

1) Patera V., Prezado Y., Azaiez F., Battistoni G., Bettoni D., Bugay A., Cuttone G., Dauvergne D., de France G., Graeff C., Haberer T., Inaniwa T., Incerti S., Nasonova E., Navin A., Pullia M., Rossi S., Vandevoorde C. and Durante M. Biomedical research programs at present and future high-energy particle accelerators // Front. Phys. 2020. V.8. P.380.

Description of JINR research program.

2) Hausmann M., Neitzel C., Bobkova E., Nagel D., Hofmann A., Chramko T., Smirnova E., Kopečná O., Pagáčová E., Boreyko A., Krasavin E., Falkova I., Heermann D.W., Pilarczyk G., Hildenbrand G., Bestvater F. and Falk M. Single Molecule Localization Microscopy Analyses of DNA-Repair Foci and Clusters Detected Along Particle Damage Tracks // Front. Phys. 2020. V.8. P.578662.

Supervising, performing the experiment, irradiation, data acquisition, processing and interpretation.

3) Khramko T.S., Boreyko A.V., Krasavin E.A., Krupnova M.E., Pavlova A.S., Smirnova E.V., Filatova A.S., Vasilyeva L.A. Induction and repair of DNA double-strand breaks in a primary culture of rat hippocampal cells after exposure to 60Co γ-rays and accelerated protons. // Particles and Nuclei Letters. 2021, in press (in Russian).

100% JINR contribution

4) Abdullaev S., Bulanov T., Gaziev A., Timoshenko G. Increase of mtDNA and its mutant copies in rat brain after exposure to 150 MeV protons // Molecular Biology Reports 2020. https://doi.org/10.1007/s11033-020-05491-7.

Performing the experiment, irradiation, data acquisition.

5) Kowalska A, Nasonova E, Czerski K, Kutsalo P. Initial radiation DNA damage observed in prematurely condensed chromosomes of G2-phase human lymphocytes and analytical model of ion tracks // Eur. Phys. J. D 2020 V.74. P.17.

Performing the experiment, irradiation, chromosome aberration data acquisition and processing.

6) Czerski K., Kowalska A., Nasonova E., Kutsalo P., Krasavin E. Modeling of chromosome aberration response functions induced by particle beams with different LET // Radiation and Environmental Biophysics 2020. V59: P. 79-87.

Performing the experiment, irradiation, chromosome aberration data acquisition and processing.

7) Pereira W., Kowalska A., Czerski K., Nasonova E., Kutsalo P., Valerievich L.E. Deviation from Poisson statistics observed in chromosome aberrations induced by 252Cf neutrons // Acta Physica Polonica. 2020. V.51. No.3. P. 881-886.

Performing the experiment, irradiation, chromosome aberration data acquisition and processing.

8) Stemberg A.S., Klotz I.N., Belyaeva A.G., Blokhina T.M., Yashkina E.I., Osipov A.N., Bazyan A.S., Kudrin V.S., Perevezentsev A.A., Koshlan N.A., Bogdanova Yu.V., Koshlan I.V., Timoshenko G.N., Lapin B.A. Hematologic, biochemical, and molecular effects of monkey head irradiation with high-energy krypton nuclei. // Aerospace and Environmental Medicine (Aviakosmicheskaya i ekologicheskaya meditsina), 2020, Vol. 54, No 1, pp. 38–45 (in Russian).

Performing the experiment, irradiation, chromosome aberration data acquisition, and interpretation.

9) Koltovaya N.A., Zhuchkina N.I., Dushanov E.B. Distribution of mutations in the molecule of the yeast arginine permease CAN1 protein // Current Issues in Biological Physics and Chemistry (Aktual'nyye voprosy biologicheskoi fiziki i khimii). 2020, Vol. 5, No. 4, pp. 644–651 (in Russian).

100% JINR contribution

10) Severyukhin Yu.S., Lalkovičová M., Kolesnikova I.A., Utina D.M., Lyakhova K.N., Gaevsky V.N. The effect of piracetam on behavioral reactions of adult rats and morphological changes in the brain after whole body fractionated gamma irradiation – an exploratory study // Radiation and Environmental Biophysics 2020. doi:10.1007/s00411-020-00886-3

100% JINR contribution

11) Koltovaya N.A. Simulation of a mutant form of human inosine triphosphate pyrophosphohydrolase P32T-ITPA and its potential regulatory chemical modifications // Current Issues in Biological Physics and Chemistry (Aktual'nyye voprosy biologicheskoi fiziki i khimii). 2020, Vol. 5, No. 4, pp. 637–643 (in Russian).

100% JINR contribution

12) Timoshenko G.N., Gordeev I.S. Calculation of the Linear Energy Transfer Distribution in Radiobiological Experiments at the U400M Cyclotron. Physics of Particles and Nuclei Letters, 2020, V. 17, No. 7, P. 951–957

100% JINR contribution

13) Timoshenko G.N., Gordeev I.S. Simulation of radiation field inside interplanetary spacecraft. Journal of Astrophysics and Astronomy 2020 V.41. P.5

100% JINR contribution

14) Timoshenko G.N., Gordeev I.S. Estimation of the astronaut’s doses inside the spacecraft habitable module in deep space. Physics of Particles and Nuclei, 2020, V. 51, No. 5, P. 988–993.

100% JINR contribution

15) Ivanov A.A., Krylov A.R., Molokanov A.G., Вushmanov A.Yu., Samoylov A.S., Pavlik E.E., Mytsin G.V., Shvidky S.V., Timoshenko G.N. Modeling of Laboratory Animals Exposure Conditions behind Local Concrete Shielding Bombarded by 650-MeV Protons. // Medical Radiology and Radiation Safety (Meditsinskaya radiologiya i radiatsionnaya bezopasnost), 2020, Vol. 65, No. 5, pp. 77–86 (in Russian).

Performing the experiment, irradiation, dosimetry, pathomorphological data processing and interpretation.

16) Timoshenko G.N., Gordeev I.S. Forecasting Radiation Environment around the NICA Booster. Physics of Particles and Nuclei Letters, 2020, V. 17, No. 3, P. 379–388.

100% JINR contribution

17) I. G. Mitrofanov, M. L. Litvak, D. V. Golovin, C. Yu. Nikiforov, A. B. Sanin, A. A. Anikin, M. I. Mokrousov, G. N. Timoshenko, V. A. Krylov, E. E. Pavlik, V. N. Shvetsov, G. V. Mytsin, A. G. Molokanov, Gamma spectrometry of composite models of planetary matter at JINR's proton accelerator beam using the tagged proton method. Particles and Nuclei Letters, 2020, Vol. 17, No. 3, pp. 348–357.

Performing the experiment, irradiation, test stand for models of planetary matter, data processing and interpretation.

3.   PhD theses:

- completed:

L. Ježková, “DNA damage and repair after exposure to ionizing radiation with different linear energy transfer” 2018

P. Blaha, “Induction of HPRT mutations in mammalian cells after irradiation with heavy ions” 2018

-expected to be completed within 2021:

M. Batmunkh, “Computer modeling of mechanisms of CNS cell damage when exposed to heavy charged particles”

L. Bayarchimeg, “The study of track structures in a biological targets induced by ionizing radiation”

V.N. Chausov, “Effect of DNA synthesis inhibitors on the formation of double-strand breaks in human cells under the action of radiation with different linear energy transfer”

M.G. Zadneprianetc “Formation and repair of cluster double-strand DNA breaks under the action of accelerated heavy ions”

4.   Talks:

A.N. Bugay, "Modern approaches to improve the efficiency of radiotherapy of tumors" // XXVII International Conference "Mathematics Computer Education" (Dubna, January 27 - February 1, 2020)

A. Bugay, E. Nasonova, "Nuclear Applied Physics and Biophysics at NICA" // International Biophysics Collaboration meeting (INFN headquarter, Rome, February 20-21, 2020)

A.N. Bugay, "Promising approaches for increasing the efficiency of ionizing radiation action on tumor tissue cells " // International Summer Online School "Innovative Technologies of Nuclear Medicine and Radiation Therapy" (MEPhI, Moscow, July 27 — August 02, 2020)

D. Chevizovich, A. Chizhov, Z. Ivic, A. Reshetnyak, “On the long-distance charge transport in DNA-like macromolecules” Mathematical Challenge of Quantum Transport in Nanosystems.   
Pierre Duclos Workshop (ITMO, Saint Petersburg, September 14 - 16, 2020)

\*Note: most of 2020 Conferences and Workshops were postponed to 2021.

**PART B: Plans and requests**

5.   Plans

* Research on the mechanisms of the development of DNA molecular damage and its repair in cultures of human and mammalian normal and tumor cells and in histological sections of tissues of different parts of animals' central nervous system after exposure to radiations of different LET.
* Research on the induction and molecular nature of different types of gene and structural mutations in mammalian and lower eukaryote cells depending on the radiation dose and LET, repair status, oxidative stress development, and genetic stability mechanisms.
* Research on the formation of complex chromosomal aberrations in normal and tumor cells of humans and laboratory animals. Evaluation of long-term consequences of exposure to radiations of different LET.
* Research on behavioral reaction disorders and pathomorphological changes in different structures of the brain, spinal cord, and critical organs and systems of irradiated laboratory animals. Conducting a search for new radioprotective drugs.
* Research on radiation-induced effects in microglia, oligodendrocytes and their precursors, and in the myelin sheath after exposure to densely ionizing radiation.
* Research on the mechanisms of the action of Ara-C and other radiosensitizers for the irradiation of different normal and tumor cell cultures and mice with transplanted tumors.
* Development of a hierarchy of mathematical models of radiation-induced biological effects that would describe the development of radiation-induced pathologies at different organization levels (from molecules to cell populations) and at different times (acute and long-term consequences).
* Improvement of accelerator-based radiobiological experiment procedures. Calculation of shieldings for new nuclear physics facilities; evaluation of the radiation conditions and development of radiation safety systems for them. Participation in the creation and tests of nuclear planetary science instruments.

6.   Group size, composition and budget

Project Leaders: E.A. Krasavin, A.N. Bugay

Researcher leaders: A.V. Boreyko, A.V. Chizhov, E.B. Dushanov, N.A. Koltovaya, O.V. Komova, I.V. Koshlan, M.A. Ostrovsky, G.N. Timoshenko,

Researchers:

S.V. Aksenova, A.S. Batova, L.G. Beskrovnaya, T.Zh. Bezhanyan, Yu.V. Bogdanova, N.N. Budennaya, V.N. Chausov, O.O. Chernyak, I.M. Enyagina, V.O. Fateev, A.A. Glebov, I.S. Gordeev, D.-N. Gureu, E.M. Ignat, E.V. Ilyina, A.A. Ivanov, T.S. Khramko, A.N. Kokoreva, E.A. Kolesnikova, I.A. Kolesnikova, D.A. Komarov, V.L. Korogodina, N.A. Koshlan, M.A. Kovalenko, R.A. Kozhina, E.A. Kruglyakova, V.A. Krylov, P.V. Kutsalo, E.A. Kuzmina, M. Lalkovičova, E.N. Lesovaya, B. Lkhagva, K.N. Lyakhova, B. Munkhbaatar, E.A. Nasonova, A. Nurkasova., M.S. Panina, A.Yu. Parkhomenko, D.V. Petrova, M. Piotrowski, Yu.S. Severyukhin, D.D. Shamina, N.V. Shvaneva, E.V. Smirnova, S.I. Tiunchik, D.M. Utina, M.A. Vasilyeva, Yu.V. Vinogradova, M.G. Zadneprianetc, N.I. Zhuchkina,

Engineers: T.A. Fadeeva, L.A. Melnikova, E.E. Pavlik, E.V. Pronskikh, V.N. Gaevsky (DLNP), A.A. Bezbakh (FLNR), Yu.G. Teterev (FLNR),

Technicians: T.N. Bazlova,

Laboratory assistants: A.S. Filatova, M.D. Isakova, M.E. Krupnova, P.-O. Lkhasuren, A.S. Pavlova.

FTE – 67.4

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| --- | --- | --- | --- | --- | --- |
|  | Expenditure items | Full cost, k$ | 1st year | 2nd year | 3rd year |
| 1.  2.  3.  4. | Materials  Equipment  Payments for agreement-based research  Travel allowance, including: | 240  158.2  -  150 | 70  84.2  -  50 | 70  43.2  -  50 | 100  30.8  -  50 |
|  | Total direct expenses | 548.2 | 204.2 | 163.2 | 180.8 |

Needs of JINR computing resources: 2 CPU nodes and 1 GPU node at “Govorun” for simulations;

dataspace for Information System (Biohlit).