Biological effects of reduced natural background radiation: transcriptome profiling of model organism developed in the deep underground low-background laboratory DULB-4900 BNO INR RAS

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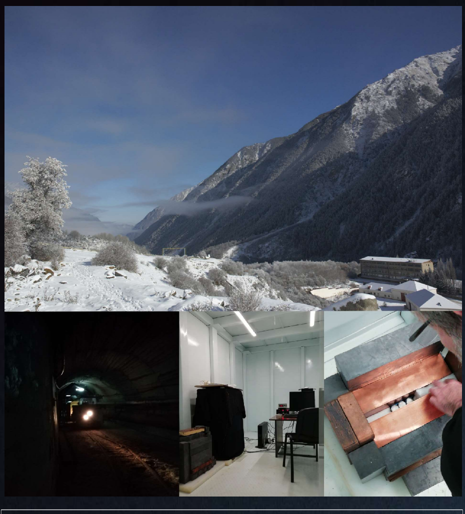


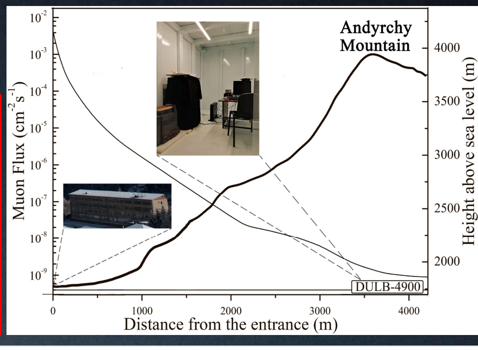
***Fig.1** (left)*: Locations and facilities at world's first underground neutrino observatory BNO INR RAS (1966): institute building and the DULB-4900 low-background laboratory at the ~ 4000 m tunnel in the Andyrchy mountain. ***Fig.2** (down, right)*: Physical characteristics of two laboratories

Natural background radiation is a permanent multicomponent environmental factor of terrestrial and cosmic origin influencing all living organisms, but effects of its deprivation still remain uncertain. On the surface of the Earth it consists of γ-rays, α- and β-particles, neutrons, radon, secondary cosmic particles etc. and gives rise to dose rates of 10^2–10^3 nGy/h.

End of 2010s: Number of biophysical studies, rapidly evolving at physical research centers with deep underground low background laboratories as LNGS Gran Sasso, CNRS Modane, SNOLAB Sudbary etc., attempt to reveal mechanisms of biological responses to chronic absence of natural background radiation with implementation of new experimental methods as omics techniques.

Dec. 2019-Present: Deep underground low background laboratory DULB-4900 of Baksan Neutrino Observatory INR RAS (*Fig.1*, *Fig.2*) encouraged Dzhelepov Laboratory of Nuclear Problems JINR initiative of collaboration in Life Science studies and hosted experiments concerning determination of low radiation background impact on model organisms.

Our goal was to determine for the first time a response of complex multicellular organism *D. melanogaster* Oregon-R line to the reduced natural background radiation at the whole transcriptome level after complete developmental cycle (14 days of exposure) in low (DULB-4900) and natural radiation background laboratories by comparison RNA-seq gene expression profiles and by comparative transcriptome analysis with data deposited at NCBI GEO and NASA GeneLab databases (*Fig.3*).



Experiment was performed at equalized environmental conditions (*Fig.3*) except radiation background: ~190 nGy/h in surface laboratory and ~ 16.4 nGy/h in DULB-4900.

Background component	Data source	Ground laboratory in the institute building, BNO (INR, RAS)	Chamber of DULB-4900, BNO (INR, RAS)
Gamma, nGy h^{-1}	NaI(Tl) crystal scintillation detector [32]	120	0.02
Neutrons, nGy h^{-1} (cm^{-2}s^{-1})	Helium proportional counter [32, 33]	3.45 (4.67 × 10^{-3})	~0 (3.8 × 10^{-7})
Muons and cosmic rays, nGy h^{-1} (cm^{-2}s^{-1})	Determined by the altitude (m.a.s.l.) and covering rock massive (m.w.e) [32]	24.4 (2.0 × 10^{-2})	~0 (3.0 × 10^{-9})
Radon, nGy h^{-1} (Bq m^{-3})	Experimental set-up to continuously measuring the radon activity [33, 34]	1.19 (35)	0.85 (25)
Nutrition medium ^{40}K, nGy h^{-1} (Bq kg^{-1})	Spectrometer SNEG	15.5 (6.7)	15.5 (6.7)
Total dose rate, nGy h^{-1}	Estimation	164.5 (190.7—based on UNSCEAR data)	16.4

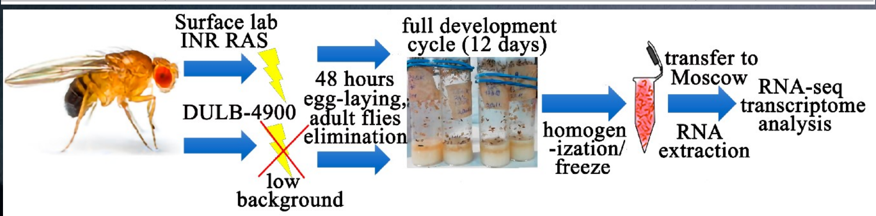
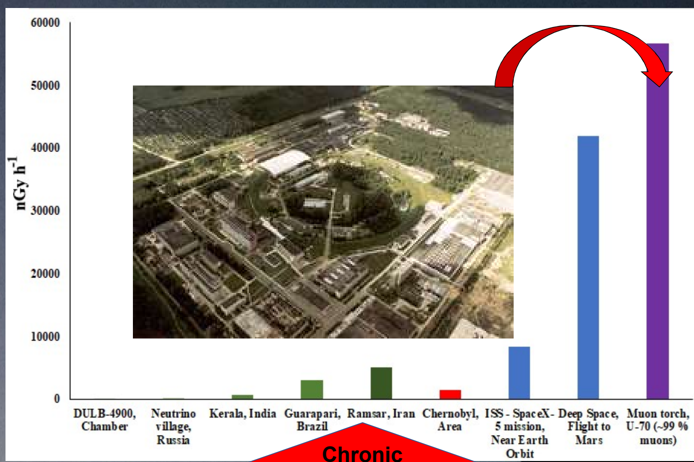


Fig.3: Scheme of the experiment for determianation of low background effects on *D.melanogaster,* organisms were placed deep-underground in DULB-4900 and to the surface laboratory



Chronic μ-exposure experiment at U-70 (NRCI IHEP)
Dec. 2021-present

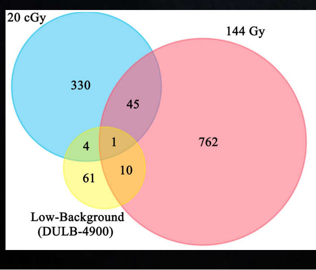
We identified differentially expressed genes in low radiation background laboratory, biological process, in which they are involved, and biological network for total response was created.

In DULB-4900, we observe, up-regulation of genes related to immune response, response to stimuli and down-regulation of genes involved in primary metabolic processes.

Comparative transcriptome analysis of obtained data and transcriptome profiles from NCBI GEO and NASA GeneLab databases reveals low similarity of responses to various kinds of ionizing radiation treatments (*Fig.4*) and to several deep underground environmental stress.

D. melanogaster responses to DULB-4900 conditions were not specific to radiation-related stress and may be a result of chronic lack of external natural stimuli, necessary for normal functioning of terrestrial organism which leads to an activation of immune response and response to stimuli with down-regulation of primal metabolic processes

***Fig.4** (down)*: Venn diagram representing the quantity of shared genes for *D.melanogaster* developed in DULB-4900 and after γ-ray exposure with low (20 cGy) and high doses (144 Gy). ***Fig.5** (right)*: Dose rates for some high radiation background environments, components of secondary cosmic radiation and prospect for the chronic μ-exposure experiment at U-70 (NRCI IHEP)



Perspectives

In this work (*M. Zarubin et al., 2021*) we determined full picture of complex organism's responses to reduced natural background radiation, however ongoing long-term 3-year experiment at LNGS Gran Sasso (RENOIR project) will accomplish this experiment.

We declare our work to be the first initiative of biological studies at Baksan Neutrino Observatory INR RAS, which links tasks of biophysics, radiobiology, astrobiology and medicine. We expect that this unique facility poses outstanding scientific potential for interdisciplinary studies.

With this study, we underline necessity to focus on chronic radiation exposures of biological organism, which differs in effects from acute doses. Such studies are more relevant to industrial disaster, natural high background areas, biology of spaceflight and aircrew exposures (*Fig. 5*). For further step we will focus on components of secondary cosmic radiation, especially muons. Biological impact of muons is actively studied recently, but few experimental results exist in this field.

References

1. M. Zarubin, A. Gangapshev, Y. Gavriljuk, V. Kazalov, E. Kravchenko. First transcriptome profiling of *D. melanogaster* after development in a deep underground low radiation background laboratory. *PLoS ONE.* 2021
2. M. Zarubin, O. Kuldoshina, E. Kravchenko. Biological Effects of Low Background Radiation: Prospects for Future Research in the Low-Background Laboratory DULB-4900 of Baksan Neutrino Observatory INR RAS. *Physics of Particles and Nuclei.* 2021.
3. M. Zarubin, A. Gangapshev, Y. Gavrilyuk, V. Kazalov, E. Kravchenko. Transcriptome profiling of D. melanogaster after development in a deep underground low radiation background laboratory DULB-4900 of BNO INR RAS Radiation Research Society`s 67th Annual Meeting. USA. 3-6 October 2021.