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dedicated to N.W. Timofeeff-Ressovsky and his scientific school

MODERN PROBLEMS OF GENETICS, RADIOBIOLOGY, RADIOECOLOGY, AND EVOLUTION

Fourth Readings after V.I. Korogodin & V.I. Shevchenko

IUR Advanced Research Workshop

RADIOECOLOGY MEETS RADIOBIOLOGY:
A REAPPRAISAL OF BASIC MECHANISMS OF RADIATION

St. Petersburg, 2-6 June 2015

ABSTRACTS

PAPERS BY YOUNG SCIENTISTS

Dubna, 2015

The collection contains Theses of the reports presented at the Meeting of St. Petersburg and Short papers by young scientists submitted to the competition after N.W. Timofeeff-Ressovsky. The Theses and young scientists Papers are published in the authors' wording.

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TOPICS OF THE CONFERENCE

Genetics

- Genome integrity
- Protein inheritance
- Mechanisms of global and region-specific control of mutagenesis
- Stress-induced mutagenesis
- Cancer genetics

Sections: Mechanisms of genetic processes;
Cancer genetics and cancer therapy
Discussion: Variability laws

Radiobiology

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- Modulating effect of linear energy transfer
- Epigenetics of radiation-induced genome instability
- Genomic instability in the offspring of irradiated parents
- Epidemiology of radiation

Sections: Radiobiology effects;
Radiation effects on human
Discussion: Low radiation: mechanisms and effects

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- Regularities of radionuclide migration
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- Biodiversity: formation of species/degradation of species community
- Influence of environment conditions on radiation effects

Sections: Radiation terrestrial & hydroecology;
Radionuclide migration & distribution;
Accumulation of radionuclides & radiation exposure
Discussion: Dependence of biodiversity on radiation characteristics and environment conditions

Evolution

- Progressive evolution in terms of physics
- Evolution of the genomic universe
- Evolution of biodiversity
- Possibility space for evolution
- Evolution of bacterial genomes
- Evolution of ethological structure of populations
- Anthropogenesis

Discussion: evolution principles in biology

Memorial

ABSTRACTS
OF PRESENTATIONS

GENETICS

Mechanisms of genetic processes

THE CORRECTION OF THE UV-INDUCED MUTAGENESIS BY EXTRACT FROM KIWI FRUIT

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It were done experiments on the Escherichia coli cells with normal genotype (B/r WP2 K-12 and AB 1157) and their derivatives with defects in the reparation genes: 1885 AV (uvrB^{-}), BHL 1 (rec A^{-}), JC 5519 (rec BC^{-}), JC 9239 (rec F^{-}) and SM 561 (lex A^{-}) to identify the characteristics of the correction of the UV-induced mutagenesis by kiwifruit extract.

There was mutagenesis decreased by 0,001% extract in UV-irradiated cells as wild type and rec BC^{-}cells with a high efficiency and in recA^{-} lexA^{-}cells with substantially reduced efficiency. The efficiency of mutagenesis modifications practically absent in uvrB^{-} and rec F^{-} mutants. Thereby the management of resistant of E.coli cells to mutagenic UV-radiation on the given stage of the mutation process is largely due to the state of activity of the uvr B и rec F genes products and relatively less - rec A and lex A genes products.

The modifying effect of kiwifruit extract at the final stages of the mutagenesis is realized in the interaction between the two main ways of eliminating of induced primary damages of DNA. One of them is related to the state of the activity of the error-free DNA repair system, which is under the control of the constitutive enzyme of the excision and post-replicate repair: products of uvr B (uvr AB-dependent exonuclease), rec F gene (reparations, but not recombination function of the unidentified product), rec BC gene (UV-induced endonuclease) and is always active of one of the two centers of recA gene (protein RecA). Another way depends on the allelic state of lex A genes (protein Lex A) and the second center of rec A gene and is associated with the suppression of flowing with errors the inducible DNA repair system. Its important feature is that increasing the viability of cells carrying DNA damage, it also increases the total number of mutations.

It indicates that the related part of kiwifruit extract in two main process of elimination of the primary damage of the DNA determines the sufficiently high efficiency of modifications of induced mutagenesis at the final stages of mutations formation.

INSTABILITY OF INTERSTITIAL TELOMERIC SEQUENCES

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Besides chromosomal ends, telomeric repeats are also present in internal parts of the chromosomes. Such sequences are called Interstitial Telomeric Sequences (ITSs) and are present in many eukaryotic genomes. For instance, human genome contains more than 50 sites of short ITSs (s-ITSs). Some of these sequences are polymorphic in length and their role in the genome is unclear. Various observations imply that ITS can trigger genome instability potentially leading to human disease. For instance ITSs were linked to some cancer-related chromosomal rearrangements. Yet the mechanisms responsible for length polymorphism, chromosomal fragility and rearrangements mediated by s-ITSs, including the relative contribution of replication, repair, recombination and transcription to these processes, are little known.

This prompted us to study genome instabilities mediated by telomeric repeats placed into internal chromosomal positions in our model yeast system. We found that the generic yeast telomeric repeat (Ytel) was unstable. When its G-rich strand served as a lagging strand template for replication, Ytel repeats triggered gross chromosomal rearrangements (GCRs) and mutagenesis at a distance [1]. In striking contrast with the G-orientation, no GCRs mediated by Ytel repeats were detected in C-orientation. Instead, those repeats were exceptionally prone to small-to-medium scale expansions. Our genetic analysis revealed that two important pathways, post-replication repair and homologous recombination, appeared to account for Ytel repeat expansions. The same pathways were implicated in the process of alternative telomere lengthening (ALT). Thus, our data on the expansion of ITSs in yeast shed new light on the mechanisms of genome stability and telomere maintenance.

[1] Anna Y. Aksenova, Patricia W. Greenwell, Margaret Dominska, Alexander A. Shishkin, Jane C. Kim, Thomas D. Petes, and Sergei M. Mirkin; Genome rearrangements caused by interstitial telomeric sequences in yeast. 2013 PNAS 110 (49) 19866-19871.

COMBINING OF RECOMBINATION METHODS WITH BIOTECHNOLOGY IN POTATO BREEDING IN TAJIKISTAN

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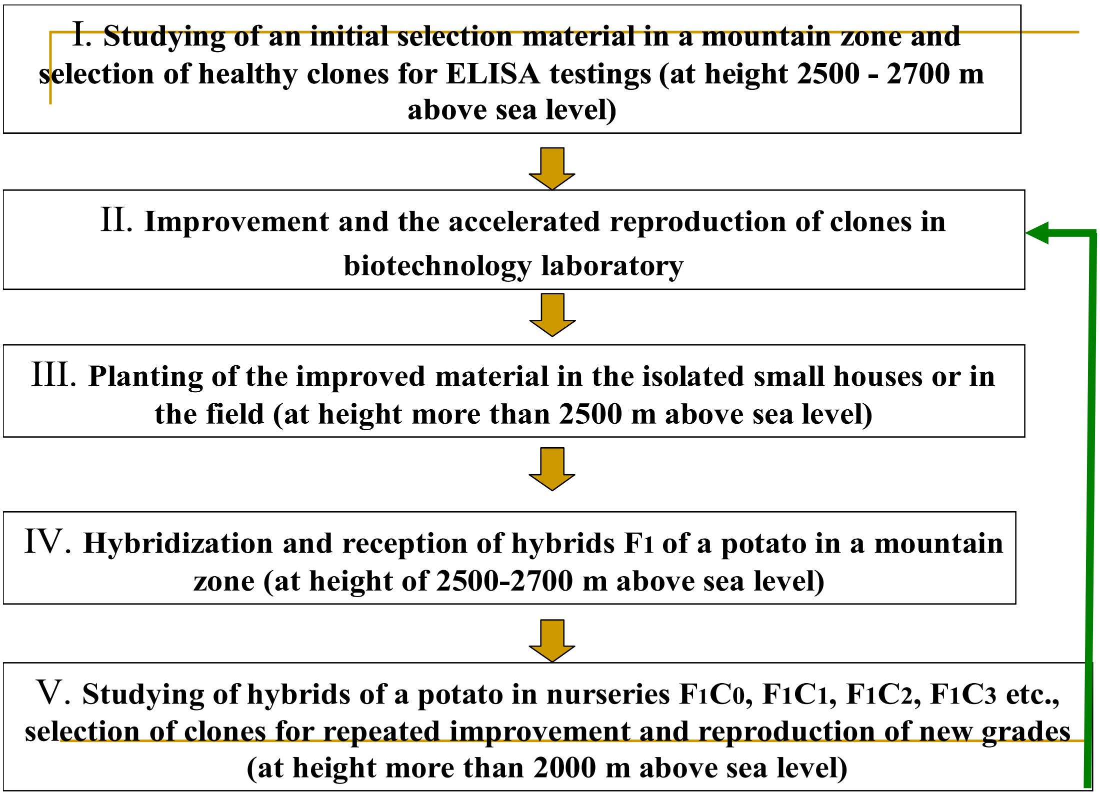
In our opinion, for increase of efficiency of breeding and seed-growing work in the future the special role belongs to knowledge of biological features of growth and development of plants of potato in various ecological conditions of a mountain zone of republic, to a complex combination of traditional methods of selection of a potato to methods of biotechnology which is schematically resulted in the below figure:



I. Studying of an initial selection material in a mountain zone and selection of healthy clones for ELISA testings (at height 2500 - 2700 m above sea level)

II. Improvement and the accelerated reproduction of clones in biotechnology laboratory

III. Planting of the improved material in the isolated small houses or in the field (at height more than 2500 m above sea level)

IV. Hybridization and reception of hybrids F_1 of a potato in a mountain zone (at height of 2500-2700 m above sea level)

V. Studying of hybrids of a potato in nurseries F_1C_0, F_1C_1, F_1C_2, F_1C_3 etc., selection of clones for repeated improvement and reproduction of new grades (at height more than 2000 m above sea level)

Thanks to a combination of methods recombination and biotechnologies process we was reception of new potato varieties, such “Dusti”, Faizobod”, “Rasht” and “Tajikistan”, which are zoned in republics from agriculture party Ministry of Agriculture of the Republic of Tajikistan.

PRION [PSI+] HAS AN IMPACT IN THE CONTROL OF GENOME STABILITY IN YEAST *SACCHAROMYCES CEREVISIAE*

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Prions are the form of the proteins with modified tertiary structure. They also possess the ability to self-propagating by converting the normal protein molecules into the prion form. There were also noted the increased frequency of genome instability in the neurons from the patients suffered from the neuromental diseases caused by prions. In yeast *Saccharomyces cerevisiae* the prion [PSI+], the research model of mammal prions, is the prion form of translation termination factor Sup35. The yeast strains with the mutations in the *SUP35* gene also showed increased chromosome instability.

We proposed the idea that the prions may cause neurodegenerative symptoms by increasing genome instability. The strains with prion [PSI+] and with the normal conformation of the Sup35 were investigated in the alpha–test. The alpha-test is a convenient test-system in yeast Saccharomyces cerevisiae to reveal high range of genetic changes, such as loss of chromosome, mutations, gene conversion, loss of the arm of the III chromosome, recombination and temporary lessions. These events interfere the expression of the the*MAT* locus, maped in the chromosomeIII. It leads to the mating type switching α→a, which could be observed as appearance of “illegitimate” hybrids in the mixture of two alpha-mating type strains.

In our experiments we showed that the prion [PSI+] reduces twice the frequency of both chromosome loss and gene mutations, and causes 5-fold increase of the gene conversionfrequency. The canavanine test also showed double decrease in mutation frequency in the strain with the prion.Our data suggests that prions may participate in mutagenesis.Acknowledgements: Grant RFBR # 15-04-08625 and Research Grant of St. Petersburg State University #1.38.426.2015.

AMYLOIDOGENIC PROPERTIES OF ARCHEAL PROTEINS DEPEND ON ENVIRONMENTAL CONDITIONS

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Amyloids are fibrillary protein aggregates possessing cross-beta structure. These aggregates are highly resistant to different environmental factors. That is why it is an interesting question, whether extreme habitats of some prokaryotes and amyloidogenic properties of their proteins are connected? To answer this question, we analyzed proteomes of 76 archaeal and 104 bacterial species. The fraction of amyloidogenic proteins in proteomes of acidophilic, thermophilic and hyperthermophilic archeae was shown to be significantly increased in comparison with neutrophilic and mesophilic species. It is interesting to note, that the fraction of such proteins of halophilic archeae was decreased, and we did not notice similar patterns in bacterial proteomes. Next, we analyzed distribution of amyloidogeneic proteins among different functional classes. We have shown that amyloidogenic proteins tend to be in the relatively big functional groups, and identified the groups, proteins of which tend to become amyloidogenic at extreme conditions. Proteins, connected with dynamics and structure of chromatin, appeared to be more influenced by environmental conditions. Taken together, in the current work the dependence of amyloidogenic properties on habitual conditions was first shown.

The study was supported by RFBR (Project 14-04-31838) and by the grant of the President of the Russian Federation № MK-4854.2015.4.

THE INFLUENCE OF THE LONG DIRECT SELECTION ON A MUTAGENESIS OF HETEROZYGOTES *vg*$^+$*vg*.

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The vestigial strain was chosen in our work as the initial parental strain for further crossing with wild type strains. The wild type strains were caught in different habitats. It is known that wild type strains can characterize by different parameters of viability, and also differ to the frequency of occurrence of damage like "cutting" on a wing, and respectively to degree of apoptosis. We made the assumption that the difference in the frequency of damages is based on amount of dihydrofolate reductase enzyme in wild type strains.

In our work we conduct the reciprocal crosses: wild type strains and vestigial strain. We used next strains:"*Host*" (Yekaterinburg, 2005), "*Belgorod*" (Belgorod, 2006), "*Bios-3*" (Dvurechensk, 2007) and "*Degtyarsk*" (Degtyarsk, 2011). In experiments were used "+" selection on existence of damage like "cutting" on both wings. The phenotypes, which were corresponding to various mutations, were found in three hybrid strains. First mutant phenotype “white” was found in *Bios-3xvg* F_{50}. Second mutant phenotype “scalloped” was found in *Hostxvg* F_{10}. Third mutant phenotype “yellow” was found in *vgxDegtyarsk* F_8. In *Belgorodxvg* F_{147} was not found any mutant`s phenotypes. Transposable elements can influence on emergence of white and yellow mutations. Transposons can be the reason of absence of mutations in *Belgorodxvg*. In our laboratory was revealed that *Belgorodxvg* is characterized by a *hobo*-element excision in the condition of a chemical stress testify (in the presence of a methotrexate) at the long direct selection on the frequency of ”wing`s cutting”. The hybrid strains were placed on medium with a methotrexate. The genomic instability in somatic cells was determined by the morphometric analysis of a wing as an indirect method. We established that after the influence by a methotrexate the spatial structure of a wing was changed. Thus, it is possible to suggest that hybrid strains during long selection are subject to a mutagenesis, and also the increased activity of transposable elements can be a cause of this mutagenesis. Work is financial support by a grant of the Russian Foundation For Basic Research - *14-04-31654*.

CALORIC RESTRICTION INFLUENCES LIFESPAN OF *DROSOPHILA MELANOGASTER* INDIVIDUALS WHOSE GENES CONTROLLING CIRCADIAN RHYTHMS ARE OVEREXPRESSED IN PERIPHERAL TISSUES

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The aging process is associated with various genes' expression level changes. Genes forming a system of "biological clock" of the body are not an exception, it evidenced by the worsening with age violations in rhythms of physiological activity and aperiodizm of sleep and wakefulness cycles phenomenon in old specimens. The molecular clock found in each cell of the peripheral tissues of multicellular organisms, are present and all unicellular, including prokaryotes (Shnol, 1996). The main environmental factor connected to the rhythms of biological processes is light, with daily and annual variations in the light intensity are associated such phenomena as sleep, physical activity, rest, growth, reproduction, sexual behavior, moult and migration. Most human genes of circadian rhythms are evolutionarily conserved and have orthologs in the fruit fly *Drosophila melanogaster*. It is found that adults of *D. melanogaster* show the decrease in gene expression of photosensitive protein Cryptochrome, while its overexpression in old specimens slows down the rate of aging (Rakshit, Jadwiga, 2013). On the other hand, fruit flies with mutations in the genes of circadian rhythms are characterized by a reduced life expectancy (Kondratov, Antoch, 2007). One of the *cyc* gene ortholog profed roles is way dTOR inhibition, resulting in metabolism supression, which prevents uncontrolled flow of resources and prolonging life of an organism (Giebultovicz et al., 2010). The purpose of this study was to investigate wheather caloric restriction affected the life span of *Drosophila melanogaster* which genes of circadian rhythms (*Period, Timeless, Doubletime, Clock, Cycle, Cryptochrome*) had been overexpressed. We chose UAS / GAL4 system to ensure conditioned (mifepristone-inducible) gene overexpression in flies' muscules. Next, Drosophila lines were placed on standard media with different caloric values life expectancy had been being observed once a day. The results of this study demonstrate the relationship of circadian rhythms' gene regulation mechanisms and aging components such as insulin-like and TOR signaling pathways. This work was supported by a grant from the President of the Russian Federation № MD-1090.2014.4 "Comparison of response mechanisms *Drosophila melanogaster* to oxidative, heat, cold, and genotoxic stresses using genome-wide transcriptome analysis."

NUCLEOTIDE SEQUENCE CONTEXT AND MUTABILITY OF *ESCHERICHIA COLI* GENES

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Suppose that individual variability of genes was the stress-induced mutagenesis consequences. This gene variation program is manifested in such features of the nucleotide sequence context, as potential quadruplex-forming sequences (PQS), repeated motif(s) (RM), GGGG homopolymer tract (poly-$dG_{n>4}$), sites of recombination (*chi*), and also overlapping with poly-$dG_{n>4}$ sites methylated by Dcm or Dam enzymes (GGGGATC, CCWGGGG).

To test this supposition we have carried out computational analysis by QGRS Mapper, Tandemswan, and diffseq EMBOSS programs to detect both regions consisting of PQS, RM on the plus strand, and mutation spectrum in 72 genes (GC% 52.95 ± 2.49) of 11 strains of *E. coli* (NCBI GenBank). Reference strain was *E. coli* MG1655. Analytical grouping method, Student's *t* distributions, ANOVA, regression, and clustering analysis were used to reveal the dependence of transitions and transversion frequency variability on the changes in density distribution or proportions of annotated sequence features.

It was found that the rows of both the frequency of mutations or transitions, and density distribution of PQS possessed increasing tendencies. Parallel to that, the rows of transversions, RM, and poly-dGn>4 frequencies/proportions had decreasing tendencies. The variational rows of PQS, RM, poly-$dG_{n>4}$ affected the frequencies of both mutations and transversions/transitions ($F_{mut} = 115.72$, $p < 0.001$, $F_{trasitions} = 115.72$, $p < 0.001$, $F_{trasversions} = 133.49$, $p < 0.001$). There was a moderate impact of density distribution of sequence motives on mutability of genes ($p < 0.05$). There were two major clusters of genes in grouped variational series. The first cluster included genes having a higher distribution level of GGGGATC (74% sites), the second – *chi* (100%) and CCWGGGG (93%). Decline in the levels of RM or transversions (cluster 1) and increase in the level of PQS or transitions (cluster 2) in nucleotide sequences of genes was observed. We suggest that the changes in the proportions of annotated sequence features are responsible for the level of gene mutability.

THE TEMPLATE PRINCIPLE IN BIOLOGY

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The template principle had been proposed for chromosome replication by N.K.Kolzov (1928) – the teacher of N.V.Timofeeff-Ressovsky, who in his turn, developed this idea in the form of con-variant reduplication concept (1930s) which explained origin of inherent variations (mutations) as a by-product of genetic material multiplication. Later on M.E.Lobashev proposed physiological hypothesis of mutation process (1946), in which he put together two terms: mutation and repair and suggested that any mutation is preceded by a pre-mutational event – a primary lesion of genetic material, as we used to say now.

Now the template principle is known as the Central Dogma of molecular biology, proposed by F.H.C.Crick (1958, 1970) and summarized: replication, transcription and translation – the first order template processes (TPI), operating with linear (or sequence) templates. This universal scheme may be completed to-day with the conformational (or space) templates and the second order templates (TPII) responsible for the protein (prion) inheritance phenomenon, in particular.

All the template processes (TPI, at least) have some universal characteristics: (1) ambiguity, which means that any encoding symbol in a template may be decoded ambiguously with a specific probability; (2) possibility of repair, or correction. These two features, working in balance, evolutionary optimize and define the final level of variability vs stability of each template process at any its stage: initiation, elongation (or copying) and termination. We accepted already ambiguity (“mistakes”) and repair for DNA replication at the elongation stage and it is easy to show the existence of the same features for transcription and translation. It is evident now that ambiguity (canalized by correction) in reading of initiation and termination signals of TPI plays a fundamental role in regulation and evolution of regulation of genetic (template) processes.

There is a considerable possibility of application of these principles not only to TPI but also to TPII organization. Study of interaction of different conformational templates with each other and of TPII with TPI is in progress now.

ORGANIZATION AND EVOLUTION OF THE DUPLICATED FLAVONOID BIOSYNTHESIS GENES IN TRITICEAE

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Gene duplication followed by subfunctionalization and neofunctionalization is of a great evolutionary importance. In plant genomes, duplicated genes may result from either polyploidization (homoeologous genes) or segmental chromosome duplications (paralogous genes). The flavonoid biosynthesis (FB) gene network is known to be a convenient model system for investigation of different issues of plant genetics. In the current study, homoeologous and/or paralogous copies were isolated for the FB regulatory gene *Myc* (encoding R/B-like bHLH transcription factor), and for the two key FB structural genes *F3h* (encoding enzyme flavanone 3-hydroxylase) and *Chi* (chalcone-flavanone isomerase) of allohexaploid wheat *Triticum aestivum* L. (genome BBAADD). Five copies of the *Myc* gene demonstrated essential structural and functional divergence. Their transcriptional activity was tissue-specific. In particular, only the *Myc1* gene is expressed in wheat pericarp, conferring purple color of grain due to accumulation of flavonoid pigments anthocyanins. Three *Myc* genes are expressed in other parts of wheat plant, while one copy is not expressed at all. The three homoeologous genes *Chi-A1*, *Chi-B1* and *Chi-D1* found in wheat encode identical enzymes, however their promoter regions diverged essentially, and the homoeologs are not always co-regulated. In particular, the three genes demonstrated different response to salinity in roots. Analysis of the duplicated *F3h* paralogue (*F3h-B2*) suggested this gene to encode functional enzyme that however differs from that encoded by the three homoeologous copies (*F3h-A1*, *-B1*, *-D1*) by replacement of some of the strictly conserved residues in the putative substrate-binding sites. *F3h-B2* promoter region diverged essentially from that of the *F3h-1* genes, and diversified transcriptional regulation of these two genes is observed. Analysis of *F3h-1* and *F3h-2* coding sequence divergence suggested *F3h* to be duplicated in the common ancestor of the Triticeae tribe. Specific occurrence of the orthologous *F3h-2* genes was demonstrated in a small group of Triticeae species having one of the closely related genomes B, G or S, and in rye. *F3h-2* could acquire a new functional specialization in the common progenitor of the B, G and S genomes, and in rye. These can be a reason for the maintenance of the duplicate *F3h* copies in these genomes, whereas in other Triticeae genomes, *F3h-2* was likely pseudogenized.

GENOME-WIDE IDENTIFICATION OF MUTATION CLUSTERING USING A NEW HIERARCHICAL METHOD

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Mutations in genomes exposed to mutagens frequently form clusters, including recently discovered *kataegis* in tumors. Clustered mutations comprise only a fraction of all mutations, while the other changes are distributed uniformly. Under this background «noise» direct identification and correct localization of clusters becomes ineffective and difficult.

We developed a new three-step procedure to detect clusters of mutations under these circumstances. The first step is estimation of approximate threshold of cluster size. On the second step, extraction of clusters from hierarchical analysis based on this threshold is performed. On the last step, the adjustment of cluster borders is performed to produce «raw» clusters of mutations. The filtration of raw clusters could be finally applied. To streamline this analysis, we developed a new file format for storage of the information about mutational clusters – *ccf* (*cluster call format*), based on *vcf* (*variant call format*). Implementation of our clustering algorithm and parsers for *vcf* and *ccf* files were included into *MACE* package (*Mutation Advanced Clustering Extractor*) that is available at https://github.com/mahajrod/MACE. Genome-wide SNV sets obtained via Next Generation Sequencing require a strict filtration because lots of false positive variants can be found in raw SNV data. *MACE* allows for incorporation of additional filtration during the clustering to get more reliable data for mutagens with well-defined signatures or substitutions patterns (for example, APOBEC deaminases).

To summarize, the new approach and user-friendly software developed in this study provides a reliable solution of the difficult task of the detection of mutation clusters. The work was supported by Russian Foundation for Basic Research (grant 15-04-08625) and St. Petersburg State University (grant 1.38.426.2015).

GENOME STABILITY: GENETIC AND EPIGENETIC FACTORS

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The report is dedicated to the 70th anniversary of geneticist Alexander Devin's birth (1944—2007). An important field of his work was studying the genetic control of the stability of *Saccharomyces cerevisiae* yeast's genome and a search for new genes determining cell genetic stability. Saccharomycete yeasts are especially convenient for genome stability research because they are tolerant to extra chromosomes. Besides, by the beginning of this work, the mitochondrial genome was most studied in yeasts among all eukaryotes because yeast cells can survive its degenerative rearrangements *(rho$^-$)* and even elimination *(rho^0)*. A special method was developed that allowed making a collection of nuclear mutations leading to a change in the stability of the nuclear and mitochondrial genomes *(Devin, Koltovaya, 1981; Devin et al., 1994)*. These mutations increased the chromosome loss frequency in aneuploid strains and decreased the mitochondrial mutation *(rho$^-$)* frequency. It was also found that aneuploidy has a regulating effect on mitochondrial genome stability (Devin et al., 1987). It is remarkable those for the first time mutations were obtained that stabilize the mitochondrial genome and decrease the respiratory failure mutation frequency. The nature of this phenomenon is still unclear and is very interesting.

To understand how these enzymes control genome stability and in what processes they participate, genetic appearances of mutations were studied *(Devin et al., 1990; Koltovaya et al., 2003; Koltovaya et al., 1998; Koltovaya, Kadyshevskaya, 2009)*. Besides chromosome destabilization, found were mutation influence on cell sensitivity to the damaging effect of ionizing radiation, DNA recombination and checkpoints. Among the studied mutations, isolated were the mutations leading to cell radiosensitivity and radioresistance.

Some of the nuclear mutations were mapped and sequenced *(Devin et al., 1990; Koltovaya et al., 2003)*. It turned out that the studied mutations are localized in highly hierarchical genes that play the key role in cell functioning. In terms of modern system biology, those are the so-called hubs of biological networks describing the physical interactions between the proteins. The identified genes participate in the regulation of cell processes by chemical modifications. One of them encodes the central CDC28/CDK1 kinase, which regulates cell cycle transition (*Koltovaya, 2013*). The second gene encodes the Ada1 component of the transcriptional histonacetyltransferase complex SAGA, in which it is the Gcn5 subunit that has acetylase activity. The third gene encodes the nucleolar Net1 protein, which controls Sir2 deacetylase localization. It was supposed that the observed effects are determined by the chemical modification of different substrates in particular chromatin structure elements (phosphorylation, acetylation, and deactylation of histones and non-histone proteins), and that there exist common regulatory elements of nuclear and mitochondrial DNA chromosome packing. It is interesting how the results obtained by A.B. Devin and his colleagues match modern data and how they were developed. The report will include a review of literature data on the epigenetic regulation of the molecular cell processes involving mentioned genes.

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IS THERE A NUCLEOTIDE-LEVEL GENETIC CODE FOR GENE EXPRESSION CONTROL?

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The genetic code describing the "digital storage" of genetic information remains one of the basic principles of genetics and molecular biology. Today, with the rapid development of sequencing technologies, it became clear that the majority of DNA does not directly contribute to storage of the inheritable information. Instead, a notable portion of genome controls usage of this information in different conditions and different cell types that make up a higher eukaryotic organism.

It seems there is no short answer to the question of a putative sequence-level regulatory code describing the structure of gene regulatory regions. However, modern experimental data supported with bioinformatics methods reveal not only base components of the nucleotide-level regulatory code, binding sites of regulatory proteins, but also shed light on their composition and functional roles.

We shall discuss the power and limitations of sequence motif analysis applied to study gene regulatory regions in higher eukaryotes. We shall highlight several major insights gained from such analysis, in particular, we shall point out possible regulatory effects of individual genomic variants, and demonstrate how somatic mutations reveal positive and negative selective pressure on cancer cells population.

TRANSCRIPTION DETERMINES THE LANDSCAPE AND CLUSTERING OF MUTATIONS INDUCED IN DIPLOID YEAST BY AID/APOBEC DEAMINASES

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The mechanisms and genetic consequences of non-random distribution of mutations resulting in mutation clusters, including recently discovered *kataegis* (mutational showers) in tumor genomes, are not well understood. To get insight into the origin of clusters and their significance, we analyzed the mutational single nucleotide variations (SNV) data obtained by whole-genome sequencing of yeast drug-resistant mutants induced in diploids by AID/APOBEC deaminase PmCDA1 and base analog 6-HAP. PmCDA1-induced robust clusters, while 6-HAP induced a few weak ones. We found that PmCDA1, AID, and APOBEC1 preferentially mutate the beginning of the actively transcribed genes in yeast. Inactivation of transcription initiation factor Sub1 strongly reduced deaminase-induced *can1* mutation frequency, but, surprisingly, did not decrease the total SNV load in genomes, merely redistributing them. We propose the following model of induction of clustered mutations by deaminases: 1) Exposure of ssDNA strands during transcription and loss of protection of ssDNA due to depletion of ssDNA-binding proteins, such as Sub1; 2) Achievement of physiological conditions in some cells for the optimal manifestation of APOBEC activity, leading to enzymatic deamination within the highly expressed genes. This model can apply to both initial and later stages of oncogenic transformation.

EVOLUTION OF THE MUTATION RATE

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Recent applications of whole-genome sequencing to mutation-accumulation lines have revealed that the mutation rate per nucleotide site per generation varies by about three orders of magnitude across the tree of cellular life, with some unicellular eukaryotes having the lowest rates, prokaryotes being somewhat intermediate, and multicellular species (especially mammals) having the highest rates. The observed patterns are explained by a remarkably simple set of rules. Species-specific mutation rates are inversely proportional to both the effective population size and the number of genomic sites under selective constraint, which together explain the majority of phylogenetic variation in replication fidelity. These observations are consistent with the drift-barrier hypothesis, which postulates that selection generally works to reduce the genome-wide deleterious mutation rate to the point at which the advantage of any further refinement is smaller than the power of random genetic drift. Other lines of evidence that appear to be consistent with this hypothesis include: patterns of variation in base-loading accuracy among different DNA polymerases; the direct demonstration of evolutionary changes in mutation rates in experimental populations with different effective sizes; and the extraordinary increase in the error rates of RNA polymerases, the effects of which are transient unlike inherited mutations. The case will be made that the implications of the drift-barrier hypothesis extend well beyond replication fidelity, providing a useful platform for understanding how a diversity of cellular features may have arisen over evolutionary time.

SCREENINGS FOR NOVEL AMYLOID-FORMING PROTEINS IN BACTERIA *ESCHERICHIA COLI*

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Amyloids are fibrillary protein aggregates possessing cross-beta structure. These aggregates were found in different systematic groups, from bacteria to higher eukaryotes. In bacteria, amyloids may have different functions: at least six functional groups of bacterial amyloids (curlins, hairpins, chaplins, listeriolysins, microcins and phenol-soluble modulins) are known to date. The most studied bacteria, *Escherichia coli*, have functional amyloids called curlins that are involved in the formation of biofilm matrix. The main question of this study was whether other proteins in *E. coli* proteome are able to form amyloids *in vivo*? To address this issue, proteomic method PSIA (Proteomic Screening and Identification of Amyloids), recently developed by us, was used. PSIA is based on the unusual resistance of amyloids to treatment with ionic detergents (sodium dodecyl-sulfate). At the first stage of PSIA, this feature allows separation of amyloids and amyloid-like polymers from monomeric proteins and non-amyloid polymers by detergent treatment with consequent ultracentrifugation. Next, purified detergent-resistant fractions are digested with trypsin, separated by high-resolution liquid chromatography and identified by mass-spectrometry. As a result of this experiment, we detected a set of bacterial proteins capable of forming detergent-resistant polymers *in vivo*. The detailed analysis of this set revealed that all bacterial proteins identified by PSIA have amyloidogenic regions detected by WALTZ algorithm (http://www.switchlab.org/bioinformatics/waltz). A very interesting subset of *E. coli* proteins identified by PSIA is bacteriocins. The finding of these proteins is important, since bacteriocin homologue of *Klebsiella pneumoniae* has recently been proven to have amyloid properties. Possibly, formation of amyloids by bacteriocins may be the common mechanism shared by different species of bacteria.

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CROSSING AND GRAFTING OF AMERICAN ARTICHOKE *(HELIANTHUS TUBEROSUS* L.*)* WITH SUNFLOWER *(HELIANTHUS ANNUUS* L.*)* IN THE CONDITIONS OF TAJIKISTAN

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In the first time in the conditions of the Gissar valley of Tajikistan we spend crossing and grafting of American artichoke with sunflower. As an initial selection material was used elite seed tubers of variety of American artichoke "Interest" and elite seeds of sunflower of variety "Ubileini" (they are selection varieties of the Russian Federation). In experiences on crossing of these two kinds of plants, as the parent form, we used grades American artichoke «Interest", and as fatherly, pollen of plants of sunflower of variety "Ubileini". The collected material in the form of seeds of hybrids F1 American artichoke and sunflower (grades Interest x Ubileini) will be studied in our further researches.

In experiences on grafting of these two kinds of plants (*Helianthus tuberosus* l. + *Helianthus annuus* l. And *Helianthus annuus* l. + *Helianthus tuberosus* l.*)* in both cases when as a stock sunflower plants and on the contrary served, plants of american artichoke were a stock, the imparted branches on stocks well took root and provided normal growth and development of plants. Us it is revealed, that under the influence of an elevated part of plants, that is of American artichoke, in roots the imparted plants of sunflower were formed small tubers, which represent special interest for the further researches. Also under the influence of a stock (sunflower plants) on plants of American artichoke the increase in the size of inflorescences, nimbuses and seeds was observed. Thus, by crossing and a grafting of american artichoke with sunflower, us has been received valuable breeding - genetic materials in the form of seeds of hybrids F_1 and tubers which will be studied in future our researches.

MECHANISMS OF GLOBAL AND REGION-SPECIFIC CONTROL OF MUTAGENESIS

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Mutagenesis has been traditionally studied in haploid cells – in microorganisms and in germ cells. However, most eukaryotic cells are diploid or have higher ploidy. The mechanism of the appearance of mutants in diploid cells is a classical problem in biology. In cancer research it is exemplified by the two-hit kinetics of appearance of retinoblastomas. The most common loss-of-function mutations are recessive and are not immediately seen in heterozygous diploids. In this case the manifestation of a new phenotype requires an inactivation or a loss of the second,wild-type copy of the gene. Most agents induce mutants in diploids by the mutation-segregation mechanism. A high level of replication errors leads to mutants in diploid yeast due to mutations in both copies of the gene. Their frequency is much higher than predicted by the coincidence of two independent events. Combining classical genetics and next generation DNA sequencing we found that the mutability of growing cells is uneven and ploidy is an important factor determining genetic outcomes. Haploid cells with the highest levels of mutagenesis die due to lethal mutations. Therefore, we underestimate mutation frequency in haploids. Lethal recessive mutations load is tolerated in diploids and descendants of hypermutable cells with genomes saturated with mutations are recovered. Expression of APOBEC deaminasesin diploid yeast elevated mutant frequency in reporter genes by coincident mutations and caused genome-wide accumulation of changes with prominent signs of *kataegistic*clusters. The major sources of the ssDNA target of deaminasesin the cells are replication, repair and transcription. APOBEC deaminases induced mutants in stationary phase diploid yeast cells in transcription-dependent manner, mutating predominantly the beginning of the genes. A sharp increase of yield of mutant clones during progression of stationary phaseis due to induction of recombination. Therefore, several mechanisms contribute to the induction of mutant clones in non-dividing diploid cells. This model could be applied to the explanation of initiation of cancer in terminally differentiated cells.

THE INFLUENCE OF THE ACTIVITY OF DNA DAMAGE RECOGNITION AND REPAIR GENES ON THE LIFESPAN OF *DROSOPHILA MELANOGASTER*

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The ability to appropriately respond to environmental and physiological stresses influences on vitality and longevity of organisms. Stress factors both directly and indirectly lead to DNA damage, which is a critical event for cell and organism. Key cellular mechanisms that resist against their action and provide genome integrity are DNA damage recognition and DNA repair. The aim of this work was to study the role of genes involved in DNA damage response regulation (*Drosophila* homologous of *HUS1, ATR, ATM, CHK2, p53, GADD45* genes), DNA excision repair (homologous of *PCNA, XPC, XPF, APE1* genes), and double-strand break repair (homologous of *BRCA2, KU80, WRNexo, XRCC3, RAD54, BLM* genes) in the determination of aging and longevity. To study their action on lifespan and aging rate we applied two approaches. Firstly, we analyzed the lifespan changes in *Drosophila melanogaster* flies with mutations in DNA damage recognition and repair genes, and showed the negative effect of loss-of-function of these genes. An alternative approach is based on the investigation of lifespan changes of flies with ectopic activation of studied genes. We used transgenic flies with both ubiquitous and tissue-specific overexpression of DNA damage recognition and repair genes by GAL4/UAS system. However, in the most cases overactivation of DNA repair genes led to lifespan decrease. Reasons of this adverse effect can include insufficient epigenetic regulation, superfluous energetic expenses and enhanced aging-related hyperfunction of cellular and organism systems.

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PROTEIN ASSEMBLY DISORDERS AND PROTEIN-BASED INHERITANCE

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Amyloids are fiber-like ordered aggregates generated via intermolecular cross-ß interactions. *In vivo* amyloid formation is a widespread phenomenon in eukaryotes. Self-perpetuating amyloids provide a basis for the transmissible protein isoforms (prions) that cause infectious neurodegenerative diseases in mammals (including humans) and manifest themselves as non-Mendelian heritable elements in yeast and other fungi. A variety of human amyloid diseases, including such widespread disorders as Alzheimer's and Parkinson's diseases, are caused by self-perpetuating amyloids possessing at least some prion properties. Initial formation of prion aggregates in yeast is counteracted by ribosome-associated chaperones and assisted by cytoskeletal networks. Association of misfolded proteins with certain intracellular locations plays an important role in prion formation. Propagation of the prion state is controlled by the concerted action of the chaperone proteins, promoting breakage of amyloids into smaller oligomeric seeds that initiate new rounds of prion proliferation. Therefore, prion propagation employs the enzymatic machinery which is normally supposed to protect cells from environmental stresses. Amyloid-forming potential of yeast prion proteins appears to be conserved in evolution despite divergence of the amino acid sequences. However, transmission of prion state even between closely related proteins could be impaired by sequence differences, resulting in the so called "species barrier". Both sequence divergence and structural variability of prion aggregates contribute to the species barrier. As an additional mechanism of heritable change, prion formation may play an important role in heritable variability at the population level.

THE ORIGIN OF STERILE CYTODUCTANTS OBTAINED IN THE ALPHA-TEST

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The alpha-test is a sensitive system for genetic toxicology. The system utilizes heterotallic strains of yeast *Saccharomyces cerevisiae*. It is based on genetic system controlling the mating type in yeast. The mating type of yeast strains is controlled by the *MAT* locus which is located on the right arm of chromosome III. The *MAT* locus determines “a” or “α” cell type of haploid cells. Normally haploids of the opposite cell types can mate and form diploid cells. Primary lesions, mutations and recombination events in *MATα* as well as loss of the chromosome III or its right arm impair the *MATα* expression. It causes mating type switch from α to a and mating of two initially α-type cells. The frequency of the "illegitimate" hybridization is a criterion of genome instability in the alpha-test.

Different phenotypes of hybrids in the alpha-test correspond to different molecular events of the mating type switch. It was predicted that sterile cells obtained in "illegitimate" cytoduction (the modification of the alpha-test) contain mutations in the *MATα* locus. Our new data indicate that two thirds of sterile cytoductants do hold mutations in the *MATα*. We demonstrate that the other sterile cells are different in their ploidy. One of the reasons for sterility is forming of triploid cells α/a/α. We show that overexpression of *STE12* transcription factor restores mating type “α” to triploid cells α/a/α as well as to diploid cells α/a. Our findings open new opportunities for further improvement of the alpha-test.

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Fe-S CLUSTERS ASSOCIATED WITH THE C-TERMINUS OF THE DNA POLYMERASE DELTA ARE ESSENTIAL FOR DNA POLYMERASES SWITCH AND IN THIS WAY CONTROL SPONTANEOUS AND INDUCED MUTAGENESIS

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Mutation rates are precisely controlled by multiple cellular mechanisms. Loss of these controls increases genome instability, changes the evolutionary fate of cells and leads to diseases, including cancer. DNA polymerases are critical guards of genome during replication, repair and recombination. Eukaryotes have about 15 different DNA polymerases whose activity and fidelity broadly varies. Most amount of the genomic DNA is synthesized by the accurate processive replicative polymerases Polα, Polδ and Polε, with some involvement of a specialized error-prone Polζ, which is recruited when DNA synthesis is impeded. This prevents major genome rearrangements and cell death in expense of the increase of rates of point mutations. Several molecular mechanisms controlling polymerases switches during replication and repair have been described. None of them are fully understood. We focus on the mechanism by which C-terminal domains of the B-family polymerases control the polymerase switch during replication. DNA polymerases Polδ and Polζ have conservative motives on the C-terminus (CTD), which are required for interaction with Fe-S clusters. We propose that Fe-S clusters are essential for the communication between the two DNA polymerase and regulate their switches during replication on damaged DNA. To check this, we constructed yeast *S. cerevisiae* strains with a change of the conservative cysteine in CTD of the Polδ (*pol3-13* allele). We have confirmed that the *pol3-13* mutation leads to the five-fold increase of spontaneous mutation rates. This effect was completely depended on the functional Polζ. The *pol3-13* mutant is UV-sensitive but has defects in UV light induced mutagenesis. Our results reveal the differential control of spontaneous and UV induced Polζ-dependent mutagenesis by the Fe-S clusters present in replicative Polδ.

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ANTIBIOTIC RESISTANCE OF STRAINS *PSEUDOMONAS AERUGINOSA* ATCC 27853 AND SMALL-COLONY VARIANTS

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Pseudomonas aeruginosa is an opportunistic pathogen. This microorganism is a ubiquitous Gram-negative bacterium found in diverse ecological habitats. *P. aeruginosa* can efficiently adopt diverse strategies to evade antimicrobial stresses. Compared to wild-type *P. aeruginosa* its small-colony variants (SCVs) show an increased antibiotic resistance. The aim of the work was to study the ciprofloxacin antibiotic resistance induced in cells of reference strain and strain with SCV phenotype. We observed cell survival and frequency of stress-induced mutants to ciprofloxacin in the cultures of planktonic and biofilm cells of the reference strain ATCC 27853 and SCV strain from the swimming pool of bacterial populations. Biofilms prior to incubation with ciprofloxacin were grown for 4 days. Concentration of ciprofloxacin was determined experimentally. Cells were pre-incubated in LB with antibiotic within 90 minutes. Every 15 minutes one portion was seeded on LB-agar to study the frequency of stress-induced mutants and to examine cell survival. Cell survival of biofilms under the action of ciprofloxacin was higher compared to cell survival of planktonic cultures of both strains. The results indicated direct dependence of the frequency of stress-induced mutants on the growth phase culture of a SCV strain. However, we observed high sensitivity to ciprofloxacin in SCV cells. Then, biofilm cells of both strains were incubated with ciprofloxacin up to 16 days. Extending the time of incubation with ciprofloxacin to 16 days showed that SCV strain evoked the ciprofloxacin resistant mutants by the end of incubation. At the same time cells of the reference strain of ATCC 27853 died by the end of incubation. We propose that the antibiotic-induced stress in cells of ATCC 27853 triggers the temporary mutagenesis. This strategy allows gradually reducing the number of surviving cells. Some of them would develop the ciprofloxacin resistance. Cells of SCV strain used a different strategy to develop the antibiotic resistance. It is required quite a long period of time that mutagenesis could be realized. Results of our study have shown that the acquisition of antibiotic resistance is more effective strategy of SCV strain.

THE USE OF DNA TECHNOLOGY TO MONITOR GENETIC HETEROGENEITY IN BROILER LINES

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It is known that in broiler industry the essential issue is the homogeneity of chicken lines. However, this situation contradicts the requirement for a certain diversity of populations that contributes to the genetic progress. In this paper we develop ways to control the genetic diversity through the analysis of gene polymorphism and microsatellite DNA repeats that are scattered throughout the genome. The current level of DNA technology allows the use of polymerase chain reaction (PCR), DNA fingerprinting and sequencing. The object of the study was DNA isolated from the blood of autosex four-line cross "Smena 8" chickens. In the study maternal chicken lines of White Plymouth Rock and paternal line of White Cornish along with final broiler hybrid have been used. The data obtained by DNA fingerprinting allows sufficiently objective evaluations concerning the degree of divergence between groups within chicken lines as well as between total lines. The correlation analysis of the relationship between the occurrence of certain minisatellite markers (DNA fragments) and the live weight of broiler chickens showed a statistical significance. The calculation of basic genetic parameters (intra and -intergroup genetic similarity coefficients, genetic distance and level of heterozygosity) provides data as to the degree of within population genetic diversity and divergence between populations. Using PCR analysis of the frequency of polymorphic genes with certain types of single nucleotide polymorphisms (SNPs) in releasing hormone growth factor, pituitary and myostatin transcription factor the discovery of certain types of polymorphisms with growth rate has been demonstarated. Thus, the analysis of DNA polymorphism enables quantifying genetic diversity in broiler lines, as well as their heterozygosity and divergence and monitoring these parameters in grandparent, parent forms and final hybrids. Potential for chicken selection based on DNA and gene polymorphism has been evaluated. Such a control can be an effective tool in the breeding and improvement of broiler lines.

MOLECULAR NATURE OF PRIMARY DNA LESIONS DETECTED IN THE ALPHA-TEST

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Primary DNA lesions by way of error-prone repair cause heritable changes in genetic material. The genetic consequences of DNA damages when they are transformed into gene and genomic mutations are well documented, however less is known about the impact of DNA lesions on cellular phenotype before lesions are eliminated by repair. To investigate the phenotypic expression of primary DNA lesions, we use an yeast-based assay that is called the alpha-test. The alpha-test based on illegitimate α×α hybridization of heterothallic yeast *Saccharomyces cerevisiae*. Analysis of illegitimate hybrids allows to distinguish primary lesions that are transformed through inaccurate repair into gene mutations, or induce chromosome aberrations, gene conversion and recombination from primary lesions that were correctly eliminated by repair. We suppose that in the alpha-test DNA lesions that are fixed in the error-free manner phenotypically express as a temporary mating type switch α →a in yeast cells. To identify molecular nature of primary lesions that are able to affect phenotype of yeast cells we determined the spectra of genetic changes in the alpha-test. We studied effects of several mutagens, which cause specific DNA damage, in combination with defects of different repair systems. Our results show that base modifications induced by 6-N-hydroxylaminopurine and 8-oxoguanine and camptothecin-induced double-strand breaks may cause phenotypic changes in yeast cells that results in a temporary mating type switch α →a before repair take a place. Unpaired nucleotides induced by the inactivation of mismatch repair by disruption of the *PMS1* gene were detected in the alpha-test mostly as inherited genetic changes after their error-prone repair. Our results reveal that the alpha-test allows to detect phenotypic expression of primary lesions that occur mostly during the G1 stage of the cell cycle. Acknowledgements: Grant RFBR # 15-04-08625 and Research Grant of SPbU #1.38.426.2015.

Cancer genetics & cancer therapy

ASSOCIATION BETWEEN METABOLIC SYNDROME AND GENE POLYMORPHISM IN BELARUSIAN POPULATION

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Metabolic syndrome (MS) is regarded now as a public health problem. Its prevalence and morbidity in developed countries rises each year. The aim of the present study was to determine the association of *ACE, BDKRB2, UCP2, TCF7L2, PPARG* gene polymorphisms with MS in Belarusian population.

A total of 121 patients (58 women and 63 men) with MS were included in this study. The control group consisted of 362 randomly selected Belarusians. All gene polymorphisms were determined using polymerase chain reaction with specially designed allele specific primers. The statistical analysis was performed using STATISTICA 10 for Windows (Statsoft Inc., USA). Differences were considered significant at $P<0.05$.

The analysis of distribution of genotype and allele frequencies of analyzed gene polymorphisms did not reveal statistically significant difference in the genotype frequencies of *I/D* polymorphism of *BDKRB2* gene. At the same time the risk of MS was significantly higher for *I* allele careers (OR=1.35 95% CI, 1.01-1.82). We have also shown that the risk of MS is much higher for carriers of *Ala/Ala* genotype of *UCP2* gene, *C/T* genotype of *TCF7L2* gene (OR=1.81 and OR=2.08 respectively, $P<0.05$).

For all patients, ranges of triglycerides, total cholesterol, creatinine, total bilirubin, alanine transaminase, aspartate transaminase and urea were measured. Body mass index was also included in the analyze. The correlation between patient's genotype and AST, ALT, TG levels was revealed. The observed correlation was weak but it may be explained by the quantity of analyzed individuals, which is insufficient for achieving statistical power. Further analysis of association of clinic-biochemical parameters with gene polymorphisms predisposing to MS is required.

This study clearly indicates that tested polymorphisms of *ACE, UCP2, TCF7L2, BDKRB2* genes play the important role in predisposition to metabolic syndrome. Screening of these polymorphisms may enable early revealing of population groups with increased risk of MS groups to perform preventive measures in a timely manner, to improve treatment effectiveness, to avoid complications, as well as to cut down the

TUMOUR TREATING FIELDS - NEW TYPE OF CANCER THERAPY

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The current forms of cancer treatments (mainly surgery, chemotherapy, radiotherapy) are effective but often contribute to the complications and side effects. Patients may suffer during and after the cancer therapies. There are risks concerned with the various forms of treatments. Some of them are invasive which has limitations and can cause complications. Others are non-invasive but are known to damage healthy cells in the process and, as a result, shorten the patient's survival and or quality of life over time. If there is an effective alternative form of cancer treatment which is non-invasive and can slow or reverse tumour progression, by inducing cell death in solid tumours without damaging healthy cell, then the patient's survival over time will increase together with life quality. This research seeks to determine if low intensity intermediate-frequency electric fields /Tumour Treating Fields (TTF) therapy, which is a new alternative form of cancer treatment therapy, can be used as this effective alternative that can disrupt the rapid cell division of cancer cells, without the associated risks that patients suffer from the current treatments available. Using in vitro techniques, low intensity electric fields of frequencies within the intermediate range (between 1 kHz and 10 MHz) was applied across cultured cells. Disturbance and arrest of cell proliferation were observed. The same effects were reported in literature and the TTF treatment for certain types of cancers was approved in some countries. The possible mechanisms of the TTF action as well as limitations are discussed.

ANALYSIS OF CRITICAL REGIONS OF CANDIDATE GENES FOR FAMILIAL AND SPORADIC COLORECTAL CANCER CASES

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In recent years there has been considerable worldwide increase in colorectal cancer (CRC) morbidity and a significant rejuvenation of this type of cancer. Despite the fact that the majority of colorectal cancers cases are sporadic, about 20-30% of patients present with familial history of CRC. Identification of association between key candidate genes and risk of CRC is intensively studied on different populations. Here we present the results of molecular-epidemiological study of different types of colorectal cancer in population from Kazakhstan.

Blood samples were collected from patients diagnosed with rectal or colon cancer (249 individuals) as well as a matched control cohort of healthy volunteers (245 individuals). Among CRC patients there were 32 patients with early onset CRC (28-50 yrs), including 10 patients with a family history of cancer. The candidate polymorphisms of *DCC*, *TP53*, *hMLH1*, *GSTT1* and *GSTM1* genes were genotyped for sporadic CRC cases. The mutation hot spots regions of genes *APC, KRAS, MLH1,* and *TP53* associated with famous familial syndromes were studied for the suspected familial cases.

Our results showed a significant association with increased CRC risk in the following genotypes: *DCC* (32008376 G/G and G/A vs. A/A; OR=3.45, $p<0.0002$), *MLH1* (-93G/G vs. G/A and A/A, OR=1.45, $p<0.04$), *TP53 (Pro72Pro; OR=3.80,* $p<0.0001$), and *GSTM1* deletions (OR=1.83, $p<0.001$). Analysis for ethnicity and smoking for each of the investigated polymorphisms showed that some genotypes can have a predictive value for susceptibility to CRC, at least those that demonstrate statistically significant ORs either for the combined mixed population of Kazakhstan or for both main ethnic groups separately (Kazakhs and Russians): *TP53* Pro72Pro homozygous (for Kazakh - OR=3.40, $p<0.003$; for Russian - OR=4.69, $p<0.0001$) and *GSTM1* deletions (for Kazakh - OR=2.30, $p<0.01$; for Russian - OR=1.64, $p<0.02$).

The spectrum of mutations (8 mutations) in “hotspots” regions of genes (*APC, TP53, MLH1, MSH2*) associated with early CRC development and possible family inheritance were defined. In a cohort of patients with early CRC onset 3 new previously non-described mutations were identified (mutation in intron 15 of *MLH1* gene (c.1732-90C>A), mutation in intron 4 (c.376-19C>T) and intron 9 (c .993 + 12T>C) of *TP53* gene). Well known coding polymorphisms were observed in exon 8 of *MLH1* (rs1799977 - A655G/Ile219Val), in exon 7 of *MSH2* (rs5028341 - C1168T/Leu390Phe), in exon 15 of *APC* (rs1801166 - G3949C/p.Glu1317Gln and rs41115 – 4479G>A). The single deletion, c.3613delA (p.Ser1205fs), located in exon 15 of *APC* gene, was found in the heterozygous state in two patients with a family history of adenomatous polyposis.

The results of the research will significantly enhance the ability of the national screening program for colon and rectum neoplasms and increase the efficiency of measures for the prevention of this disease in Kazakhstan.

EVOLUTION BY TUMOR NEOFUNCTIONALIZATION AND PHENOMENON OF CARCINO-EVO-DEVO GENES

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Earlier I formulated the hypothesis of the possible evolutionary role of tumors. This hypothesis suggests that tumors supply evolving multicellular organisms with extra cell masses for the expression of newly evolving genes. After expression of novel genes in tumor cells, tumors differentiate in new directions and give rise to new cell types, tissues and organs.

In the presentation, the bulk of data supporting the positive evolutionary role of tumors will be reviewed, obtained both in the lab of the author and from the literature sources.

The following issues will be addressed: the widespread occurrence of tumors in multicellular organisms; features of tumors that could be used in evolution; the relationship of tumors to evo-devo; examples of recapitulation of some tumor features in recently evolved organs; the types of tumors that might play the role in evolution; examples of tumors that have played the role in evolution.

The discussion of experimental confirmation of nontrivial predictions of the hypothesis will include the analysis of evolutionary novelty of tumor-specifically expressed EST sequences; *ELFNI – AS1*, a human gene with possible microRNA function expressed predominantly in tumors and originated in primates; *PBOV1*, a human gene of the recent *de novo* origin with predicted highly tumor-specific expression profile; and the evolutionary novelty of human cancer/testis antigen genes.

The conclusion is made that expression of protogenes, evolutionarily young and/or novel genes in tumors might be a new biological phenomenon, a phenomenon of *carcino-evo-devo* genes, predicted by the hypothesis of evolution by tumor neofunctionalization.

EFFECTS OF PHOTODYNAMIC THERAPY ON CANCER STEM CELLS (CSCs) *IN VITRO*

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According to modern concepts, most of the tumors are characterized by hierarchical structure and includes cancer stem or cancer-stem like cells (CSC). It was shown, that CSCs have resistance to low-LET radiation and a couple of anticancer drugs. This resistance is one of the possible reasons of cancer recurrence. However photodynamic therapy efficiency for CSCs elimination is poorly studied. The aim of the study was to determine accumulation of a clorine e6 photosensitizer “Photolon”(PS) by CSC and non-CSC and to compare total cell death after photodynamic treatment in vitro on stable cancer lines (murine melanoma B-16, human breast adenocarcinoma MCF-7, and cervical carcinoma Hela).

We have shown difference in accumulation of PS in CSCs (which were identified by flow cytometry using side population (SP) technique by the ability to exclude fluorescent dye Hoechst 33342) and other bulk of cancer cells (non-SP). It was found, that intracellular concentration of PS (measured by its fluorescence) has linear dependence on its medium concentration (within range of 0.75-15ug/ml) both for SP and non-SP ($R>0.93$; $p<0.01$) for all cultures used. However, SP cells accumulate PS much slower, than non-SP (1.8-fold for B-16 and 1.5 for MCF-7 and Hela, $p<0.05$). Accumulation process of PS has non-linear dependence on incubation duration and differs in SP and non-SP. Analysis of the dependences shows that intracellular concentration of PS significantly differs in SP and non-SP 1 hour after addition of the preparation ($p<0.05$), suggesting that CSCs could have ability to exclude this substance. In spite of difference in PS accumulation, we have shown that death rate after activation of PS with 661nm laser radiation ($6.2 mW/cm^2$) does not significantly differ in SP and non-SP cells under all experimental conditions (PS concentration range of 0.375-1.5ug/ml, that is 0.5-1-fold of therapeutic dose, and exposure during 30-60s) which are actual for all cell cultures used.

Thus, these results show firstly high efficiency of photodynamic treatment in terms of CSC elimination.

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GENETIC BASIS OF FUTURE MEDICINE

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Future medicine will be personal, predictive, preventive and participative (they say "medicine 4p"). All these characteristics of future medicine are based on DNA-testing.

Personal medicine have to treat patient but not decease and drugs have to be used according to patient genotype. There are more than 30 drugs nowadays which can be recommended only after genetic testing. For instance using of interferon for virus hepatitis C treatment will be successful or unsuccessful in dependence of patient interleukin 28b (C/T, rs12979860) polymorphism. The same situation is with many other drugs. Various medicine and various its doses will be prescribed to humans with different genotypes for illness treatment in future.

Molecular-genetic diagnostic allows estimate genetic predisposition to multifactorial diseases. We elaborated molecular genetic technologies for risk evaluation of cardiovascular pathology, diabetes, metabolic syndrome, osteoporosis, pregnancy miscarriage and so on. Detection of genetic predisposition to such pathologies provides possibility to reveal high risk people groups (*predictive medicine*) and to provide required prophylaxis (*preventive medicine*).

DNA-testing allows to reveal genetic predisposition to diseases just after child birth. If human knows about high risk of some multifactorial pathology he can correct his life style in order to avoid environmental risk factors and to prevent a development of disease in this way. This is *participative medicine* (participation of potential patients) .

We can propose the fifth name for future medicine – "*population medicine*". Indeed it is known that rates of illnesses and rates of pathology gene polymorphisms in different ethnos and different populations are very diverse. For instance the frequencies of Leiden mutation, which is responsible for arterial thrombosis, vary from 11% in Sweden till 0% in most Africa countries (44 % altogether in Europe and practically 0% in Africa). It is necessary to take into account such facts for prophylactic medicine measure choice.

Thus, molecular - genetic testing provides possibility for morbidity and mortality decreasing, as well as life longevity increasing, that is why genotyping is basis for future medicine ("medicine 5p").

RADIOBIOLOGICAL BASIS OF DENSELY IONIZING RADIATION APPLICATION IN NUCLEAR MEDICINE

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The main advantages of densely ionizing radiation application in nuclear medicine are well known: the reduction or complete inhibition of cell ability to recover from sublethal and potentially radiation damage, and increased biological effectiveness to produce primary radiation damage, resulting in the higher relative biological effectiveness (RBE) about of 3–10 in dependence of dose radiation, biological test and object. Moreover, the increased values of the RBE are displayed for low doses used in fractionated radiotherapy. The purpose of this paper is to present new experimental data concerning the features of the densely ionizing radiation action.

In experiments, haploid and diploid yeast cells of *Saccharomyces cerevisiae* were used. Sources of densely ionizing radiation were α-particles of ^{239}Pu (25 Gy/min) and sparsely ionizing radiation – γ-rays of ^{60}Co (20 Gy/min). Cell viability was assessed by their ability to form colonies visible by the naked eyes after 5-day incubation on a solid nutritious medium at 30 °C.

The ability of cells to recover from potentially lethal damage after repeated exposures have been studied insufficiently. Our new data related with this problem showed the retarded rate of recovery and the decrease in the volume of recovery after the repeated exposures. This effect was particularly pronounced after exposure to high LET radiation: after repeated irradiation the recovery process decreased dramatically, and after the third irradiation was completely stopped. Hence, the repeated exposures by high LET radiation result in both the cell ability to recover from sublethal and lethal radiation damage. These data indicate the additional advantage of high LET radiation application in radiotherapy.

It is shown that the RBE of α-particles for diploid yeast cells capable to recover from radiation damage due to the double set of chromosomes was 5.4 while for haploid cells incapable of such kind of recovery the RBE with dramatically reduced and was 1.7. These data confirm earlier findings indicating the participation of the recovery processes in the manifestation of the RBE of densely ionizing radiation. In addition, the correlation between radiosensitivity and RBE of densely ionizing radiation was demonstrated; the RBE was significantly greater for more resistant cells capable of recovery. These data indicate the perspective application of high LET radiation for more resistant tumors, in particular in neutron and neutron capture therapy, proton and other charged particles, π^--exposure and *etc*.

The effect of the late appearance of colonies by irradiated yeast cells was studied in the dependence of radiation quality. It was shown that this effect, characterizing genetic instability, was more pronounced after exposure to alpha particles than after irradiation with gamma rays.

RADIOMODIFYING EFFECT OF DIMERIC BISBENZIMIDAZOLES ON CANCER STEM CELLS (CSCs) OF BREAST ADENICARCINOMA LINE MCF-7

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Tumor DNA represents one of the most promising targets for anticancer drugs. Therefore, synthetic dimeric bisbenzimidazoles **DB**(**n**) (Ivanov et al.) which demonstrate the site-specific minor groove binding to DNA A-T enriched sequences in minor groove are considered to be possible anticancer agents (**n** is length of oligomethylene linker between the two bisbenzimidazole blocks) .

The aim of the study was to elucidate combined effect of gamma radiation at dose of 4 Gy with compounds **DB**(**5**) or **DB**(**7**) on the CSCs of breast adenocarcinoma line MCF-7. CSCs were isolated by $CD44^{+}CD24^{low/-}$ immunophenotype with flow cytometry. Both compounds had cytotoxic effect on the cancer cells and furthermore significantly reduced the CSC proportion at a concentration of 20 μM. Approximately two-fold increase in CSC content was found 48 h after radiation exposure. **DB**(**5**) and **DB**(**7**) in combination with irradiation reduced the proportion of CSCs multiply compared with that after radiation exposure ($p<0.05$). Thus, these results showed that the compounds **DB**(**5**) and **DB**(**7**) could potentially be used to develop anticancer drugs for elimination of CSCs and increase the effectiveness of cancer patient radiotherapy.

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REALIZATION OF CYTOGENETIC DAMAGE IN IRRADIATED HUMAN CELLS FOR ADDITIONAL ACTION OF CO-MUTAGEN

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The impact of co-mutagens on the realization of radiation-induced genetic damage in human cells is an important research topic in radiobiology nowadays. A phenomenon of co-mutagenesis can be observed when the substances without an own mutagenic activity are able to significantly modify, namely amplify, the effects of mutagens. Some of the medical drugs, such as verapamil (V), ascorbic acid (AA) were recently shown to be dangerous co-mutagens. The aim was to determine the changes cytogenetic parameters in peripheral blood lymphocytes (PBL) of healthy individuals at low dose ionizing radiation (IR) and different concentrations of co-mutagens V and AA. Materials and methods: PBL culture as a test-system, IR of 0,3 Gy; co-mutagen V treatment in concentrations (1.5-4.0 mg/ml), AA (20,0-80,0 mg/ml). Results. Our studies showed the effect of co-mutagenes V and AA on the formation of radiation-induced chromosomal rearrangements in human somatic cells and the dependence of co-mutagenesis on the ionizing radiation at low doses and concentration of co-mutagenes. The obtained data indicates that V exhibits co-mutagenic effect with low doses of IR (0.3 Gy) only at high concentrations. Co-mutagen V (4,0 mg/ml) potentiates the damaging effects of ionizing radiation, increasing the overall frequency of chromosome aberrations by 1.5 times. At exposure to radiation of cell culture AA in concentration 20,0 µg/m shows radioprotective effect, which becomes apparent in decrease of overall frequency of chromosome aberrations by 1.5 times compared with effect of IR alone. It has been determined that post-radial effect of AA on the PBL culture in concentrations 40,0-80,0 µg/ml increases overall frequency of chromosome aberrations compared with effect of exposure to radiation in low dose in 1,4 times. Conclusion. Some medical drugs (V, AA), the combined action of IR can exhibit a co-mutagenic effects depending on the concentration that results increased frequency of radiation-induced chromosome aberrations. These facts should be taken into account during the purpose medical drugs with co-mutagene effects for individuals occupationally exposed to IR.

ANALYSIS OF MUTATIONS IN THE GENES *BRCA1, BRCA2, CHEK2, NBN, BLM* IN PATIENTS WITH INFLAMMATORY BREAST CANCER

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Germinal mutations in highly penetrant suppressor genes *BRCA1, BRCA2* and medium penetrant *CHEK2, NBM, BLM1* can be a are cause of hereditary breast cancer (BC), which is 5-10% of the total pathology (according to the literature data). Inflammatory BC is a rare and most aggressive invasive form of breast cancer, with has a high metastatic potential.

The aim of the study was to finding hereditary mutations in the genes *BRCA1, BRCA2, CHEK2, NBN, BLM1* in patients with inflammatory breast cancer.

41 patients with inflammatory BC and 432 patients with non-inflammatory BC (a comparison group) were examined. Analysis of mutations in the *BRCA1* (5382insC, 185delAG, 4153delA, 300T>G, 2080delA, 3819del), *BRCA2* (6174delT), *CHEK2* (1100del, IVS2+1G>A, 470T>C(Ile157Thr)), *NBM* (675del5), *BLM1* (Q548X) genes was carried out by the method of allele-specific real-time PCR. After detection of mutations the results were confirm as by Sanger for DNA sequencing. Information about relatives with the same or any cancer was collected for all patients.

The frequency of mutations in patients with inflammatory BC was more than 3 times higher comparing with the frequency of mutations in patients from the comparison group (9.7% and 3%, respectively). Mutations (5382insC and 2080delA) in the *BRCA1* gene were detected in 7.3% of patients with inflammatory BC and 2.3% of patients from the comparison group. In 2.4% of patients from inflammatory BC and 1.4% of patients from the comparison group mutations in gene CHEK2 (470T> C(Ile157Thr)) were revealed. In the genes *BRCA2, NBM* and *BLM1* mutations were not found.

The results obtained allow carrying out more exact diagnostics for optimal tactics of the surgical treatment and the specific therapy in patients with inflammatory BC. It is also very important for the prevention of BC in their relatives.

FISH ANALYSIS OF EXFOLIATED URINE CELLS FOR DETECTION OF BLADDER CANCER

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Bladder cancer (BC) not being the most frequent among neoplasia is one of very dangerous due to the tendency to recur after treatment. The gold standard for detection of BC is cystoscopy followed by histopathologic study of bioptate. This procedure is very traumatic, painful and sometime noninformative. Noninvasive diagnostic methods are needed especially for monitoring patients for tumor recurrence. Two cytogenetic assays based on FISH of exfoliated cells in urine were developed during last decade: UroVysion (UV) and AURKA (AK). For UV test a mixture of fluorescent labeled probes to centromeres of chromosomes 3, 7 and 17 and band 9p21 is used to assess urinary cells for chromosomal abnormalities indicative of malignancy. For AK assay fluorescent DNA probe to 20q13 band (Aurora kinase A gene location) is used to identify aneuploid tumor cells on the slides of urine sediments.

On the sample of 170 patients with BC the diagnostic potency of these two assays was assessed. The result of UV and AK tests coincided with cystoscipy results in 87% and in 93% cases correspondingly. In 5 cases the recurrence of BC after treatment was revealed by FISH methods earlier than by cystoscopy. In 13 cases with equivocal result of cystoscopy for 11 ones the results of the FISH assays were positive and for 2 cases – negative. The number of cells with abnormal pattern of fluorescent signals (polisomy, aneuploidy) correlated positively with aggressiveness of tumor (stage, grade).

AK test gave comparable results with UV test and being less expensive may be recommended as promising clinical biomarker for detection of BC, especially of its recurrences.

ROLE OF *CYP1A1* POLYMORPHISM OF CYTOCHROME P450 FAMILY GENES IN SUSCEPTIBILITY TO LUNG CANCER IN MAYAK PA WORKERS

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Workers of the ‘Mayak Production Association (PA)’ nuclear facility occupationally exposed to external gamma-rays and internal alpha-particles due to incorporated plutonium-239 were found to be at risk of lung cancer. An excess of foreign to an organism active substances – xenobiotics – is known to be accumulated from radiation exposure in humans and potentially plays an important role in tumorogenesis. Xenobiotics are counteracted by genes of the enzymatic biotransformation of xenobiotics (EBTX) system. Individual inheritable genome features are pivotal for the activity of EBTX. Certain gene polymorphisms of the cytochrome P450 superfamily, in particular, *CYP1A1* gene, were shown to be associated with lung cancer risks. Among them we detect a thymine/cytosine point mutation in m1 (3801 region) as *CYP1A1* polymorphism. The current study examines the association of lung cancer in Mayak PA workers occupationally exposed to external gamma-rays and internal alpha-particles due to incorporated plutonium–239 over prolonged periods with genetic polymorphism of *CYP1A1*2A* (m1 polymorphism). The research is designed as a case-control study. It includes 77 Mayak PA workers diagnosed with verified lung cancer (cases). The mean absorbed lung dose from external gamma-rays is 1.19 ± 0.13 Gy at the time of cancer diagnosis; the mean absorbed lung dose from internal alpha-particles due to incorporated plutonium-239 is 0.31 ± 0.06 Gy. 141 Mayak PA workers serve as sex- and year of birth – matched controls without lung cancer diagnosis at the time of the study. Lung cancer risk is found to be significantly increased in Mayak PA workers who were defined as homozygous carriers of the minor *CYP1A1*2A* allele (OR = 12.45, p = 0.0035). The current study confirms the role of individual genome features in lung cancer risks.

ECOLOGICAL-HYGIENIC APPROACHES TO RESTRICTION OF MEDICAL IRRADIATION FOR PREVENTION OF MALIGNANT TUMORS DEVELOPMENT

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At present in Belarus there is a steady significant growth of malignant tumors (MT) morbidity. According to official statistics given for a forty-year period (from 1971 to 2011) oncological morbidity increased almost 3-fold and death-rate nearly doubled. One of the factors of the growing cancer incidence among population is the influence on the human organism of widely-spread environmental carcinogenic factors; cessation or restriction of their effect can bring about steep (up to 70%) reduction of oncological diseases. The ionizing radiation pertains to factors with proved carcinogenic activity, whereas medical irradiation is the main anthropogenic factor of population irradiation, the scope of its use is constantly growing. Thus, it is medical irradiation that warrants particular attention and studies in terms of possible restriction. The purpose of the study is to review from the ekologo-hygienic position the main reserve reductions of medical irradiation and the decrease of risk origin of stochastic radioactive effects similar to medical irradiation.

In Belarus since 2005 a number of diagnostic investigations performed with the use of radiation technology have exceeded 7 mln. For early diagnostics of tuberculosis and lung cancer up to 99% patients undergo annual prophylactic investigations of the thorax. In addition, the constantly growing number of computer tomography investigations together with high information value give almost ten times higher dose load as compared to standard X-ray radiography. In Belarus since 2008 more than 200 thousand of such investigations have been carried out. Over the last years a full renovation of proper equipment for modern low-dose digital fluorographs has occurred. However, non-optimal use of ionizing radiation sources in medicine is one of the main reasons which accounts for the increase in the importance of average annual efficient irradiation dose preservation for population, which in Belarus in 2013 was 1.4 мSv/year and exceeded the specified dose limit.

In relation to the proved and currently accepted the linear-nonthreshold theory of stochastic radioactive effects origin, the main efforts in the provision of radiation safety of patients should be made following the principle of justifiability that is to say propriety of practical activity, and the principle of optimization directed to the reduction of dose load. In sanitary legislation of Belarus the main concern is directed to mandatory control of irradiation doses for patients under medical irradiation.

In conclusion, the avoidance of unwarranted medical irradiation and its reasonable restriction as well as the introduction of new, more efficient equipment, using modern means of individual protection, goal-directed education and refresher course for the personnel on the issues of radiation safety, make an important aspect in the restriction of medical irradiation and reduction of the risk origin of stochastic radiation effects such as malignant tumors.

RADIOBIOLOGY

Radiobiology effects

MOLECULAR NATURE OF THE HERITABLE GENE MUTATIONS INDUCED BY γ-RAYS AND NEUTRONS IN *DROSOPHILA* GERM CELLS

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As a further development of Timofeeff-Ressovsky's classical work (1930-1933) on the issue of the nature of radiation-induced gene/"point" mutations in *Drosophila* germ cells, the DNA alterations underlying the γ- and neutron-induced *vestigial* (*vg*) gene mutations were studied by the polymerase chain reaction (PCR), conformation sensitive gel electrophoresis (CSGE) and sequencing. For the PCR-screening of the 43 γ-ray- and 16 neutron-induced *vg* gene mutations the *vg* gene (15.1 kb, 8 exons, 7 introns) was divided to 16 overlapping fragments. All mutations were divided into 4 classes: (i) PCR$^+$ - without the detected changes; (ii) "single-site" - with the loss of a single fragment; (iii) partial detections as a loss of 2–9 adjacent fragments and (iv) "cluster" mutants having 2-3 independent changes. γ-rays and neutrons cause all classes of damages, however, γ-rays are more effective in induction of PCR$^+$ mutations, while neutrons induce clusters in 10 time more frequently than γ-rays. To detect the molecular alterations which are not detectable by PCR, for some part of the γ- and neutron-induced mutants 3 functional regions of the gene were studied by CSGE method. According to the obtained results, 11 out of 27 γ-induced mutants and 1 out of 11 neutron-induced mutants have base substitutions and micro-deletion or insertion of the DNA. The sequencing of these gene regions in these mutants permitted to identify the nature and exact location of this DNA alterations. Clusters of lesions at the gene level were identified by PCR and sequencing. A large proportion of all these cluster mutants after neutrons compared to γ-rays showed it's greater effectiveness in the induction of complex lesions within the gene. Significantly, the neutrons are more effective than γ-rays in induction of this cluster mutations (26.3% and 16.7% respectively). Thus the gene/"point" mutations induced by both rare and densely ionizing radiations are presented by wide spectrum of DNA alterations. Therefore to obtain a whole picture of radiation damage of the gene it is necessary to use a complex of methods. So, our findings show necessity of new approaches for the assessment of the genetic risks of different quality radiation in induction of damages on the molecular level.

SYNTHETIC ANALOGS OF NATURAL PHENOLIC ANTIOXIDANTS AND ANTIMUTAGENS FROM RASPBERRY AND GINGER

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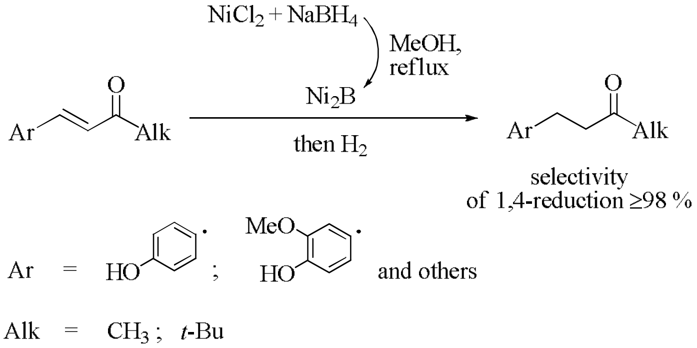
Raspberry ketone and zingerone are well-known natural substances isolated from raspberry and ginger which became the objects of both laboratory studies and commercial production. Investigations of the biological activity of these phenolic compounds, in particular antioxidant and anti-inflammatory actions, cancer prevention, influence on the mutagenesis and metabolism are still ongoing. Zingerone can potentially be used for the selective protection of the normal tissues in the course of the radiotherapy of tumor diseases. Also zingerone and related compound dehydrozingerone found to inhibit growth of the colon cancer cells.

Now we report an efficient synthetic way for the preparation of zingerone, raspberry ketone and different structural analogs of these natural compounds based on the aldol condensation – enone reduction reaction sequence. Simple procedure for the selective hydrogenation of the double bonds of enones was developed [1].



Radical-regulating properties of the synthesized compounds were tested during the radiolysis of the model systems.

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TRANSGENERATION TRANSFER OF RESPONSE TO A CHEMICAL MUTAGEN IN ORGANISMS OF ANIMALS AFTER DIFFERENT-TIME IONIZING RADIATION

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The study concerned genome damages of bone marrow (BN) cells in organisms of tundra voles (*Microtus oeconomus*) which have lived under anthropogenically-increased (by 10-100 times) natural radioactivity level for more than 50 years including next generations (F_1-F_3) of tundra voles bred in vivarium. Voles from radium plot have an increased amount of BN cells with micronuclei (MN), a low mitotic index (MI), and a high apoptosis index. Background F_1-F_3 voles demonstrate a gradually increasing amount of BN cells with micronuclei which gets stable at 20 ‰. F_1 voles at radium plot have a share of cells with MN being equal to background values whereby F_3 already have a truly higher amount of these cells than it is observed at background F_3. This fact may indicate inheritance of unstable genome. The sensitivity to a chemical mutagen was assessed by reaction to urethane. The provoking agent of urethane revealed a heterogeneous response of BN cells in organisms of animals from regions with different radio-ecological conditions. For background animals, urethane truly increased the amount of aberrant cells, lowered the mitotic activity, and sharply reduced cases of apoptotic death. For radium-affected voles and their offspring, we observed urethane decreased amount of cells with MN, also mitotic activity and apoptosis index. Such reaction to chemical agent evidences animals which have lived under ionizing radiation (IR) for many generations are resistant to its action. The trial with urethane indicated different generations of irradiated animals showed different sensitivity to the chemical mutagen. Finally, voles in natural populations having lived under IR for a long period of time are low-sensitive to mutagen. This phenomenon speaks for inheriting of instable genome.

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THE EFFICIENCY OF DNA REPAIR IN THE PRIMING OF SUGAR AND RED BEET SEEDS

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Advancing treatments of seeds by osmotics (priming) are leading to the activation of biochemical processes in seeds allowing repair of damage in embryo cells and resulting in completion of all essential pre-germination processes. Priming is widely used in the world to improve seed material quality of agricultural and horticultural species. This process can be further tuned, if we can identify risks from overpriming and find reliable molecular markers for the priming optimisation.

The aim of the work was to study the efficiency of reparative DNA as a molecular marker to optimize the priming of seeds beet.

We analysed an integrity of DNA after different regimes of priming for sugar and red beet. It turned out that all treatments lead to an increased level of high molecular weight DNA in cells because of DNA repair function. However, during the drying of primed seed we also see accumulation of degraded (low molecular weight) DNA, concentration of which is proportional to the priming intensity. Using ratio content values of high to low molecular weight DNA in the embryos of treated seeds, it is possible to estimate priming quality and predict (to the certain extend) risk of overpriming. It is also shown that reparative DNA synthesis that occurs during first two hours of primed beet seeds germination reflects DNA repair intensity for the damages accumulated during priming.

It turned out that efficiency of DNA repair in primed beet seed can be tested by introduction of additional DNA damage into embryo cells via gamma-irradiation.

The data obtained suggest that potential capability of repair systems to recover from such additional DNA damage together with measurements of DNA-ligase I induction can be used as a reliable molecular marker for priming optimisation of sugar and red beet seeds.

PHENOTYPIC MANIFESTATIONS OF GROWTH DISORDERS IN PROGENY OF HENS CHRONICALLY EXPOSED TO ^{131}I

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The investigations were carried out using hens of Russian white breed which were given equal doses o f ^{131}I for 30 days at daily quantities of 0.11, 1.1, 2.1 and 4.6 MBk/kg, and their progeny belonging to seven generations (2573 test chickens and 2782 control ones). The radiation doses absorbed with hen thyroid were 10.4, 34.9, 96.9 and 112.2 g, respectively. Injection of ^{131}I to hens in the quantities of 0.11 и 1.1 MBk/kg stimulated egg laying, of 2.1 MBk/kg inhibited it, and of 4.1 MBk/kg irreversibly stopped the reproductive function.

Egg-laying quality levels for three generations of hens that received ^{131}I at a dose of 0.11 MBk/kg, of generations 3 and 5 of hens that received 1.1 MBk/kg, and generation 1 that received 2.1 MBk/kg were increased, the ones for hen generations 1, 2, 4 and 6 that had received ^{131}I at 1.1 MBk/kg were within the normal range or decreased. Hatchability levels of chickens from eggs laid by the tested progeny were decreased because of higher embryo death rates both within early and later periods of the embryogenesis. This effect appeared in the majority of generations at all isotopic doses that had been administered to their parents. In generations 4 and 5, chickens produced from hens that had received ^{131}I at a dose of 1.1 MBk/kg in 0.75% of cases manifested various malformations like absence or deformation of eyes and/or X-shaped jaw decussation. In the offspring of these hens that were older than 7 months of age and belonged to the first four generations, neoplasms in cephalic and cervical areas were found, also in soft tissues some neoplasms structurally similar to reticulosarcoma were seen in 0.8 to 4.7% of cases. The progeny birds under test had decreased body weights and survivability levels.

Thus, phenotypic manifestations of disorders observed in the growth of offspring of hens chronically exposed to ^{131}I admininstered at daily quantities of 0.11 до 2.1 MBk/kg comprised raised embryo death rates, stillbirths, inborn malformations, proneness to neoplasia, and drops in body weight and survivability levels.

NON-MUTAGENIC NON-TARGETED RADIATION EFFECTS AS ONE OF THE MECHANISMS OF DECREASE OF LIFE SPAN IN MULTICELLULAR ORGANISMS

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Non-mutagenic, non-targeted radiation effects (NNE) differ from usually observed mutagenic ones. Those differences are as follows: abrupt appearance of alterations which increase probability of cellular senescence; irreversibility; effectiveness of low-dose irradiation; presence of threshold level; absence of dose-effect regression in wide range; cellular alterations are not connected with proliferation; primary injuries are localized in cytoplasm; high probability of appearance.

NNE were discovered in a set of unicellular organisms (amoeba, infusoria, yeasts) and rat tissues. These permit us to argue evolutionary conservatism of the phenomenon. These injuries appears predominantly in postmitotic cell populations, which are “doomed” for step by step degradation due to absence of substitution of dying cells by newborn ones.

We analyzed our data obtained in billbugs *Calandra granaria syn. Sitophilus granarius* (LINNAEUS, 1758). The specia is characterizes by long life span and extreme radioresisitance. Imago consists from postmitotic tissues predominantly. We found several NNE traits in the organisms.

Traits were as follows: mass character, irreversibility, effectiveness of low doses, abrupt nature of transformation, its high probability,

Thus, we argue, that NNE traits may appear in multicellular organisms leading to life span shortening.

A set of NNE traits promote us to think about epigenetic nature of the phenomenon. However, concrete mechanisms are still unknown.

MUTATION INDUCTION IN THE MOUSE GERMLINE: A GENOME-WIDE PERSPECTIVE

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The ability to predict the genetic consequences for humans of exposure to ionising radiation and chemical mutagens has been one of the most important goals of human genetics in the past fifty years. However, despite numerous efforts, little is known about the genetic effects of radiation exposure in humans and the only definitive evidence for germline mutation induction *in vivo* in mammals comes from mouse studies.

Recent advances in genetic technologies have provided new microarray-based and next generation sequencing-based tools for the genome-wide analysis of genetic variation, which have the potential for characterising germline mutation in humans and mice. Using microarray-based comparative genomic hybridisation and high depth (>22X) whole genome HiSeq sequencing we have recently carried out a matched case control experiment to investigate the effects of ionising radiation on germline mutation in mice. We found that the frequency of *de novo* Copy Number Variants (CNVs) and insertion/deletion events indels was significantly elevated in offspring of exposed fathers. We also showed that the spectrum of induced *de novo* SNVs is strikingly different; with clustered mutations being significantly over-represented in the offspring of irradiated males. Our study highlights the specific classes of radiation-induced DNA lesions that evade repair and result in germline mutation and paves the way for similarly comprehensive characterisations of other germline mutagens.

INDUCTION OF GENOMIC INSTABILITY ON THREE GENERATIONS OF MICE IRRADIATED BY INFRARED LIGHT

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In the last time, the phenomenon of adaptive response (AR) has attracted considerable attention of investigators. It is considered as a form of cell defense from mutagenic action of different factors. Therefore the search for adaptogens of physical and chemical nature which are able to transform the organisms to a new adapted state similarly as low doses is an actual problem. Various devices, based on the action of electromagnetic waves of the infrared subspectrum are currently used in clinical practice.

Previously, in our experiments it was shown that exposure of mice to infrared light (IRL) as well as low doses of X- and γ-rays, induced AR in bone marrow cells, remained unchanged thymus weight after irradiation with a challenging dose (1.5 Gy) and decreased tumor growth rate. The aim of the present work was to investigate the biological action of IRL (850 nm, 101 Hz, 22 mW/cm^2) on the induction of adaptive response in hemopoietic organs (the bone marrow and thymus) and the rate of Ehrlich carcinoma growth on the mice offspring (F_1, F_2 and F_3).

To induce the AR the standard scheme of radiation (0.1 Gy + 1.5 Gy) was used. The level of cytogenetic damage was assessed in bone marrow cells using a micronucleus test. The weight of the thymus was determined from the ratio of the average weight of the organ to the average weight of animals in the group. The influence of the adaptive exposures on the tumor growth was estimated by measuring the size of the tumor at different times after the inoculation of ascitic cells into the femur.

Our investigation of three generations from males irradiated by IRL demonstrated that: there level of spontaneous cytogenetic damages did not differ from that of unirradiated mice, the radiosensitivity decreased, no AR takes place, the thymus weight decreased and the tumor growth rate did not differ from that of the unirradiated males offspring. The obtained experimental data demonstrated the induction of genomic instability on three generations of mice irradiated by IRL; for detection of genomic instability in descendants it is necessary to use different tests.

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EFFECTS OF LOW-DOSE GAMMA IRRADIATION DURING EARLY LIFE STAGES IN THE ZEBRAFISH MODEL

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Human and zebrafish genome share 70% of the genes.The aim of this study was to assess phenotypic and genotypic changes in zebrafish embryos after exposure to low dose and chronic dose-rates of γ-radiation during two sensitive developmental stages. Zebrafish embryos AB wild type were exposed to dose-rates ranging from 0.5 to 40 mGy/h external^{60}Co gamma irradiationfor a period of 3 hours (hpf) and 5 days post fertilization (dpf), for a total of 118 hours. Samples for gene expression analysis were collected at 5.5hpf. Mortality, malformations, and the hatching rate were observed at 48 and 118 hpf. Total RNA for gene transcription analysis was isolated from embryos exposed between 2.5 hours and 5.5 hpfwhich are across the mid blastula transition and early gastrula stage of development. The quality of RNA sequenced samples was determined by photometric parameters (260/280>1.8, 260/230>2, yield>200ng/µl) and RNA integrity number (RIN>8.5)(Bioanalyzer;Agilent technologies, USA).The RNA was sequenced at BGI Tech Solutions Co., Ltd., Hong Kong. Embryo hatching rate and number of malformations were significantly different from controls in all exposure groups. Mortality observed at 5dpf was higher than in controls for all groups except for the lowest dose-rate(0.5 mGy/h). This suggests that γ-radiationin the range of 1mGy/h and higher during embryogenesis and early larval stage (equivalent to total doses of ca. 100 mGy or higher) induces acute toxic effects in zebrafish. Bioinformatic analysis of RNA-seq data showed a clear dose response relationship between the number of differentially regulated genes compared to controls, which increased with the γ-radiation dose. Analyzes of the gene expression data sets using Ingenuity Pathway Analysis (IPA) showed significant changes in gene networks around hnf4α (hepatocyte nuclear factor 4α) and cebpa (CCAAT/enhancer binding protein) and genes involved ineif2 signaling. Interestingly, corresponding gene transcription changes were also found in cancer patients in the post-Chernobyl period suggesting that the same mechanisms are involved in humans and zebrafish exposed to ionizing radiation.

EFFECT OF RADIATION AND EMOTIONAL STRESS ON BEHAVIOUR OF RATS IN THE OPEN FIELD TEST

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Today found that thin integral indices functioning of the central nervous system (CNS) show a high sensitivity to ionizing and electromagnetic radiation (EMR), and the degree of central nervous system disorders may be determined by electrophysiological, biochemical, and behaviour parameters.

Purpose of the investigation - to determine the characteristics of behaviour responses in male and female rats under emotional (immobilization stress) and physical (external irradiation and EMR) stress.

Methods. Experiments were carried out on male and female rats (6 months age). The rats were exposed to the outside of radiation in a doses of 0.5; 1.0 and 2.0 Gy (^{137}Cs, 46,2 sGy /min) and prolonged EMR (900±3 MHz for 10 days/8 hours a day). Model of emotional stress were caused by placing the animals in the narrow plastic tubes ("soft" immobilization): 1) for two hours for 5 days; 2) for three hours for 7 days on end. The animals were examined using the “Open field” test (Of) on the next day after immobilization.

Results. The emotional stress was resulted in complex degenerative changes of internal organs: the involution of lymphoid organs, including reduction of thymus weight, reduction of spleen weight compared with the control. It was shown that chronic immobilization stress leads to inhibition of the horizontal and vertical motor activity in experimental animals (male and female) in Of test.

There were sex differences in the behaviour change in the Of test after exposure to ionizing radiation at doses of 0.5 and 1.0 Gy.

It was shown that exposure of EMR modifies the level of integrative reaction of CNS rats which were exposed to ionizing radiation in the Of.

It was found that more pronounced negative changes of orientation and exploratory activity and of the levels of emotionality observed in the groups after exposure to ionizing radiation and immobilization.

CYTOGENETIC EVIDENCE OF HRS/IRS EFFECTS IN HUMAN LYMPHOCYTES AND CHINESE HAMSTER CELLS FOLLOWING 14.5 MEV NEUTRONS AND GAMMA IRRADIATION

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To investigate LET modification of hyper-radiosensitivity and induced radioresistance (HRS/IRR) human lymphocytes and Chinese hamster CHO-K1 cells were irradiated either with 14.5 MeV neutrons ($LET_d \approx 100$ keV/μm) or with ^{60}Co γ-rays ($LET_d \approx 0.3$ keV/μm). Both cell cultures were irradiated with doses of 0.1-1.2 Gy in pre synthesis stages of the mitotic cycle, G_0 (lymphocytes) and the late stationary growth phase (CHO-K1). Therefore, chromosome type aberrations (dicentrics, centric and acentric rings, deletions) contributed mainly to the total chromosomal aberration (CA) yield, 85-95%. For both cell cultures and for both radiations dose-effect curves demonstrated, in general, the same shape. Namely, the sharp rise of CA at doses of 0.08-0.15 Gy (HRS) followed by a (quasi)plateau (IRR) up to 0.3-0.6 Gy, and, finally, transition to regular linear-quadratic dependence. Those patterns of dose-effect curves have been observed for total aberration frequencies and for yields of the major types of CA, dicentrics in the case of human lymphocytes and deletions in the case of Chinese hamster cells. Experimental data were reasonably well fitted using Induced Repair Model by B. Marples and M.C. Joiner.

Despite the overall likelihood of dose curves for both radiation a certain LET-modifying effect was observed. The dose range of HRS was 0.08-0.1 Gy in the case of neutron irradiation and 0.12-0.15 Gy in the case of irradiation with γ-rays. The plateau region was 0.1-0.3 Gy for neutrons and 0.25-0. 6 Gy for γ-rays. It suggests that despite general mechanisms of both effects (HRS/IRR) some features of their performance are LET-dependent. One reason of possible differences may be the different spectra of radiation damages induced by high- and low-LET radiations.

THE HIERARCHY MECHANISMS OF RADIOGORMESIS EFFECTS ON PLANTS

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The radiogormesis effects (RGE) are observed for the representatives of practically all taxonomic groups of organisms and at all levels of biological integration. Of course, each object requires selecting the appropriate dosage regimes – dose and its power. The report substantiates the position that the RGE is a form of stress-reactions, namely eustress by H. Selye. Obviously, in the basis of the primary mechanism of action of radiogormesis doses is ionization of the atoms and molecules of the irradiated object, i.e. disintegrative process, a fact which makes the RGE paradoxically, when the primary destructive acting factor, ultimately, has a beneficial effect on the organism. The fact of the hierarchical type of organization requires the study of biological mechanisms RGE as a consistent description of the reactions of all the sublevels (subsystems) of a biological object for which it is described.

The studies of RGE carried out on pea seedlings, derived from the pre-gamma irradiated dry seed. According to the dose dependence of the growth parameters of the main root seedlings (organ level) was identified radiogormesis dose, range of that starts with 1.0 Gy and does not exceed 10.0 Gy (radiation power at 4.0 cGy/s). Then were established the level of proliferative activity and parameters of the root apical meristem cells (the critical root system – cellular and tissue level) in the range radiogormesis doses by using standard cyto-histological methods. Assuming a direct relationship between of cell proliferation and level of cytokinin (endocell or biochemical level), was determined the intensity of the synthesis by using a liquid chromatograph Agilent 1200 Series LC. The idea of the experiment was that the dynamics of the parameters that characterize the responses of different levels of integration of seedlings grown from irradiated gormesis doses of gamma irradiation of pea seeds, to restore the sequence of cause and effect relationships that lead to the RGE. The gormesis effect of irradiation on the growth activity of the main root seedlings appear only in the first few days of their growth, that indicating the transitive nature of the RGE. The histological analysis of the root apical meristem of radiostimulation roots showed that the size of the cells that irradiated in gormesis dose did not differ significantly from control values. In this proliferative activity of meristematic cells in the experiment was stimulated by that, together with the previous evidence, indicating on increase in meristem volume by increasing the number of its constituent elements, ie, meristematic cells. The RGE manifestation of the parameter proliferative activity of meristematic cells indicates an increased the reliability (in this case – radioresistance) of the system (the root), which manifests itself in our previously studied by using the classical scheme of radioadaptive response studying. In samples of roots, experienced the radiogormesis effect of irradiation, was also observed the increased levels of cytokinin synthesis, which preceded the stimulation of proliferative activity of meristematic cells, which indirectly confirmed our hypothesis about the possible role of post-irradiation DNA degradation products (especially guanine) as an additional substrate for the synthesis of cytokinins with which at the biochemical level begins to “line up” the entire hierarchy of their own biological mechanisms RGE.

COMPARISON OF DOSE-RESPONSE TRANSCRIPTOMICS AND LONGEVITY EFFECTS OF GAMMA RADIATION IN *DROSOPHILA* MALES

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Throughout the history of the living things the natural background radiation of the Earth and cosmic rays are one of the key environmental factors that affect the rate of evolutionary processes. As a result of nuclear weapons testing, nuclear accidents and the activities of the nuclear fuel cycle, large areas were contaminated with artificial radionuclides. In addition, people are exposed to radiation during medical procedures, air travel and on a number of enterprises. Thus, the problem of biological effects of low doses of ionizing radiation is becoming increasingly important.

The goal of this work was to identify changes of lifespan and expression of genes by γ-irradiation in broad doze range (5, 10, 20, 40, 100, 200, 500 cGy) on the imaginal stage of development *Drosophila melanogaster* males.

In a dose-dependent manner were observed hypersensitivity, hormesis or inhibitory action of radiation on lifespan and identified radiation-induced molecular pathways in Drosophila imago.

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LOW DOSE GAMMA IRRADIATION STIMULATES PROLIFERATION OF STEM CELLS AND TUMOR CELLS BUT DIMINISHES THE SIZE OF SP FRACTION

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Stem cells (SC) play a major role in tissue regeneration. The effects of low dose gamma-irradiation on various types of SC are still scarcely known. Aim of this work was to investigate the effects of gamma-irradiation at low doses on epithelial stem cells (ESC) - keratinocytes of human skin, on mouse mesenchymal stem cells (MSC) and on cells of small cell lung cancer line H69. MSC were derived from mouse brain (MSC_{BR}) and from mouse bone marrow (MSC_{BM}). The cultures of ESC and of MSC include as the subpopulation of SC and also the population of early progenitor cells. The capability of SC to efflux fluorescent dyes like Hoechst 33346 or Rhodamine-123 and to form the side population (SP) on dot-plot diagrams during flow cytometry is used as an indirect marker of normal and cancer SC. Cells were exposed to gamma-radiation (Cs-137) in doses 1, 5, 10 and 20 cGy at dose rate 1cGy/min, higher doses were achieved at dose rates of 20 and 50 cGy/min. The cell survival was assessed by counting vital cells after staining with trypan blue in the Goryaev's chamber on the 1, 3, 7, and 14th day after irradiation. SP fraction was measured during flow cytometry after incubation with rhodamine-123. Exposure to doses in range of 1 to 50 cGy stimulated proliferation of H69 cells and of all SCs except of MSC_{BM} and lowered the size of SP fraction in all cells. Decreasing in the size of the fraction SP apparently is due to the rapid transition of the SC into the progenitor cells pool. Thus, the stimulation of cell proliferation after gamma-radiation at low doses is accompanied by the redistribution of distinct cell subpopulations: the decreasing of the percent of cells that make up the SP fraction and the increasing of the general population of cells.

BYSTANDER EFFECTS, ADAPTIVE RESPONSES, AND HORMESIS: BEING ON THE RIGHT PART OF THE STRESS RESPONSE CURVE

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The dose response relationship for ionizing radiation is very controversial. There is the assumption in radiation protection of a linear dose response and a single dose dependent DNA strand break mechanism. Despite many studies showing non-targeted, adaptive, hormetic and various inducible responses, the linear-non-threshold (LNT) -DNA centric paradigm dominates in both basic science and in radiation protection. This is not only costly but restricts development of new ideas in radiobiology which could have profound consequences for our approaches to environmental and medical issues involving radiation and other stressors. The latest data from our laboratory strongly suggest that the low dose mechanisms are completely independent of mechanisms operating at higher doses and may not even be temporally related. We have found that a low dose delivered after a high dose can produce the same type of adaptive response as is seen when the low or conditioning dose is given first. Important endpoints at low doses are apoptosis and changes in gene or protein expression patterns, which often play out as hormetic, protective and adaptive effects rather than harmful or potentially carcinogenic effects. Genotype is important in determining outcome as are system level micro and macro environmental effects. While targeted doses are kept within accepted safety limits, little is known about the non-targeted effects (NTE) of exposure such as the role of bystander effects in mediating response to stressors. In particular it is unclear whether the radiation weighting factors and dose rate effectiveness factors used in radiation protection apply following non-targeted or low dose exposures. The literature is confusing and controversial. Low energy protons and neutrons do not appear to produce NTE, although high energy protons, alpha, beta and gamma radiations do and NTE have also been reported following UVA/B exposures. The dose responses for NTE typically saturate around 0.5Gy acute dose and have a low dose threshold for induction of only a few mGy. They should therefore be expressed at doses typically used in nuclear imaging and in targeted therapy. We suggest that understanding the factors controlling low dose effects and in particular the post-conditioning effect could be critical to resolving the debate about the benefits or dangers of radiation exposure.

RELATIVE BIOLOGICAL EFFECTIVENESS OF ENVIRONMENTALLY RELEVANT LEVELS OF ^{226}Ra AND X-RAYS ON GROWTH AND ON BYSTANDER EFFECTS IN FATHEAD MINNOWS (PIMEPHALES *PROMELAS,* RAFINESQUE, 1820)

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The relative biological effectiveness (RBE) of alpha internal emitters such as radium is highly controversial and the precautionary RBE values suggested range from 10-40. However there are very few data concerning RBE for non-human species or for endpoints other than cancer or reproduction. The aim of this work was to examine longterm effects of one off acute exposures to low doses of ^{226}Ra compared with x-rays using endpoints known to show perturbations after low dose exposures. To investigate this fathead minnows were given low dose acute x-rays or a one-off meal of fish pellets containing ^{226}Ra to the equivalent dose of the x-ray. Endpoints relating to growth and bystander effects were measured at 6 and 12 months after the acute exposure. The results show significant persistent effects of both radiation qualities using growth, biochemical indices and bystander effects as endpoints but no indication for these doses and endpoints of any greater effect of high versus low LET radiation. It is suggested that the use of weighted doses (i.e. Sv) for reporting impacts of low dose ionising radiation in non-human species is misleading.

COMBINED ACTION OF IONIZING RADIATION AND FOOD SUPPLEMENTS ON THE INDUCTION OF ADAPTIVE RESPONSE AND TUMOR GROWTH ON MICE *IN VIVO*

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The purpose of this study is to investigate the combined action of food supplement, low dose rate high-LET and X-ray radiations on sensitivity, induction of adaptive response (AR) and tumor growth on mice in vivo. The SHK mice were being irradiated with 11,6 cGy (0,5 cGy/day) of low-dose-rate high-LET radiation behind the concrete shield of the 70 GeV protons accelerator. The X-ray irradiation was carried out on the RTH device (1 Gy/min). The diet composition included products containing big amount of biologically active substances, such as: soybeam meat, buckwheat, lettuce leaves and drug of cod-liver oil. Four groups of mice were fed with selected products mentioned above during the whole irradiation period of 22 days. The control groups received the same food without irradiation. For induction of AR the animals were irradiated according to the scheme 10 cGy+1,5 Gy. The influence of food supplement on the growth of solid tumor was estimated by measuring the size of the tumor at different times after the inoculation of ascitic cells s.c. into the femur. The percent of polychromatic erythrocytes (PCE) with micronucleus (MN) in bone marrow served as definition criteria of cytogenetic level of damage. The results of the study indicate that: due to influence of high-LET radiation with the dose of 11,6 Gy, mice who had dietary supplement demonstrated reduction of PCE with MN to the level of natural background radiation comparing with mice who had only standard food; diet containing soybean, buckwheat or greens unlike cod-liver oil reduces the sensitivity of mice to X-radiation with the dose of 1,5 Gy and causes significant slowdown in growth of Ehrlich carcinoma; the combined effect of high-LET radiation and the food supplements (except for cod-liver oil) reduces the sensitivity of mice to irradiation with the dose of 1,5 Gy, which demonstrate ability of AR induction unlike the mice only irradiated with high-LET radiation and causes the slowdown in growth rate of Ehrlich carcinoma in contrast to the mice only irradiated with high-LET with the dose of 11,6 Gy; the combined effect of high-LET radiation and the food supplements (except for cod-liver oil) does not action on the level of AR.

THE PROBLEM OF THE INFLUENCE OF LOW-INTENSITY LASER RADIATION ON BIOLOGICALLY ACTIVE SUBSTANCES

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It is known that chemical and biological agents can produce low-intensive electromagnetic fields. Remote reproduce properties of biologically active substances by using their characteristic electromagnetic radiation has been known for a relatively long time (J. Benveniste et al., 1987, 1988, 1998; L. Montagnier et al., 2009, 2012). The mechanisms of such phenomena have not a clear theoretical justification.

It was shown previously that the ability of low-intensive laser radiation to reproduce the basic properties of individual drugs in neutral carrier, presumably due to induced secondary radiation (B. P. Surinov et al., 2012, 2013, 2014).

It was shown that thus treated carriers and exposed them saline reproduce immunosuppressive activity Dekson or immunostimulant activity pharmaceutical drug Arbidol, Galavit, L-Tyrosine, which was affected by the laser radiation. In immunodeficiency states after exposure to ionizing radiation or stressed mice was the restoration of immune reactivity.

Similar laser processing on carriers of samples blood serum or urine samples irradiated at a dose of 4 Gy mice allowed to reproduce in the exposed water the ability to influence on olfactory behavioral response of intact mice. We are talking about attractive, attracting the intact recepients properties that were previously discovered in post-irradiation volatile components of urine or blood of mice irradiated by ionizing radiation in sub-lethal doses (B. P. Surinov et al., 2000-2012).

Reproduce the olfactory property on a neutral carrier under the influence of laser radiation showed a chemical analogue of the pheromone stress mice, such as 2,5-dimethylpyrazine.

The ability of laser radiation to modify the properties of biologically active substances not only demonstrates a new phenomenon, but also provides new opportunities for practical application, including the reduction of the effects of ionizing radiation.

GOMEOREZ IS THE KEY MODEL TRANSFORMATION OF LIVING SYSTEMS UNDER THE INFLUENCE OF LOW RADIATION DOSES

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More thanhalf a century ago, N.W. Timofeeff-Ressovsky hypothesized multipleways of human evolution in environment contaminated with artificial radionuclides. Our 20 years of research dedicated to finding the mechanisms of this process. Literature data on the dynamics of ecosystems and author'sempirical researches of functional status of the liquidators of the Chernobyl accident were analyzed.

The transition to the new regime of self-regulation is described by the following studies: a concentration gradient Ca, Mg, K in system "plasma - blood cells"; the electrical conductivity of the skin; the level of energy consumption per unit of work performed during bicycle ergometer; daily, weekly, seasonal, and 7-year monitoring of physiological parameters. Gradientsof potassium, calcium and magnesium LCA displayed different scenario of transformation compared with the control group. Three algorithms found: a coincidence, a slight decrease, multiple increase. The first is typical for potassium in system "blood plasma - red blood cells" and magnesium in system"plasmablood-platelets." The second is typical for magnesium in system"plasmablood-red blood cells." The third recorded for calcium and potassium in system "blood plasma -platelets."

The concept of human evolution lightning formulated on the basis of the results obtained. The main mechanisms of this concept are biorhythmological and biocybernetic mechanisms.

Detailed results of the research presented in monographs: "ROFES diagnostics for environmental monitoring" (2004); "Time, radiation and technogenesis: biological rhythms residents of industrial areas" (2006); "Population aspects of self-preservation behavior" (2008); in the articles "Gomeorezis-keymodel transformation biota in anthropogenic habitat" (Materials of the II InternationalConference"Fundamental and Applied Science today", 2013); "Signs gomeorezisain mineral metabolism liquidators of the Chernobyl accident" (International Journal of Experimental Education,2013, № 11, p.2.).

ASSESSMENT OF ADAPTIVE REACTION IN FISH TO CHRONIC RADIATION EXPOSURE IN THE *IN SITU* EXPERIMENTS

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The purpose of work was to study the adaptive reactions of erythropoiesis in fish to chronic radiation exposure in the in situ experiments. The principle of experimental studies suggests replace roach from radioactively polluted watercourses to the «pure» water flow and vice versa roach from «pure» watercourse to the radioactively contaminated. We used Techa River as radioactively contaminated flow. As "pure" water flows we used Miass River and Zyuzelga River. Roach which was caught in the Techa River was partitioned into three groups: one group was placed in a cage in the Techa River. The second group was placed in a cage in the «clear» Zyuzelga River; the third group of fish was analyzed after harvest in order to determine the initial state of hematopoiesis in roach of Techa River. Roach which was caught in the Miass River was subjected the same manipulations.

Analysis of the results showed that in roach of Techa River the adaptive reaction to chronic radiation exposure is enable to support the production of erythropoiesis at physiological norm. However, the effect of additional stress factor ("cage") in the context of the ongoing chronic radiation exposure, leads to insufficient production of erythropoiesis. This is may indicate that the adaptive capacity of fish erythropoiesis to additional stress are reduced. At the same time, changes in erythropoiesis caused by the influence of chronic irradiation at a dose rate of 108 μGy /day, are reversible, and the elimination of the radiation factor, allowed to return to normal operation and recover adaptive capacity to the action of stress factors other non-radiation nature.

The work was supported by the NRPA.

QUALITATIVE DISTINCTIONS OF DOSE-EFFECT RELATIONSHIPS BETWEEN DIFFERENT STRESS RESPONSES TO IONIZING RADIATION IN NORMAL HUMAN FIBROBLASTS

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Understanding the mechanisms producing low dose ionizing radiation specific biological effects represents one of the major challenges of radiation biology. Although experimental evidence does suggest that various molecular stress response pathways may be involved in the production of low dose effects, much of the detail of those mechanisms remains elusive. We hypothesized that the regulation of various stress response pathways upon irradiation may differ from one another in complex dose-response manners, causing the specific and subtle low dose radiation effects. To verify this hypothesis in the present study, the DNA damage induction, DNA repair, caspase-3 induction, and the transcription level of 22 genes involved in stress responses were analyzed in normal human fibroblasts (HELF-104) exposed to a range of gamma-doses from 1 to 200 cGy. Furthermore, the senescence dynamic of irradiated cell were analyzed using histochemical staining for β-galactosidase until a complete stop of culture growth.

We found non-linear dose responses for the repair of DNA damage after exposure to gamma-radiation. Alterations in gene expression were also not linear with dose for several of the genes examined and did not follow a single pattern. Rather, several patterns could be seen. In addition, qualitatively different changes in dynamic of β-galactosidase accumulation in cells irradiated by different doses were shown. Low dose irradiation may delay the onset of senescence in normal human fibroblasts. The latter result confirms our earlier data, that shows for the first time the effect of radioinduced delay of senescense in HFL-1 cell line. Our results suggest a complex interplay of various stress response pathways triggered by low radiation doses, with various low dose thresholds for reactions of different systems. Funding for this study was provided by the Russian Fund for Fundamental Research Grant 13-04-01750.

MIX LYMPHOCYTE CULTURE FROM HUMANS OF DIFFERENT GENDER – NOVEL MODEL FOR STUDY THE RADIATION INDUCED BYSTANDER EFFECT

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Mix culture of lymphocytes from humans of opposite gender represents a unique model for investigation of radiation induced bystander effect (RIBE). Karyotype difference between male (XY) and female (XX) allows to observe in mix culture chromosomal aberrations (ChA) both in irradiated lymphocytes and in neighboring unexposed ones from opposite gender donor.

Two endpoints were used in our study to reveal RIBE – spontaneous frequency of ChA and the ability to develop the adaptive response (AR). Experiments were performed on the blood samples donated by six pairs of male and female donors at the age 23-25 years.

The spontaneous yield of ChA was increased in XX/XY lymphocytes in mix culture with XY/XX lymphocytes irradiated at the dose 1 Gy as compared to corresponding monoculture (Kolesnikova, 2012). If male/female lymphocytes were irradiated at the adaptive dose 0,05 Gy the AR was observed not only in these cells, but as well in co cultivated with them lymphocytes of opposite gender donor (Vorobtsova, Kolesnikova, 2007).

These data provide supportive evidence on the existence of indirect mechanism of radiobiological effect.

EPIGENETIC EFFECTS *MUS*-MUTATIONS IN THE RADIATION-INDUCED ACTIVATION OF TRANSPOSABLE ELEMENTS IN *DROSOPHILA*

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The molecular-genetic reaction formation mechanisms of living organisms to a low-intensity radiation are a significant topic of the radiation genetics. Now, we possess not only the knowledge on the principal mechanisms of the radiation-induced effects (DNA damage repair, detoxification of free radicals, cell cycle control, and apoptosis) but also on certain regulatory processes of epigenetic reaction which base on the transposition activity of transposable (mobile) elements (TEs).

There are data proving the certain similarity between the mechanisms of DNA damage formation induced by radiation and by TE transposition activity. Both of them activate the cell repair systems and their genes. The repair genes are highly important here because repair the DNA strand breaks induced by both radiation and TEs. They also provide for interaction between induction of the cell repair systems and transposition of mobile elements in conditions of a long-term external radiation.

The study concerns the effects of a chronic low-intensity γ-radiation and induction of transposition of TEs (*P*, *hobo*) in *Drosophila* individuals being mutant on reparation (*mus101, mus205, mus304, mus308, mus309*). A clear "transpozonspetsifichnost" enable repair processes and their genes was shown.

Radiation effects on human

RADIATION INDUCED CHANGES IN DYNAMICS OF NEURAL NETWORK MODEL FOR WORKING MEMORY

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Exposure to galactic cosmic radiation is represents a potential risk for central nervous system in long-term space travel. Heavy charged particles constitute a large component of the biological radiation dose due to their high LET and complex energy deposition track structure. In ground-based experiments, exposure to heavy ion radiation induces pronounced deficits in cognitive functions. The precise mechanisms underlying these impairments are mostly unknown, however, recent findings suggest radiation-induced changes in synaptosomes within individual neurons. The synchronization of neuronal activity within a neural network is required for cognitive performance. Thus, in order to make a theoretical background for study of cognitive impairments we have developed a detailed biophysical network model for a population of neurons. The model network describes the neural activity in the prefrontal cortex that is responsible for short-term retention of information about the object (object working memory). We consider two principal types of cells - pyramidal neurons (excitatory population) and interneurons (inhibitory population), connected to each other by synapses with GABA, AMPA and NMDA receptors. Dose-dependent changes in basic structural elements of neurons (synaptic receptors, ion channels, etc) were introduced by phenomenological models, based on the experimental data for heavy ion irradiation. The calculations of network spatiotemporal dynamics were performed. It is demonstrated, that radiation-induced alterations in the properties of synaptic receptors cause loss of stability for specific patterns of activity. This instability arises at the excess of threshold radiation dose. Proposed mathematical approach can be extended for theoretical estimation of other cognitive impairments under ionizing radiation of different quality in the course of solution for various problems of space radiobiology.

THE DYNAMICS OF APOPTOSIS AND REPARATION OF GENOMIC DNA INDICATORS IN RADIATION INDUCED DISEASES FORMATION AT CHILDREN OF 1 - 2 GENERATIONS AFTER THE CHERNOBYL ACCIDENT

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The phenomenon of radiation induced genomic instability has essential impact on a health state in irradiated persons, and also in their off-sprigs, leading to increase of oncogenic risk and effect of a disembriogenesis. Cytogenetic examination of children living in the radiation polluted regions testify the increase of the average levels of the radiation induced chromosomes aberrations in groups of children of the 1-st and 2-nd generations living in radiation polluted regions. At most of children of 1-st generation – radiation-exposed - reparation activity of DNA is reduced, at children of the 2-nd generation this parameter is expressed to a lesser extent. High level of readiness for apoptosis is registered, and at children of the 2-nd generation is higher, than at children of the 1-st generation. This fact can be also considered as a phenomenon of "early cell aging".

DNA damage leads to turning on of the protective mechanism, activation of the P53 protein controlling integrity of genomic DNA, arrest of abnormal cells (with cytogenetic disorders) with the subsequent induction of apoptosis that allows to keep a cellular homeostasis and to avoid formation of a clone of cells with tumoral transformation and development of oncogenic effects at the population which underwent chronic radiation in the small doses, and at their off-spring. So, it was shown that at the irradiated children increase of an indicator of readiness for apoptosis is twice higher than in non-irradiated children. In regions of radionuclide pollution there is an accumulation of mutagenic freight that further may be realized in activation of carcinogenesis and a disembriogenesis.

TIME-DEPENDENT YIELDS OF WATER RADIOLYSIS PRODUCTS IN CA1 HIPPOCAMPAL NEURONS EXPOSED TO HIGH-ENERGY IONS

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Study of the effects induced by high-energy ions in the central nervous system has become increasingly important in recent years. In this regard, identifying the biophysical mechanisms responsible for observed radiation-induced cognitive impairments is one of the major questions in the field. The current work deals with numerical simulation of earliest events in action of high-energy ions on brain neurons. Using the Monte Carlo-based simulation technique, we estimated the indirect radiation damage to synapses of CA1 rat hippocampal neurons placed in the physiological medium. ^{56}Fe particles of 100–5000 MeV/nucleon energy are selected for the analysis. The amounts of seven main water radiolysis products (e^{-}_{aq}, $^{\bullet}OH$, H_3O^+, $H^{\bullet}$, OH^{-}, $H_2^{\bullet}$, $H_2O_2^{\bullet}$) are estimated. It was shown that the levels of e^{-}_{aq}, $^{\bullet}OH$, and H_3O^+ decrease at the reaction time range from 10^{-12} s to 10^{-6} s, while $H^{\bullet}$, OH^{-}, $H_2^{\bullet}$, and $H_2O_2^{\bullet}$ increase up to about 10^{-8} s and then drop down. The data obtained suggest a possibility of radiation damage to synapses due to large amounts of e^{-}_{aq}, $^{\bullet}OH$, and H_3O^+ species at about 10^{-12} s and $H^{\bullet}$, OH^{-}, $H_2^{\bullet}$, and $H_2O_2^{\bullet}$ at about 10^{-8} s. In contrast, the distributions of main four radicals are freely diffusible and their amounts are very different at end of time 10^{-6} s. In this regards, we estimated radiolytic yields that are defined as amount of products formed depending on the total energy deposition in synapses. The amount of water radiolysis after irradiation was found to decrease and their yields increases with increasing energy of particle at time of 10^{-6} s. The large energy deposition and large amount of water radiolysis in small volumes most likely enables heavy ions nuclei to induce violations in the synaptic active zone. The quantification of water radiolysis yields obtained in our study may also enable a better understanding of radiation effects in single neurons. Although the precise mechanism of radiation effects on synapses is unknown, it can be hypothesized that synaptic transmission may be disturbed via overproduction of free water radiolysis and direct interaction of charged particles with certain sensitive structures in the synaptic zone.

IDENTIFICATION OF GENE VARIANTS PREDISPOSING TO INCREASED RADIOSENSITIVITY

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Numerous data demonstrate unequal sensitivity to radiation both at the cellular level and at the level of the organism. In addition, it is proved that the radiosensitivity is an individual feature, which varies from individual to individual within a species. Individual radiosensitivity is a complex trait which is due to the influence of both genetic and environmental factors. One of the important factors that shape individual radiosensitivity is polymorphisms of genes involved in the reparation, cell cycle control and apoptosis, induction of radioprotection mechanisms, detoxification of xenobiotics and others.

Complex molecular genetic analysis of genes polymorphisms involved to the repair of one- and double-strand breaks DNA (*XRCC1* Arg194Trp, *XRCC1* Arg399Gln and *XRCC3* Trp241Met, *XPD* Asp312Asn and *XPD* Lys751Gln.), genes of xenobiotics detoxification (*GSTM1*, *GSTT1* and *GSTP1*), regulation and control the cell cycle (*TP53* Arg72Pro, *ATM* G5557A) and induction of radioprotection mechanisms (*eNOS* 4a/b) allowed us to determine the frequency of polymorphic alleles in representatives 3- & 4-generational families, exposed to irradiation as a result of the Semipalatinsk nuclear test site action and in control population from unpolluted areas of Almaty region. A statistical analysis of association between the studied species polymorphisms and the irradiation factor, as well as increased frequency of 8 minisatellite loci mutations and chromosome aberrations was carried out.

Our results revealed that next genotypes associate with radiosensitivity: *XRCC1* (Trp194Trp; OR=3.39), *XRCC1* (Gln399Gln; OR=1.83), *XRCC3* (Met241Met; OR=2.22), *GSTM1* deletion (OR=3.19), *GSTP1* (Val105Val; OR=1.30); *ATM* (G5557A; OR=1.19), *TP53* (Arg72Pro; OR=1.28), *eNOS* (a/a; OR=1.33). In the analysis of *XPD* was observed that under conditions of acute exposure risk associated with an increased frequency of minisatellite mutations occur in carriers of the homozygous genotypes Gln751Gln (OR=2.19) and Asn312Asn (OR=1.22).

DYNAMICS OF AGE-RELATED CHANGES IN THE EXCHANGE OF MONOAMINES AND THEIR METABOLITES IN RAT BRAIN STRUCTURES AFTER ^{12}C ION IRRADIATION

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Research on the neuroradiobiological effects of high-energy heavy charged particles has become in recent years quite a topical issue due to the necessity of solving a number of important scientific and practical tasks. In this work, the dynamics is studied of age-related changes in the exchange of monoamines and their metabolites in some structures of the rat brain after irradiation with 500 MeV/nucleon 12C ions. The radiation dose and linear energy transfer were, respectively, 1 Gy and 10.6 keV/µm. The times chosen for the analysis of age-related changes were 30 and 90 days after irradiation. Changes of the levels of the following compounds were evaluated in the prefrontal cortex, hippocampus, striatum, nucleus accumbens, and hypothalamus: noradrenaline (NA); dopamine (DA) and its metabolites: 3,4-dihydroxyphenylacetic acid (DOPAC), homovanillic acid (HVA), and 3-methoxytyramine (3-MT); and serotonin (5-OT) and its metabolite 5-hydroxyindolacetic acid (5-HIAA). Also, the concentration ratios DOPAC/DA, HVA/DA, and 5-HIAA/5-OT were analyzed. The most significant differences in the character of the age-related changes were observed in the prefrontal cortex, hypothalamus, and nucleus accumbens. In the prefrontal cortex of the control animals, reliable ($p \leq 0.05$) changes were found in the levels of the four studied compounds: an increase was observed in the concentration of NA, HVA, 5-OT, and 5-HIAA; and a decrease, in the exchange of serotonin determined by the ratio 5-HIAA/5-OT. In the nucleus accumbens, the differences between the control and irradiated animals were in exchange of NA, 3-MT, and 5-HIAA. On the whole, the obtained results show that irradiation influences the dynamics of the temporal changes in the exchange of monoamines and their metabolites.

SOMATIC, BEHAVIORAL, AND CYTOGENETIC EFFECTS AFTER γ-IRRADIATION IN LOW DOSES

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During space flight, the astronauts are exposed to radiation exposure at low doses with low dose rates, so one of the actual areas of Radiobiology is research of action of ionizing radiation in low and ultra-low doses. The aim of our work was the study of earliest effects of ionizing radiation in vivo in mice irradiated with low doses of γ-irradiation of 10 to 200 mGy in the first 24 hours after exposure, i.e. within the first post-radiation exposure cell cycle. Studies were carried out on adult female mice outbred ICR (CD-1) - SPF category at the age of 4-4.5 months with an average body mass of 31 g. Experimental animals were totally irradiated from one side by gamma rays ^{60}Co on the device Rokus-M MTC JINR at doses of 10, 25, 50, 75, 100, 200 mGy with a dose rate of 6.916 mGy / min. Animals were euthanized by cervical dislocation in 21-22 hours after irradiation. Objects for research mice were selected blood system, including cytogenetic indices of bone marrow cells and the immune system, as one of the most radiosensitive. Also the behavioral reactions allowing receiving ideas of a condition of the central nervous system were used. In 21-22 hours after irradiation was observed statistically decrease in number of kariotsit in bone marrow, spleen and thymus mass in the group of animals irradiated in a dose of 50 mGy and 200 mGy whereas decrease in these indicators in the group of mice irradiated at 75 mGy was less expressed. Statistically significant characteristic increase in number of chromosomal aberrations which didn't have complete dose dependence at the mice irradiated in low doses was observed. After 19-20 hours after exposure the reference research behavioral response, estimated in the "open field", in groups of animals irradiated at doses of 10 and 25 mGy, was significantly higher than in the biological control, and the emotional status of mice after 10 mGy exposure was significantly reduced. In the group of mice irradiated at a dose of 50 mGy a statistically significant decrease grip strength of forepaws was registered. The zones of hyperradioresistance and hyperradiosensitivity differing on radiobiological effects and their dependence on the used indicator are identified.

RADIOACTIVE AREAS AND HEALTH IN TIEN-SHEN

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We studied tailings-water-land-grass-meat-human spreading uranium for last four years. It was determined radioactive background around of old tailings situated in rivers cost (MailuuSuu, Sumsar, MinKush) in Tien-Shen. There are determined high content of uranium in soil of gardens (very vary depending of landslides in tailing points), in irrigating water, drinking water, vegetables, in cow meet (1.2±0.15 mg/g uranium in Min-Kush, 0.06±0.0002 mg/kg in Mailuu-Suu), and in milk (2.27±0.031 and 0.107±0.001 mg/kg of wet weight) . Human teeth uranium content in MailuSuu: in milk-teeth 0.481±0.002 x 10^{-6} g/g; but in elderly people groups, from 0.7684 x 10^{-6} g/g to 0.6876 x 10^{-6} g/g. It has been shown in all three areas under-normal inheritage diseases level, and latent illness blood data (lymphocytes and neutrophyles cells; immunity proteins). The blood data similar with light level of radioactive disease. Concerning radon emanation – data were vary variability day-to-day and week-to-week, but in several buildings were high um during year determination in all three areas. So, there are aggravating radioactive impacts to human health: polluted food and drinking water, stones of buildings radioactivity, radon emanation.

MORTALITY RATES AMONG THE OFFSPRING, WHOSE FATHERS WERE OCCUPATIONALLY EXPOSED TO THE IONIZING RADIATION SOURCES

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The study of mortality rates among the offspring of men occupationally exposed due to the contact with ionizing radiation sources at Mayak PA, is the objective of the present work.

Two cohorts were formed based on database “Children’s Register” of Ozersk. The cohort under study comprised 14562 children born from 1949 through 1996 in Ozersk. Their fathers received external gamma-radiation dose by the time of conception due to their work at Mayak PA. Average dose of external gamma-radiation dose, accumulated by the fathers for the whole period of work by the moment of conception, was measured by individual dosimetric control equipment and equaled 29.25 cSv, and average dose accumulated for a year equaled 55.79 mSv. The control cohort comprised children whose parents did not have occupational contact with ionizing radiation sources at the nuclear enterprise. This cohort comprised 23049 individuals born in the same calendar years. 1218 individuals died in the cohort of the offspring of the exposed fathers, 2223 – in the control group.

Trauma and intoxication made a big contribution into the structure of death causes and took the first place both in the main and control groups. Circulatory diseases took the second place, and the third place was for various conditions of perinatal period. No gender differences were observed. It should be noted that the proportion of malignant neoplasms and fatal congenital abnormalities in the cause of death structure both in male and female offspring was higher than in controls.

Evaluation of the effect of the fathers’ exposure for 1 calendar year prior conception with preconceptive dose over 100 mSv showed that the close to significant excess of mortality risk from malignant neoplasms was higher by factor of 1.5 than in the group of the offspring whose fathers had “zero dose” (SIR = 1.54, confidence interval 0.99-2.56)

Epidemiological analysis of mortality risk in the offspring cohort under study have not given evidence yet for speaking about a role of radiation factor in the increase of mortality from all causes and malignant neoplasms.

THE EPIGENETIC DISTURBANCES IN HUMAN BLOOD LEUKOCYTES IN REMOTE PERIOD AFTER RADIATION EXPOSURE

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DNA methylation is a main epigenetic genomic modification, which not only plays an important role in gene regulation but also is crucial for maintaining stability of genome. The aberrant hypermethylation of cytosines in CpG islands (CGIs) associated with active promoters is one of the main mechanisms of gene inactivation.

Methylation-sensitive PCR assay was used to analyze promoter hypermethylation of *p16/CDKN2A, p14/ARF, RASSF1A* and *GSTP1* genes in blood leukocytes from 208 unirradiated volunteers and 124 irradiated subjects (83 Chernobyl Nuclear Power Plant liquidators, 21 nuclear specialists, 20 residents of territories with radioactive contamination, 4 persons evacuated in 1986 from the zone of Chernobyl NPP). The age of unirradiated and irradiated subjects at the time of examination was 19 to 77 years and 24 to 77 years, respectively. Besides, 74 non-exposed offsprings (2.5 – 49 years) born from irradiated parents were examined. As a whole, a frequency of individuals with promoter methylation of at least one of the analyzed genes in exposed group is significantly higher compared to the control group (OR = 5.44, 95% CI = 2.62 - 11.76, p-value = $3{,}9 \bullet 10^{-7}$). No significant differences were found in the frequency of children born to irradiated and unirradiated (control group) parents with the revealed promoter hypermethylation of studied genes (power of the test is about 90%). On this account, upon further analysis, the offsprings of irradiated individuals were assigned to the control group. Multiple regression analysis showed that the growth in the number of methylated loci of a set of *RASSF1A* and *p14* genes is due to the age factor ($\beta = 0.242$; p-value = $1.7 \cdot 10^{-5}$). In contrast, the growth in the number of methylated loci of a set of *p16* and *GSTP1* genes is exclusively due to the fact of radiation exposure ($\beta = 0.290$; p-value = $1.7 \cdot 10^{-7}$). Thus the reality of hypermethylation of CpG islands in gene promoters is revealed in blood leukocytes in remote periods after irradiation of human body. Differential role of age and radiation exposure factor in the hypermethylation of various genes was identified.

MAGISTRACY INTERDISCIPLINARY STUDIES CURRICULUM ON HUMAN SECURITY IN TERRITORIES CONTAMINATED WITH RADIOACTIVE AGENTS

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There is no doubt for the need of specialist's training, owning modern interdisciplinary approaches in the security of population living on areas affected by radioactive contamination in modern conditions.

Objective: To evaluate the effectiveness of curriculum designed to train specialists of the second stage of higher education (Master's degree) on Hygiene within an interdisciplinary approach.

The curriculum was developed on the basis of European partner universities experience study and a multidisciplinary approach. It includes the following sections: radioactivity, radiation doses, radiation sensitivity; exposure due to technologically altered background radiation; radiation accidents; principles of radiation dose reduction on the human organism; legislation and human rights in the contaminated areas; catering of population living in radioactive contamination areas; operation of geographic information systems (SNUNEI) and IT-technologies; principles of exposure reduction and health protection of the population living in the areas contaminated with radionuclides.

Mastering of the curriculum will enable undergraduates to receive academic, social, personal and professional competencies that will help to prepare specialists with modern interdisciplinary approach in the field of security of the population living in areas affected by radioactive contamination.

MATHEMATICAL MODELING OF THE RADIATION-INDUCED DNA DOUBLE-STRAND BREAK REPAIR IN MAMMALIAN AND HUMAN CELLS

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We suggested a mathematical model to simulate the major pathways for repair of radiation-induced DNA double-strand breaks (DSB) in mammalian and human cells. As it is known, DSB is one of the most deleterious types of DNA lesions, since it can lead to induction of structural gene mutations, chromosome aberrations, and possible initiation of the malignant cell transformation, which can be a causal event of carcinogenesis. In this regard, simulation of DNA double-strand break (DSB) rejoining in eukaryotic cells is of great interest. The proposed model shows a possible mechanistic explanation of the basic regularities of DSB processing through the non-homologous end-joining (NHEJ), homologous recombination (HR), single-strand annealing (SSA) and two alternative end-joining pathways. It reconstructs the time-courses of radiation-induced foci specific to particular repair processes including the major intermediate stages. The model is validated for ionizing radiations of a wide range of LET (0.2–236 keV/μm) including a relatively broad spectrum of heavy ions with atomic number up to and including Z=26 (i.e.,^{56}Fe). It provides topological views of the NHEJ, HR, SSA, and two alternative end-joining systems, which contributes to clarifying their biological relations. The model shows possible connections between the biochemical processes of the repair pathways, some of which are still hardly accessible by real experiments. Additionally, with the use of the proposed approach, we reproduced several experimental data sets on γ-H2AX foci remaining in different types of cells including those defective in NHEJ, HR, or SSA functions. The results produced meet the hypothesis that the alternative end-joining pathways represented by micro-SSA and Alt-NHEJ can eliminate some amount of DSBs when classical NHEJ fails.

DOSE THRESHOLD FOR DETECTION OF MUTATIONS IN OFF-SPRINGS OF MAYAK PA WORKERS OCCUPATIONALLY EXPOSED TO IONIZING RADIATION

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Analysis of radiation-induced genome instability (RIGI) and assessment of thresholds for RIGI are crucial tasks of radiobiology. The latter has been the objective of a number of research programs and discussions. To date the dose threshold for RIGI has been estimated to be approximately 0.5 Gy.

To assess risks of long-term genetic effects of radiation exposure we studied RIGI in 95 Mayak PA worker families in which solely paternal prolonged occupational radiation exposure was registered. The mean total absorbed preconception dose (MTAPD) from external gamma-rays to paternal gonads was 1.65 Gy and MTAPD from internal alpha-particles due to incorporated plutonium–239 to gonads was 0.0015 Gy. 50 families with occupationally unexposed parents were selected as controls. Mutagenesis in the study individuals was examined by PCR-assay based on CEB1 hypervariable minisatellite. CEB1 minisatellite mutations were found to be significantly increased in families with fathers exposed to ionizing radiation vs. controls (chi-square based p-value of significance = 0.109).

Weibull model was used to calculate the dose threshold for mutation detection. It took into account MTAPDs from both external gamma-rays and internal alpha-particles due to incorporated plutonium–239 jointly in terms of equivalent doses to gonads. 5% quantile of the estimated dose distribution was used as a dose threshold value. It was estimated to be approximately 0.37 Sv. Thus, the estimated dose threshold for mutation detection agrees with radiation dose levels reported by international organizations at which genome instability may be potentially revealed.

RELEVANCE OF THE CHERNOBYL RESEARCH FOR THE EVALUATION OF GENETIC RADIATION RISKS IN HUMANS

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The committee of the United Nations for the evaluation of radiation effects UNSCEAR up to now derives a very low risk for hereditary diseases from experiments in mice. They claim that there are no human data to refer on, and missing effects in the Japanese A-bomb survivors are erroneously generalized for cases of chronical exposures. Vladimir A. Sevchenko criticized their estimates already soon after the Chernobyl accident. He stated that the main contribution of possible effects as many congenital malformations and all polygenic diseases are leaved out. He also demanded that the estimates must include the following generations until an equilibrium of heritable defects is reached, while the committee considers only the first generation. Sevchenko referred to the rising rates in the Belarussian central registry for congenital anomalies after 1986 and emphasized the importance of biological dosimetry by cytogenetic analysis in order to receive realistic information about the population exposure. We made a compilation of findings about early deaths, congenital malformations, Down´s syndrome, cancer and other effects, which were observed in humans after exposure of parents. Few of them are available from occupationally exposed collectives, much information can be drawn from studies in populations exposed by Chernobyl fallout and from the descendants of liquidators. Nearly all types of hereditary defects were found, which are to be expected according to our general knowledge about. It can clearly be shown that the official risk estimates are much too low. No threshold can be defined below which genetic damage due to exposure to ionizing radiation does not occur. Rising radiation burdens to mankind by medical exposures make necessary to realize the danger to the following generations and to implement the Chernobyl results in a new concept of radiation protection for patients and occupationally exposed people.

PATHOLOGICAL AND MORPHOLOGICAL CHANGES OF PURKINJE CELLS IN THE CEREBELLAR CORTEX OF RATS EXPOSED TO IONIZING RADIATION OF DIFFERENT TYPES

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Humanity is developing space. At the moment, there is the problem of radiation safety of space flights. The least studied the damaging effect of radiation on the central nervous system. Galactic cosmic rays affect on astronaut.

Analysis of pathological and morphological changes of Purkinje cells in the cerebellum is a good method for assessing the degree of the damaging effects of ionizing radiation, and in particular of heavy charged particles.

The report will be presented data on the effect of ionizing radiation (carbon ions with energy C^{12} 500 MeV / u and γ-rays) at a dose of 1 Gy to the morphological changes of Purkinje cells in the cerebellum of rats at 30 and 90 days after irradiation.

To obtain quantitative data were analyzed state of the cerebellar cortex. Was determined by the percentage of normal neurons, easy-changes neurons (morpho-functional and adaptive) and dystrophic neurons. An indicator of the severity of degenerative processes is the number neurocyte with degenerative changes.

The data indicate a substantial increase in the number of destruction changes in the cerebellar cortex of rats under the influence of heavy ions of carbon.

STATISTICAL RECONSTRUCTION OF RADIATION BACKGROUND DOSES OF RURAL RESIDENTS OF THE URALS BASED ON EPR DOSIMETRY OF TOOTH ENAMEL

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The aim of the present work was to investigate the radiation background detected by EPR method for rural residents of Chelyabinsk region (Russia). Rural residents of Urals can be assumed as epidemiological control for the Extended Techa River Cohort exposed due to releases of liquid radioactive effluent into the Techa River during 1949–1956. The method of Electron Paramagnetic Resonance (EPR) dosimetry using tooth enamel is widely used for individual dose reconstruction as well as it is an instrument for retrospective population studies. The method gives an opportunity to measure a cumulative dose of ionizing radiation absorbed due to both radiation background and anthropogenic sources of exposure during lifetime (from the enamel calcification up to tooth extraction). The background dose in this study is meant a dose formed by natural sources of exposure (such as environmental photons and cosmic rays, internal beta emitting radionuclides from uranium and thorium series, and also ^{40}K, ^{14}C and ^{3}H) as well as trace amounts of anthropogenic ^{90}Sr and ^{137}Cs due to nuclear weapon tests (global fallouts) and exposure for medical reasons.

Three hundred ninety-five EPR measurements were performed for 297 teeth of 255 donors, which were born in 1908-1968 and lived in villages of the Southern Urals not exposed to radioactive contamination. The age of donors at time of tooth extraction was in the range from 37 to 93 years old with 70% of ages belonged to a range of 50 - 70 years; mean age was 64±11 years. Actually, EPR detected background doses are close to detection limit of EPR dosimetry and cannot be assumed as a precise. Dealing with the noisy data is not trivial. The method of statistical reconstruction of the background doses was suggested to solve this problem. Assuming the lognormality of background dose distribution, the mean background dose was found as 63±47 mGy that corresponds to the dose rate equal to 0.98 mGy year^{-1}; 25-95% dose range is 0.47-1.25 mGy year^{-1}.

Obtained results will be used for interpretation of the results of EPR tooth dosimetry for the Techa River residents.

RADIATION EPIDEMIOLOGY STUDIES OF MAYAK WORKERS

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Mayak is the first Soviet industrial complex built to provide Plutonium-239 for defense purpose. The plants started operation in 1948 and the first Soviet nuclear device was tested in 1949. During the period of technology development (1948 – 1958) number of workers were exposed to substantial doses of exposure to ionizing radiation including exposure to external gamma-rays and to internally deposited alpha-emitter Plutonium-239 (primarily by inhalation intake).

In 1980-ies the cohort of Mayak workers had been created, which includes today about 26,000 workers, (25% females), 12,000 deaths and 950,000 person-years. Each worker had data of individual monitoring of external exposure level but only about 40% of workers with potential to exposure to Plutonium had been monitored for levels of internal alpha-exposure. Average dose of external gamma-exposure in the cohort is 0.26 Gy whereas maximum dose reaches 6.3 Gy (colon dose). Average dose of alpha exposure (liver dose) is 0.25 Gy whilst maximum liver dose of alpha-exposure is about 16 Gy.

Workers included in the cohort developed both deterministic and stochastic effects resulted from radiation exposure, deterministic are, however, beyond the scope of current report. Leukemia risk was one of the first effects clearly demonstrated having ERR/Gy of 0.57 (95% CI 0.05 – 2.04) sharply declining with age attained and time after exposure: the highest risk is associated with external dose received 2-4 years before leukemia death. Risk of death from solid cancers other than lung, liver and bone (which are organs receiving the highest doses of exposure to alpha-particles) increased with level of external exposure with excess relative risk per Gray (ERR/Gy) 0.16 (95% CI 0.07 – 0.26). Neither of cancers described above have shown any association with exposure to Plutonium.

Cancers in organs of primary Plutonium deposition showed significant alpha-particles dose-response with most deaths attributed to Plutonium. ERR/Gy for lung cancer is 7.1 (95% CI 5.0 - 11), for liver cancer 2.6 (0.7 – 6.9) and for bone cancer 0.76 (<0 – 5.2). Among these sites only lung cancer responded (although insignificantly) to gamma-exposure with ERR/Gy of 0.13 (95% CI -0.04 – 0.38).

HEMATOLOGICAL MALIGNANCIES IN THE OFFSPRING OF RADIATION-EXPOSED PARENTS

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Malignancies of the hematopoietic and lymphatic tissues in children have polyetiological nature. Causal relation of parental exposure to ionizing radiation and hematological malignancies in their offspring are subject to discussion.

In this study we tried to find the relations between preconceptional exposure to prolonged external γ-radiation of the Mayak Production Association (PA) workers and haematological malignancies in their children.

This epidemiological study is based on the registry which includes all children, who were born in 1949 – 2009 in the city of Ozyorsk, located near the first Russian nuclear industry complex Mayak, which started operation in 1948. We used nested case-control approach, defining case as person with hemolymphoblastose diagnosed and control as person with no such diagnosis matched to case on sex, birth year and parents age at birth. We calculated odds ratio (OR) with 95% confidence interval (CI). The study group included children under 15 years old (51 child, among them 23 boys and 28 girls), diagnosed with hematologic malignancy while living in Ozyorsk in 1949 – 2009. The control group included 197 children with no malignancies diagnosed (boys-107, girls-90). Average total whole-body external γ-ray dose before conception in parents of study group was 445.5 mSv (2.7-3,122); in parents of control group – 374.8 mSv (0.3-3,026). Average age at diagnose is 6 years without any gender difference. Acute leukaemia (34 diagnoses, 66.7% of all hemolymphoblastoses diagnosed) was the main contributor to the structure of hematologic malignancies. The odds ratio OR 0.92 (CI 0.56-1.53) indicated no relation between the level of preconceptional radiation exposure in parents and haematological malignancies in their offspring.

Conclusion: In this study we did not see any impact of preconceptional prolonged external γ-radiation exposure in parents on risk of hematologic malignancies. Supposedly, this is caused by natural reparation mechanisms, reducing damage resulting from external risk factors, in particular ionizing radiation.

LOCAL BONE MARROW EXPOSURE: HOW TO INTERPRET THE DATA ON STABLE CHROMOSOME ABERRATIONS IN CIRCULATING LYMPHOCYTES?

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The method of fluorescence in situ hybridization (FISH) applied to peripheral blood T-lymphocytes is used for retrospective dose estimation, and the results obtained from the stable-chromosomal-aberrations analysis are usually interpreted as a dose accumulated in the red bone marrow (RBM). However, after the local exposure of RBM, the doses derived from the FISH-study were found to be lower than those derived from direct measurements of radionuclides accumulated in the bodies of exposed persons. These results were obtained for people residing near the Techa River contaminated by ^{89,90}Sr (beta-emitters) in 1949-1956 (Chelyabinsk Oblast, Russia). It has been suggested that some portion of T-cells remained unexposed because they represented the offspring (clones) of thymocytes which had matured before the start of ^{89,90}Sr intakes. To clarify this problem, the number of T-cell-clonotypes produced by the thymus over different age-periods of human life was estimated with the use of the mathematic model of T-cell homeostasis (Bains I, 2010) describing the production of recent thymic emigrants. According to our estimates, as of the time of blood sampling, the fraction of exposed T-cells (and their progeny) ranged from 80% to 20% depending on the patients' age at the start of ^{89,90}Sr exposure. A comparison of the model estimates and actual FISH-based doses for donors from the Techa riverside villages aged 10 years (at the start of ^{89,90}Sr exposure) has shown that our approach to FISH-data interpretation does not contradict the experimental data. A two-fold excess of doses based on in vivo measurements of ^{90}Sr body-burdens versus FISH-based doses was correctly predicted for Techa riverside residents. The approach presented is also applicable to data on human exposure to plutonium isotopes distributed mostly between the skeleton and liver. FISH-based Pu-doses may reflect the cumulative effect of exposure of the lymphoid-progenitors in the bone marrow cavities, periodic exposure of T lymphocytes (in circulation) in the liver and lung lymph nodes; as a result, FISH-based Pu-doses and also ^{89,90}Sr- doses cannot be directly interpreted as RBM doses.

BODY POTASSIUM CONTENT AND RADIATION DOSES FROM 40K TO THE URALS POPULATION (RUSSIA)

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Long-term monitoring of whole-body radionuclides in residents of Urals Region occurred in Urals Research Center for Radiation Medicine (URCRM, Chelyabinsk). Quantification of ^{90}Sr was achieved by measuring a 'phoswich' detector the bremsstrahlung of ^{90}Y (daughter of ^{90}Sr) beta rays with use of with Whole Body Counter (WBC) SICH-9.1M. Analyses of ^{137}Cs and ^{40}K were accomplished at the same time with the same detectors by the measurement of their photopeaks. Current study presents the results of ^{40}K measurements in 3,651 women and 1,965 man aged 11-90; measurements were performed in 2006 - 2014. The levels of ^{40}K-body contents depend upon gender, age, and body mass. The residents belonged to two ethnic groups, Turkic (Tatars) and Slavs (Russian). However, it was not found significant ethnic-differences in ^{40}K-body contents and values normalized per kg of body weight (in groups homogenous by age and gender). Both ^{40}K-body contents and normalized values were significantly higher in men then in women in all age-groups, the difference was about 25%. The measured ^{40}K-body contents in men of 20-50 years were about 4200 Bq and about 3000 Bq in women. By the age of 80 these values decreased up to 3200 Bq in men and 2500 Bq in women. The dose coefficients according to Storm et al., 2009 (in terms of mGy/year per 1 Bq of ^{40}K in kg of body weight) were used to calculate the individual doses absorbed in the whole body. Annual dose rates were maximal in the age group of 20-30 years: 0.16 ±0.02 mGy/y for men and 0.13±0.01 mGy/y for women. Further, the dose-rates decreased with age and in the group of 60-80 years they were 0.13± 0.02 mGy/y for men and 0.10±0.01 mGy/y for women. Individual dose rates are described by a normal statistical distribution within the groups homogeneous in terms of age and gender. Variation coefficient makes up from 9 to 14%, on the average – 12.5%. Doses from naturally occurring ^{40}K accumulated over 70 years were 9.9 mGy for men and 8.3 mGy for women; over 90 years - 12.5 and 10.4 mGy correspondently.

SIGNIFICANCE OF CYTOGENETIC STUDY FOR ESTIMATION OF BIOLOGICAL EFFECTS OF LOW-DOSE IRRADIATION OF PEOPLE

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Cytogenetic study was performed on various groups of people survived the low-dose irradiation: liquidators of the consequences of Chernobyl accident, their children, evacuees (adults and children) and control groups, in total about 1500 persons at the age range 3-87 years. In exposed groups increased frequencies of unstable and stable (FISH) chromosomal aberrations (CA), micronuclei, HPRT-mutations were found.

Cytogenetic injuries in exposed group were accompanied by negative health effects. In lymphocytes of children irradiated prezygotically or postnatally increased chromosomal sensitivity to the challenge irradiation in vitro was observed (genomic instability). The positive correlation has been found between the spontaneous level of CA and morbidity (cardiovascular and gastrointestinal systems) in adults. The frequency of translocations in lymphocytes increased with age as quadratic function, faster in exposed people than in control ones (accelerated ageing).

On the lymphocytes of cancer patients undergone whole-body fractionated irradiation every other day at the single dose 0,115 Gy up to the total dose 1,15 Gy in vivo the dose-response for dicentrics was constructed and compared with their dose-response for in vitro irradiated lymphocytes. The lower frequency of events per unit dose was observed after in vivo irradiation of lymphocytes. It means that individual dose reconstructed using in vitro dose-effect calibration curve is underestimated as well as risk of possible health effects.

Bystander effect was studied using novel model – mix culture of male and female lymphocytes. In non irradiated female/male lymphocytes neighboring the irradiated (1 Gy) ones from humans of opposite gender increased level of CA was observed. Moreover non irradiated female/male lymphocytes developed adaptive response (on the CA index) in mix culture with pre irradiated at low dose (0,05 Gy) lymphocytes of opposite gender donor.

LASER DEVICE FOR THE PROTECTION OF BIOLOGICAL OBJECTS FROM THE DAMAGING ACTION OF IONIZING RADIATION

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The search for ideal protective agents for use in radiotherapy or post-exposure treatment of victims of radiation accidents is one of the actual problems of radiation protection.

Laser irradiation devices for the protection of biological objects from the action of ionizing radiation to be used in practice has been manufactured (invention patents RU 2 428 228 C2).

Laser device is used to study the action of various doses of laser radiation and combined irradiation with laser and gamma-radiation, on peripheral blood parameters and number of bone marrow karyocytes of the experimental mice line C57BL/6. The mice were irradiated with ionizing and laser radiation, separately one by one in a special bench. The time interval between two types of irradiation did not exceed 30 min. First, the mice were exposed to γ-radiation then to laser radiation.

It was shown that the laser radiation can be applied to improve the recovery of hematogenesis after the action of ionizing radiation on biological objects.

Then, experiments were conducted to study the action of γ-rays and the combined action of laser radiation and γ -rays on survival, weight and skin of experimental mice. The authors investigated also the action of gamma-rays and combined effects of 650 nm laser radiation and gamma-rays on general mitotic index of bone marrow cells of mice.

The method of the laser radiation-protection of biological objects contributes to an increase in the viability of mice, prevents the damages of skin and also increases the mitotic activity of mice bone marrow cells.

It was also demonstrated that laser can manage protection from a broad range of ionizing radiation doses and mitigate the adverse effects of equally acute and prolonged radiation exposure.

RADIOECOLOGY

Radiation terrestrial & hydroecology

VIABILITY OF PLANT SEED PROGENY FROM THE EAST-URAL RADIOACTIVE TRACE: RADIATION AND WEATHER CONDITIONS

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The East-Ural Radioactive Trace (EURT) was formed in 1957 as a result of the accident at the PA "Mayak" (Russia). This territory was contaminated again in 1967 with radioactive silt and sand transferred by wind from the shores of Lake Karachay. Modern absorbed dose rates for plants in buffer areas exceed the background values by 2-5 times, and in impact one – by 43-110 times. We summarized the long-term investigations of viability of 20 species seed progeny from the EURT area: *Taraxacum officinale*, *Plantago major*, *Silene latifolia*, *Stellaria graminea*, *Bromopsis inermis*, *Cirsium setosum*, *Centaurea scabiosa*, *Berteroa incana*, *Trifolium medium*, *Galium aparine*, *Leonurus quinquelobatus* etc. More than 180 weather parameters were analyzed to estimate the weather condition effects on seed maturation. For same species within-year and interannual variability of seedling survival, growth rate of the roots and true leaves were assessed. The interaction of radiation with environmental factors plays the important role in forming the high-quality seeds because it modifies intra- and interpopulation variability. It was found that in 2005, the survival rate of seedlings of different plant species at the EURT area was below background plots. From 2007 to 2013 differences between samples in the pollution gradient were insignificant for most plants. The manifestation of synchronous interannual variability in different species indicates the priority influence of weather conditions. For instance, *Stellaria graminea* high-quality seeds in impact populations were formed in cool and wet conditions in June followed by warm and dry August. The opposite pattern was found for *Bromopsis inermis* populations: significant effects of weather had not been identified at the EURT, but high-quality seeds of background populations were formed in dry and warm seasons. The same weather conditions were necessary for seed formation of *Silene latifolia*, regardless of the total absorbed doses. The peculiarity of the observed effects in *Arctium tomentosum* populations consisted in the opposite dependencies: the background seeds need in warm and humid conditions but impact seeds need in cool and dry conditions. Thus, the weather conditions can modify significantly the radiation effects on seed progeny. This work was supported by Federal Special Scientific and Technical Program in support of leading scientific schools (SS-2840.2014.4) and RFBR (15-04-01023, and 15-34-20639).

ECOGENETIC STUDIES IN ARMENIA

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An integrated approach including genotoxicity biomarkers and chemical analysis of environmental pollutants is used in the biomonitoring programs in Armenia. This approach allows to get a comprehensive picture of the pollution-related genetic effects and evaluate the status of ecosystems. Analysis of genotoxicity of soils around Armenian Nuclear Power station using Tradescantia (clone 02) bioassay showed increased frequencies of micronuclei (Trad-MCN) and stamen hair mutations (Trad-SHM) along with the ^{137}Cs pollution gradient at significant inter-location. Evaluation of genotoxicity of waters of Hrazdan, Getar, Marmarik and Sevjur rivers revealed dependence of levels of Trad-MCN and Trad-SHM from the concentrations of 14 heavy metals. The reason for this increase may be draining of domestic and industrial wastes. Annual monitoring of Hrazdan River showed the seasonal increase of water genotoxicity caused by accumulation of pollutants after summer and spring rains. Application of the comet assay (single cell gel electrophoresis) in erythrocytes of *Carassius auratus gibelio* fish and Trad-MCN demonstrated significant inter-site differences in the level of water genotoxicity in basin of Lake Sevan. Positive correlation between DNA damage in fish and content of nitrate ions, Si, Al, P_{total}, Fe, Mn and Cu, as well as between the Trad-MCN and the level of nitrate ions, Si, Al, Fe, Mn and Cu in water has been revealed. The comet assay in haemocytes of crayfish *Astacus leptodactylus,* widespread in basin of Lake Sevan, allowed estimating the genotoxicity of benthic zone pollution, which considerably differs from the genotoxicity of surface waters. For the first time native species of lizards *Darevskia armeniaca* (parthenogenetic) and *Darevskia raddei* (bisexual) were used as bioindicators of environmental pollution. Estimation of DNA damage in lizard erythrocytes using the comet assay demonstrated higher sensitivity of parthenogenetic species towards environmental mutagens in comparison with bisexuals. Moreover, females were more sensitive than males.

The sensitivity and efficiency of applied test systems and their capacity to reflect the level of environmental pollution will be summarized to develop principles of local and integral monitoring of mutagenicity/genotoxicity in Armenia.

INTERNATIONAL UNION OF RADIOECOLOGY (IUR): TASKS, ACHIEVEMENTS AND STRATEGY DIRECTED TO PROTECTION OF PEOPLE AND ECOSYSTEMS

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The first founding pioneers of Radioecology started by investigations of the biological and ecological effects of radiation. IUR was founded in the seventies as a non-governmental knowing society dedicated to the development of radioecology worldwide. The scientific directions taken in Radioecology have been drastically influenced by the Chernobyl accident. The immediate need to assess risk to man emphasized a focus on environmental transfers through the environment to feed human radiation protection appropriate measures. This initially exclusive anthropocentric attitude has been next influenced by an evolution prompted by emerging society's concern on environmental issues calling for better assessment of ecological risk from toxicants and other stressors, including anthropogenic radioactivity. This has prompted an evolution of radioecology towards a more ecocentric view which aims at building capacity for assessing/predicting risks to animals, plants and their ecosystems as well as human beings (who form an integral part of the later). Indeed, as indicated by scientific investigations carried out in contaminated territories (Chernobyl and more recently also Fukushima), results interpreted in terms of ecological risk still remain controversial, undermining public trust in nuclear generation technology. The IUR plays a central role within this evolution which will be detailed further. After a historical analysis of the development of Radioecology as viewed from IUR, an explanation of its most significant current tools of action and their recent achievements will be given. Finally, paying due account of the questions raised by the Fukushima accident and the challenges faced today by the Radioecology community when attempting to integrate human and environment radiological protection, the overall strategy of the Union for the future will be drawn and explained.

PLUTOPIA: THE GREAT SOVIET AND AMERICAN PLUTONIUM DISASTERS

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In *Plutopia,* the author draws on official records and dozens of interviews to tell the extraordinary stories of Richland, Washington and Ozersk, Russia-the first two cities in the world to produce plutonium. To contain secrets, American and Soviet leaders created plutopias--communities of nuclear families living in highly-subsidized, limited-access atomic cities. Fully employed and medically monitored, the residents of Richland and Ozersk enjoyed all the pleasures of consumer society, while nearby, migrants, prisoners, and soldiers were banned from plutopia--they lived in temporary "staging grounds" and often performed the most dangerous work at the plant. Brown shows that the plants' segregation of permanent and temporary workers and of nuclear and non-nuclear zones created a bubble of immunity, where dumps and accidents were glossed over and plant managers freely embezzled and polluted. In four decades, the Hanford plant near Richland and the Maiak plant near Ozersk each issued at least 200 million curies of radioactive isotopes into the surrounding environment--equaling four Chernobyls--laying waste to hundreds of square miles and contaminating rivers, fields, forests, and food supplies. Because of the decades of secrecy, downwind and downriver neighbors of the plutonium plants had difficulty proving what they suspected, that the rash of illnesses, cancers, and birth defects in their communities were caused by the plants' radioactive emissions. Plutopia was successful because in its zoned-off isolation it appeared to deliver the promises of the American dream and Soviet communism; in reality, it concealed disasters that remain unstable and threatening today.

EFFECTS OF PRECEDING GAMMA IRRADIATION OF SEEDS *HORDEUM VULGARE L.*

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One of the main uses of radiation technologies in agriculture is presowing seed treatment - technology, which is based on the phenomenon of radiation hormesis. However, many questions about the use of pre-sowing treatment remain: 1) mechanisms of short-term and long-acting effects of stimulation; 2) incomplete reproducible stimulation effect in the field. To answer the questions submitted is necessary to conduct comprehensive studies on the biochemical, organisms, as well as, on the population levels of biological organization.

Step 1. In our research, we have shown the stimulatory effects of γ-irradiation of barley seeds (variety NUR) in the early stages of ontogeny. Increasing the length of the germ and root was observed with a dose of 8-20 Gy (dose rate of 60 Gy /hr).

Irradiation was carried out on an experimental-industrial gamma setting GUR-120 (RIARAE, Obninsk, Russia). Shows the influence of the shelf life of irradiated seeds before planting, as well as the impact of the quality of the irradiated seeds. Better the effect of hormesis is displayed on the seeds of poorer quality (1 reproduction). On the weight of the root system of the irradiation of seeds are mostly not affected.

Step 2: To evaluate the stimulation of plant growth in the early stages of ontogeny affects their productivity and quality of the harvest, we performed a field experiment. After evaluating the structure and quality of the crop produced the following results: an increase in the height of the stems of plants (10.4%, 8 Gy); increase in tillering (16, 20 Gy); increasing the number of stalks with ears (8, 20, and 50 Gy); 1000 seed weight increase of 11 and 15.7% at a dose of 16 and 20 Gy. When assessing the resulting yield (t / ha), can increase to 37, 34, 38 and 37% of seeds by irradiation doses of 8, 16, 20 and 50 Gy, respectively.

In the grain observed significant decrease in the level of fat (14.6%) at a dose of 20 Gy and dry matter (1.2%) at a dose of 50 Gy, as well as a significant increase in the level of protein (9.7%) and fat (14.1 %) at a dose of 50 Gy irradiation. In the straw significantly alter the level of fiber: ↑ 4,3%, ↑ 3,8% and ↓ 2,2% at doses of 8, 16 and 50 Gy, respectively. Significant differences in other indicators of straw have been identified.

MICROEVOLUTIONARY PROCESSES IN THE 30-KM CHERNOBYL EXCLUSION ZONE

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As a result of severe technogenic accidents, microevolutionary processes in plants and their pathogens could occur and affect the ecological balance in ecosystems. The aim of the work was to study the effect of combined stress (biotic and radiation) on plants and their pathogens in the 30-km Chernobyl exclusion zone.

It was found that low dose chronic irradiation leads to a decrease in plant disease resistance. In pot experiments it was established that infection with powdery mildew and brown rust of three wheat (*Triticum aestivum* L.) cultivars seedlings grown from seeds, collected in the Chernobyl exclusion zone, was 1.5–2.0 times higher than of plants grown from control seeds. On field plots in the Chernobyl zone, wheat plant resistance to biotic stress was reduced. At artificial infection with brown rust, the disease development was enhanced on plots with increased radiation background. One of the mechanisms of declined phytoimmunity potential under the action of low dose chronic irradiation is evidently a reduced activity of plant proteinase inhibitors. Thus, in wheat and rye kernels, their activity reduced by 35–60% as compared to control. The decrease in the activity of these inhibitors could lead to decrease of plant innate disease resistance. This assumption was confirmed in experiments with high-lysine *opaque*-mutant of maize.

Active form- and race-formation processes in the population of the stem rust causal agent (*Puccinia graminis* Pers.) were observed in the Chernobyl exclusion zone. A "new" population of this fungus with high frequency of more virulent clones than in other Ukraine regions was distinguished. The results obtained independently in greenhouse and field trials performed in the Chernobyl zone demonstrated radiation stress influence on the plant-pathogen system. Other researchers, who have studied the consequences of Chernobyl disaster for biological objects, have also found some changes in the populations of plant pathogens. The results obtained suggest a necessity of monitoring the microevolutionary processes occurring in both plants and their pathogens under severe technogenic accidents because it may pose a threat to the ecological balance in biocenoses.

EFFECTS OF IONIZING RADIATION ON POPULATIONS AND ECOSYSTEMS

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Release of radionuclides into the environment as a result of human activity is a new evolutionary factor which creates the risk of additional exposure of all living organisms, including mans. Responses of populations and ecosystems to low and high doses of ionizing radiation as well as to radinouclide contamination are discussed in this contribution. Typical reactions of ecosystems to high dose irradiation such as reduction in species diversity, changes in species dominance, decline of productivity and alterations in community structure are considered. Absorbed doses form differently in case of acute irradiation and in the course of large radiation accidents. There are essential differences in absorbed doses for humans and typical biota representatives in the same radioecological situation. Particular attention should be paid to the phenomenon of radioadaptation, changes in sex, age and genetic structure of populations since such effects cannot be reduced to the basic mechanisms of biological action of radionuclides. The results of field studies carried out on different plant species (winter rye and wheat, spring barley, oats, Scots pine, wild vetch, crested hairgrass) in various radioecological situations (nuclear weapon testing, the Chernobyl accident, uranium and radium processing) are discussed. Populations growing in areas with relatively low levels of pollution are characterized by the increased level of both cytogenetic alterations and genetic diversity. Contamination of the plants environment activates genetic mechanisms, changing a population's resistance to exposure. However, there are ecological situations where enhanced resistance has not evolved or has not persisted. Experience gained in many studies allows to list main challenges of up-to-date radioecology: analysis and formalization of mathematical models of key processes determining the migration of radionuclides in major natural environments; development of dosimetry models for reference biota species; analysis of the mechanisms underlying the formation of radiobiological effects at different levels of biological organization - from molecular to the ecosystem, especially in conditions of chronic radiation exposure; development of a unified system of radiation protection of man and the environment that is compatible with the risk assessment of chemical pollutants.

PATTERNS OF RODENTS POPULATION' RESPONSE TO ACUTE AND LOW DOSE CHRONIC RADIATION

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In this report patterns of rodents population' response to acute (laboratory experiment) and chronic irradiation (inhabiting the Eastern Urals Radioactive Trace zone – EURT - resulted from the Kyshtym accident 1957, Chelyabinsk region) will be considered. It will be shown the basis of biological effects and radionuclide' accumulation at the population level is the polyalternativeness of small mammals' ontogeny development (a belonging of individuals to one of two alternative pathway of ontogeny (Olenev, 2002)). Small rodents are cyclomorphic mammals, which characterized by cyclic changes in the most biological parameters over a period of approximately one year; mass breeding and generation overlap in the presence of two alternative ontogenetic pathways. These pathways are supposed to divide natural population into groups of individuals with the same functional status, i. e. with the uniform patterns of growth and/or maturation rate as well as their participation in reproduction. Results of own radiobiological experiments (acute irradiation) concerning studying of radioresistance, lifespan, reaction of haemopoietic system of mouse-like rodents of different ontogeny' pathways will be given. Besides the data of long-term investigations of ^{90}Sr accumulation (osteotropic radionuclide) in rodents skeleton from the radiocontaminated zone (EURT) at the level of intrapopulational structure-functional units will be submitted. Specific patterns of rodent's population response to both: an acute and chronic low doses radiation exposure will be characterized. Individuals of similar chronological age, but different functional status differ significantly for all analyzed parameters. It is discussed both (1) the functionally-ecological role of biodiversity of small mammals in stability of population as a homeostatic system and (2) ontogenetic polyalternativeness as an important mechanism of radioadaptation at the population level which decrease the damaging action at non-human biota in radiocontaminated environment.

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MICROEVOLUTION PROCESSES IN ANTHROPOGENIC RADIONUCLIDE ANOMALIES

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There are territories of different size contaminated with fission products of uranium due to nuclear accidents and nuclear weapons testing in the continent and water area. Radioactive contamination in these areas is responsible for the existence of a permanent ionizing radiation. Field. Examples include Chernobyl Exclusion Zone, part of the land and waters of the ocean near the Fukushima nuclear power plant, the Ural radioactive trace. Such radioactive anomalies are hot spots for the flora and fauna in ecosystems because all kinds of animals, plants, fungi, bacteria and viruses are affected by chronic exposure to ionizing radiation throughout their life cycles. Increasing doses are accompanied by an augmentation in the incidence of mutations. In addition, irradiation is perceived by the organism as stress effect and ontogenetic and phylogenetic adaptations should be formed in response to this stress. The first is associated with the activation of genes controlling DNA reparation, membrane currents, and the synthesis of antioxidants as well as a repopulation in meristem tissues. The second phenomenon is manifested in the processes that lead to an increase in phenotypic diversity in populations thus increases the efficiency of natural selection for enhanced radioresistance in species. Phenotypic polymorphism population is also increasing due to epigenetic mechanisms that lead to appearance of pseudo mutations. In plants capable to apomixes, the frequency of sexual reproduction increases and therefore the contribution of apomictic seed formation decreases. A similar phenomenon is observed in some polychaetes in which with increasing dose of chronic exposure the role of sexual reproduction increases and the value of vegetative fragmentation weakens. Reported events constituting microevolution cause accelerated evolutionary changes in the intra-specific level. Because some of the species populations are composed of a relatively small number of individuals in hotspots ecosystems, the probability of genetic drift also due to declining fertility of some species population is replenished by immigration from areas adjacent to anthropogenic radionuclide anomaly. This process is accompanied by an increase in the intensity of gene flow. Naturally, the high rate of microevolution processes can be revealed only in those species that are characterized by short periods of the life cycle and whereby they a sufficiently large number of generations under conditions of chronic exposure. The examples of stem rust pathogen of cereals fungus *Puccinia graminis* Pers. and mildew *Erysiphe sp*. demonstrated an increase in the development of these pathogens due to the emergence of new highly virulent races in the Chernobyl exclusion zone, The hotspots are gradually becoming the nidus of new virulent forms of pathogens. Risks to biota due to an increase in micro-evolutionary processes in the anthropogenic radionuclide anomalies can result in the appearance of rare mutations, increase the genetic and epigenetic polymorphism of populations and loss of balance of species in ecosystems. Of course, it is necessary to create a monitoring of microevolution processes in hot spots as a helpful security measure. In natural radionuclide anomalies associated with uranium deposits range of deviation in genetic variation is not as significant as in the conditions of anthropogenic anomalies. Apparently mechanisms stabilizing the variability in populations evolved over a long period of time.

AQUATIC PLANTS AND ANIMALS IN THE CHERNOBYL EXCLUSION ZONE: EFFECTS OF LONG-TERM RADIATION EXPOSURE ON DIFFERENT LEVELS OF BIOLOGICAL ORGANIZATION

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Currently the radioecological situation in the Chernobyl Exclusion Zone (EZ) determining primarily by long-lived radionuclides ^{90}Sr, ^{137}Cs, ^{238}Pu, ^{239}Pu, ^{240}Pu and ^{241}Am. The absorbed dose rate for hydrobionts of the researched water bodies within the EZ during 1997-2014 was registered in range 1.3 mGy - 3.4 Gy per year. The highest levels were registered in lakes of the dammed territory of the left-bank floodplain of the Pripyat River, the lowest one - for running water objects. Different radiation effects of ionizing radiation on hydrobionts in lakes within the EZ were registered in post-accident period. Some of these effects appear shortly, while an increasing importance expected by the remote consequences - genetic damages induced by a long-term irradiation. These remote consequences are a long-drawn realization of changes in molecules of heredity, where the initial molecular damages have a latent period without any display and can be transfer through the many generations of cells to be a reason of genome instability in future. The established dose-related effects in hydrobionts of lakes within the EZ indicates a damage of biological systems at subcellular, cellular, tissue, organ, organism and population levels as a result of chronic exposure to low doses of ionizing radiation. The rate of chromosomal aberrations in cells of aquatic species in many times exceeds the level of spontaneous mutagenesis level to aquatic biota. Increased levels of chromosome damages may be a manifestation of radiation-induced genetic instability, which is one of the main mechanisms for the protection of living organisms from exposure to stressors with subsequent implementation at higher levels of organization of biological systems. Haematological research of fish in the exclusion zone shows essential changes in leukogram structure and high amount of red cells with atypical shape of nucleus as different type of invaginations, ramifications etc. as well as cells without nucleus in the blood of fishes from the water bodies with high levels of radioactive contamination that allows to assume that the qualitative indexes of red cells of peripheral blood of fishes are more sensible to chronic radiation influence in comparison with the elements of white blood.

INHERITANCE OF *ARABIDOPSIS THALIANA* ADAPTATION TO UV-B RADIATION

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Transgenerational transfer of adaptive effects against UV-B radiation in three A. thaliana genotypes: wild type (Col-0) and deficient in salicylate (NahG) and jasmonate (jin1) inducible defenses were analyzed.

3-5 days A. thaliana seedlings were irradiated and effects were estimated based on the roots length after 3-5 days. In another set of experiments, plants grown on soil were irradiated 5-6 times (0.1 to 0.5 kJ/m^2) since 3 days old till the beginning of the generative phase with an interval of 2-3 days. Three days after the last adaptive irradiation plants were irradiated with a damage dose of 6 kJ/m^2. Number of pods formed in F0 and roots length of F1 seedlings were determined.

Pre-irradiation of seedlings (Col-0) at a dose of 35 J/m^2 resulted in the formation of adaptive response. The damaging effect of irradiation at a dose of 170 J/m^2 on root growth was significantly reduced.

Repeated exposure of A. thaliana plants in doses of 0.1-0.5 kJ/m^2 resulted in hormesis and the formation of adaptive response (number of pods). The effect varied depending on the dose, genotype and age of plants. Mainly growth of generative potential was revealed.

Adapting irradiation of F0 plants of three genotypes resulted in stimulation of root growth in seedlings of the next (F1) unirradiated generation. The irradiation dose of 10 kJ/m^2 had a less damaging effect on the F1 seedlings that emerged from seeds in the variants subjected to adaptation irradiation in F0 in all three genotypes.

The data obtained suggest that low dose UV-B irradiation of plants in F0 leads to the formation and transgenerational transfer of hormesis and adaptive response. The degree of manifestation of the investigated effects was dependent upon plant age and functioning of salicylate and jasmonate signal systems. Stimulation and adaptive effects have been decreased with increasing plant age at the time of adapting exposure.

STUDY OF PLANT ADAPTATION TO SALT STRESS, WHOSE SEEDS BEFORE SOWING ARE EXPOSED TO γ – IRRADIATION AT DIFFERENT DOSES

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Plants in the real environment, usually subjected simultaneously to several stressors. In certain conditions the effect of these factors leads to adapt plants. Adaptation of plants to adverse environmental conditions due to the presence in them of an effective antioxidant defense system.

In this study, based on the individual components of defense system we attempted to clarify the nature of the operation of this system for several agricultural crops. Objects of investigation were beans, eggplant, cucumber and tomato. The seeds of these plants before seeding in soil salinity using source ^{60}Co γ-ray irradiated at doses of 1, 5, 10, 50, 100, 200 and 300 Gy (the dose rate in all cases was 0.048 Gy / s).

Were shown that: in some cases the experimental and control samples of plants differ in biometric parameters; malondialdehyde content, as a result of destruction of membrane lipids, increases with increasing dose of ionizing radiation; content of low molecular weight component - proline and activity of macromolecular components - superoxide dismutase, catalase, ascorbate peroxidase, forming antioxidant protection of plants under stress conditions, are subject to significant change. These changes depend on the plant species as well as the radiation dose.

It is shown the active participation of both components defense system in plant protection from radiation and salt stress.

It is assumed that increasing the dose in the low-dose radiation causes increased formation of reactive oxygen species. This is accompanied by a great destruction of lipid membranes, resulting in the increase of malondialdehyde content - a product of lipid peroxidation by free radicals of oxygen. The defense system functioning under these conditions leads to increased synthesis of proline which plays the role of "traps" for the reactive oxygen species under stress conditions and to activation of antioxidant enzymes. And at higher doses of radiation in addition to the destructive effects of lipid peroxidation also covers the biological macromolecules.

ADAPTIVE, POPULATION, AND GENETIC CHANGES IN EARTHWORMS UNDER ANTHROPOGENIC CONTAMINATION

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Though some modern articles published cover effects of chronic anthropogenic stress in plant and animal natural populations but just little of them discover mechanisms of adaptation. However survival of population exposed to adverse conditions results evidently from changes occurs on all organization levels of living matter from the molecules up to populations.

The present investigation goal was simultaneous analysis of genome stability, individual stress tolerance and population changes in earthworms *Aporrectodea caliginosa* inhabiting anthropogenically contaminated soils.

Results obtained shows no difference in levels of DNA damage detected with alkaline and neutral versions of Comet assay in earthworms from contaminated territories and spontaneous level found in animals from reference population. This is could of indicate adaptive changes in the animals inhabited the contaminated sites. The rate of DNA-damage repair induced in *A. caliginosa* sampled from the contaminated site with an additional acute γ-irradiation (4 Gy) was found to be considerably higher as compared with earthworms from reference sites. At the same time earthworms sampled from the contaminated site were less resistant to additional exposure to high Cd concentration in the soil.

Genetic distances between populations inhabiting the areas with varying degrees of soil contamination was shown using AFLP method. At the same time no correlation was found between genetic and geographic distance. Moreover, the genetic diversity within groups of worms did not differ between experimental sites.

ANALYSIS OF AN ISOZYME POLYMORPHISM OF GLUCOSE-6-PHOSPHATE DEHYDROGENASE IN THE CHRONIC IRRADIATED SCOTS PINE POPULATIONS

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As a result of the Chernobyl accident the vast forested areas are exposed with chronic low-dose radiation. Long-term effects of such exposure still remain the subject of scientific debate. Using electrophoretic methods for the analysis of the protein polymorphism allows to figure out the effects of a chronic radiation exposure influence on biological processes. This influence may change the genetic structure of natural populations.

Polymorphism of the glucose-6-phosphate dehydrogenase enzyme was studied in the Scots pine populations growing on the sites in Bryansk region (Russia) which were heavily radioactively contaminated as a result of the Chernobyl accident. It was revealed that frequency of mutations in isozymes loci increased along the level of a dose rate (7-130 mGy/year) in the study sites. We investigated parameters which characterized genetic structure of studied populations and revealed, that there was no significant correlation between proportion of rare alleles, the effective number of alleles and the level of radioactive contamination. Genotypic diversity characterized by an average level of volatility.

Evaluation of biochemical activity of G6PD showed that with increasing the level of contamination enzymatic activity in seeds does not change.

Thus, level of radioactive contamination in study sites insufficient for inducing significant effects at the biochemical level, although frequency of mutational events in G6PD increases along the level of radiation exposure. Consequently, mutational events taking place under the influence of chronic radiation exposure do not lead to changes at higher levels of biological organization.

BEHAVIOR OF SOME SPECIES OF SOIL BACTERIA IN THE AREA ADJOINING ARMENIAN NPP

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By the use of detectors with NaI and pure germanium, supplied with corresponding programs, the distribution of ^{137}Cs in soil in the region of Armenian Nuclear Power Plant (ANPP) location along a primary direction of winds movement has been investigated. It is shown, that on the curve of ^{137}Cs distribution there is a maximum alee, specifying the contribution from NPP that makes up approximately 20-25 % from a background caused by global fallouts. Investigation of total amount of bacteria in samples of the soil, taken from the sites adjoining to the ANPP executed by traditional methods of microbiology, has shown that from the windward side of NPP are not registered considerable variations of number of bacteria. Alee from the NPP statistically authentic increase in the general number of microorganisms is revealed, and their maximum number is revealed in the point corresponding to a maximum on the curve of ^{137}Cs distribution. Also, from the samples of soils, representatives of rather radiosensitive closely-related species of bacteria *Pseudomonas putida* and *P. fluorescense,* and rather radioresistant bacilli *Bacillus mesentericus* and *B. subtilis* were isolated. Their quantitative content in the soils of monitoring points and radiosensitivity is investigated. It is shown that in the soils with the raised quantity of ^{137}Cs the amount of Pseudomonas cells is understated; contrariwise their radioresistance is a little bit raised. The maintenance of cells of Bacillus species varies without certain law, and survival curves have practically identical characteristics in all the points.

Naturally, such type of study requires periodic monitoring in time. The authors hope to get a possibility to repeat this cycle of investigations.

BUCCAL EPITHELIUM AS INDICATOR OF THE CONDITIONS OF ENVIRONMENT

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Purpose of our work is to examine the possibility of using micronucleus test of buccal epithelium for investigation of chemical, radiation and combined radiation and chemical pollution of environment.

In the Bryansk region exist the areas of intense radiation contamination after the Chernobyl accident (up to 2997 kBq/m^2 for ^{137}Cs and 42,5 kBq/m^2 for ^{90}Sr), and the areas of combined radiation and chemical exposures.

Assessment of the cytogenetic status in buccal epithelium was carried out in 2010-2011 for 242 children 7-9 years old.

The maximal number of deviations in cytogenetic characteristics of buccal epithelium was found in regions with the combined radiation and chemical contamination. This probably indicates the additive nature of the action of radiation and of chemical factors on the frequency of cytogenetic abnormalities. High level of degradation of the nucleus in the contaminated area suggests the existence of synergy, and the low level of cytogenetic damages by the number of cells with micronuclei and protrusions of several shapes suggests the effect of inhibition of the combined effect of physical and chemical contaminants.

The collected data imply the necessity to improve the hygienic standards for people exposed to combined influence of chemical and radiation environmental factors.

We plan to accumulate data about the level of cytogenetic damage of buccal epithelium in different regions and develop the method of "biological dosimetry" of the pollution of environment.

EFFECTS OF IONIZING RADIATION ON MARINE BACTERIA

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The purpose of the work was to study chronic low-dose effects of radionuclides on marine microorganisms. Luminous bacteria *Photobacterium Phosphoreum* were chosen as model microorganisms. Bacterial growth and bioluminescence (BL) intensity were used as parameters of physiological activity of the bacteria. Chronic low-dose effects of alpha-emitting nuclides Am-241 and U-(235+238), and beta-emitting nuclide H-3 were studied. The bacteria were grown in the presence of the radionuclides of different activity concentrations – up to 10 kBq/L for alpha-radionuclides, and 100 MBq/L for H-3. The Am-241 and U-(235+238) inhibited bacterial growth at all activities of the nutrient media. The H-3 increased bacterial growth at activity <30 MBq/L, and inhibited it at >30 MBq/L. Three stages of bacterial BL response to radionuclides were found in BL kinetics in solutions of Am-241 and H-3: (1) absence of effect, (2) activation, and (3) inhibition. The bacterial response was interpreted in terms of standard reaction of organisms to stress-factor; it includes the following successive stages: (1) stress recognition, (2) adaptive response/syndrome, and (3) suppression of physiological function. Stage (1) demonstrates the “threshold effect”, stage (2) – radiation hormesis, and stage (3) – radiation toxicity.

Effect of U-(235+238), alpha-radionuclide of low specific radioactivity, was similar to that of stable metals: they showed high effective concentrations (appr. 10^{-6}M) and the absence of stages (1) and (2) in BL kinetics. Hence, the effect of U was attributed to chemical toxicity, not radioactive one. Physico-chemical mechanisms of activation and suppression of physiological functions of the bacteria were discussed. BL time-course of enzymatic reactions in the presence of Am-241 and H-3 was compared to that of bacterial BL. The results showed higher stability of bacterial cells as compared to enzymesRole of peroxides (as secondary products of ionizing radiation in water) in the radionuclide’ effects was studied. Peroxides were found to be responsible for the effects of Am-241, and were not – for the effects of H-3. Mutagenic effects were studied using restriction and sequence analyses. Mutations were not found in bacterial DNA.

USE OF CELLULAR REGULATION SYSTEMS AT FORECASTING ENVIRONMENTAL RADIOACTIVE CONTAMINATION CONSEQUENCES FOR MOUSE-LIKE RODENTS OF NATURAL POPULATION

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Integrated monitoring of cellular regulation systems state has been carried out and the interrelation between the parameters of various elements of lipid peroxidation regulatory system and energy supply in tissues of mouse-like rodents of natural populations from 7 localities with different levels of radioactive pollution from the exclusion zone of the Chernobyl Nuclear Power Plant (1987-1991, 2007) and from 4 stationary localities with normal and increased levels of natural radioactivity of the Komi Republic (1981-1984, 2005-2006) has been studied. Depletion of organ lipids by antioxidants, increase of the number of lysoforms and the rate of phospholipids fractions resistant to oxidation, decrease of phospholipids content in common lipids, increase of free fatty acids, depression of the Krebs cycle enzymes activity and glycolysis activation should be referred to homogenous changes at chronic low-intensity radiation of the rodents populations which can be compared to the effects of acute radiation. Disorder in the organ distribution by the value of lipid antioxidant activity and activity of energy metabolism enzymes, emergence of irregular forms of methyl oleate oxidation kinetic curves, imbalance between the processes of dehydration and separate elements of lipid peroxidation, non-linear dependence of effects, significant heterogeneity of the indicators should be considered as the peculiarities of biochemical processes characterizing the degree of the animals' adaptation on cellular level. This can be explained by cumulative effect of external and internal radiation and ecologic factors of the habitat. The disorder mentioned in the relations between the elements of lipid peroxidation and the tissues functional activity, the degree of manifestation and the occurrence time of these disorders depend on the character of the indicators, the level of contamination, the rodents species, the organ under study and the duration of radioactive contamination action. The biochemical tests used for the studies can also be used to forecast biological effects determined by prolonged exposure to low doses of ionizing radiation in the habitat.

RADIOECOLOGICAL RELIABILITY AND RADIOCAPACITY OF DIFFERENT ECOSYSTEMS

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The models and theory of radiocapacity of ecosystems worked out by us have allowed entering an adequate parameter - factor of radiocapacity for the definition of a condition and reliability of an ecosystem biota. The radiocapacity can be determined as a limit of acceptable radionuclides contamination of an ecosystem; its elevation leads to biota depressing. It was experimentally and theoretically established that radiocapacity parameter indicates a level of biota reliability in a given ecosystem. It was shown by us for the plant ecosystems that biota capacity to store and to retain radionuclide tracer - ^{137}Cs that is included into plant mineral chain – K characterizes the stability and reliability of an ecosystem. A decreasing of a radiocapacity parameter at chemical pollutants effect is accompanied by biota well-being lowering and reliability reduction. It is possible when the radiocapacity parameters reflect as a reliability of each component of an ecosystem and ecosystem as a whole. We can estimate reliability of an ecosystem using the components' parameters and its structure that provide adequate distribution and reallocating of tracer in this ecosystem. On the basis of this new approach to reliability prediction of ecosystems, the calculation of reliability on an example of concrete types of ecosystems (slope and mining ecosystems, for instance) is conducted.

This method allows one to determine places of deporting and warehousing pollutants, the doses' load and risks in different types of ecosystems.

MORPHOMETRY OF SCOTS PINE NEEDLE UNDER CHRONIC RADIATION EXPOSURE

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Phytotoxic effects of acute impact are well known, but the consequences of long-term chronic exposure to low pollutant concentrations are neither well understood nor adequately included in environmental assessment. The aim of this work was to estimate biological effects of chronic radiation impact for pine trees using needle indexes as test-functions. Scots pine populations have been growing at doses up to 130 mGy per year in the Bryansk region contaminated after the Chernobyl accident. 2-years old needle were sampled from 15 trees at every of 6 study-sites; there were picked up 20, 40 and 40 paired needles per tree in 2011, 2013 and 2014, respectively. Morphometric parameters (length, weight) and occurrence of necrosis and morphosis in the needles were studied. Fluctuating asymmetry (FA) was estimated for paired needles length and weight.

Needle length and weight ranged from 65 to 80 mm and from 18 to 31 mg, correspondingly. There were observed essential fluctuations of studied parameters between sites and years with a tendency for a stimulating effect of low-level exposures (7-20 mGy/year) on needle length. There were not revealed any significant dependence of morphometric parameters from annual dos. In 2011, frequency of needles with severe degree of necrosis increased with dose rate (r=0.92, $p<0.05$), while percentage of healthy needle was decreasing (r=-0.86; $p<0.05$). FA of needle length at the most polluted sites (with dose rates 91 and 130 mGy/year) in 2013 was significantly higher ($p<0.01$) than at reference site. Also, FA of needle length correlate with dose rate in 2011 (r=0.97, $p<0.01$) and 2013 (r=0.75, p=0.08). Triple needles have been found on the impacted sites, but never on the references sites.

Thus, needle length asymmetry can be used as an indicator of disturbance in the stability of needle development, and degree of necrotic processes can used for bioindication in dose rate of 90-130 mGy/year or above.

RADIOECOLOGICAL RELIABILITY AND RADIOCAPACITY OF LOCAL AGROECOSYSTEMS

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Our results on the evaluation of the distribution and redistribution of radionuclides in the agroecosystem showed a significant trend of formation of radiation exposure on humans. For the evaluation and prediction of such processes we proposed to use the model and theory of reliability. Therefore the agroecosystem is seen as a system of transport of radionuclides from soil to human. We propose quantitative methods for assessing the reliability of separate elements of the agroecosystem and agroecosystems in general. Studies of radioecological processes in agroecosystems are particularly important for the assessment and prediction of their environmental safety for the population, especially in the formation of radiation exposures. It is analysis of the agroecosystem as a system of radionuclides transport from soil to human, means and methods of modifying these processes.Our task is to apply effective analysis for agroecosystem as a system of radionuclides transport from the operating system to human using the theory and models of reliability. Implementation of this task will greatly expand the range of ways in theoretical radioecology and can complement significantly the existing method of chamber models.

In studies with plant ecosystems it is showed that the ability of the biota to accumulate and retain the radionuclide tracer ^{137}Cs, the equivalent of mineral plant nutrient - potassium, shows the stability and reliability of the biota of this ecosystem. It is established that the decrease of radiocapacity of the biota in plant ecosystem under the influence of chemical pollutants and gamma-irradiation of plants, clearly shows the decrease of well-being of the biota and the reliability of the ecosystem .Thus, it can be asserted that the radiocapacity parameter can act as a measure of the reliability of each element of the ecosystem, as well as the ecosystem as a whole. The higher is the radiocapacity factor and / or the likelihood of tracer retention in each element of the ecosystem, the higher is the reliability of the constituent elements of the ecosystem. Using these parameters of reliability of the ecosystem elements and knowing the structure of a particular ecosystem, we have the possibility to adequately assess the reliability of the entire ecosystem in terms of its ability to provide the distribution and redistribution of the tracer, which reflect its steady state.

BIOLOGICAL EFFECTS IN COMMUNITIES OF WILD PLANTS AT DIFFERENT INTENSITIES AND DURATION OF CHRONIC EXPOSURE

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Results of laboratory and natural experiments published up to nowadays shows essential differences in living organism responses on acute and chronic irradiation. But still there is lack of data on generation of regularities in biological effects observed in natural populations of plants and animals under chronic radiation exposure to find out causes of differences in responses registered in nature (Geras'kin et al., 2010). At the same time preliminary estimation of effects observed for terrestrial species from the Chernobyl-Exclusion Zone supposed (Garnier-Laplace et al., 2013) natural populations of plants and animals to be higher radiosensitive as compared with the laboratory ones.

We have analyzed our own data on responses of natural plant population inhabiting territories contaminated with radionuclides of natural origin (chiefly with ^{226}Ra and it's radioactive-decay products) on cell, organism, population and community levels and make a comparison with results obtained on the same area 30–50 years ago. Particularly reproductive capacity of *Vicia cracca* plants from sites with the highest soil activity concentration of radionuclides is found at present to be still significantly lower on low aberration frequency background, but lethal embryonic mutations higher as compared with less contaminated and reference sites. As for *Ranunculus acris* seeds germination capacity, sampled from sites with lower soil radioactive contamination and the survival of the seedlings – were shown to be similar with observed in reference site populations. Although in the early years of population formation on the impacted territory decrease in the reproductive capacity was registered. Our studies indicated also lower rate of the plant communities' progress for the higher contaminated sites, but vascular plant species distribution in phytocenoses structure gives evidence on demutation processes unidirectionality of recovery of the vegetation in case of contaminated and reference landscape.

Long-term studies of wild plants, covering data from the beginning of radiation exposure and results obtained on different structural and functional levels of organization, allows to improve database on biological effects in natural populations and to approximate to the patterns of relationship for living organisms survival in adverse conditions.

NARROW-HEADED VOLE EXPERIMENT DOES NOT CONFIRM A FAMILY SPECIFICITY OF THE ^{90}SR METABOLISM HYPOTHESIS

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Northern mole vole is subterranean rodent, colonies of this animals consist of families. 84% of a variability of ^{90}Sr accumulation for northern mole voles, caught in East-Ural radioactive trace (EURT), referred to a factor "a family" (Starichenko, 2011). The author associates this fact with a heterogeneity of ^{90}Sr contamination or family specificity of the ^{90}Sr metabolism. It is important to explore ^{90}Sr metabolism differences for EURT-rodents population for a comprehension the adaptation to the radiation. This activity is our pilot research of this area. The object of the research is narrow-headed vole. Colonies of voles consist of initial couple of animals and its progeny. Animals had been caught by live-traps in the EURT-area dimensions 80*100 sq. m. We took mandibles for radiometry analysis (Malinovsky et al., 2012). We defined allelic composition of four microsatellite loci: MSMoe02, Mar49, Mar80, MSMM2 (Ruda et al., 2009). Genotypes of voles were analyzed using program Structure v. 2.3.4 (Pritchard et al., 2000). This method identifies genetically distinct clusters on the basis of individual genotypes at multiple loci. We marked out three groups of animals. 32 of 38 individuals were included in one of these groups with support more than 75%. Most of animals, included in one cluster, were caught in traps, located in close from each other. These aggregations of voles we consider as a colony. One individual was put to the cluster №2, but this animal was caught in a territory of the colony, populated by animals from cluster №1. We considered this individual as a migrant. Specific activity of accumulated in vole's mandibles ^{90}Sr for colony № 1 is (N=7, mean=493, min-max=433-534), for colony №2 is (N=7, mean=392, min-max=341-426,), for the migrant it is 529 Bq/g. Colony №1 and №2 animals differ in specific activity of ^{90}Sr and in genotypes. The migrant has genotype as colony №2 animals, but specific activity of ^{90}Sr as colony №1 animals. A mosaic structure of contamination is more simple explanation of this fact, then metabolism of ^{90}Sr differences of different families. This study was supported by Russian Foundation for Basic Research (project 14-04-01484_a)

THE IMPACTS OF THE CHERNOBYL AND FUKUSHIMA DISASTERS ON WILDLIFE

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Recent advances in genetic and ecological studies of wild animal populations in Chernobyl and Fukushima have demonstrated significant genetic, physiological, developmental, and fitness effects stemming from exposure to radioactive contaminants. The genetic studies that have been conducted in Chernobyl generally show elevated rates of genetic damage and mutation rates. All major taxonomic groups investigated (i.e. birds, bees, butterflies, grasshoppers, dragonflies, spiders, mammals) displayed reduced population sizes in highly radioactive parts of the Chernobyl Exclusion Zone. In Fukushima, population censuses of birds, butterflies and cicadas suggested that abundances were negatively impacted by exposure to radioactive contaminants, while other groups (e.g. dragonflies, grasshoppers, bees, spiders) showed no significant declines, at least during the first summer following the disaster. Bird abundances and biodiversity continued to decline for four years following the disaster and the relationship with radiation was significantly higher in Fukushima than in Chernobyl folowing 20+ years. Insufficient information exists for groups other than insects and birds to assess effects on life history at this time. The differences observed between Fukushima and Chernobyl may reflect the different times of exposure and the significance of multigenerational mutation accumulation in Chernobyl compared to Fukushima. There was considerable variation among taxa in their apparent sensitivity to radiation and this reflects in part life history, physiology, behavior and evolutionary history. Interestingly, for birds, population declines in Chernobyl can be predicted by historical mitochondrial DNA base-pair substitution rates that may reflect intrinsic DNA repair ability.

THE DOSE-DEPENDENT FUNCTIONAL-METABOLIC EFFECTS OF *APODEMUS URALENSIS* FROM THE RADIATION CONTAMINATED AREA GIVEN THE NUMBER OF ITS POPULATION

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The population dynamics, radiometrical and biochemical parameters of *Apodemus uralensis* inhabiting the East Ural Radioactive Trace (EURT) were analyzed. The recent data available on the functional-metabolic myocardial reactivity in animals from the EURT area (Orekhova, Modorov, 2013) is evidence of the high sensitivity of cardiomyocytes (CMC). Effects, comparatively reference group, in the reduced participation of lipids in energy supply of CMC, decrease in the levels of mitochondrial oxidation and antioxidant protection, induction of lipid peroxidation were expressed. Activation of anaerobic glycolytic system, the protein-synthesizing and genetic apparatus is regarded as compensatory mechanisms used for improve myocardial contractile function at a low efficiency of energy production in the CMC and the development of functional defects in them. The response level of organism within the EURT area depends not only on the internal radiation dose of animals (determined by specific activity of ^{90}Sr in the lower mandible), but refracted through the number of the population. In particular, the level of functional-metabolic shifts, dependent on the dose, is higher at a high abundance of animals (from 20 to 43 ind./100 trap–day) than the population number from 4 to 20 ind./100 trap–day. This indicates increased radiation effect under the simultaneous action of overpopulation as of environmental stressors. Furthermore, at high number of population the individuals with a high degree of radiation dose in the samples were not provided, which were present in the collected material at a depression. Synergies of radiation and non-radiation effects suggests the probability of elimination from the environment of animals with a high degree of specific activity of ^{90}Sr in mind the possibility of transition adaptation to the decompensate stage and development of pathology incompatible with life. The results obtained allow us to estimate the "weight" of radiation influence to make informed decisions about radio-ecological situations and on what basis should take measures to limit radiation effects on biota. This work was supported by the Program for Basic Research, UB of RAS (Project № 15-4-2-21).

ZOOPLANKTON COMMUNITY OF SPECIAL INDUSTRIAL RESERVOIR R-11 "MAYAK" PA

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R-11 is a locking reservoir in the cascade of Mayak PA reservoirs. The volumetric activity of ^{90}Sr in water is 1,3×10^3 Bq dm^{-3}, ^{137}Cs - 1,0 Bq dm^{-3}. Also, there is high concentration of sulfate (about 500 mg dm^{-3}).

In the period from 2009 to 2012 condition of the zooplankton community in R-11, as sensitive component of biocenosis, which plays an important role in transformation of energy and biotic turnover, was studied. Shershnyovskoe Reservoir, an artificial reservoir on the Miass River, created to water supply of Chelyabinsk, was used as a comparison waterbody.

Analysis of species diversity of zooplankton in R-11 did not show decrease in the average number of species in a sample compared to the control. The level of quantitative development of zooplankton in the reservoir also did not differ from control. In both reservoirs rotifers dominated in abundance. Among the dominant species, *Keratella cochlearis cochlearis* (Gosse, 1851) was the most frequent. In biomass in the reservoirs dominated large cladocerans of the genus *Daphnia* O.F. Müller, 1785 and *Diaphanosoma* Fischer, 1850 and a copepod *Eudiaptomus graciloides* (Lilljeborg, 1888).

In general, the state of zooplankton communities in both reservoirs can be described as positive, with high species diversity and without overwhelming dominance of single species.

Thus, for zooplankton in the reservoir R-11, despite the significant contamination of the environment by radionuclides, were not found significant differences in the structure and quantitative development from community in the comparision reservoir were found.

ENVIRONMENT BIOLOGICAL MONITORING AT A FACILITY FOR RADIOACTIVE WASTE TREATMENT IN THE FAR-EAST OF RUSSIA

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Anthropogenic nuclear and industrial activities can substantially increase environmental exposure levels. Contamination of territories through human civil and military activities such as nuclear facilities operation, mining sites, nuclear weapon testing involves a complex impact so that there are a number of situations where a mixture of radionuclides is supplemented by other potentially hazardous substances. There is still a large lack of knowledge on actual hazard of such combined contamination for biota and human health.

This work was aimed at an estimation of impact from the Far-Eastern center on radioactive waste treatment (FEC) on the environment with techniques of biological monitoring. The FEC is located about 40 km of Vladivostok, Russia on the shores of the Sea of Japan, and it is considered as a potential source of radiation hazard. Two main technologies were used: bioindication of plant populations growing in the impacted environment, and a bioassay of underground waters collected from the site. In first case, a fluctuating asymmetry of leaves and pollen fertility in three plant species were used as indexes of the environmental well-being. Genotoxicity of underground waters sampled at the territory of the FEC was studied with *Allium cepa* bioassay, and cytogenetic and cytotoxic effects were used as biological endpoints.

Complex issues are involved in evaluating environmental risk, and an effectively linking of bioindication screening assays to the well-established environmental pollution monitoring approach is a way of improving and upgrading an existing system of the public and the environment protection to meet requirements of consistency between nowadays scientific knowledge and decision-making process.

QUALITY OF *TARAXACUM OFFICINALE* S.L. AND *PLANTAGO MAJOR* L. SEED PROGENY FROM RADIOACTIVE OR CHEMICAL POLLUTION AREAS

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Adaptations of living organisms to different types of human-induced impacts may be diverse and include both universal and specific components caused by nature of factors and biological characteristics of species. It is well established the quality of seed reproduction deteriorates under contamination conditions because the stages of gametogenesis, zygote and early seed germination are very sensitive to toxic impacts. A comparative study of the seed progeny of dandelion (*Taraxacum officiale*) and plantain (*Plantago major*) was performed with samples from cenopopulations growing for a long time under conditions of radioactive contamination (the zone of the Eastern Ural Radioactive Trace, EURT) or chemical pollution (the impact zone of the Nizhnii Tagil Metallurgical Plant, NTMP).

Viability of seeds was assessed by the complex of parameters, including seedling survival rates, true leaves formation rates and root length. Dandelion seed viability decreased by as anthropogenic pressure increased, regardless of the factor nature. At the same time, viability of plantain seed from EURT area was high and the same to background samples, the seed progeny from NTMP area had low viability. Adaptation potential of plants from background and impact populations was revealed by additional provocative heavy metal and г-radiation exposure. The dandelion seeds from background samples were resistant to radiation exposure and sensitive to chemical stress. The seedlings from EURT and NTMP areas demonstrated non-specific responses to provocation exposure to both «usual» and «new» factors. The plantain seeds from background and EURT plots were radiosensitive, but seed samples from chemical pollution area (NTMP) were resistant to «new» agent (radiation). The frequency of abnormal seedlings in the impact populations (EURT and NTMP) was higher than in background samples for both species. The most part of morphological anomalies was revealed in the dandelion samples at the first month, but anomalies of plantain became apparent only on late stages of plant development. Thus, *T. officinale* and *P. major* have different adaptation mechanisms to man-made contamination.

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REACTION OF WATER ECOSYSTEM TO CHRONIC RADIATION EXPOSURE

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Study of ecosystem of storage-reservoirs of liquid radioactive wastes of «Mayak» Production Association («Mayak» PA) with different levels of radioactive contamination allows to assess the influence of chronic radiation exposure to biocenosis. The analysis of 5 years research into the status of biocenosis of these storage reservoirs of liquid radioactive wastes of «Mayak» PA was performed. The status of biocenosis was evaluated in accordance with the status of following communities: bacterioplankton, phytoplankton, zooplankton, zoobenthos, macrophytes and ichthyofauna. The status of ecosystems was determined by radioactive and chemical contamination of water bodies. The results of hydrobiological investigations showed that no changes in the status of biota in reservoir R-11 (total activity of β-emitting radionuclides, or TBA, is 2.3×10^{3} Bq dm^{-3}) were revealed as compared to the biological parameters of the water bodies of this geographical zone. The ecosystem of the reservoir R-10 (TBA is 4.7×10^{3} Bq dm^{-3}, total activity of α-emitting radionuclides, or TAA, is 1.6×10^{-1} Bq dm^{-3}) maintains its functional integrity, although there were registered negative effects in the zoobenthos community. In reservoir R-4 (TBA is 6.4×10^{3} Bq dm^{-3}, TAA is 4.2×10^{0} Bq dm^{-3}) a significant reduction in the quantity of Cladocera and Copepoda was registered in the zooplankton community, while in the zoobenthos there were no small mollusks. In reservoir R-3 (TBA is 6.5×10^{3} Bq dm^{-3}, TAA is 7.2×10^{1} Bq dm^{-3}) there was no small pelophylic mollusks either, 90% of zooplankton community was represented by rotifers, in species composition of ichthyofauna there was no carnivorous species of fish. In reservoir R-17 (TBA is 4.7×10^{5} Bq dm^{-3}, TAA is 2.2×10^{2} Bq dm^{-3}) ichthyofauna was completely absent, species diversity of phytoplankton and zooplankton was significantly reduced. In reservoir R-9 (TBA is 3.0×10^{7} Bq dm^{-3}, TAA is 8.3×10^{4} Bq dm^{-3}) there was no ichthyofauna; phytoplankton and zooplankton was almost a monoculture of cyanobacteria and rotifers. In all of the above mentioned reservoirs, the development of bacterial plankton was at the levels characteristic of the standing water bodies of this geographical zone.

CYTOGENETIC ESTIMATION THYROID GLAND VOLES FROM INCREASED RADIOACTIVE BACKGROUND TERRITORIES

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The response of cells of the thyroid gland of tundra voles (*Microtus oeconomus Pall.*) living in areas with normal (10-15 mR/h) and high (50-2000 mR/h) the level of natural radioactivity (Ukhta region of the Komi Republic, Russia) was studied. Voles from both sites were brought to the vivarium experimental animals. Offspring F_1, F_2 and F3 was obtained in the vivarium. It was showed, that chronic exposure of animals at low dose-rate induces increasing of the number of cells with micronucleuses compared with the control. At the same time the level of apoptotic cells and cells with single-stranded and double-stranded DNA breaks remained unchanged._ In the thyroid gland of the offspring (F_1-F_3), whose parents were exposed by elevated environmental radiation, the number of thyrocytes with micronucleus was same to control. But levels of DNA damages (F_1 and F_3) and apoptosis (F_2 and F_3) was significantly higher. The results show that the exposure of high environmental radioactivity to tundra voles can lead to genetic instability in their offspring.

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PLANT BIODIVERSITY IN THE DRYING SOUTH SEA FLOOR OF THE ARAL SEA

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This work presents the results of floristic and geo-botanic investigations of the dry seafloor of Aral Sea in its south part. Biological diversity of the dried up part of Aral Sea basically was characterized by specific structure of flora and vegetation. For the first time 216 species of the higher plants has been shown to be growing in the south drying seafloor of Aral Sea.

Especially, the division of gymnospermous plants (*Pynophyta*) includes only 3 species (0.01%). Division of magnolia make up 212 species from 216 types of vascular plants of the dry seafloor of Aral Sea (98.14%) members of the division of magnolia: *Magnoliopsida* has 185 species (85.64%; 99 genera and 31 families); *Liliopsida* has 27 species (12.50%; 21 genera and 8 families). Analysis of division of genera and species according to the family shows that the large 7 families (*Chenopodiaceae* (59:27.31%), *Asteraceae* (25:11.57%), *Brassicaceae* (21:9.72%), *Polygonaceae* (15:6.94%), *Poaceae* (15:6.94%), *Fabaceae* (13:6.01%), *Boraginaceae* (10:4.62%)) unite make up 158 species (73.14%). The largest family is *Chenopodiaceae* includes 24 genera and 59 species. Other 6 large families compose 58 genera and 99 species (45.83%); 20 families (*Equusetaceae, Hypecoaceae, Caryophyllaceae, Frankeniaceae, Capparaceae, Euphorbiaceae, Geraniaceae, Biebersteiniaceae, Peganaceae, Elaeagnaceae, Apiaceae, Apocynaceae, Solanaceae, Scrophulariaceae, Plantaginaceae, Alliaceae, Asparagaceae, Najadaceae, Zosteraceae, Typhaceae*) have only one genus and one species (9.25%).

These data are the results of seven years of author's research on the classification of plants of south part of Aralkum. The amount of species and taxonomic units certainly may change because of continue of flora formation.

TOXICITY ASSESSMENT OF NATURAL WATERS NEAR RADIOACTIVE WASTE DISPOSAL FACILITY BY ALLIUM-TEST

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Currently, nuclear energy has become one of the most promising sources of energy. In this regard, the problem of radiation safety attracts attention of many people and makes necessary radiation monitoring in the vicinity of nuclear industry enterprises. In addition to traditional physical and chemical methods for environmental assessment, biological control methods have increasingly being incorporated in total monitoring scheme. At biological monitoring, test-responses of living beings to the combined effect of factors are estimated. Among plant bioassays, the Allium-test has got highly informative qualities at the cellular and genetic level. This technique showed its effectiveness in assessing the toxicity of natural and waste waters, soil samples from areas exposed to radioactive and chemical contamination.

The aim of this work was to evaluate the cyto- and genotoxicity of water samples from the territory of the regional radioactive waste storage Obninsk.

To assess potential biological hazard, water samples were collected from three control wells at territory of the radioactive waste disposal facility (№4, №7, and №10) as well as from a stream originating in the territory of the facility. As a control sample, tap water was used. Testing of natural waters was repeated in triplicate. Water samples were collected in May, July and October 2013.

Bioassay results indicate a high degree of cyto- and genotoxicity of waters from the well №4. An elevated frequency of cells with chromosome aberrations in comparison to the control was also registered for other test water samples. The spectrum of aberrations was mainly represented by disorders of chromatid type. Sporadically alterations at genome level were observed. The indicators of genotoxicity used correlated with data from radiochemical analysis.

BIOLOGICAL EFFECTS OF INTERNAL RADIATION DOSE OF LONG-TERM CHRONIC EXPOSURE ON HIGHER AQUATIC PLANTS IN THE CHERNOBYL EXCLUSION ZONE

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Long-term radioecological monitoring of water bodies in the Chernobyl Exclusion Zone (ChEZ) allowed collecting an extensive database of variety radiobiological effects on plant organisms. The following biological indexes were analysed: set of cytogenetic indexes – range and number of chromosomal aberrations, number of aberrations per aberrant cell in root meristems of eight species of helophytes; for one of the ChEZ water-bodies referent species (the common reed) - panicles and seeds morphometry; set of reproductive indexes, set of indexes of seed vitality and abnormalities at earliest stages of ontogenesis. Analysis revealed a linear dose curves for morphometric, reproductive and seed vitality indexes. Exponential and polynomial dose curves were observed for cytogenetic indexes and sprout abnormalities. Biological effectiveness of internal radiation dose IRD of long-term chronic exposure on wildlife referent species was calculated. The existence of "pseudo-safe" range of low doses based on the analysis of IRD bio-effectiveness under cytogenetic and seed vitality sets was revealed. Hormesis phenomenon at the level of seed vitality is accompanied by maximum level of sprout abnormalities and cytogenetic damages. Obtained field data of bio-effectiveness of long-term low-level chronic exposure on aquatic plants have a great importance for creating the model the expected biological effects on chronically irradiated non-human biota and for the calculation of the radiation risks to aquatic ecosystems.

HISTOLOGICAL CHANGES OF INTERNAL ORGANS OF FISH IN WATER BODIES WITHIN THE CHERNOBYL EXCLUSION ZONE

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The mounts of internal organs of the silver carp (*Carassius gibelio*), gold carp (*Carassius carassius*), perch (*Perca fluviatilis*), tench (*Tinca tinca*), common carp (*Cyprinus carpio*) and rudd (*Scardinius erythrophthalmus*), inhabiting the most contaminated water bodies of the Chernobyl exclusion zone were analyzed. Collection of material was carried out during spring and summer of 2013 and 2014 in lakes Azbuchin, Glubokoye, Dalyokoye as well as Yanovsky Crawl and cooling pond of the Chernobyl NPP. In total was collected about 100 specimens of fish. The absorbed dose rate for the studied species of fish in closed water bodies of the Chernobyl exclusion zone registered within 25-240 mcGy h^{-1}, while in control water bodies the radiation dose for fish does not exceed 0.12 mcGy h^{-1}. Histological studies were carried out using tissues of gills, muscles, liver and spleen. Hematoxylin and Eosin staining procedure was used. Almost all selected specimens of fish were characterized by histological changes of gill tissues, among which were the most typical the hypertrophy of secondary lamellar epithelium, dilatation of capillaries, aneurysm and hyperplasia of epithelial cells. In liver tissues of investigated fish observed the hypertrophy of hepatocytes, increase of Kupffer cells, poor blood circulation, and nuclear pyknosis. In turn, in the tissues of the spleen we recorded a decrease in the number of lymph nodules and the size of their centers, and coarsening of reticular fibers in white and red pulp and the acquisition of a winding structure. We did not register any significant histological changes in the muscle tissue of studied fish species.

SQUALENE CONTENTS AND WEIGHT SEED PROGENIES TWO GENERATIONS OF *AMARANTHUS RETROFLEXUS L.* UNDER γ-IRRADIATION PRESOWING OF PARENTAL SEEDS

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Amaranthus retroflexus L. - is a wild annual herbaceous plant about 15-100 cm height with pink root. Genus *Amaranthus* seeds contains oil (from 6 to 17%), in which fat-soluble antioxidant squalene was found. Oil also contains up to 67% of polyunsaturated fatty acids (omega-6, linoleic, oleic, palmitic, stearic and others.), lecithin, tocopherol. Typical reaction of plants to an irradiation is change in growth processes and biochemical parameters, depending on the received dose seed observed both stimulatory and inhibitory effects. **Objective:** To study the effect of ionizing radiation on the content of squalene and seed's weight of *Amaranthus retroflexus* L.

Results and Discussion. During two generations when it's grown under the conditions of Central Yakutia. During the considering of weather conditions were revealed that the most favorable growing conditions were reported in the second generation (F2), because of gentle temperature and elevated rainfall amount. By obtained data was revealed that the effects of ionizing radiation caused non-monotonic decrease in weight of seeds of the first generation in the range from 0.5 to 300 Gr but the second generation has not changed the indicator in reference to the non-irradiated seeds. Squalene content in the seed oil *A. retroflexus* L. in two F1 and F2 generations non-monotonically increased with doses of 0.5 to 5 Gy. Also recorded is non-monotonic decrease in squalene oil within the range from 10 to 300 Gy.

Conclusion It is proved that the content of squalene in the oil and seed's weight is higher in the second generation, which can be connected by the influence of pre-sowing γ-irradiation on the parent seeds or weather conditions. Revealed that the second generation has repaired the weight of seed progeny in all the studied dose ranges preplant γ-irradiation parent seeds. Was found a stimulating dose - 0.5 and 5 Gy, which increase the content of squalene in the oil and seed weight in two generations.

EQUIDOSIMETRIC APPROACH TO THE ASSESSMENT OF ECOLOGICAL EFFECTS OF CHRONIC EXPOSURE FROM THE ALPHA- RADIATION OF INCORPORATED ^{239,240}Pu ON THE BLACK SEA HYDROBIONTS

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Due to the accident at the Chernobyl nuclear power plant the Black Sea ecosystem were contaminated with alpha-radionuclides of plutonium (^{239,240}Pu). These radioactive isotopes, serving as tracers, provide an opportunity for in vivo determination of radioecological parameters of anthropogenic radionuclide redistribution processes in the marine ecosystems components. This, in turn, serves as a scientific basis of approaches development for the assessment of potential radiation effects on living organisms in natural ecosystems caused by the expected levels of radionuclides.

The aim of our study was to investigate the contamination of the Black Sea hydrobionts and marine environment with transuranic radionuclides as well as usage of the comparative equidosimetric approach to the ^{239,240}Pu ecological effects assessment on hydrobionts within a wide range of these radionuclides concentrations in seawater.

Based on field observations and model calculations as well as on the conceptual model of chronic action zonality of ionizing radiations dose rates in the nature (Polikarpov, 1998, 2008), the levels of expected ecological effects on marine organisms in the wide range of radionuclides concentrations in seawater and the critical ^{239,240}Pu concentrations in marine environment have been determined.

Depending on the accumulative ability of marine organisms against ^{239,240}Pu, the critical concentrations of these radionuclides in seawater varied in the range of 3 orders of magnitude for different groups of the studied Black Sea hydrobionts. Since species radiosensitivity, being characterized by LD_{50} (the dose causing 50% death rate of organisms), within each taxonomic group is known to vary in a range from 1 to 3 orders of magnitude (Santschi, Honeyman, 1989, Polikarpov, 2008), then for radioresistant species, being able to tolerate higher radiation doses, the critical radionuclides concentrations in seawater will be accordingly higher by 1-3 orders of magnitude.

CHANGING IN A GENETIC STRUCTURE OF THE CHRONIC IRRADIATED PLANT POPULATIONS

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A gene pool of natural population is constantly changing in order to provide the greatest fitness at this time. An ability of population to adapt to changing environmental conditions depends on genetic polymorphism of traits which are operates by selection. Chronic stress exposure can change an amount or structure of an intra-population variability. Therefore, it is necessary to analyze the relationships between genetic polymorphism and stress factors, such as radiation exposure.

Our study has been conducted in several districts of Bryansk region, the most contaminated region of Russia. Dose rates on 6 experimental sites vary from 0.14 to 130 mGy/year. The experimental object is *Pinus sylvestris* L. populations, the dominant tree species in North European and Asian boreal forests. Scots pine has a long maturation period (18-20 month), which means that significant DNA damage may accumulate in the undifferentiated stem cells during exposure to low concentrations of contaminants. We evaluated an isozyme polymorphism and activity of a number of enzymes:

It was shown that frequency of rare alleles increase in chronic irradiated populations, as far as indices of genotype diversity, and proportion of rare alleles is increased along the level of radiation exposure. Observed and expected heterozygosity values increased with the level of radioactive contamination. There were null-mutations without protein biosynthesis in experiment. We observed significant increase of null-mutations frequency in populations from experimental sites.

We obtained data about enzyme activity in studied populations. Mostly, studied enzymes didn't show any significant changes in their activity in impact populations.

It was showed that chronic radiation exposure increased general mutation frequency in isozyme loci and proportion of rare alleles in studied populations. So far as mutational events in seeds of Scots pine relatively rare, they don't make a significant contribution to observed enzymes activities. In whole our study suggests that present dose rates insufficient for form significant changes on physiological level, in spite of revealed changing in genetic structure of populations.

CHROMOSOMAL AND DEVELOPMENTAL INSTABILITY IN NATURAL RODENT POPULATIONS IN ZONES OF THE RADIATION INCIDENTS IN THE URALS

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Results of long-term investigations of chromosomal (frequency of bone marrow cells with structural and numerical mutatons) and developmental (fluctuating asymmetry of craniological traits) instability in natural rodent populations in zones of radiation incidents in the Urals are presented. Our investigations were started over 20 years ago in Institute of Plant and Animal Ecology by Dr. E.A. Gileva and were continued in the laboratory of Phylogenetics and Biochronology. Rodent species of the two families (Crecitedae - *Microtus arvalis*, *M. rossiaemeridionalis*, *Ellobius talpinus*, *Clethrionomys glareolus*, *Cl. rutilus*; Muridae - *Apodemus agrarius*, *A. uralensis*, *Mus musculus*) were chosen as model objects because of their wide spread and abundance in different natural zones of the Urals. The Urals Radioactive Trace zone (Kyshtym radiation accident in 1957; initial pollution by ^{90}Sr from 500-1000 to 1,2 Ci/km^2), and the settlements in Sverdlovsk region polluted by wastes containing ^{232}Th in the beginning of the second half of the XX century, were investigated. The following effects of chronic irradiation are observed: - the increase of chromosomal and developmental instability in most species including rare mutations and mutant karyotypes; - species specificity of genome reaction and developmental processes under conditions of chronic radiation exposure; - possible effect on interspecific reproductive isolation barriers in chromosomal sibling species *M. arvalis* and *M. rossiaemeridionalis*.

Parallelism of the incidence rates of cancer in human population and the rates of chromosomal instability in synanthropic *M. musculus* was demonstrated.

Obtained results could be used when estimating the consequences of radiation incidents for ecosystems and human.

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MORPHO-ANATOMICAL RESEARCH OF PLANTS AT THE TERRITORY OF SEMIPALATINSK TEST SITE

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By nuclear testing at the Semipalatinsk Test Site (STS) was the formation of high doses to biota. An additional factor may be the impact of the increased content of toxic elements.

Research was performed at the STS territory to reveal consequences of influence of radionuclides and toxic elements and morpho-anatomical parameters of chee reed grass (*Calamagróstis epigéjos*). Investigated parameters of leaf: thickness of upper and lower epidermis, thickness of mesophil, area of conducting bundles; investigated parameters of steam: diameter, thickness of epidermis, sclerenchyma, area of conducting bundles in parenchyma.

Upon the results of research it was found, that with increase of specific activity of ^{137}Cs in investigated samples of plants from 1.7×10^3 Bq/kg to 7.3×10^4 Bq/kg decrease of area of conducting bundle of leaf from 1.9×10^4 µm^2 to 9.7×10^3 µm^2 is observed. With increase of specific activity of ^{90}Sr from 0.7×10^4 Bq/kg to 9.9×10^4 Bq/kg in plants increase in thickness of leaf mesophil from 100 to 350 µm is observed.

During research concentrations of: Al, Li, Be, Cr, Mn, Fe, Co, Ni, Cu, Zn, Sr, Y, Cd, La, Ce, Nd, Sm, Gd, U, Pb in plants were determined. The dependence between the changes of anatomical parameters and the concentrations of the elements Al, Li, Cd. Area of conducting bundles in the steam parenchyma increase from 0.8×10^4 µm^2 to $2,5\times10^4$ µm^2 with increase of Al concentration from 250 µg/g to 500 µg/g. Increase in area of conducting bundles of the leaf from 0.6×10^4 µm^2 to 1.9×10^4 µm^2 can be observed with increase of Li concentration from 0.5 to 20 µg. With increase of Cd concentration from 0.4 to 1.2 µg/g insignificant increase in thickness of steam epidermis from 16 to 7 µm is observed. Thus, as a result of the net effect of toxic elements and radionuclides observed change the selected plant tissue anatomical level.

THE EFFECT OF γ-RADIATION ON HATCHING SUCCESS OF RESTING EGGS AND LIFE CYCLE OF HATCHED FEMALES OF CLADOCERAN *MOINA MACROCOPA*

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Aquatic ecosystems are contaminated with technogenic radionuclides due to various nuclear activities and accidents. Bottom sediments serve as a sink of artificial radionuclides. Many zooplankton species under the unfavorable conditions produce resting eggs that form egg banks in the bottom sediments. Egg banks are important for ecology and evolution of aquatic communities. However little is known about the effect of ionizing radiation on the resting eggs. In this study we tested the effect of γ-radiation on resting eggs of cladocerans *Moina macrocopa*, species widely used as test organism, in order to determine the dose-response relationship and reveal sensitive endpoints in the life cycle of this species. We exposed the resting eggs to the range of doses (from 4 to 2400 mGy) from a point source of ^{137}Cs. The following endpoints were tested: hatching success of dormant eggs; somatic growth rate, fecundity, sex of progeny and mortality of hatched animals; based on life cycle experiments we also calculated net reproductive rate, generation time and rate of population increase. The hatching success of resting eggs strongly depended on the resting time and was only slightly affected by the γ-radiation. The average lifespan of hatched females was highly variable and did not sensitive to the effect of low doses. The responses in fecundity and male/female ratio of the progeny to the different doses were irregular. Responses of the somatic growth rate and rate of population increase of animals hatched from the eggs exposed to γ-radiation were similar to the dose-response curve for the effects of low doses with the significant effects of intermediate and maximal doses. We can conclude that resting eggs of Cladocera can sustain in natural habitats the low doses of γ-radiation without significant effect on the hatching success. However hatched females will demonstrate irregular but significantly reduced reproductive output and growth success. Further research is needed to test the effect of wider range of doses on the survival and success of resting eggs and to extrapolate the detected individual effects on the performance of the populations and communities.

EFFECTS OF ELECTROMAGNETIC RADIATION ON *PHOTOBACTERIUM PHOSPHOREUM* CELL POPULATION

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The constant increasing of number and diversity of non-ionizing electromagnetic radiation (EMR) sources is an important problem of ecology. Within the next years it should be expected changes in natural microbial associations as a result of man-made electromagnetic radiation generated with diverse electrical equipment. Bioluminescence intensity of luminous bacteria reflects the state of their metabolism and can be used as sensor for monitoring the environment radiotoxicity. The aim of this research was studying the non-ionizing EMR irradiation effect on luminous bacteria *Photobacterium phosphoreum.*

Bacterial biomass was grown for 8 hours in liquid medium and exposed to UHF (ultra-high frequency)- and UV-radiation. The absorbed dose for both type of radiation was the same and equal to EMR effects were evaluated as the changes in the luminescence intensity, cell survival rate and genome stability. Exposure bacterial cells for 15 min to both UHF and UV EMR led to the decreasing of luminescence intensity by 68% and 89%, respectively, while irradiation for 5 min evoked increasing of this index up to 45% after UHF and, on contrary, decreasing it up to 40% after UV EMR. Analysis of cell survival rate in bacterial suspension after EMR irradiation showed that that all radiation modes were accompanied by a reduction in *P. phosphoreum* cell viability. After UHF EMR for 5 min the cell survival rate was 50%, and 15 min exposure resulted in 4%. After the same absorbed dose of UV cell survival rate was dramatically decreased and insignificant number of cells (lower than 1%) was revealed. As a result of amplification with primers to short nucleotide repeats no differences in amplicon patterns between irradiated and non-irradiated bacterial cells were detected, although the intensity of some bands after UV-exposure was lower than in control and treated with UHF EMR. Thus, results obtained in our study suggested that under the same absorbed dose UV-irradiation caused more essential effects than UHF EMR.

TOXICITY AND GENOTOXICITY OF BOTTOM SEDIMENTS OF THE YENISEI RIVER CONTAMINATED WITH RADIOACTIVE AND CHEMICAL XENOBIOTICS

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Bottom sediments (BS) provide habitat for aquatic plants and animals, that is why, the quality of sediments play an important role in ecosystem functioning. BS of the Yenisei Rive are polluted with a mixture of potentially toxic xenobiotics: artificial radionuclides (^{60}Co, ^{137}Cs, ^{152} Eu, ^{241}Am, ^{238,239,240,241}Pu) heavy metals, and persistent organic pollutants resulting from industrial, urban, and farming activities in the water catchment area. The purpose of this work was to assess the toxicity and genotoixicity of BS of the Yenisei River. Toxicity and genotoxicity of sediments was estimated in laboratory contact tests using macrophyte *Elodea canadensis* (elodea) as an indicator species. Root and shoot growth endpoints were used as indicators of toxicity and the occurrence (%) of cells with abnormal chromosomes in apical root meristem – as indicators of genotoxicity. Genotoxicity of BS of the Yenisei River was also estimated *in situ*, using roots of *E.canadensis* sampled from its natural habitat.

The experiments showed that among toxicity endpoints, root length was more sensitive than shoot length. Despite the difference in variability and sensitivity, the responses of shoot and root length to the quality of BS were similar. The response of the genotoxicity endpoint was the highest on the sediments with chemical pollution, while the inhibition of toxicity endpoints occurred on the sediments with the highest level of radioactive pollution. Abnormalities caused by the damage of chromosomes were the most frequent in our experiments (55.6–83.3 % of total number of abnormal cells). Abnormalities caused by spindle poisoning occurred in 12.2 – 31.8 % of abnormal cells of elodea. The spectrum of chromosome abnormalities registered in laboratory tests was similar to the spectrum occurring in the natural population of elodea in the Yenisei River.

Based on the results obtained, *E.canadensis* can be proposed as a sensitive indicator of toxicity and genotoxicity of natural BS in laboratory contact tests and in ecotoxicological monitoring of freshwater environments.

ARTIFICIAL RADIONUCLIDES IN FISH FAUNA OF THE YENISEI RIVER BEFORE AND AFTER THE SHUTDOWN OF THE NUCLEAR REACTOR PLANT AT THE MINING-AND-CHEMICAL COMBINE (ZHELEZNOGORSK, RUSSIA)

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The Yenisei River is contaminated with artificial radionuclides due to the weapon-grade plutonium production at the Mining-and-Chemical Combine (MCC) in Zheleznogorsk (Russia) for more than 50 years. The last reactor plant at the MCC was shut down in 2010. The research presents the data on accumulation of artificial radionuclides in wild wish inhabiting the radioactively contaminated part of the Yenisei River in 2005–2014. Among artificial radionuclides that occurred in fish muscles when the nuclear reactor plant was operating (^{32}P, ^{60}Co, ^{65}Zn, ^{137}Cs), only ^{137}Cs was registered four years after the shutdown of the nuclear power plant at the MCC. The concentrations of ^{137}Cs in fish muscles were considerably below the sanitary norms for this radionuclide in the Russian Federation. Piscivorous and non-predatory fish species differed in accumulation of ^{137}Cs in muscles. The calculation of concentration factors (CF) revealed a possibility of biomagnification of ^{137}Cs in muscles of pike (CF up to 4.7) and ^{60}Co in muscles of freshwater cod (CF up to 3.3) from bodies of dace and grayling. Concentration of ^{137}Cs in fish fauna of the Yenisei River did not decrease after the shutdown of the nuclear power plant at the MCC, while the concentration of radionuclides with induced activity decreased considerably. From this we can conclude that the bottom sediments may be the main source of ^{137}Cs for fish in the Yenisei River. We can expect that the concentration of ^{137}Cs in fish muscles will not decrease in the next few decades.

Radionuclides migration & distribution

RADIOECOLOGICAL CONDITION OF THE TERRITORIES ADJACENT TO SEMIPALATINSK TEST SITE, SUBJECTED TO RADIOACTIVE CONTAMINATION

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The main plumes of radioactive fallouts from nuclear plumes at Semipalatinsk Test Site were directed to the northeast, southeast and south. Herewith, radioactive contamination was spread beyond the test site territory for hundreds of kilometers, forming plumes with the width of dozens of kilometers. As a result radioactive contamination affected the territories located beyond the STS inhabited by local population.

According to the Law of the Republic of Kazakhstan of 18.12.1992 N 1787-XII "About social protection of citizens, suffered from nuclear tests at Semipalatinsk Test Site" territories affected by nuclear tests were classified, based on the data of radiological survey performed during the testing period. By the present time there is nearly no objective information about radioecological situation at these territories.

Within the frame of complex survey of the territory adjacent to the STS boundary character and peculiarities of radioactive contamination of the environmental objects (air, water, soil, flora and fauna) were studied. Radiation doses for population, living at this territory have been assessed. In addition, mechanisms and peculiarities of contamination of environmental components, typical for the specified territory were investigated: Irtysh river, pine forest, forest-steppe.

According to results of performed investigations, spatial distribution of cesium and americium has a uniform character for inhabited localities, there was no zones with increased specific activity values for artificial radionuclides. It was found, that concentration of natural and artificial radionuclides in air and water environment, and vegetative products does not exceed established norms.

Results on spatial distribution of radionuclides in the plumes' area have shown that average specific activities of radionuclides in soil of the plume zone and at the "background" territory differ several times from one another. So, average concentration of ^{137}Cs on the fallout plume is almost 3 times higher than at the rest of the territory. It was found that vegetation cover of investigated territory can be considered as suitable for all kind of economic activities without limitation, and does not pose any radiation hazard.

Some physical and chemical properties of soils and forms of radionuclides occurrence in them were studied. Obtained results did not reveal any new regularities in behavior of ^{137}Cs radionuclide in soil, however they allow to make a conclusion about its low biological availability. Numeric values of ^{241}Am have been determined only in tightly bound form. There were noticed some peculiarities and differences in character of radionuclides in depth distribution, depending on types of ecosystems.According to results of radiation exposure assessment for population of Beskaragay and Kanonerka villages in case of residential scenario it was found, that expected annual effective dose from artificial radionuclides per person will not exceed the value of 0.3 mSv.

INVESTIGATION OF CHARACTER OF DISTRIBUTION OF RADIOACTIVE CONTAMINATION IN WATER OBJECTS OF SEMIPALATINSK TEST SITE AND ADJACENT TERRITORIES

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For complex assessment of condition of surface water objects (water reservoirs and streamflows) it is very important to have an information about radioactive contamination of both water and sediments. Accumulating contamination during a long time, sediments can serve as an indicator of radioecological state of the water object. Herewith, they can accumulate radionuclides and be the source of secondary radioactive contamination of the water object. The aim of this work is to study the character of distribution of radioactive contamination in the "water – sediments" system of objects of the Semipalatinsk Test Site (STS) and adjacent territories.

As the research objects there were chosen water reservoirs and streamflows of "Experimental Field", "Balapan", "Degelen", "Telkem" sites, adjacent territories as well as Shagan river. At selected objects conjugated samples of water and bottom sediments were taken. Samples were taken at he distance of 1 – 2m from the costal line, and as mainly all the water objects are not deep-water ones, the depth in sampling points was about 20 – 30 cm. Sampling of sediments was made to the depth of 0 – 10 cm, water – from the surface 0 – 20 cm. Collected samples were used to determine concentration of artificial radionuclides ^{90}Sr, $^{239+240}$Pu, ^{241}Am, ^{137}Cs, ^{152}Eu.

As a result of performed researches transfer factors (TF), determining character of distribution of radioactive contamination in water objects were calculated. According to obtained data the TF is decreasing in the range $^{239+240}$Pu>^{137}Cs>^{241}Am>^{90}Sr i.e. $n\times10^6>n\times10^5>n\times10^4>n\times10^3$ respectively. However, obtained TF is >>1. It indicates that, the major part of investigated radionuclides in the "water – sediments" system is concentrated in sediments.

CHARACTER OF RADIOACTIVE CONTAMINATION WITH ARTIFICIAL RADIONUCLIDES OF THE SHAGAN RIVER AND “ATOMIC” LAKE

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The work provides results of research on distribution of artificial radionuclides in water of "Atomic" lake and Shagan river, located at the territory of the former Semipalatinsk Test Site.

To determine content of artificial radionuclides in water of "Atomic" lake, point sampling of surface water was made as well as in-depth sampling with the vertical interval of 5-10 m. Water samples from Shagan river were collected with sampler from different depths with the vertical interval of 5 cm.

According to obtained data, in “Atomic” lake non uniform spatial distribution of concentrations of artificial radionuclides was observed. Maximal values of tritium and strontium-90 were found in the central part of the body of water at the depth of 60-80 m, and they were 20 000 and 15 Bq/kg, respectively, and the minimal values were found at the depth of up to 10 m. According to monitoring data, artificial radionuclides distribution in the central part of the lake has a stable character.

Presence of tritium was noticed in water of Shagan river, from the "Atomic" lake to inflow into Irtysh river. Maximal concentration of tritium was found at the distance of 5 km downstream from "Atomic" lake, with activity of 350 000 Bq/kg. Also at the area with maximal concentrations non uniform areal distribution of tritium is observed, both in width and depth of the stream.

In the place of flowing of Shagan river into Irtysh river specific activity of tritium does not exceed 100 Bq/kg.

RECONSTRUCTION OF THE TECHA RIVER CONTAMINATION AS A RESULT OF RADIOACTIVE RELEASES FROM THE "MAYAK" PRODUCTION ASSOCIATION IN 1949-1956

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The Mayak Production Association (MPA) was the first site for the production of weapon-grade plutonium in Russia. Early operations led to routine and accidental waterborne release of large amounts of radioactive materials into the small Techa River. The major releases occurred during 1950–1951. The releases and subsequent flooding resulted in the deposition of sediments along the shoreline and on floodplain soil. Pioneer studies of the processes of the distribution of uranium fission products in biomass and non-living components of water bodies were started under supervision of Nikolay Timofeeff-Ressovsky in the so-called "laboratory B" established at 40 km from the MPA. Initial aim of the study was physical modeling of radionuclide behavior in flowing and stagnant reservoirs in order to clarify the situation of the contaminated Techa River and its lakes. More accurate reconstruction of the radioactive contamination of the Techa River system has been made recently on the basis of refined data on the amounts and the rate of discharge of radionuclides from the MPA. This improved understanding is possible because of access to many archive documents that have been declassified and become available. An improved Techa River model has been developed that describes transport of radionuclides through the up-river ponds and along free-flowing river as well as deposition of radionuclides in bottom sediments and flooded areas. The model considers transport of radionuclides adsorbed on solid particles and in soluble form. The output of the model provides concentrations of all source-term radionuclides in the river water, bottom sediments and floodplain soils at different distances from the site of radioactive releases. The outputs of the model show good agreement with historical measurements of water and soil contamination. The model will be used for reconstruction of internal and external doses received by residents of the Techa riverside communities.

SPATIAL DISTRIBUTION OF RADIONUCLIDES AND HEAVY METALS IN BOTTOM SEDIMENTS OF THE YENISEI RIVER

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For decades, the Yenisei River has received artificial radionuclides and heavy metals from the Mining-and-Chemical Combine (MCC) ROSATOM and industrial facilities of the city of Krasnoyarsk. Bottom sediments (BS) of the River accumulate radionuclides and heavy metals from water. Thus, BS both store information on the range of contaminants present in the water and provide habitat for many species of living organisms, which may be adversely affected by high concentrations of these contaminants. Therefore, it is important to obtain the data on the distribution of radionuclides and metals in BS. Sediment layers located downstream of the MCC discharge point contain a wide range of artificial radionuclides: Eu isotopes, ^{137}Cs, ^{60}Co, ^{90}Sr, and transuranium elements. The vertical distribution of radionuclides in bottom sediments is rather complex, with a number of extrema. Different radioisotope methods have been used to calculate sedimentation rates in several regions of the Yenisei River and date the maxima of radionuclide concentrations. In addition to artificial radionuclides, heavy metal concentrations have also been determined in the layers of sediments of the Yenisei River. For the metals studied, no significant concentration increases or consistent effects of industrial facilities on the chemical composition of bottom sediments have been revealed. In some parts of the River, Cd and Ni concentrations were higher than their threshold values, above which these metals may adversely affect the biota. Downstream of Krasnoyarsk, U and Th concentrations were increased. Thus, in some parts of the Yenisei River, aquatic organisms may be subjected to the joint adverse effects of contaminants, under increased concentrations of both radionuclides and heavy metals in bottom sediments.

THE MODEL OF RADIONUCLIDE TRANSPORT AT THE SYSTEM OF WATER CONSUMPTION OF NPP FOR ASSESSMENT OF THE ACTIVITY DISCHARGED TO THE ENVIRONMENT

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Nuclear power plants (NPP) operate in an environment with the natural and technogenic radiation background. As a result, water supply and water removal systems of NPP contain artificial radionuclides, the source of which are global fallout due to nuclear weapons testing, The Chernobyl accident, Fukushima, etc. Normative legal acts of the Russian Federation and guidelines in the field of radiation safety do not contain direct requirements to take into account the content of natural and artificial radionuclides in water bodies in justifying standards for allowable discharges. At the same time control of the content of radionuclides in surface water monitoring zones near NPP is an essential part of monitoring of the radiation situation. Thus, the responsibility for radionuclide in liquid effluents falls on the NPP even in the case of presence of ^{3}H, ^{90}Sr, ^{137}Cs due to global fallout in the water used.

The task of our study is to develop the approach that allows to estimate the fraction of radionuclides in effluents due to operation of the NPP and due to activity in the incoming water. For this purpose, the model describing the transport of radionuclides in the system of water supply and water removal of NPP was designed. Activity of radionuclides in each compartment of the model depending on time can be found by solving a system of differential equations. The model gives the possibility to estimate the fractions of radionuclides in discharges due to each source basing on the data as follow: measured values of water activity concentration in the place of water intake and in discharge channel and characteristic of water system such as volumes of the various section of the system, water flows between sections, the effectiveness of filtering.

Control of radionuclide transport in the system of water consumption of NPP gives possibility to: justify the values of allowable discharges taking to account the features of specific territory; assess the impact on water bodies; control the radioecological situation.

Developed approach will be tested in the operating NPP. (Project UB RAS 15-2-2-19)

RIVER FLOODPLAINS AS RADIONUCLIDE SINK: EXAMPLES FROM CONTRASTING ENVIRONMENT

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Lateral migration of ^{137}Cs and other radionuclides is associated with sediment transport in the river basin. River floodplain is the one of major radionuclide sink within the fluvial system. Amount of sediment-associated fallout radionuclides redeposited within floodplain strongly depends on morphological characteristics of river valley bottoms, water discharges and turbidity and the distance from the most contaminated area of the river basin. Radionuclide inventory within the different floodplain sections and it possible influence on the environment of two contrasting river basins is discussed, which are the Niida River basin, Japan (Fukushima accident affected area) and the Plava River basin, Russia (Chernobyl accident affected area).

It is found that only differences in sediment concentrations associated with different levels of initial contamination in different parts of basin is influenced on ^{137}Cs inventory on the different level floodplains of the River Plava, because the sedimentation rate is relatively uniform along the different reaches of the river. Maximum radionuclide inventory is found on the lower floodplain level. Minor ^{137}Cs deposition is detected on the middle and high floodplain levels. Completely different situation is observed within the different sections of the River Niida floodplain, where^{137}Cs deposition in addition is strongly dependent on the gradient of the river valley bottom and type of anthropogenic impact on river channel (floodplain) in each particular floodplain section.

RADIOACTIVE TRACERS IN THE BLACK SEA: A TOOL FOR ENVIRONMENTAL ASSESSMENT AND ECOLOGICAL REGULATION

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The study deals with the development of radiochemoecological approach for evaluation of maximum allowable discharge of radioactive and toxic chemicals to marine ecosystems to be used as a numeric measure for environmental regulation of the human impact. This approach combines assessment of capability of seawater for self-purification against the nuclear and non-nuclear pollutants and determination of their toxicity, on the example of the Black Sea. The rate of decontamination of the upper marine waters is proposed to estimate from the time-series data on concentration and inventory of the fallout radionuclides, both well-soluble (^{137}Cs, ^{90}Sr) and particle-reactive plutonium isotopes. In areas which would otherwise be difficult to investigate due to a lack, incompleteness, poor comparability or absence of the previous observations and monitoring data, the contamination history was reconstructed using the methods of nuclear geochronology, which is based upon the tracing of deposition signatures (or records) of pollutants in the seabed sediments dated with the fallout (^{134,137}Cs, ^{238,239,240,241}Pu, ^{241}Am) and naturally occurring (^{234}Th/^{238}U, ^{210}Po/^{210}Pb/^{226}Ra) radionuclides. ^{40}K was applied as a proxy to estimate separately biogenic and lithogenic sedimentation. The parallel measurement of sediment-depth profiles of the persistent non-radioactive pollutants (PCBs, pesticides, mercury etc.) has allowed recovery the deposition chronology of their input to the marine environments at an uninterrupted and comparable basis over the last 50-150 years, i.e. throughout the entire nuclear epoch and the whole history of pollution of the Black Sea with the harmful chemical substances. Combining of such approaches provides opportunity for estimation of levels of the maximum allowable discharge into marine environments of nuclear and non-nuclear pollutants, to differentiate between their effective and ecological half-lives, and to assess capacity of aquatic ecosystems regarding the assimilation of contaminations, and their ability to take up an impact without unacceptable changes.

FUKUSHIMA-1 AND CHERNOBYL: COMPARISON OF RADIOACTIVITY RELEASE AND CONTAMINATION

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The Fukushima-1 accident was a failure-of-cooling accident due to the station blackout triggered by the tsunami the height of which was over 10 m against the anti-tsunami design of 5.7 m. At the time of the earthquake on March 11, 2011, three BWR units (Unit-1; 460 MWe, Unit-2 and -3; 784 MWe) were in operation out of six units at the Fukushima-1 NPS. Melt-down/melt-through of reactor core took place at all three units, which led to a large amount of radioactivity release into the environment. The process of the biggest release began in the early morning of March 15 when the containment of Unit-2 suffered a serious damage. In the evening of that day, when the radioactive plume moved to the north-west direction, strong deposition occurred by rain and snow, which formed the north-west trace of contamination over Namie town, Iitate village and Fukushima city. Radioactivity release from Fukushima-1 NPS continued up to the end of March 2011. The difference of radionuclide composition between Fukushima-1 and Chernobyl should be noted. A similar radionuclide composition to the reactor core inventory was released in the case of Chernobyl because the explosion occurred at the reactor itself. Meanwhile, explosions did not happen at the reactor cores, and mainly gaseous and volatile radionuclides escaping from high-temperature melted cores were released in Fukushima-1. According to UNSCEAR2013, the total amount of radioactivity release into the atmosphere of ^{131}I, ^{132}Te/^{132}I and ^{137}Cs were 120, 29, and 8.8 PBq, while they were 1,760, 1,150 and 85 in Chernobyl. Other than these nuclides, significant contamination such nuclides as ^{90}Sr, ^{95}Zr, ^{103}Ru, ^{140}Ba and Pu were reported around Chernobyl. On the contrary, it was found from soil measurement that contamination of ^{90}Sr and ^{239,240}Pu in Iitate village were 0.04 – 0.05 % and 10^{-5} – 10^{-6} %, respectivelty, of that of ^{137}Cs. The land area contaminated more than 555 kBq/m^2 of ^{137}Cs amounted about 1,000 km^2 around Fukushima-1, while it was about 10,000 km^2 around Chernobyl. In addition, high level radioactive liquid was directly released into the Pacific Ocean: estimates about 3 – 6 PBq of ^{137}Cs and three times larger ^{131}I are given in UNSCEAR2013.

INITIAL EXTERNAL RADIATION DOSE TO RESIDENTS IN IITATE VILLAGE UNTIL EVACUATION DUE TO THE FUKUSHIMA-1 NPP ACCIDENT

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In the aftermath of the Fukushima-1 NPP accident, most residents in Iitate village remained at home for several months after the severe radioactive contamination occurred in the evening of March 15, 2011. Consequently they received higher radiation dose than the people within the 20-km zone around the Fukushima-1 NPP who evacuated on March 12 following the quick instruction by the Japanese government. In order to evaluate radiation dose delivered to residents in Iitate village, we reconstructed the temporal change of radiation exposure rate at 1 m above ground for 1,700 housing points in Iitate village, using the Cs-137 deposition map elaborated from the aerial survey data released by US NNSA (National Nuclear Security Administration) as well as radionuclides compositions in soil samples measured by us at the end of March, 2011. During July – October 2013, we took interview of residents of Iitate village about the place where they were during the accident and the time of evacuation from the village. We collected the information of 496 families with 1,812 residents, about 30 % of the population of the village. Combining the temporal change of radiation exposure rate with the behavior of residents, individual external doses until evacuation were estimated. The average external radiation dose for 1,812 residents of Iitate village accumulated was estimated to be 7.0 mSv, while the maximum was 23.5 mSv was for a male in sixties. Collective external dose for the total population of 6,132 residents in Iitate village was obtained to be 42.7 person-Sv.

DISTRIBUTION OF RADIONUCLIDES IN GRANULOMETRIC SOIL FRACTIONS IN PLACES OF NUCLEAR EXPLOSIONS AT SEMIPALATINSK TEST SITE

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Distribution of artificial radionuclides in components of soil granulometric composition was researched in places where atmospheric and surface nuclear tests were carried out as well as on plumes from their fallout, at sites of underground and excavation tests and also at conditionally "background" territories. By results of research, distribution of ^{137}Cs, ^{90}Sr, ^{241}Am and $^{239+240}$Pu in granulometric fractions of soil has its peculiarities depending on character and mechanism of radioactive contamination. So directly in places of nuclear tests and on plumes definite fractions, significantly enriched with artificial radionuclides are found in soil. In addition to presence of "enriched" fraction there is a tendency for natural redistribution of radionuclides in granulometric fractions of soil, expressed in increasing of their accumulation with decrease of fraction size. Natural redistribution can be the most clearly observed for ^{137}Cs and ^{90}Sr if compared with transuranium radionuclides as ^{241}Am and $^{239+240}$Pu.

At conditionally "background" territories distribution of radionuclides by granulometric fractions of soil mainly depends on their natural redistribution, however in character of distribution of $^{239+240}$Pu we can see the impact from nuclear tests performed at the Semipalatinsk test site.

So as a result of performed researches the main mechanisms of radionuclides distribution in granulometric fractions of soil in places where nuclear tests were carried out at the Semipalatinsk test site were revealed: "enrichment " of some definite soil fraction, presumably due to presence of radioactive materials of nuclear explosion and natural redistribution of radionuclides due to sorption and other physical and chemical processes in soil.

ABOUT SOME CHARACTERISTIC PARAMETERS OF THE FORMER SEMIPALATINSK TEST SITE RADIONUCLIDE CONTAMINATION

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This work is a generalization of accumulated materials on radionuclide contamination of the most researched areas of the former Semipalatinsk nuclear test site. The main objective of the present work was generalization of accumulated materials and, on their basis, optimization of comprehensive environmental research implementation in order to reduce expensive radiochemical analysis of plutonium isotopes. For obtaining of radionuclide contamination distribution pattern were collected materials about well-studied test site areas (about 7000 sq. km). Analysis results of main artificial radionuclides determination were conducted (^{137}Cs, ^{90}Sr, $^{239+240}$Pu, ^{241}Am) in more than 8,000 soil samples. A comparative analysis of radionuclide contamination were carried out for the most researched STS areas, such as the northern, western, southeastern, and other objects of the test site. Maps of ^{90}Sr, ^{241}Am, ^{137}Cs, $^{239+240}$Pu artificial radionuclides contamination were built and values of isotopic ratios were calculated for ^{137}Cs / ^{90}Sr, $^{239+240}$Pu / ^{241}Am, ^{238}Pu / $^{239+240}$Pu.

According to the results were revealed that there are objective prerequisites for the introduction of the concept - "background STS territory." These areas are characterized by the following parameters: the average content of ^{137}Cs - 18 Bq / kg, the average content of ^{241}Am - <0, 9 Bq / kg, the average ratio for $^{239+240}$Pu / ^{241}Am - 5, 3. It’s also possible to talk about the average ratio for ^{238}Pu / ^{241}Am in background areas, but there is a presence of ^{238}Pu, unrelated to the nuclear tests conducted at the test site. In our case, evaluated activity for one introduced ^{238}Pu is 0.13 Bq / kg.

During the research of background territories in assessing of plutonium isotopes activity possible to use the average values of $^{239+240}$Pu/ ^{241}Am isotopic ratios which is 5.3 and ^{238}Pu / ^{241}Am which is equal to 0.08 * ^{241}Am + 0.13. Therefore, taking into account obtained results, it’s possible on their basis optimize comprehensive environmental research implementation and abandon extremely expensive plutonium isotopes radiochemical analyzes, conducting them only for authentication of obtained data. Based on these results, was viewed the southeastern part of the test site, located between the test site "Delegen" and the village Sarzhal. Defined approach to categorizing of surveyed sites in the "background" and subjected to the influence of STS.

THREE-YEAR MONITORING STUDY OF RADIOCESIUM TRANSFER AND AMBIENT DOSE RATE IN FOREST ENVIRONMENT AFFECTED BY THE FUKUSHIMA DAI-ICHI NUCLEAR POWER PLANT ACCIDENT

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We investigated the transfer of canopy-intercepted radiocesium to the forest floor during 3 years (July 2011~) following the Fukushima Dai-ichi Nuclear Power Plant (NPP) accident. The cesium-137 (Cs-137) contents of throughfall, stemflow, and litterfall were monitored in two coniferous stands (plantation of Japanese cedar) and a deciduous broad-leaved forest stand (Japanese oak with red pine). We also measured ambient dose rate at different height in the forest by using a survey meter (TCS-172B, Hitachi-Aloka Medical, LTD.) and a portable Ge gamma-ray detector (Detective-DX-100T, Ortec, Ametek, Inc.). Furthermore, effects of forest decontamination on the reduction of ambient dose rate were assessed quantitatively.

Total Cs-137 deposition flux from the canopy to forest floor for the mature cedar, young cedar, and the mixed broad-leaved stands were 157 kBq/m^2, 167 kBq/m^2, and 54 kBq/m^2, respectively. These values correspond to 36%, 39% and 12% of total atmospheric input after the accident. The ambient dose rate showed an exponential decrease with time for all the forest sites, however the decreasing trend differed depending on the forest type. These data suggested that an ambient dose rate in forest environment can be variable in spatially and temporally reflecting the transfer of radiocesium from canopy to forest floor. In this study, we presented the analysis results of the relationship between radiocesium deposition flux and ambient dose rate at the forest floor. In addition to that, we reported the effects of forest decontamination (e.g., tree felling, removal of organic materials, woodchip pavement) on the reduction of ambient dose rate in the forest environment.

MICROBIAL INFLUENCE ON THE MIGRATION OF RADIONUCLIDE IN GROUNDWATER; FROM LABORATORY EXPERIMENT AND *IN SITU* OBSERVATION

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To understand the transport of radionuclides once they are spread into groundwater, not only physic-chemical condition but microbial influence on their movement must be taken into consideration carefully as the biomass of microbes in subsurface environment is far abundant than taken before. Laboratory experiment together with *in site* observation suggested some radionuclides adsorb to microbial cells and the strength of adsorption depends on pH and Eh. Furthermore, microbial activity in groundwater may affect dissolution and sedimentation characteristics of some radionuclides through denitrification if sufficient nitrate were supplied as a neutralizer when they were deposited. Possibility of denitrification is suggested from 100 m deep groundwater where some radionuclides migrate together with very abundant nitrate in Siberia. We show the results obtained from four years collaboration from 2011 to 2014 supported by JSPS and RFBR for the team consisted of Russian and Japanese geochemists, radio-chemists and microbiologists.

FATE AND TRANSPORT OF RADIOCESIUM IN SOIL-WATER ENVIRONMENT: COMPARATIVE ANALYSIS OF CHERNOBYL AND FUKUSHIMA CASES

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Comparative analysis is provided for radiocesium (^{134}Cs and ^{137}Cs) distribution between particulate and dissolved forms and wash-off parameters for rivers and surface runoff in Fukushima and Chernobyl contaminated areas for the first 3 years after the accidents. It is found that radiocesium distribution coefficient K_d in Fukushima area is essentially higher (1-2 orders of magnitude) than correspondent values for rivers and surface runoff of the Chernobyl zone. Quantitative characteristics of dissolved and particulate radiocesium wash-off from contaminated watersheds after the FDNPP accident are calculated based on available monitoring data. Normalized dissolved wash-off coefficients for Fukushima river watersheds are 1-2 orders of magnitude lower correspondent values for Chernobyl zone. Normalized particulate wash-off coefficients are comparable for Fukushima and Chernobyl.

Results of the investigation of radiocesium vertical distribution in soils of the close-in area of the Fukushima Dai-ichi NPP – Ohkuma town and research forest site at Yamakia (Kawamata) are presented. It is shown that radiocesium dispersion in undisturbed forest and grassland soils at Fukushima contaminated area is significantly faster as compared to the Chernobyl 30-km zone during the first three years after the accidents. Similar to the Chernobyl case forest soils of Fukushima area are characterized by faster radiocesium migration in upper layer.

Investigation and analysis of Fukushima origin radiocesium distribution in soils of River Niida basin allowed identifying accumulation zones of contaminated sediments on the river floodplain. Average sediment deposition rate for sites under study varied in range 0.3-3.3 cm/year depending on the floodplain type.

OPTIMIZATION OF RESEARCH OF THE TERRITORY OF SEMIPALATINSK TEST SITE FOR THE PURPOSE OF ITS TRANSFER INTO ECONOMIC TURNOVER

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According to legal acts of the Republic of Kazakhstan, now the whole territory of Semipalatinsk Test Site (STS) is currently categorized as reserve lands (Decree of RK of the 7th of February, 1996 № 172). The whole complex of obtained experimental data allows conclude that currently the STS have no adversely impact on the population, living in the surrounding areas. There can definitely state that following to law and special rules related to activities in the STS territory will provide radiation safety, when performing economic activities in the STS. In order to transfer parts of STS lands into economic turnover, a complex ecological survey of would-be transferred lands was performed in order to determine the conditions of safe human habitation and performance of economic activities by population.

As a result of performed works all the basic components of environment (soil and vegetation, water sources, water objects, air basin) were characterized from the point of view of radionuclide contamination. It was found that average concentrations of the main dose-forming artificial radionuclides in soils correspond to the level of global fallouts and are: ^{137}Cs – 17; ^{90}Sr – 10; ^{241}Am – <0,8; $^{239+240}$Pu – <3,9; ^{238}Pu <0,2 Bq/kg. Herewith about 90% of total content is located in the upper 5-cm layer of soil. Concentrations of all the artificial radionuclides ^{137}Cs, ^{90}Sr, ^{241}Am, $^{239+240}$Pu, ^{3}H in water sources, water objects and in air basins are at 10-1000 times lower than maximum permissible concentrations for the population. Agricultural crop and livestock products produced in the researched territory will completely meet established criteria of radiation safety. There are no factors (migration of radionuclides with ground water, air transfer) could lead to a negative change of radioecological situation in researched territory. Accommodation of the population in the researched territory may lead to receiving of additional dose from artificial radionuclides more than 0,04 mSv per year.

REGULARITIES OF TRITIUM DISTRIBUTION IN THE AIR OF RADIATION-HAZARDOUS OBJECTS OF THE SEMIPALATINSK TEST SITE

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Radioecological research, taking place at the Semipalatinsk test site (STS) have shown that tritium is currently the main radionuclide posing a hazard to air in terms of a radionuclide contamination. The purpose of research was to study regularities of tritium distribution in air of radiation-hazardous sites of the STS.

Tritium distribution in air was studied in details at the area of test sites - «Degelen», «Balapan», «Experimental Field» where nuclear tests of different character were made, as well as within the radiation-hazardous objects of the STS – the «Atomic» lake and Shagan river that were formed as a consequences of nuclear explosions. Special attention should be paid to the fact that two forms of tritium were determined in air at the researched territory – as tritiated water (HTO) and as gaseous compounds (H_{gas}).

Maximal concentration of HTO was determined at the «Degelen» testing site, where underground nuclear explosions (UNE) were made in tunnels. Presence of HTO was noted in atmospheric, soil air and tunnel air, maximal volumetric activity was about 1300 Bq/m^3, significant concentrations of HTO in air, up to $1*10^2$ Bq/m^3 were also found beyond the «Degelen» testing site, at the distance over 5 km. Presence of H_{gas} was found in soil air in the immediate vicinity of tunnel entries. Volumetric activity was about 0.5 Bq/m^3.

Interesting facts about tritium distribution were determined at the «Balapan» test site, where UNEs were made in horizontal wells called «boreholes». There was observed other regularity of tritium distribution in the air and fixed maximal concentration of tritium as a gaseous form up to 200 Bq/m^3. Tritium in the air at the boreholes location was only determined near to mouth of wells, at the distance of no more than 500 m from ones. Much less focus can be given to tritium distribution in the air at the places of surface and atmospheric nuclear explosions at the «Experimental Field». Volumetric activity of HTO did not exceed 0.5 Bq/m^3.

Research at the point of excavation explosion at the territory of «Atomic» lake showed unexpected results. There was determined of tritium presence in both forms of HTO and H_{gas} as in atmospheric as in soil air. Concentration of HTO at the cone dump of the lake varied from 1 to 90 Bq/m^3, concentration of H_{gas} was range from 0.2 to 4 Bq/m^3. Tritium distribution in the air has local character and it is limited by the explosion crater area.

Results of research in the bed of Shagan river that is going through the «Atomic» lake and spreading far beyond the boundaries of the STS, have shown a high concentrations of HTO in air, volumetric activity of tritium there was up to 700 Bq/m^3. Concentration of H_{gas} in this area was about 0.2 Bq/m^3. Concentration of tritium sharply decreases with the distance from the riverbed and achieves of background levels about 200 m far from it.

REGULARITIES OF THE ^{90}Sr AND ^{137}Cs MIGRATION IN THE ECOSYSTEMS OF THE SEVASTOPOL BAYS OF THE BLACK SEA AFTER THE CHERNOBYL NPP ACCIDENT

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The regularities of change of the ^{90}Sr and ^{137}Cs concentrations in water and hydrobionts of the Sevastopol bays in the period 1986–2014 years after the Chernobyl NPP accident were described by the obtained results of the investigations. They were characterized by a sharp increase of the ^{90}Sr and ^{137}Cs concentrations in components of sea ecosystems in 1986 and an exponential decrease since 1987. The time constants of the exponential decrease twice of the ^{90}Sr and ^{137}Cs concentrations in the components of the Sevastopol bays ecosystems were determined. These time periods are: for sea water – 8.8 and 6.1 years, for seaweeds (*Cystoseira crinita* (Desf.) Bory) – 4.9 and 4.7 years, for mollusc (*Mytilus galloprovincialis* Lamark) – 6.7 and 7.6 years, accordingly. Rates of the self-purification of water of the Sevastopol bays ecosystems from post-accident ^{90}Sr and ^{137}Cs were: for ^{90}Sr – 0.5 ± 0.08 GBq per year, for ^{137}Cs – 5.74 GBq per year. At the same time on the radioactive decay accounted to 48.6 % of ^{90}Sr and 46.4 % of ^{137}Cs of the total radionuclide content in the components of the ecosystem, which was defined in 1986. The main factors that ensure self-purification of marine ecosystems from ^{90}Sr are the radioactive decay and water exchange between the open sea area, and from ^{137}Cs, in addition to these both factors, the deposition this radionuclide into the bottom sediments is the main process, as well, for self-purification of the marine ecosystems. Over 28 years after the Chernobyl NPP accident the value of stocks of the radionuclides in bottom sediments of the Sevastopol bays amounted to 1.5 GBq for ^{90}Sr and 31.8 GBq for ^{137}Cs. The biogeochemical and hydrological processes in marine ecosystems of the Sevastopol bays reduce the time of presence of the post-accident radionuclides in the marine environment on 106–127 years.

MIGRATION OF TRITIUM NEAR RADIATION DANGEROUS OBJECTS

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In 1995 when testing Obninsk groundwater sources of the Protva left bank where all enterprises are placed, the SPA "Typhoon" employees had found that the higher tritium content was observed at all outlets of groundwater sources in the sanitary zone of Obninsk water intakes, including those upstream of the town and NPP. Maximum tritium concentrations up to 46.9 kBq/l refer to water in the first above floodplain terrace of Protva near the new IPPE radioactive waste (RAW) repository (Makhon'ko, 1996).

Monitoring of tritium dispersal at the IPPE industrial site and near Obninsk had been performed by analyzing tritium content in the reference wells of the RAW repository, water and snow in the IPPE area and adjacent territories and water from four Obninsk water intakes.

Consider the data on tritium distribution within the anomaly in groundwater intakes near the IPPE industrial site. Based on data of water well testing, it could be said with the approximation probability $R^2 = 0.80$ that as the distance from a research centre increases the power dependence of tritium distribution. Generally, tritium migration in groundwater is thought as being a polluted flow which is directed along a chain of water intakes from the IPPE industrial site to distant intake.

The dilution degree of a tritium flow arriving from the IPPE industrial site is considered in profiles transverse to the river valley. In the Central water intake the degree of tritium dilution as the distance from the river increases is characterized by a linear function $C_T = 1.2\,L - 141$, where C_T is the tritium concentration in water, Bq/l; L is the distance to the river, m.

The analyzed tritium dispersal in a water bearing horizon allows the qualitative assessment to be made of some essential parameters of a filtration flow: the direction of a flow, the rate of mass transport, the mixed volumes of ground and river water and etc.

Reference

Makhon'ko, K.P., 1996, Radiation situation in the territory of Russia and the adjacent states in 1995, SPA "Typhoon", Obninsk. (In Russian)

TIME CHANGES IN RADIOCESIUM TRANSFER TO RIVER SYSTEMS AFFECTED BY THE FUKUSHIMA DAIICHI NPP

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Due to Fukushima Daiichi Nuclear Power Plant accident, radioactive materials including Cs-137 were widely distributed in surrounded area. Detailed field monitoring has been conducted in Yamakiya-district, Kawamata town, Fukushima prefecture. These monitoring includes, 1) Radiocesium wash-off from the runoff-erosion plot under different land use, 2) Radiocesium transfer in forest environment, such as throughfall and overlandflow, 3) Radiocesium concentration in soil water, ground water, and spring water, 4)Dissolved and particulate radiocesium concentration in river water, and stream water from the forested catchment, and 5) Radiocesium content in drain water and suspended sediment from paddy field. We also monitored flow and turbidity in downstream rivers. The monitoring started at 6 sites from June 2011. Subsequently, additional 24 monitoring sites were installed between October 2012 and January 2013, to measure Cs-137 activity concentrations by gamma spectrometry.

Our monitoring result demonstrated that the Cs-137 concentration in eroded sediment from the runoff-erosion plot has been almost constant for the past 3 years, however the Cs-137 concentration of suspended sediment from the forested catchment showed slight decrease through time. On the other hand, the suspended sediment from paddy field and those in river water from large catchments exhibited rapid decrease in Cs-137 concentration with time. The decreasing trend of Cs-137 concentration were fitted by the double-component exponential model, differences in decreasing rate of the model were compared and discussed among various land uses and catchment scales. Such analysis can provide important insights into the future prediction of the radiocesium wash-off from catchments from different land uses. The decerasing trend of river system vaired with catchments. Our analysis suggest that these differences can be explained by upstream landuse with different decreasing trend.

VERIFICATION OF THE ^{137}Cs SOURCE BY MEANS OF PLUTONIUM ISOTOPIC ANALYSIS IN THE BLACK SEA DEEP-WATER SEDIMENTS

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The world's largest marine anoxic basin of the Black Sea is known to be affected by two major sources of anthropogenic radioactivity quite separated in time: the global radioactive fallout after the nuclear weapons testing in the open environments (peaked in the early 1960s) and the atmospheric fallout caused by Chernobyl NPP accident in April-May 1986). Both mentioned sources had contained a wide variety of fission and activation products including cesium and plutonium isotopes, which can be considered as one of the most informative tracers for the dating of seabed sediments. During the deep-sea sediment stratification analysis, due to the time localization of ^{137}Cs maximum inputs in the Black Sea, this isotope demonstrate typically two well recognized activity peaks, thereby giving a rapid information about sedimentation rate, taking into account its usually simple measurement procedure by non-destructive gamma-spectrometry. At the same time, anthropogenic plutonium is always introduced into the environment as a mixture of relatively long-lived isotopes characterized by significant variety of its composition from source to source. For example ^{238}Pu/^{239,240}Pu activity ratio for global (at the Northern Hemisphere) and Chernobyl fallouts are 0.036 and 0.4-0.5, respectively. This gives unique opportunity to improve greatly the reliability of determination of origin of the peaks. In this study, an undisturbed core of the abyssal Black Sea sediments sliced into very thin layers (0.25 cm thickness) was analyzed. The absence of any significant bioturbation at the Black Sea anoxic deep-water sediments allows obtaining adequate results by such a thin stratification. ^{137}Cs concentration profile, obtained by non-destructive gamma-spectrometry of each layer, showed 3 peaks. The largest peak was strictly localized at the sediment depths of 2.75-3.00 cm with activity of almost 600 Bq/kg that is approximately 5 times higher than in other peaks and up to 10 times higher as compared to the general trend of ^{137}Cs concentration in the profile. The ^{238}Pu/$^{239-240}$Pu ratio in this peak at the level of 0.34 as well as 0.035 below and 0.037 above the peak implies the Chernobyl dating of 2.75-3.00 cm deep layer with up to 80% of plutonium characterized by Chernobyl origin.

RADIOACTIVITY AND RADIOACTIVE ELEMENTS IN THE ENVIRONMENT

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Nowadays all existing radioactive elements in the geospheres of our planet, including biosphere, can be divided into three essential groups: 1. natural radioactive elements (NRE: U, Th, ^{40}K and others); 2. technogenic (artificial or anthropogenic) radioactive elements (TRE: ^{137}Cs, ^{90}Sr and others); 3. radioactive elements, forming at the interaction of neutrons of cosmic radiation (cosmogenic radionuclides) and neutrons from nuclear decay of ^{235}U or ^{239}Pu with some stable nuclides (^{14}C, ^{3}H and others). NRE occur absolutely in all objects of the material world. These components determine the general radioactivity of the human environment. These elements and their decay products (Ra, Rn, and Po for U) compose the main radioecological hazard for the biosphere. First of all this concerns radioactive gas without odor and colour – radon, emitting alpha-radiation. This gas occurs elsewhere and determines the development of lung cancer. Considerable NRE contents of real hazard occur in the biosphere quite rare and the places of their accumulations are well known (Kerala state in India, etc.). In the places of anomalously high radioactivity people have specific cytogenetic and other deviations. Since 1945 the radionuclide composition of the biosphere became substantially different. New radioactive elements (Pu, Am, etc.) and isotopes (^{137}Cs, ^{90}Sr, ^{85}Kr, ^{131,139}I, etc.), which had not been existed in the biosphere, appeared and entered into the biological cycle. The amount of ^{3}H and ^{14}C has also sharply increased in the environment. Nowadays, the quantity of TRE became statistically meaningful factor of high teratogenic, cancerogenic, and genetic risk.

An especial attitude in radioecological aspect should be directed to the Pu, Am, and other trasuranium elements input, which are alien to the biosphere in their chemical and radiation nature. Nowadays Pu of various contents can be found in all biological objects, including people, especially in technogenic zones of nuclear facilities and in nuclear testing sites. Pu is capable of forming fine-grained systems, that makes it extremely penetrating and long-way mobile radionuclide. According to our data (Rikhvanov et al., 2002), the accumulation level of the alpha-decaying radionuclides for the last 150 years has increased more than three times.

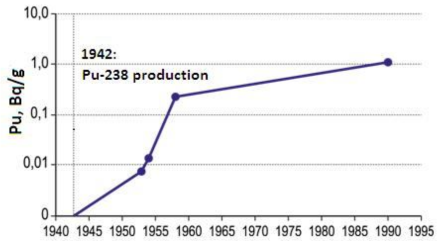

Fig.1.Schematic graph of the change of the specific activity of Pu in the human lung tissue for the last 70 years (according to separate data from literature) in the nuclear facilities sites.

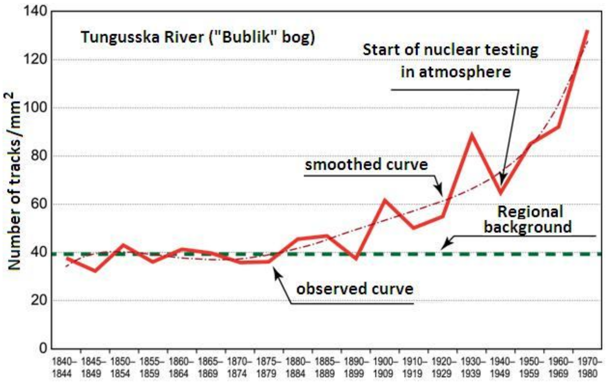

Fig.2.Thechangeofthe global background of decay in alpha-emitting radionuclides (^{235}U, Pu, Am, etc.) for the last 150 years by the data of fragmentation radiography (f-radiography) in annual tree rings.

CHARACTER OF DISTRIBUTION OF TRITIUM AND MECHANISMS OF ITS FORMATION IN THE SNOWCOVER AT THE STS TERRITORY

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For the last 5 years a complex investigation of the main environmental components was carried out at the territory of testing sites of Semipalatinsk Test Site (STS). All the biological environmental components, located at or adjacent to the territories with high concentrations of tritium in the channel water accumulate tritium. Also at underground nuclear explosion (UNE) and excavation nuclear explosions sites at «Balapan» site entry of tritium into air environment was found. It can be assumed that all the well mouth sites for underground nuclear tests at «Balapan» site are potential sources of tritium entry into environmental objects. Investigations of tritium concentrations in the snow cover at the STS were not carried out before. The aim of this work is research of character of distribution and study of mechanisms of tritium entry into soil cover.

Maximal concentrations of tritium in snow cover were found directly in streamflows of the STS (creeks at «Degelen» site and Shagan river) and they reach concentrations of tritium in surface waters (40 kBq/kg). The main way of tritium entry into the snow cover is emanation of tritium from the soil or ice cover.

At UNE sites of «Balapan» testing site tritium was also found in snow cover. At that concentration of tritium in near surface layer of snow is greater than in surface layer of the snow cover. At all the geological rocks research sites tritium was found. At the wellhead area of the well 1355 maximal concentration of tritium at the depth of 5 m is up to 90 kBq/kg. It was found during this research, that spatial distribution of tritium at the STS has a larger scale than we expected before. Developed method is cheap enough in material expenses and simple in implementation. This method can be successfully used in identification of UNE sites.

At the distance of 0-10 km from «Degelen» site, in places of surface tests at the «Experimental Field» site, and in inhabited locations adjacent to the STS no tritium was found. It means that tritium is not distributed by air at large distances.

When pasturing cattle in places with high concentrations of tritium in environmental objects there is a probability of accumulation of tritium in cattle breeding products. In the winter period snow cover and plants located near the STS streamflows can serve as a source of tritium entry into animal organism.

MODELING TRANSFER OF FUKUSHIMA-DERIVED CESIUM-137 BASED ON A DISTRIBUTED MODEL CALIBRATED BY WASH-OFF OBSERVATIONS ON VARIOUS LAND USES

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Predicting spatial distributions in cesium-137 is required for mitigating radiological risks on residents in area affected by the accident of Fukushima Dai-ichi Nuclear Power Plant (FDNPP) accident. For the prediction, estimations of soil erosion and associated ceasium-137 wash-off are indispensable because of high affinity of ceasium-137 to soil particle. In this study, we present a calculation of transfer of cesium-137 based on a distributed model of Universal Soil Loss Equation (USLE). Our calculation targeted an area within 80 km from FDNPP with resolution of 25m mesh DEM basis. Parameters of USLE model and entrainment coefficients of cesium-137 wash-off were derived from erosion plot observations at various land uses in Yamakiya district, an area affected by the accident. Calculated soil loss and cesium-137 discharge were counted on a river basin basis which divides the targeted area into 30 basins.

Annual specific cesium-137 discharge at the points was in a range from 10^{-2} to 10^{0} kBq m^{-2} $year^{-1}$. Annual cesium-137 wash-off rates, annual specific discharge divided by initial cesium-137 fallout, were below 1 %. Estimates of cesium-137 discharge at two points on Abukuma and Kuchibuto rivers agreed with observed discharges obtained by previous study. At the points on main stream of Abukuma river, more than 50 % of cesium-137 was discharged from paddy fields at the first year and the total cesium-137 discharge decreased in subsequent years. By contrast, at points on rivers on Hamadori area, almost cesium-137 was discharged from forest lands and annual cesium-137 discharge showed no decreasing trends and depends on the magnitudes of annual soil loss. Our calculation suggests that land uses significantly affect fate of cesium-137.

Accumulation of radionuclides & Radiation exposure

PARAMETERS OF ^{137}Cs, ^{90}Sr, ^{241}Am, AND $^{239+240}$Pu TRANSFER INTO ORGANS AND TISSUES OF SHEEP IN DISTANT PERIOD AFTER NUCLEAR TESTS AT SEMIPALATINSK TEST SITE

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Full scale experiments with animals were carried out in the summer period when animals were kept in confinedness and some individual sheep groups were supplied with contaminated feed, soil, water, in some cases mixed intake took place. Feed and soil were supplied from contaminated spots, where surface and underground nuclear tests were previously carried out.

As a result of performed works dynamics of radionuclides transfer into sheep organs and tissues was determined and peculiarities of their distribution in sheep organism were studied. During performance of works parameters of radionuclide transfer in «feed-sheep breeding products», «soil- sheep breeding products», «water-sheep breeding products» systems were studied.

It was found that the main, ^{137}Cs depositing organs are muscular tissue and kidneys, for ^{90}Sr they are – bone tissue and wool, for ^{241}Am and $^{239+240}$Pu – bone tissue and hepar. The time of dynamic equilibrium for ^{137}Cs in the main depositing organs comes after 2 months. For ^{90}Sr, ^{241}Am and $^{239+240}$Pu in chosen time intervals (up to 112 days) such equilibrium was not found.

In general obtained results of f research approve already existing data on dynamics of accumulation and character of distribution of ^{90}Sr and ^{137}Cs radionuclides in animal body. However obtained transfer factors (T_f) were an order less than average T_f values, presented in the IAEA database (TRS#472, 2010).

It was found that transuranium radionuclides, entering with soil, are less digested than when enter with feed. At that T_f of $^{239+240}$Pu could be compared to existing single data in the world.

PREDICTION OF ^{137}Cs CONTAMINATION IN THE FOOD CHAIN FOLLOWING A NUCLEAR ACCIDENT

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A very reliable model developed in the ’60 at the Euratom Joint Nuclear Research Centre of Ispra, Italy, for the prediction of the food chain contamination due to the radioactive fallout deposition. Such a model was later applied to foresee the behaviour of the contamination released by the Chernobyl accident. A comparison between the experimental measurements carried on in the years after the accident and the model led to the evaluation of reliable prediction functions to be used for cost effective countermeasures.

Keywords: food chain contamination, nuclear accident, prediction.

FRACTAL DIMENSION OF BILATERAL LEAVES IN HIGH BACKGROUND RADIATION AREA

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Fractals, i.e. self-similar structures, are ubiquitous in nature. Fractal dimension is a measure of the complexity of the object and it can be used to characterize the morphological properties of natural objects. The dependence of this parameter on the factors affecting the growth of a biological object (temperature, humidity, the dose of radiation, etc) is of particular interest. A sample of Alchemilla leaves related to different species and grown in high-level radiation area has been chosen for the study. The subject of the study was the fractal dimension of the Alchemilla leaves contour.

One of the common methods for determining the fractal dimension of the curves is the box-counting method, which involves sequential covering of the curve by squares with different size. Then dependence of squares number on length of the square side is plotted in log-logarithmic coordinates. The fractal dimension is calculated as the slope of the straight area of the dependence. We have tested several programs for calculating the fractal dimension of the curve using known fractal figures and modeled fractal figure, close to studied form of Alchemilla leaf. The program that defines known fractal dimension most accurately was chosen. By means of chosen program the fractal dimension of digitized Alchemilla leaves contour was determined.

It was found, that fractal dimension is an objective and significant criteria for characterization the object's shape. However, it is not informative enough to provide the differentiation of Alchemilla leaves sample by its specie. The fractal dimension of the contour of the leaves, related to one specie, but grown in different sites, was different, but it is most likely not due to exposure to radiation, but due to other external parameters, such as light, humidity and others.

THE BIOACCUMULATION RATIO OF CAESIUM-137 BY WILD-GROWING EDIBLE FUNGI ON PEAT SOIL OF A RIDING SPHAGNOUS BOG

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Earlier by us it has been established that fungi fruit bodies of *Leccinum* S.F. Gray species in riding sphagnous bog accumulate caesium-137 with excess of admissible values, and in beside woods such accumulation does not occur (Leningrad reg., Gatchinsky distr.).

The purpose of research – to lead monitoring of caesium-137 in the riding bog ecosystem on the basis of mass gathering wild-growing edible fungi and to define bioaccumulation ratio (BAR) in relation to peat soil.

Gathering of fungi fruit bodies was spent by route method on a bog (area of 10 ha). The monolith of peat soil has been selected in the point with coordinates (N 59°04.775', E030°25.527') up to the bog mineral part. Fungi fruit bodies and peat soil samples have been dried up in a stream of warm air for constant weight. Measurements of a radio-activity have been lead by method of scintillation gamma-spectroscopy. Activity is specified in relation to samples dry weight. In all samples activity has been caused by presence of caesium-137.

Following results have been received. In sphagnum (height 10-15 cm) the activity of caesium-137 has made 830±83 Bq/kg. The in peat horizon (up to depth 30 cm) 540±60 Bq/kg. Humus-peat horizon (from up 30 to 45 cm) 420±50 Bq/kg. Humus horizon (45 - 55 cm) 380±38 Bq/kg. Mineral gley horizon (55-80 cm) 330±43 Бк/кг. For calculation of BAR we used activity in peat horizon because the most part of fungous mycelium there is located.

According to SANR&S 2.3.2.1078-01 the admissible level of caesium-137 in dry fungi – 2500 Bq/kg. The activity in wild-growing edible fungi species and BAR: *Lactarius helvus* (Fr.) Fr. 10718±1179 Bq/kg, BAR 19,9; *Leccinum holopus* (Rostk.) Watling 14862±2230 Bq/kg, BAR 27,5; *Russula emetica* (Schaeff.) Pers. 14303±2174 Bq/kg, BAR 25,5; *Suillus variegatus* (Sw.) Kuntze 17247±1897 Bq/kg, BAR 31,9; *Suillus flavidus* (Fr.) J. Presl 14431±2742 Bq/kg, BAR 26,7. Accumulation of caesium-137 in fungi fruit bodies is caused by acidity of peat soil (pH 3,5-4,0). The surveyed bog is on distance of 16 and 22 km from two known zones of pollution 1 Ci/km^2 (Mshinshoye Boloto Zakaznik).

RESEARCH OF PECULIARITIES OF ARTIFICIAL RADIONUCLIDES TRANSFER INTO PIG BREEDING PRODUCTS WHEN ENTERING WITH SOIL

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This paper provides results of research of peculiarities of ^{137}Cs and ^{241}Am transfer into organs and tissues of young pigs when artificial radionuclides enter during a long period of time with radioactively contaminated soil from surface testing sites of the STS. Dynamycs of removal of these radionuclides was studied as well.

Upon the results of performed works it was found that concentration of ^{137}Cs radionuclide in muscular tissue, hepar and bone tissue is approximately the same. It was found that one month after everyday entry of ^{137}Cs into animal body dynamic equilibrium between intake and removal appears.

Dynamics of ^{137}Cs removal from animal body shows that the period of half-decrease of ^{137}Cs activity is 7 days. At the 56th day content of ^{137}Cs achieves the value of 0.3% from average daily intake.

According to results of investigation of dynamics of ^{241}Am transfer into muscular tissue, hepar and bone tissue, equilibrium state of radionuclide in muscular tissue appears at the 28th day, while in hepar and bone tissue within the selected time interval of experiment (up to 56 days) equilibrium state was not achieved.

Removal of ^{241}Am from hepar and bone tissue take longer time, comparing with muscular tissue. At the 7th day concentration of this radionuclide in muscular tissue, hepar and bone tissue is 0.006%, 0.054% and 0.09% of average daily intake of this radionuclide, at the 56th day these values are 0.0001%, 0.047% and 0.05%.

CONCENTRATIONS AND FORMS OF OCCURRENCE OF URANIUM IN SOILS OF SEMIPALATINSK TESTS SITE

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According to historical data, hydronuclear experiments with charges containing not only plutonium, but also uranium were made at the territory of Semipalatinsk Test Site. Due to this the following **aim of research** was set: study of gross content of uranium and its isotope composition, as well as forms of its occurrence in STS soils using more sensitive mass-spectrometric method. As a material for research there were used soil samples, taken from the depth of 0-2.5 cm at the following sites of the «Experimental Field»: P2-P7, P2-G, P-3-P5 and «U-1» technical object.

Concentration of uranium in soil at these sites lies within the range of 0.40-33 mg/kg. Herewith for the most of samples under research isotopic composition of uranium (mixture of natural and artificial uranium) was offset from natural concentration to enrichment by ^{235}U isotope (3%-90 %). At the territory of "U-1" object, points with abnormally high concentration of artificial uranium in soil within the range of 95–32000 mg/kg with isotopic ratio, respecting to depleted uranium was found: (^{235}U 0,2–0,4 %).

General tendency for all the researched soil samples with different content of uranium and isotopic ratio was minimal content of its easily accessible forms (water-soluble and exchange forms) that is in average less than 2 %. For uranium compound forms in relative expression with insignificant deviation the following range was typical: $U_{water}<U_{exch}<U_{org}<U_{\text{пtigdly bound}}<U_{mobile.}$. The main percentage of uranium in soil was in potentially mobile form (1 н HCl).

In case of change in soil conditions, mainly pH, Eh, and salt content, these compounds can become mobile and migrate from soil. At that of ecological situation deterioration can appear. The most dangerous here is migration in «soil-ground waters » and «soil-plants» systems.

EXPERIMENTAL ASSESSMENT OF PECULIARITIES OF ACCUMULATION OF ARTIFICIAL RADIONUCLIDES IN AGRICULTURAL PLANTS AT THE STS TERRITORY

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In the worldwide practice processes of migration and transfer of individual radionuclides into agricultural plants are studied well enough, but information about character of ^{241}Am and $^{239+240}$Pu transuranium radionuclides accumulation in agricultural plants is still fragmentary. That is why the main objective of the work was to obtain quantitative parameters of radionuclides migration in “soil- plant” system and first of all for transuranium elements.

Experimental works for study of artificial radionuclides accumulation by agricultural crops at the Semipalatinsk Test Site were carried out at the territory with high radioactive contamination. Concentration of radionuclides in soil (0-5 cm) was: ^{241}Am – n*10^4 Bq/kg, ^{137}Cs – n*10^3 Bq/kg, ^{90}Sr – n*10^3 Bq/kg and $^{239+240}$Pu- n*10^5 Bq/kg.

As research objects, crops, cultivated in Kazakhstan were chosen: wheat, barley, watermelon, potato, eggplant, pepper, tomato, sunflower, onion, carrot and cabbage.

As a result of work basic ^{137}Cs, ^{90}Sr, $^{239+240}$Pu and ^{241}Am accumulation factors (Fv) were obtained for agricultural products. Range Fv of ^{90}Sr values for all the plant samples is 3 orders of magnitude, Fvs of $^{239+240}$Pu, ^{241}Am and ^{137}Cs - 2 orders of magnitude each.

It was found, that radionuclides are the most intensively accumulated in roots, leaves and steams, and in generative organs (fruits, grains, bulbs) accumulate radionuclides least of all. The difference in accumulation of radionuclides between different vegetative and generative organs of plants is up to 1-2 orders of magnitude. For all the investigated radionuclides the following decrease range was constructed:
Fv ^{90}Sr > Fv ^{137}Cs > Fv $^{239+240}$Pu > Fv ^{241}Am.

RESEARCH OF SPECIES OF ARTIFICIAL RADIONUCLIDES ^{137}Cs, ^{90}Sr, $^{239+240}$Pu, AND ^{241}Am IN SOILS OF CONDITIONALLY «BACKGROUND» TERRITORIES OF SEMIPALATINSK TEST SITE

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The work provides results of research of species of artificial radionuclides in soils of conditionally «background» territories of the STS. These territories include «northern», «western», «southeastern» and «southern» parts of the STS, specified in this way according to their geographic location at the test site territory. In spite being closely located to testing spots, radiological situation at the most of conditionally «background» territories mainly depends on global fallouts, except for zones of «plumes» from local fallouts of surface nuclear tests, conducted at the «Experimental Field». «Plumes» of fallouts, crossing «southeastern» and «southern» parts of the STS, could determine another character of radioactive contamination of the soil cover.

As a result of performed researches low mobility of ^{137}Cs and $^{239+240}$Pu was found in soils notwithstanding type of fallouts, conditioned radioactive contamination of soils. The main concentration of ^{241}Am transuranium radionuclide in soils was found in tightly bound form, that is not accessible for plants, less significant concentration was noticed in mobile (acid-soluble) form, representing potential reserve for plants. As it was noted, ^{90}Sr radionuclide is the most soluble in soils Along with tightly bound forms of ^{90}Sr, presence of easily accessible forms (exchangeable form) and forms representing potential reserve for plants (mobile form) was also found in soil. Herewith, the ratio between exchangeable and non- exchangeable forms of radionuclide is different, both for background sites and for the zones with increased radiation background. So the result of investigation of ^{90}Sr radionuclide mobility can be used as an additional parameter when studying the character of radioactive contamination of soil cover and when determining the impact of fallouts from surface nuclear tests on the territories under research.

ARTIFICIAL RADIONUCLIDES IN THE VEGETATION COVER OF SEMIPALATINSK TEST SITE

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The main radioactive contamination of the vegetation cover of Semipalatinsk Test Site (STS) was formed as a result of surface (including excavation) nuclear tests, radioactive fallouts (nearby and remote) and migration of radionuclides from surface and ground waters and testing of warfare radioactive agents (WRA). Research on levels of radioactive contamination and accumulation parameters of artificial radionuclide's in plants were performed at all know sites of the STS, characterized by different types of radioactive contamination. The highest accumulation in vegetation observed for radionuclide's ^{137}Cs and ^{90}Sr. Specific activity (SA) of these radionuclides is dozens of kBq/kg in the areas of radioactive watercourses. Maximal values of SA for ^{90}Sr are up to several thousands of kBq/kg in the WRA test sites. Also for these radionuclide's characteristic of the biggest differences in the accumulation factors (Af), which, depending on the nature of the radioactive contamination of soils can be up to 71 times for ^{137}Cs and 74 times for ^{90}Sr. In these specific peculiarities of plants determine differences in accumulation of radionuclide ^{137}Cs from 2 to 10 times, ^{90}Sr – from 2 to 6 times.

Transuranium radionuclide's $^{239+240}$Pu and ^{241}Am in plants accumulating significantly less than ^{137}Cs and ^{90}Sr, and in a narrow range of Af which, depending on the nature of radioactive contaminated soil are 14 times for $^{239+240}$Pu, 11 times for ^{241}Am. The greatest accumulation of $^{239+240}$Pu, as well as of ^{90}Sr, was found in WRA testing sites (hundreds of Bq/kg). Quantity values of ^{241}Am SA in plants was found only for epicenters of ground surface tests and on « plumes» of radioactive fallouts (Bq/kg and dozens of Bq/kg). Specific peculiarities of plants cause differences in accumulation of $^{239+240}$Pu from 2 to 3 times, ^{241}Am – from 2 to 5 times. High concentrations of ^{3}H radionuclide in the vegetation cover are mainly attributed to the areas with groundwater and surface water contaminated with ^{3}H. SA of this radionuclide in free water of plans in some specific sites of the STS reaches hundreds of kBq/kg

MONITORING OF SR-90 CONTAMINATION OF TERRESTRIAL ECOSYSTEMS NEAR A RADIOACTIVE WASTE STORAGE

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The paper presents radioecological studies in the territory of a regional RAW storage. This object had been put into operation in the 50-70s of the last century. Now the object is a closure. In 1998-1999 the increased specific activity of Sr-90 had been revealed in the surveying wells and in the following this was stipulated by surface water penetration in one of the facility. In reservoir overfilling, 90Sr and Cs-137 radionuclide exposed water escaped outside. Multi-year studies allowed one to establish that Sr-90 contributes much to radioactive contamination on the territory near the storage and in the adjacent territory. The analysis of long-term data (2004-2007) on the 90Sr radionuclide content in the soil of the studied site and the continued experimental work (2010-2013) allowed us to establish the following. A 1.5-2-fold reduction of the specific Sr-90 activity in soil near the studied object had been observed from 2005 to 2012. The increase was observed of Sr-90 concentration gradient from the contamination source (emergency storage) to the sampling sites located beyond the object territory. The texture of the soil (silt, clay) of the adjacent territory contribute to minimization of the Sr-90 migration processes. The area of radioactive contamination to be calculated with a value which exceeds the minimum significant activity 1kBq/kg for the tested soil layers: the contaminated area for the 0-5 cm soil layer amounted to 1800 ±85 m2, for the 5-10 cm soil layer amounted to 300±12 m2, for the 10-15 cm soil layer amounted to 180±10 m2. It is found that Sr-90 accumulation proceeds in a natural sorption geochemical barrier of the marshy terrace near flood plain.

Terrestrial mollusks Bradybaena fruticum have been chosen as reference species most properly reflecting the ecosystem Sr-90 effect. Practically the whole amount of radioactive strontium is concentrated in a mollusk shell. The exposure doses for terrestrial mollusks Bradybaena fruticum from Sr-90 in the study area are 35-653 mGy/year. Screening analysis of biota conditions during radioecological studies has shown that this contamination is local in character.

RADIOECOLOGICAL STUDY OF THE BLACK SEA MUSSELS: THE ACCUMULATION OF ^{210}Po IN DIFFERENT HABITAT CONDITIONS AND ASSESSMENT OF DOSES

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As well known, ^{210}Po is the dominant contributor to the natural radiation dose received by marine biota. The purpose of this work was to study an ability of the Black Sea mussels *Mytilus galloprovincialis* Lam. to accumulate ^{210}Po and to evaluate the doses formed this radionuclide in animals. The specified criterions taken into consideration were the habitation mode and the food set. The sampling places were located in different bays of Sevastopol marine region and in the Karadag Bay. For the determination of ^{210}Po in samples the radiochemical procedure was used. ^{208}Po was added as a yield tracer. Polonium was spontaneously plated onto silver disks. Alpha counting of ^{208}Po and ^{210}Po was done using a silicon surface-barrier detector and alpha-spectrometer EG&G ORTEC. ^{210}Po concentrations in the samples are given in Bq·kg^{-1} wet weight (ww). The results of the comparative study shown that this radionuclide may serve as an indicator of biological features of *M. galloprovincialis* in different environmental condition in the areas of their dwelling. It should be noted that the range of ^{210}Po concentrations in mussels may vary significantly from bay to bay and inside of each of investigated areas. The highest ^{210}Po concentrations were determined in mollusks from the Karadag Bay and the Kazachya Bay which are characterized as relatively clean marine regions. The lowest concentrations of ^{210}Po were determined in animals collected in the Martunova Bay which is characterized as most polluted between investigated areas. The differences are due to not synchronized stages of the mollusks development and different environmental conditions. Thus, in the study of an accumulative ability of the Black Sea mussels necessary to take into consideration the ecological conditions of the animals in the areas of their dwelling. A radiation weighting factor of 20 was applied for the calculation of equivalent doses delivered by ^{210}Po to the Black Sea mussels. The data presented in this study shown that the highest doses, calculated for investigated mollusks are about two orders lower than the dose limit (4 Gy·a^{1}) proposed by IAEA for the protection of aquatic organisms from ionizing irradiation.

ESTIMATION OF ORGAN DOSES OF MURINE RODENTS INHABITING TERRITORIES CONTAMINATED WITH SR-90

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In recent decades, protection of non-human biota against radiation exposure is considered as one of the important tasks of radiation safety. Contemporary ICRP approach to radiation protection of the environment is based on Reference Animals and Plants, Representative Organism and Derived Consideration Reference Levels (DCRL). Implementation of such approach can be demonstrated on the example of East-Ural Radioactive Trace, the territory contaminated by radioactive elements after the accident at the Mayak nuclear plant in 1957, where the murine rodents can be chosen as the representative animals. In our study we estimated doses to organs and tissues of mice and voles caused by Sr-90 accumulated in skeleton. Estimations were made using the coefficients linking the skeleton Sr-90 activity concentration and absorbed doses. The distribution of Sr-90 by organs and tissues was estimated using developed biokinetic model for mouse-like rodent. Calculated values of internal dose rate at the last day before trapping are 0.83; 0.092 и 0.023 mGy/day for the animals trapped at the area with initial Sr-90 surface contamination of >37 MBq/m^2, 18.5-37 MBq/m^2 и 0.074-18.5 MBq/m^2 respectively. External dose rate at the most contaminated territory amounts 0.43 mGy/day.

Contemporary doses to murine rodents inhabiting the EURT are still rather high. Whole body dose rate exceeds the upper boundary of the DCRL (1 mGy/day) at the most contaminated territory. Mean internal doses accumulated during 45 days are approximately 100 mGy. Such levels of exposure of bone and bone marrow can result in adverse effects to the hematopoietic and immune systems that are observed in animals. Currently, the most contaminated part of the EURT refers to the East-Ural State Reserve. It can be assumed that the restriction of human activities in this territory to some extent compensates the negative effect of irradiation of the local biota. Taking in account high levels of radiation exposure presence of the reserve is necessary to ensure the radiation safety of the environment.

FORMATION OF RADIOACTIVE CONTAMINATION OF POLLUTING PRODUCTS WHEN ^{137}CS AND ^{241}AM ENTERS WITH SOIL

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The paper provides results of full-scale studies, performed under conditions of Semipalatinsk Test Site, on parameters of transfer of ^{137}Cs and ^{241}Am into organs and tissues of birds with radioactively contaminated soil. Dynamics of transfer and elimination of these radionuclides was studied.

During research it was found that intensive transfer of ^{137}Cs in organs and tissues is observed during first 2 weeks, then dynamical equilibrium appears. Maximal values of factors of ^{137}Cs transfer into meat and hepar when coming with soil were 1.5×10^{-1} and 7.8×10^{-2} respectively, bon tissue – 4.4×10^{-2}, stomach –1.5×10^{-1}. Half-life elimination of ^{137}Cs from organs and tissues of birds is 7-14 days after putting on radioactively clean diet.

Availability of ^{241}Am radionuclide for stomach and bone tissue is more than for meat and hepar. Equilibrium state for this radionuclide in organs and tissues comes at 10th -14th day of feeding. Coefficient of transfer of ^{241}Am radionuclide into muscular tissue and hepar was $2{,}6\times10^{-4}$ and $3{,}6\times10^{-4}$ respectively, into bone tissue – $1{,}87\times10^{-4}$, stomach – $9{,}05\times10^{-4}$.

Equilibrium of ^{137}Cs in eggs comes at the 6th -7th day. No further increase of activity appears. At that time concentration of radionuclide in the egg achieves its maximal value and becomes 4.4% of daily average intake. Transfer of ^{241}Am into chicken differs from ^{137}Cs. Equilibrium state comes at the 11th day. Transfer factor for ^{137}Cs in eggs in case of long-time intake with soil is 4.4×10^{-2}, that is 3 orders higher than the ^{241}Am transfer factor, that is 3.5×10^{-5}. Concentration of ^{137}Cs radionuclide in eggs already at the 5th day after putting birds on clean diet does not exceed 50% of the maximal concentration. First half-life elimination period for ^{241}Am comes at the 3rd -4th day of experiment.

ARTIFICIAL RADIONUCLIDES IN THE SOIL-PLANT COVER OF THE KAMCHATKA PENINSULA

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The purpose of this study is the assessment of the total content of artificial radionuclides in the soil-plant cover of the Kamchatka Peninsula and the identification of the ^{137}Cs contribution from the emergency NPP "Fukushima-1". South-east part of the Kamchatka Peninsula was investigated by our research team in 2013-2014. Investigations were carried out on four reference sites located on the coast, at the foot of the hills, on the gentle relief elements. The experimental soil fields are classified as Fluvisols, Glaysols and Andasols according to World Reference Base for Soil Resources. Most of the soils have well expressed profiles, which includes horizons of ash typical for this area.

In the examined soils of Kamchatka the ^{90}Sr stock varies within 0.4-1.6 kBq/m^2, ^{137}Cs - 0.68-2.66 kBq/m^2. It should be noted that the content of these radionuclides on the southern tip of the Peninsula in the vicinity of the city of Petropavlovsk-Kamchatsky is approximately 2 times higher than in the central part. The level of soil contamination with plutonium at the Kamchatka is independent of the sites location and varies within 54-106 Bq/m^2. In general, the deposition of radionuclides in the surveyed soils does not exceed levels due to global fallout from the atmosphere. The variability of radionuclides stocks in soil cover associated with landscape diversity, as well as the physical and chemical properties of soils from different sites. Distribution of the ^{137}Cs from Fukushima-1 was not uniform on the Kamchatka territory. The contribution of accidental ^{137}Cs to the contamination of soil varied from 47 to 290 Bq/m^2; on average, this amounted to about 13% of the total radionuclide content in the soils. The comparison of the above data with the results of earlier studies shows the good similarity with the levels of soil contamination in the Primorsky Krai and Sakhalin Island. Contribution of emergency fallout ^{137}Cs to the contamination of mosses and lichens of the Kamchatka did not exceed 3.6 Bq/kg of dry matter; this is close to the level of contamination which observed in the Urals and in the Primorye.

CONCENTRATIONS OF RADIONUCLIDES IN ORGANISMS OF SOME SPECIES OF WILD ANIMALS LIVING AT THE TERRITORY OF THE FORMER SEMIPALATINSK TEST SITE

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Researches of fauna conducted at the territory of Semipalatinsk Test Site (STS) allowed to characterize species diversity and peculiarities of seasonal variations in population and density of occupation of the test site territory.An issue of concentrations of artificial radionuclides in organism of wild animals living at the STS have excited a big interest.

Territory of the test site varies both in landscape peculiarities, and character of radioactive contamination. There are places of surface tests, plumes of radioactive fallouts, places of testing of warfare radioactive agents (WRA), meadow soils of ecosystems, associated with radioactively contaminated flows from testing tunnels. Due to the above particularities of contamination of fauna representatives, living in this area with radionuclides become the point of interest .

The paper provides data on ^{137}Cs, ^{90}Sr,$^{239+240}$Pu,^{241}Am and ^{3}H radionuclides concentrations in individual species of mouse-like rodents, lizards, fishes and birds, and in particular- animals, used by human for food.

According to results of research, radionuclides' specific activity levels in the organism of investigated animals are different, and depend on living environment of animals and character of radioactive contamination of their inhabitation territory as well. For example, in the organism of lizards, living at the territory of WRA testing site, specific activity of ^{90}Sr radionuclide is up to 780kBq/kg. Taking into account the fact that average weight of lizards trapped during research is about 7 g, one species can have over 5000 Bq of ^{90}Sr radionuclide in its body that can be a serious mechanism of redistribution of this radionuclide in the ecosystem.

RESEARCH OF LEACHING OF ARTIFICIAL RADIONUCLIDES FROM THE SOIL OF THE «ATOMIC» LAKE

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The «Atomic» lake was formed as a result of excavation explosion at «Balapan» testing site at the Semipalatinsk Test Site (STS). The heap of soil around the «Atomic» lake is a serious potential source of radioactive contamination of other environmental objects. The existing radiation situation can be aggravated because Shagan river is flowing through the «Atomic» lake and flows into Irtysh river. It can be cause of possible transfer of artificial radionuclides from «Atomic» lake to the other environmental objects.

This work aimed at research of possibility of artificial radionuclides transfer from soil into natural water by leaching. The main problems of research involved with the determination the degree of radionuclide leaching and study of factors, having influence on this process (dependence of degree of leaching on phase contact time and soil texture).

Samples of soil from the soil heap of the "Atomic" lake were taken as a research objects. They were sampled at the distance of 50 and 100 m from the coast line of the lake. Concentration of artificial radionuclides at these points differs by an order. Experiment on leaching were carried out under static conditions. Distilled water was used as a leaching solution (ratio of solid to liquid phase was 1:2). Aqueous extracts have been collecting in some definite time intervals (from 1 h to 100 days) for determining of artificial radionuclides concentrations. The analysis of soil was also performed after leaching. The degree of radionuclide leaching from the soil have been assessed based on obtained data.

According to the research results it was found a linear dependence the leaching degree of radionuclide ^{3}H and ^{90}Sr on the time. Concentration of $^{239+240}$Pu in water extracts have sharply increased during first 5 days, then it started to decrease and on the 60th day concentration of $^{239+240}$Pu in the water extract was below the detection limit of the technique used. Concentration of gamma-emitting radionuclides (^{137}Cs, ^{241}Am, ^{152,154}Eu) in the solution was below the detection limit of the used technique. It was confirmed that transfer of radionuclides from soil of the «Atomic» lake into water is possible

INVESTIGATION SPECIATION OF TRITIUM IN SOIL OF RADIATION-DANGEROUS OBJECTS AT THE SEMIPALATINSK TEST SITE

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Nuclear explosions at the Semipalatinsk Test Site (STS) have resulted in radioactive contamination of environmental objects. One of the most widely spread artificial radionuclides at the STS territory is tritium. Concentration of tritium both in water and soil achieves values of several hundreds of thousands Bq/kg. Herewith speciation of this radionuclide in soil is hardly studied. It is known that tritium in water can be contained as free water, in organically bound and tightly bound form. Speciation of tritium in soil is the main parameter, characterizing its migration. This work is aimed to determine the speciation of tritium in soil at different areas of the STS, differing each from other in relief, soil-climatic and ecological conditions.

For research purposes samples of soil were collected at different radiation-dangerous objects of the STS (crater of the «Atomic» lake, external water reservoir, Shagan river). Research methodology based on consecutive extraction of each form of tritium from soil sample: surface adsorbed water, interlayer water, crystallized water, organically bound tritium and tightly bound tritium. Different speciation of tritium, contained in form of free water was determined by distillation at different temperatures. Bound forms of tritium were determined using the method of autoclave decomposition with variations of physical and chemical conditions. As a result of experimental works concentrations of tritium in obtained samples have been determined using the method of liquid scintillation spectrometry.

As a result it was found that there is some difference in speciation of tritium in soil of radiation-dangerous objects of the STS. In samples of soil in the area of Shagan river tritium mainly contains in form of surface adsorbed water (93-99%). In the northeastern part of the «Atomic» lake prevails tritium in organically bound form (81-85%) while in the opposite direction in the south-eastern part prevails tritium in form of surface adsorbed water (38-41%) and tightly bound form (34-45%). In soil samples collected around the perimeter of water reservoir organically bound 3H is the major of tritium occurrence form (55-94%).

ASSESSMENT OF EXPECTED RADIATION EXPOSURE AT INTERNAL INTAKE OF ARTIFICIAL RADIONUCLIDES FOR POPULATION LIVING IN THE ZONE OF POTENTIAL IMPACT OF SEMIPALATINSK TEST SITE

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As research objects there were chosen inhabited localities, located directly on plumes of radioactive fallouts, such as: Sarzhal, Bodene and Dolon villages. Also there were selected inhabited localities, located at enough distance from plumes of radioactive fallouts, as Mayskoe and Semenovka villages and Semey city. Total of 304 persons have participated in the research.

Concentrations of artificial radionuclides in human body were determined using whole body counter and analysis of biosubstrates. As a result of measurement on the whole body counter no numerical values of artificial radionuclides' activity was found. Average detection limits are ^{137}Cs – 10 Bq, for ^{241}Am – 40 Bq per body. In most cases no artificial radionuclides have been found in urine samples. The smallest detection limit for ^{90}Sr is 0.014 Bq, for ^{137}Cs – 0.004 Bq, for ^{241}Am – 0.002 Bq, for ^{3}H – 18 Bq and for $^{239+240}$Pu – 0.0001 Bq per one daily sample. Only in a few cases numeric values of ^{137}Cs and ^{90}Sr activity have been found in daily urine samples. Ranges of numeric values of ^{90}Sr and ^{137}Cs are 0,026 ÷ 0,71 Bq and 0,05 ÷ 0,22 Bq per daily sample respectively.

Radiation exposures were assessed with assumption, that radionuclides have been entering into organism only per oral during 50 years period. According estimations total lifelong effective dose of internal exposure will not exceed 14 mSv.

IDENTIFICATION OF REFERENCE SPECIES AND PARAMETERS IN COMPLEX DIAGNOSTICS OF CONTAMINATED AREAS BY Sr-90

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The identification and application of models of reference organisms and their indicators of vital activity is the most developed ideas in the concept of radiation safety in accordance with the publications of ICRP. The effect by Sr-90 in the system "soil-plant-mollusc" into account the nature of osteotropic accumulation of radionuclide was studied. The research was performed in territory where the content of Sr-90 in the soil varies from 246 to 2722 Bq/kg. We have tried to identify reference species and indicators for further diagnostics of Sr-90 in terrestrial ecosystems. As a candidate for the role of reference were investigated following indicators: 4 enzyme systems of soils - catalase, urease, dehydrogenase, invertase; biogeochemical indicators: accumulation factor and factor of transition; morphometric characteristics of mollusc: the height and diameter of the shell, weight, age, width of the shell. The indicators of biological activity, especially enzyme of soils are important for the biodiagnostics of soils. The change in urease, invertase, and dehydrogenase activities of soils with increasing content of Sr-90 in soils does not reveal reliable indicators. The growth in catalase activity with increasing content of Sr-90 in the soil is possible to describe by an exponential dependence $y = 3{,}29\ e^{0{,}0011x}$. It was received a model which differs from the control and is reliable within confidential probability equal to at least 95%. As a consequence, the indicator "catalase activity of soils" can pretend to the role of reference. The biogeochemical indicators "accumulation factor " and "factor of transition" in the system "plant-shell clam" can't pretend to the role of reference. Reliable model describing change of indicators from the quantity of Sr-90 in the plants within investigated range of the radionuclide content in the soil was not found. Species of mollusc *Bradybaena Fruticicola fruticum* is recommended as a candidate for the reference species. The specific activity of Sr-90 in the shell reliably exceed the value of the activities in the soil from 3 to 13 times. One indicator of 14 analyzed biogeochemical and morphometric parameters "the height of the shells of alive molluscs" is possible to pretend to the reference indicator. The variation of the height of the shell was described by the equation $y=2{,}66^{0{,}49x}$.

EFFECTS OF SOIL PHYSICAL-CHEMICAL PROPERTIES ON THE DEPTH DISTRIBUTION OF RADIOCESIUM IN SOILS AROUND THE FUKUSHIMA NPP

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The depth distribution of radiocesium in soils is basic and useful information to better understand their migration on terrestrial ecosystems and evaluate the air dose rate. There are numerous reports about the mechanisms of downward migration for a long term, but few studies about the initial depth distribution which is believed to be quite rapid because the field data had been limited. After the Fukushima NPP accident, we investigated the detailed depth distributions of radiocesium in soils under eight different land uses from very early-stage, and reported that the distribution parameters calculated by the exponential equation tended to be correlated with the cesium fixation ability of soil (RIP), macro pore, and dispersible fine particle content (Takahashi et al., 2015). The early-stage depth distributions over a wide area (85 sites) have also been monitored by the Ministry of Education, Culture, Sports, Science and Technology in Japan (MEXT). Some sampling sites were disturbed by decontamination work or soil mixing, but most sites showed the exponential distribution and little change over time (Matsuda et al., 2015). Therefore, in the present study, we measured some physic-chemical properties of soil samples and estimated the distribution parameters (relaxation depth and relaxation mass depth) on these 85 sites and discussed the relationships between these soil properties and the depth distribution and downward migration at early-stage.
As a results, no significant correlations in all sites were obtained between each soil properties and the both distribution parameters. However, the soils with quite low relaxation depth tended to have low saturated hydraulic conductivity and high macro pore, indicating that initial distributions would be influenced by the penetration ability of water. In addition, the sandy paddy fields showed quite high relaxation depth, showing that the land use patterns also have a large influence on the migration processes.

ASSESSMENT OF TRITIUM CONTAMINATION IN SOIL COVER IN THE PLACES OF REALIZATION OF NUCLEAR TESTS ON THE TERRITORY OF SEMIPALATINSK TEST SITE

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During research of the territory of Semipalatinsk Test Site (STS) tritium was found in different environmental objects – surface and ground waters, vegetation, air environment, snow cover. Analysis of obtained data have shown that, contamination of environmental objects with tritium at the STS territory is associated with places of underground nuclear tests. It was supposed that during surface nuclear tests, mainly all the tritium was emitted into the atmosphere and then transferred with air streams beyond the test site. The decision was made to investigate the soil in places of surface and excavation explosion.

Aim of the work is to assess contamination of soils at the places of excavation nuclear tests with tritium.

As objects of research at «Experimental Field» site supposed explosion epicenters were chosen. At «Balapan» test site the crater of excavation explosion and external water reservoir, formed as a result of tests were taken as objects of research.

As a result of research performed at «Experimental Field» site maximal values of specific activity of tritium in soil were found at the P-1and P-5. Sites P-2 and P-7 are distinguished by lower level of soil contamination with tritium. The smallest concentration of tritium in soil was found at the P-3 site.

At «Balapan» site concentration of tritium contained in soil in significant amount. At the bank of external water reservoir detectable amount of tritium was found only in one point, which is the closest to the explosion crater. Concentration of tritium in soil at the rest two research sites was below the detection limit.

During performance of works it was found that concentration of ^{3}H in soil correlates with concentration of ^{152}Eu. Probably, concentration of tritium in soil depends on character and yield of charges used in the tests conducted.

INTERNAL DOSES IN TOOTH ENAMEL FROM ^{90}SR/^{90}Y FOR THE TECHA RIVERSIDE RESIDENTS

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The method of Electron Paramagnetic Resonance (EPR) in the tooth enamel was used in the Urals region for external dose estimation. However, the cumulative absorbed dose in tooth enamel detected by EPR method includes the internal dose from incorporated ^{90}Sr (and daughter ^{90}Y) in tooth tissues. External dose can be assessed by subtraction of the internal dose due to ^{90}Sr/^{90}Y from the total EPR-measured dose in tooth enamel. Thus the aim of the present work was to calculate the internal doses in the tooth enamel from ^{90}Sr/^{90}Y incorporated in tooth tissues for Techa riverside residents.

The internal doses in tooth enamel were calculated for 327 teeth of 189 individuals living permanently in the Techa riverside settlements in the period of 1950-1952. Villages located along the stream of the Techa River were divided into 3 groups, viz.: the Upper Techa (7-70 km from the discharge point), the Middle Techa (75-88 km) and the Low Techa (105-237 km). The internal dose in tooth enamel was calculated as the product of the ^{90}Sr/^{90}Y concentration in the source tissue and the dose conversion factor (DC) corresponding to the dose rate absorbed in the enamel per unit ^{90}Sr/^{90}Y specific activity in the source tissue. The current ^{90}Sr concentrations in tooth tissues were measured in the enamel as well as in the crown and root dentin using the passive thermoluminescent (PTL) method of detection. If teeth or one of tooth tissues were not measured by PTL method, the ^{90}Sr concentration in tooth tissues was estimated using the models of ^{90}Sr concentrations in the enamel, crown and root dentin in 2010. The DCs were calculated using Monte Carlo simulations of electron transport (MCNP4c2 code) in the tooth tissues based on voxel phantoms of anterior teeth and analytical phantoms of posterior teeth elaborated directly for rural residents of Southern Urals. It is found the DCs of the anterior teeth are dependent on the age and the birth year of an individual. For posterior teeth only DCs of secondary dentin are dependent on the age of an individual. As a result for the teeth with crowns older than 6 years at time of ^{90}Sr intakes the internal dose in tooth enamel is about 70 mGy (from 10 to 520), 75 mGy (from 5 to 240) and 30 mGy (from 8 to 120) for the Upper Techa, the Middle Techa and the Low Techa, respectively. For the teeth with crowns younger than 6 years at time of ^{90}Sr intakes the internal dose in tooth enamel can reach 30 Gy.

FUNDAMENTAL DIFFICULTIES IN DOSE CALCULATION

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Assumptions underlying the concept of dose of radiation protection, contrary to the large amount of actual data.

The external dose for a given point and time of day drastically change during a year: its one-time measurement may not adequately reflect the value of external exposure.

The exact calculations of the absorbed dose on the basis of a retrospective analysis of the diet are dubious because of the large variability in the levels of radionuclides in each of the food, the variability of individual food preferences, seasonal and long-term variability of each radionuclide transfer coefficients for each species (varieties) food plants, animals, and mushrooms for each place.

Calculation "average half-life" of a radionuclide in a body is incorrect because of it's different exemption from different organs and tissues.

The energy of particles of different radionuclides forms a continuum from 2.5 keV to tens of MeV. Therefore, it's dubious of sharp dividing by relative biological effectiveness (four radiation weighting factors W_R). Moreover, even the same level of ionization differently affect cell depending on a stage of the cell cycle.

The assertion that the relative radiosensitivity of human organs and tissues form distinct deterministic number ("tissues weighting factors" W_t), simplifies the situation to the loss of biological sense.

It is impossible to account for the dose-forming effect of tens of radionuclides released into the environment in case of real radiation accidents as Chernobyl and Fukushima. The dose-forming ones in some places and time can be not only I-131 and Cs-137, but other radionuclides (including α-emitters) and the hot particles (e.g. Pm-144, Te-132, Nb-95 as in Chernobyl' case) .

The various voxel phantoms (Golem, Donna, etc) are inadequate for the modeling, since its can not be is applicable to the vast majority of the exposed population as because its homogeneity (fare from real organism) as soon the high group and individual variability of radiosensitivity. The assumptions underlying the calculation of effective and equivalent doses of total bear such uncertainty that the whole calculation is meaningless in terms of radiation protection.

RECONSTRUCTION OF DISTRIBUTION OF INDOOR RADON CONCENTRATION IN RUSSIA USING RESULTS OF INDOOR RADON MEASUREMENTS IN REGIONS

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The aim of our study is reconstruction of distribution and estimation arithmetic average of indoor radon concentration in Russia using the data of 4-DOZ Report published under supervision of Rospotrebnadzor. These annual reports summarize results of radiation measurements in 83 regions of Russia. Annual summary 4-DOZ Report includes the average indoor radon ECC and the number of measurements by regions and by three main types of houses: wooden, one-storey non-wooden and multi-storey non-wooden houses. All-Russian model sample is generated by integration of sub-samples created using results of each annual regional program of indoor radon measurements in each type of buildings (quasi-surveys). Arithmetic mean for each quasi-survey was obtained from the 4-DOZ annual reports. The value of geometric standard deviation (GSD) was chosen depending on the number of measurements in each quasi-survey. By results of reconstruction of indoor radon concentration distribution, all-Russian average indoor ECC of radon isotopes is 24 Bq/m^3. GSD=2.9 reflects both the dispersion of reported average values and model dispersion of indoor radon concentration in the regions. The quality of data on indoor radon collected by Rospotrebnadzor requires special consideration with regards to applicability for the reconstruction of national distribution of indoor radon concentration. The weak points are absence of rigorous requirements on inclusion of the dwellings to annual radon measurements program; application of short term measurements; absence of information on dispersion in annual reports. Despite the high uncertainty, reconstructed percentiles of indoor radon concentration distribution can be applied to preliminary consideration of strategy on protection of population against indoor radon in Russia. The reliable estimates of average indoor radon concentration and pattern of distribution should be obtained by means of survey which is based on measurements on indoor radon concentration in a representative sample of dwellings using unified, preferably, long term measurements technique. (Project 15-IIE-01)

EVOLUTION

PREDOMINANCE OF FEMALES IN THE WHITE SEA POPULATIONS OF THREE-SPINED STICKLEBACK *GASTEROSTEUS ACULEATUS*: PHENOTYPIC AND GENOTYPIC SCREENING

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The sex ratio has been estimated in 117 samples of three-spined stickleback (*Gasterosteus aculeatus* L., 1758) collected in the inshore zone of different parts of the White Sea during the summer seasons in 2008–2014. Predominance of females has been found in most populations, their average proportion during spawning period (June) was 63 %. The proportion of females in samples did not correlate notably with density of fish during spawning period (June), but positive correlation has been found in post-spawning period (first half of July), and negative in the period of when fish departure from spawning grounds (second half of July). These patterns are probably explained by stickleback migrations in the inshore zone during spawning and post-spawning periods. No difference in ectoparasite infestation has been found between males and females; however, the mean number of endoparasitic trematodes of the family Hemiuridae per individual is larger in females than in males. Random testing for two sex-specific loci has shown that the genotypic and phenotypic sexes coincide in all individuals examined; i.e., ontogenetic sex reversal does not occur in three-spined stickleback.

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NOVEL ALGORITHM FOR RECONSTRUCTION OF OPERON STRUCTURE EVOLUTION

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Patterns of gene combination within an operon vary significantly between different species of bacteria; the same set of genes can be distributed in different ways even in genomes of closely related strains. Our algorithm provides reconstruction of ancestral operons given phylogeny and data from extant species.

The common approaches to reconstruction of evolution of operon structure usually consider pairs of genes. In this paradigm, each pair in each genome can be described by one of the following two states: whether this genes are situated within the same operon or they are not. Such a consideration does not account for transitivity of 'to be in the same operon' relation, hence conflicts can arise. e.g. gene A and gene B are predicted to be within the same operon as well as genes A and C, but at the same time gene B and gene C are predicted to be in different operons.

Our approach considers operon as a collection of genes and it is free of the pairwise consideration inconsistencies. As an atomic evolutionary events we consider: a split of an operon into two or a merge of two operons into one. We reconstruct the evolution of the operon structure using the Monte-Carlo minimization of the overall number of events weighted by the tree distances. For better algorithm convergence we keep an ensemble of suboptimal solutions rather than only the best solution, in each tree node. Our approach was successfully tested on simulated data and then it was used for analysis of the operon structure of several metabolic systems in gammaproteobacteria

THE CENTRAL NERVOUS SYSTEM OF MAMMALS ACTS AS A MUTAGENIC/ANTI-MUTAGENIC FACTOR (POSSIBLE ROLE IN THE MICROEVOLUTION)

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The mutagenic/antimutagenic effects of mouse volatile pheromones serve the evidence that central nerve system (CNS) of the house mouse males modifies the level of genome instability in target cells of some peripheral organs. Olfactory cues in relatively low concentration (0,01% water solution) without direct contact with testing animals (minimal distance between animal and solution is 5 mm) nevertheless elevate the frequency of chromosome aberrations in bone marrow or germ cells. Some combinations of excreted substances decrease the level of aberrant cells induced by pheromone 2,5-dimethylpyrazine or whole body irradiation (4 Gy).

As it was shown by other researchers, pheromone effects are density-dependent, genotype-specific and are able to modulate CNS state (Brown, 1985). Therefore just CNS regardless of a nature of acting factors is able to inhibit immune and reproductive systems by means of increasing of cell genome instability. We think that CNS of animals is capable to become a mutagen under rapidly changing environment (stressful) conditions. That will selectively influence viability of the organisms and genetic heterogeneity of their germ cells. Thus, the offspring will be less numerous, but more genetically diverse. This will increase the possibilities of natural selection and accelerate the rate of microevolution.

Developing the hypothesis of Tzapigina et al. (World Congress of Landscape Ecology, IALE, Ottawa, Canada, 1991) we consider CNS as a time-saving factor of space-genetic structure formation in the house mouse populations with possible expansion to other mammalian species.

EVOLUTION OF BACTERIAL GENOMES

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Evolution of bacterial genomes at the strain, species and genus level can be analysed from several different points of view.

Comparing gene complements of related strains, one gets a description of pan-genomes (all genes of a species) and core-genomes (universal genes present in all strains). Most pan-genomes are not saturating at the present level of sequenced strains, whereas the core-genome ceases to decrease after the first several strains. However, exclusion of singletons yields relatively fast saturation of pan-genomes. An interesting phenomenon is common periphery, that is, genes present in some, but not all, strains of two species of genera. While a general theory is still lacking, empirical observations are useful for understanding gene loss and gain events, estimating their rates, etc., as well as for identification of species-specific or genus-specific genes.

Considering genomes as string of genes, one studies genome rearrangements, such as inversions, translocations, etc. One observation is that the emergence of young, aggressive pathogens (such as *Yersinia pestis*) is often accompanied with an increase in the rearrangement rates. Another observation is that some taxa and functional systems extensive operon structure is observed, while others prefer individually located genes.

To study homologous recombination and speciation, one may consider genome as a sequence of nucleotides, and identify regions with an increased frequency of single nucleotide polymorphisms. Sometimes it is possible to identify the source of inter-strain homologous recombination. In addition, comparing homologous intergenic regions, one can identify conserved regions, that are likely regulatory sites, and estimate the fraction of positions evolving under negative selection.

FUNCTIONAL CHARACTERIZATION OF *uvrD* HELICASE FROM *DEINOCOCCUS RADIODURANS* R1 IN *ESCHERICHIA COLI* K-12 CELLS

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UvrD is a highly conservative DNA helicase II involved in excision repair of nucleotides, mismatch repair, recombinational repair and replication. It plays critical role in maintenance of genome stability and DNA repair among many prokaryotes.

Fragment of genome DNA of hyperradioresistant bacterium *Deinococcus radiodurans* harboring the *uvrD* gene was amplyfied and cloned in cells of a model organism - *Escherichia coli*. Plasmid pCR 2.1-uvrD$^+$ restores radiation resistance of *E. coli uvrD* and *rep* mutants defective in reparative helicase II and replicative helicase Rep, correspondingly, practically up to wild type AB1157 (*uvrD*$^+$) level. Radioprotective effect of UvrD$_{\mathrm{Dr}}$ expression manifests also in strains with *recQ* mutation in the key helicase of recombinational repair RecQ and with mutation in *helD* gene coding helicase IV. Characteristic motifs presented by seven elements are highly conservative in helicases UvrD$_{\mathrm{Dr}}$, UvrD$_{\mathrm{Ec}}$, Rep$_{\mathrm{Ec}}$ and HelD$_{\mathrm{Ec}}$, but not in RecQ$_{\mathrm{Ec}}$.

Thus wide range of functional possibility of *D. radiodurans* UvrD helicase is established. It may take part in different pathways of DNA metabolism. These special features of UvrD$_{\mathrm{Dr}}$ may reflect its determinative contribution in increased radiation resistance.

CONSERVATIVE FULCRUM FOR EVOLUTION PROGRESS

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Whole-genome comparisons for humans/great apegive low differences andtheirlists of functional sets of the genes, driven by adaptive evolution,are similar (spermatogenesis, receptors, the immune system and signal transduction). Noted that the regulatory genesofthemorpho/ontogenesis are closes the list and very little number of the brain-specific genes among them [1]. Actually, by the clinic data mutations in them leads to pathologies that are serious even forthe civilized, not to say the ancient, human.These data cannot agree well with the main evo-devo ideas (MI). AccordingtoMIan aromorphosis (evolution with radical changes in the complexity of the organism that allows a taxon to leave and/or expand its habitat and/or ecological niche) provided by mutations in the regulatory genes(including for a norm-of-reaction expansion) and/ortheir manyduplications with the change of functions. But genes of the basic processes (housekeeping genes, HG)because of the functional conservatism almost cannot participate in the change of biological complexity through duplications [2].An alternative idea of the universal functional blocks (UFB) displays complication without duplications butthroughan expansion of the range of organismal functions where the basic genes may be involved without changing their function [3]. The rates of the strong orthologs evolution and conservatism of their functional sets (basedonGOdatabase)estimated for Metazoan wide taxaphylogenesis and taxa with different contributions MIand UFB in aromorphic evolution identified.Forants, e.g., despite high rates of the orthologues evolution, the role of UFB is extremely low, in the evolution of most mammalian aromorphic taxa both UFB and MI occurred, but in hominids, despite the presence of MI, the role of UFB has always been significant.The most typical for the UFB functional groups of basic genes revealed.This forced to allocate theservicing genesgroup different from HG.

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SPACE OF POSSIBILITIES FOR THE EVOLUTION FOR INFLORESCENCE OF *CYMBIDIUM* SW. AND *ACRIOPSIS* BL. (ORCHIDIACEAE)

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This study focuses on the analysis of the inflorescence's structure into Asians genera *Cymbidium* Sw. and *Acriopsis* Bl. The flowers may be arranged on the shoot in different ways and form fuzzy set. The inflorescences in subtropical and tropical zones have the character of the idioadaptation in contrast part of them areal. We traced the modes of transformation the inflorescence's structure based on the analysis of morphogenesis and modification variability in different environments. During morphogenesis, in structure of inflorescence arise polymorphism which promotes and divergence of taxa. As a result of our research, we came to the conclusion that the both genera have a common sequence of formation of the inflorescence' structure, however their development is stopped at different stages. The inflorescence's structure during morphogenesis have transformed in *Cymbidium* genus (single flower → monochasium → compaund monochasium → raceme) and in *Acriopsis* genus (single flower → monochasium → compaund monochasium → raceme → thyrs). Finally, we found what modus of the transformation of the inflorescence' structure are specific for the genus.

THE PRINCIPLE OF SIGNATURES IN BIOLOGY

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It is shown that both animals and machines can be included in the class of things a distinctive feature of which is the presence of control systems (Wiener, 1958). Later A.A. Lyapunov (1963) makes the logical conclusion that the management, based on the transmission of information, is an integral part of every activity, moreover, the management is a characteristic property of life in a broad sense. The main feature of living beings is their enormous complexity. All biological processes occurring in the organism, on the one hand, and carried out in its interactions with the environment of biogeocenoses, on the other, are correlated into a single system by the organism, which is the basic unit in the organic nature (Schmalhausen,1983). Thus biological evolution is a combined result of Darwinian natural selection and self-organization, in consequence of irreversible processes (Prigozhin, Kondepudi, 2002). The results of the processes of speciation, the formation of higher taxa and the forming of species complexes of biotic communities can be described through an elementary systems of signs of species. This description assumes evolutionary load, characterizing these processes as biological systems of different rank and different levels and planes of hierarchy. In the process of "analysis" by which population and coenotic matricies can determine the sequence of acting factors of the biogeocenosis, recognized not all of their pool, but only some of the signature. Organization of living beings on many levels based on the principle of signatures, according to which only one or some of the many features of any complex whole are used as information (Waterman, 1968). Under the signature comprehends the part of the characteristics of the various components involved in the integration of the entrance, law and outputs in a single whole. Conducted phenetic analysis of the painting signs mollusc's shells of Geophila order and simultaneously studied the structure of biodiversity of malacocoenoses biota of the Ural mountain country. Terrestrial molluscs, describing quite definitely biogeocenoses of the Urals as a typical mountain, at the same time largely reflect changes in the biodiversity of mountain ecosystems caused by anthropogenic pollution of the natural environment.

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THE GEOMETRIC PRINCIPLES AND MECHANISMS OF PROGRESSIVE SELF-ORGANIZATION FOR THE REPRODUCTION OF ONE'S SIMILAR

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Conclusions for or against can be described mathematically by 1 or 0, respectively, when the rounding-off rules have not remained an enigma in the cases of the selection. However, their Procrustean bed [1] usually eludes the disputants about the progressive or regressive self-organization in systems with random information transfer [2]. We would like to suggest in this connection that the rounding-off rules for the reproduction of one's similar are built into the domains of its becoming [3] and these rules may be achieved due to the mechanisms of natural percolation in the domains [4]. As a result, the laws of random geometry imply the progressive selection of childbearing in higher yield and protect the reactivity by the more complex self-organization of the cells. Notice that the rounding-off rules under consideration can come to light not only for the reproduction of one genetic line in chemical experiments [4], but also for the reproduction of more than 100 genetic lines in social experiments [5].

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MOLECULAR GENETICS AND MORPHOLOGICAL DIVERSITY OF *CANTHOCAMPTUS STAPHYLINUS* JURINE (HARPACTICOIDA, COPEPODA)

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Canthocamptus staphylinus (Jurine, 1820) (Harpacticoida, Copepoda, Crustacea) is widespread in Palearctic fresh water and rather well studied in the field of ecology and bioindication a modelling species. Wide circulation *C. staphylinus*, its high ecological plasticity, draw to it attention as possible group cryptical species. Besides, *C. staphylinus* is of interest, as one of the three species of harpacticoid (only in fresh water about 1000 species) for which duplication only females in without participation of males is installed, presumably parthenogenetically (Sarvala, 1979). The purpose of our work is revealing population distinctions among *C. staphylinus,* that recently, in connection with global audit of many species of crustaceans, is the actual problem.

In our investigation, genetics and morphometric variability of this species have been considered in common. For morphometric researches, we used males and females from eight European populations: Finland, Estonia, Switzerland and five populations from Russia. Thirty-two morphometric measurements and morphological characteristics were studied. And six of them proved to be reliable ($p<0.05$). The analysis has shown that populations differ by quantity of spikes on anal plate, by ratio of length furcal branches to their width, by ratio of spikes on the fifth pair legs and by sizes of a body.

For researches of molecular and genetic variability we used the results of sequencing mt (CO1) and nuclear (18s) DNA. The analysis of the phylogenetic trees constructed using the neighbor-joining algorithm with Tamura-Nei model indicates differentiation between geographically remote populations of C. staphylinus. Also, we are performing comparative microsatellite analysis using 11 different loci of DNA to study types of C. staphylinus reproduction. Molecular and genetic researches were conducted based on center of collective use of Institute of Biology Komi Scientific Centre Ural Branch of Russian Academy of Science. The study was supported by Russian Foundation for Basic research: 14-04-01149 A, 14-04-00932A.

EVOLUTION OF THE GENOME UNIVERSE

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Accumulations of thousands of complete genome sequences of diverse life forms allows us to reconstruct the evolution of the genome universe in unprecedented detail. The great majority of living cells and genetic material on earth belongs to prokaryotes (archaea and bacteria) and viruses. Comparative genomic analysis indicates that evolution in these major parts of the genomic universe is radically different from the traditional concepts of the modern synthesis of evolutionary biology. The genomes of prokaryotes and viruses are not stable “blueprints” of organisms but rather dynamic gene collections that at many stages of evolution rapidly gain and/or loose numerous genes. The rates of gene gain and loss in prokaryotes are high enough to justify the conclusion that these genomes primarily evolve not by Darwinian infinitesimally small changes but by much greater, at least gene-level steps. Furthermore, evolution by gene duplication that was described by Ohno and others as the central trend in the evolution of animals and plants contributes much less to than horizontal gene transfer and gene loss to the evolution of prokaryotes and viruses. Horizontal gene transfer is essential for prokaryotes to prevent accumulation of deleterious mutations and appears to be an evolvable, adaptive capacity as indicated by the discovery of dedicated gene transfer vehicles. Eukaryotes represent a distinct domain of the genome universe in which, after the founding endosymbiotic event, horizontal gene transfer was substantially curtailed although not eliminated. In eukaryotes, the role of horizontal gene transfer in eliminating deleterious mutations was taken over by sex whereas genome dynamics is maintained via extensive gene duplication and activity of mobile genetic elements. Viruses and related selfish genetic elements involved in arms races with their cellular hosts and played key roles in the evolution of life throughout its entire history.

HUMAN EVOLUTION IN THE LIGHT OF NEW ADVANCES IN PALEOANTHROPOLOGY AND GENETICS

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In the past few decades, major advances in genetics (including comparative genomics and paleogenetics) and numerous new fossils discovered by paleoanthropologists have added a lot to our understanding of human evolution, in line with Darwin's prediction that evolutionary theory "will throw much light on the origin of man and his history". Discovery of *Sahelanthropus*, *Orrorin* and *Ardipithecus*, together with the results of comparative studies of human, chimp and other primates' genomes, revealed important details of the earliest stages of hominin evolution. For instance, new paleoanthropological data demonstrates that both the transition to bipedality and the reduction of canines in males occured very early in hominin lineage. These and other traits suggest possible increase in male parental investment, transition to social monogamy, and an important role of sexual selection in shaping hominin morphology and social behaviour. In line with this possibility, comparative genomics revealed that human ancestors have lost some conservative regulatory regions of DNA, the function of which was to ensure the response of embryonic tissues to androgens, thus enhancing the development of some secondary sex characteristics which probably became disadvantageous in monogamous society. While geneticists have discovered a number of genes, mutations in which probably contributed to brain growth, paleoanthropologists have found numerous transitional fossils of australopithecines and early *Homo*, whose comparative morphology presumably suggests simultaneous parallel increase in endocranial volume in several distinct lineages (*H. habilis*, *H. rudolfensis*, and early *H. erectus*); another unexpected discovery is the astonishing variability of brain volume in early *Homo*. Major recent advances in understanding the later stages of human evolution, including the history of human dispersal out of Africa, rely to a large extent on the new field of paleogenetics, as exemplified by astonishing discovery of new hominin species, the Denisovans, based solely on the ancient DNA from scarce and morphologically uninformative bone remains. The discovery rate in human evolution studies is not showing signs of slowing down.

THE DEVELOPMENT OF THE BIOSPHERE OF THE STEPPE ZONE OF THE SOUTHERN URALS IN NATURAL AND ANTHROPOGENICALLY MODIFIED ENVIRONMENTS AND ITS PLANETARY VALUE

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Modern nature on the planet "Earth" develops without anthropogenic influence, and on the other - with different levels of its impact. To the greatest extent anthropogenically changed the biosphere. According to VG Gorshkov (1995) by the end of the twentieth century, the whole world remains unbroken 60% of the land in Russia - 65%, and in the United States - 4%. Anthropogenic influence inevitably increases. Most researchers talk about environmental security by protecting nature and the limitations of consumption beyond the economic capacity of the biosphere and must not be exceeded global stability threshold natural biota, which many believe has already been exceeded. We propose a solution to the problem arising ecological crisis, along with the strict nature protection, human involvement in the integrity of its development, increase productivity and biodiversity, taking into account their interests, increasing the economic capacity of the biosphere.

BIOLOGICAL SELF-ORGANIZATION IN TERMS OF PHYSICS

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Self-organization is observed in systems of different nature: physical, chemical, biological. The underlying mechanisms are often similar, what allows to treat them using common, synergistic, approach, but on the other hand, they are quite diverse. In the present talk I will first give examples of spatial-temporal patterns arising in different systems: Rayleigh-Benard cells in a heated liquid layer, Liesegang structures arising due to precipitation in a chemical reaction, Taylor vortices, a variety of patterns in the Belousov-Zhabotinsky reaction, various biological structures. General properties of systems in which phenomena of this kind are possible will be formulated. Then I will focus on living systems for which the ability to self-organization is one of the main distinguishing features. It comes out both at the level of an individual organism and at the level of biological communities. Vivid examples are morphogenesis of a multicellular organism and pattern formation in colonies of amoebae and bacteria. Biological morphogenesis, i.e. the emergence of new forms and structures, both in the individual development of an organism and due to interaction of communities of organisms, is a fundamental, but far from being solved, problem of the present-day biology. Certain progress, which has been achieved in recent years in understanding biological self-organization, is last but not least due to the use of physical and mathematical (synergic) methods of the theory of self-organizing nonequilibrium open systems.

TATA-BOX AS GENOME WIDE VARIABILITY VARIATOR

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Although variability (V.) is the evolution's basis, mutability is dangerous.Evolutionary progress includes a growth of the information matrix stability compensated by the growth of the V. of the access to information (*i* – the request [1]) and V. of the information realization (*iia* – combinatorial V.with different reversibility: from chromosomal rearrangements to recombinations; *iib* – V. of the gene coexpression; *iic* – within-individual V. [2]) [1]. C_v is suitable to any type of the V. Traditionally only *iia* and *iib* are developed in the theory of evolution standing on the specialized mechanisms of the genes interaction.The question of the signal that present in every gene, i.e. unspecialized signal, and might contribute to V. was not raised. It may be the TBP/TATA binding estimated by TBP/TATA-affinity, the– $ln[K_{TBP/TATA}]$,of any promoter region into -90 – -20 bp. Interaction between polymerase and DNA initiated by the TBP/TATA binding allowing to estimate both *I* and *iib*. Really, the larger is the $-ln[K_{TBP/TATA}]$, the more stable (and, *ceteris paribus*, the higher) the transcription. Transcriptomes of the yeast (stress by NaCl), Arabidopsis (miRNA of the morphogenesis management), human and mouse (brain expression according to Allen Brain Atlas) analyzed.The minor and the major clusters of genes revealed everywhere. The correlation coefficient *r* between C_v and– $ln[K_{TBP/TATA}]$ is reliable in both clusters but for yeast it significantly higher in the minor cluster (stress response genes but the major one are housekeeping and homeostasis genes), for Arabidopsis in the major cluster (the minor oneisath-miR-164 the only from an apical meristem), for human in the minor cluster (genes of the morphogenesis and reception; the major one included different other functions), similarly for mouse, but only the major cluster is possible to functionally annotate (like a human).

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TO SMALL POPULATIONS: ACCESS GRANTED YET DENIED?

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Although small populations (SP) are the forge of biodiversity [1], Haldane's dilemma completely devalues ones. The higher the number of genes under selection, the higher the death toll over a single generation. The reproductive reserve, which is, *ceteris paribus*, the smaller, the smaller the *Ne*, should compensate both cost of selection and accidental loss. In result, any growth in variability (mutability, norm of reaction, etc.) or accidental death (invasion of the novelty or even approaching the pessimal margin of the home econiche) are dangerous for SPs. Its long-term existence are possible only as a stasis. Optimally for SP to retreat in refuge – area optimality/stability of econiche – where enter into stasis. Being in stasis is time for adaptive and/or neutral storage of the (pre)adaptations for evolutionary revenge. Yet, Schmalhausen's stasis should demand a variability growth for at least enter [2] and Severtsov's stasis not so much for enter as for being [3]. In result, SPs must be useless for evolution in home and new econishes. However, data of the paleo and neontology shows otherwise. Moreover, MPs can successfully invade without the waiting of the preadaptations (Osborne effect). The new concept of stasis based on preventive adaptations (PAs) is suggested. In contrast to (pre)adaptations, PAs not counteracts with pessimal factors, but prevents any contact with them. Therefore, PA easily to produce (important for SP!) but hardly eliminate by selection. Eventually PA must become more sustainable than the protected traits of species and form possibility space for evolution locking species in refuges. But the only type of PA the stress can temporarily quench the phenotypic expression of the other PAs and ensure successful expansion of SPs even without preadaptations by *par force* evolution mechanism [4].

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EVOLUTION OF SOCIAL SYSTEMS: CONCEPTUAL AND METHODOLOGICAL PROBLEMS

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Many animal closely related species, similar in ecology and morphology, exhibit striking differences in social behavior and social organization. This evolutionary puzzle has a long history, but is far from being resolved despite the huge body of data accumulated. One problem is that studies of proximate mechanisms (behavioral, neuroendocrine, and genetic) underlying the variation in social systems have proceeded largely independently of analyses of ultimate explanations for social evolution. The other problem is that social behavior and social systems are complex multidimensional and dynamic biological phenomena difficult to describe and explain as a “whole”. Hence, distinct behavioral traits and patterns of social systems are usually studied as if they operate and are selected independently from each other. Finally, many social phenomena (e.g. “sociality” or “pairbond”) are poorly defined and still understood rather intuitively.

On a series of examples from mammals, I will demonstrate the drawbacks and advantages of various approaches to describe and explain the variation in social behavior and social organization between closely related species with the final call for an interdisciplinary approach that integrates studies of mechanisms and functions which is as old as the problem itself.

MICROEVOLUTION PROCESSES IN MICROBIAL-PLANT SYMBIOSIS

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Among the extensive scientific heritage of Nikolai Vladimirovich Timofeeff-Ressovsky papers devoted to the evolutionary process occupy main position.

Considering adaptation as a result of discrete changes in genotype, mutations on unit characters, he also recognized a limitation of this approach, noting "Behavior of *simply inherited* characters, usually monogenic in population. …. it is conflicts with the ever-increasing performance of a huge role in the evolution and selection of plants and animals"(1) The concept that we formulated about the integrated genetic system (MPS) of super-organismal formations (symbiosis) partly removes this contradiction (2).

In such a functionally integrated genetic system mutations on specific plant genes, which provide hosting of beneficial microorganisms, can lead to significant changes in adaptive capacity, because a host-plant comes into possession of thousands of genes of microsymbionts, able to rapid change in the genetic characteristics for the purpose of surviving in a complex system of soil-plant-soil.

Mutation process induced in the population of microorganisms prior to penetration of the host tissue provides the colonization ability of nodule bacteria cells. With a certain degree of conventionality this can be considered as a model of microevolution changes in which Timofeeff-Ressovsky emphazised the following elements: the mutation process, population waves, isolation and natural selection (1).

During the process of colonization of the rhizosphere the mutation process in microsymbionts sharply accelerates, exceeding a frequency by several orders of magnitude in non-symbiotic bacteria partially at the expense of suppressing the processes of reparation, further plant carries out the selection of individual cells, which penetrating into the plant are able to breed (population waves), and these populations are exposed to isolation inside the plant. As a result composition of nodule population is significantly differs from that in the soil, which corresponds to the concept of "elementary evolutionary phenomenon"(1).

Nowadays we know that recombination also plays a very important role in symbiosis, therefore it could be appropriate to add also about the activation of recombination processes in microsymbionts, for example frequencies of plasmids transfer increase enormously – it is shown for rhizobia and PGPR. Due to the clonal population structure the recombination processes for bacteria are more important than for higher organisms, as bacteria can get entirely new genes and fix them in the genome, which is restricted for higher eukaryotes.

So it becomes clear, that plant genes that direct operational (or adaptive) evolution of the nodule bacteria are of considerable interest for understanding the micro-evolutionary processes as well as for developing more effective microbial-plant systems.

In the presentation by the example of signaling genes determining the process of recognition between bacteria and plants bacterial signal receptors will be considered as well as their allelic diversity in populations of legumes, docking mechanisms of signaling molecules and other issues of the symbiotic systems evolution. You can take a fresh look at the interaction of gene-on-gene: it is not limited to a specific pair of signal-receptor (which is more typical for the pathogens). Microevolution in the symbiosis systems leads to co-adaptation of extensive gene complexes of the partners.

Modern views on symbiogenesis allow us to extend the statements of the doctrine of Nikolai Vladimirovich not only on long processes of speciation, but also on the processes leading to microevolutionary transformation within a host generation, moreover - this process turns out to be controlled by a system of symbiotic genes of the host, so microevolution processes become "working tools" of the ecologically obligate adaptations.

PAPERS
BY YOUNG SCIENTISTS

ASSOCIATION BETWEEN METABOLIC SYNDROME AND GENE POLYMORPHISM IN BELARUSIAN POPULATION

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Metabolic syndrome (MS) is regarded now as a public health problem. Its prevalence and morbidity in developed countries rises each year. MS refers to a combination of metabolic, hormonal and clinic abnormalities, based on insulin resistance, compensatory hyperinsulinemia and cardiovascular disorders [1]. The International Diabetes Federation requires as a mandatory criterion of MS the presence of abdominal obesity plus 2 any criteria: high level of triglycerides (> 1.7 mmol/L), reduced range of HDL-Cholesterol (<1 mmol/L in men and <1.3mmol/L in women), high systolic and diastolic blood pressure (≥130/85mmHg), high fasting plasma glucose (≥ 100 mg/dL) or type 2 diabetes [2]. Testing of gene polymorphisms that determine genetic predisposition to MS developing may enable an early identification of risk groups to perform preventive measures in a timely manner, to improve treatment effectiveness, to avoid complications, as well as to cut down the treatment costs. The aim of the present study was to determine the association of *ACE, BDKRB2, UCP2, TCF7L2, PPARG* gene polymorphisms with MS in Belarusian population.

Materials and Methods

A total of 121 patients (58 women and 63 men) with MS were included in this study. The control group consisted of 362 randomly selected Belarusians. All gene polymorphisms were determined using polymerase chain reaction with specially designed allele specific primers. The statistical analysis was performed using STATISTICA 10 for Windows (Statsoft Inc., USA). Differences were considered significant at $P<0.05$.

Results and Discussion

The distribution of genotype and allele frequencies of analyzed gene polymorphisms in control group and patients with MS are presented in Table 1. Pearson's chi-square test (χ^2) was used for comparison of the distribution of genotypes and alleles between tested groups.

The genotypes and alleles distribution of *ACE I/D* polymorphism in group of MS patients differs significantly from that observed in control group ($\chi^2=6.62$ and $\chi^2=5.66$, respectively, $P<0.05$). The presence of *D* allele increases the risk of MS in 1.4 times (95% CI 1.06-1.92).

The analysis of the presented data did not reveal statistically significant difference in the genotype frequencies of *I/D* polymorphism of *BDKRB2* gene. At the same time the risk of MS was significantly higher for *I* allele careers (OR=1.35 95% CI, 1.01-1.82). We have also shown that the risk of MS is much higher for carriers of *Ala/Ala* genotype of *UCP2* gene and *C/T* genotype of *TCF7L2* gene (OR=1.81 and OR=2.08 respectively, $P<0.05$).

The second aim of this study was to reveal association between gene polymorphisms and biochemical parameters in blood of MS patients. For all patients, ranges of triglycerides (TG), total cholesterol (CH), creatinine (Cr), total bilirubin (B), alanine transaminase (ALT), aspartate transaminase (AST) and urea (Ur) were measured. Body mass index (BMI) was also included in the analyze. The Kruskal–Wallis analysis was used for comparison of biochemical parameter levels in patients depending on the genotypes. Statistically significant association between analyzed gene polymorphisms and biochemical parameters was not revealed.

Table 1. Genotype and allele frequencies of analyzed gene polymorphisms in the control group and in the patients with MS

Gene, Polymorphism	Genotype, Allele	Frequency %		χ^2	P value	OR (95% CI)
		MS, n=121	Controls, n=362			
ACE *I/D*	*D/D*	33.1	26.0	6.62	**0.04**	1.41(0.90-2.20)
	I/D	53.7	50.3			1.15(0.76-1.73)
	I/I	13.2	23.7			0.49(0.27-0.87)
	D	59.9	51.1	5.66	**0.02**	1.43(1.06-1.92)
	I	40.1	48.9			0.70(0.52-0.94)
BDKRB2 *I/D*	*D/D*	15.7	22.7	3.97	0.14	0.64(0.37-1.10)
	I/D	47.9	48.9			0.96(0.64-1.45)
	I/I	36.4	28.5			1.44(0.93-2.22)
	D	39.7	47.1	4.04	**0.04**	0.74(0.55-0.99)
	I	60.3	52.9			1.35(1.01-1.82)
UCP2 *Ala/Val*	*Ala/Ala*	38.8	26.0	7.33	**0.03**	1.81(1.17-2.80)
	Ala/Val	43.8	54.1			0.66(0.44-1.00)
	Val/Val	17.4	19.9			0.85(0.49-1.45)
	Ala	60.7	53.0	4.35	**0.04**	1.37(1.02-1.84)
	Val	39.3	47.0			0.73(0.54-0.98)
TCF7L2 *C/T*	*C/C*	47.9	65.7	12.76	**0.002**	0.48(0.32-0.73)
	C/T	44.6	27.9			2.08(1.36-3.19)
	T/T	7.5	6.4			1.18(0.53-2.64)
	C	70.2	79.7	9.24	**0.002**	0.60(0.43-0.84)
	T	29.8	20.3			1.66(1.20-2.31)
PPARG *Pro/Ala*	*Pro/Pro*	78.5	74.3	1.19	0.55	1.26(0.77-2.07)
	Pro/Ala	19.8	22.7			0.84(0.51-1.41)
	Ala/Ala	1.7	3.0			0.54(0.12-2.45)
	Pro	88.4	85.6	1.20	0.27	1.28(0.82-2.00)
	Ala	11.6	14.4			0.78(0.50-1.22)

The Kendall's tau (τ) coefficient was used to evaluate the correlation between genetic and clinic-biochemical parameters of MS patients (Table 2).

Table 2. Association between genetic and clinic-biochemical parameters of MS patients

Parameters		B	Cr	Ur	AST	ALT	CH	TG	BMI
ACE *I/D*	τ	0.106	0.053	-0.009	0.010	-0.009	-0.101	-0.017	0.094
	P	0.112	0.474	0.889	0.878	0.888	0.098	0.781	0.125
ENOS *G/T*	τ	0.022	-0.048	0.024	-0.115	-0.019	-0.017	-0.037	-0.118
	P	0.747	0.518	0.722	0.086	0.780	0.779	0.544	0.055
BDKRB2 *I/D*	τ	0.064	0.061	0.010	-0.001	-0.066	-0.052	-0.084	-0.049
	P	0.341	0.412	0.882	0.991	0.327	0.400	0.171	0.426
MB *A/G*	τ	0.063	0.001	0.083	0.034	-0.035	-0.109	-0.057	0.107
	P	0.343	0.988	0.217	0.614	0.607	0.074	0.355	0.081
UCP2 *Ala/Val*	τ	0.021	0.005	0.032	**0.155**	0.102	0.078	0.066	0.045
	P	0.757	0.944	0.628	**0.021**	0.130	0.202	0.284	0.469
TCF7L2 *C/T*	τ	0.015	0.047	-0.048	0.073	**0.173**	0.098	0.011	**0.137**
	P	0.828	0.533	0.481	0.275	**0.010**	0.109	0.853	**0.026**
PPARG *Pro/Ala*	τ	0.124	-0.08	0.122	0.073	0.072	0.099	**0.132**	0.037
	P	0.064	0.279	0.071	0.279	0.283	0.104	**0.031**	0.542

Statistically significant correlation at $P<0.05$ is highlighted in bold.

The observed correlation was weak, but it may be explained by the quantity of analyzed individuals, which is insufficient for achieving statistical power. Further analysis of association of clinic-biochemical parameters with gene polymorphisms predisposing to MS is required.

Conclusion

This study clearly indicates that tested polymorphisms of *ACE, UCP2, TCF7L2, BDKRB2* genes play the important role in predisposition to metabolic syndrome. Screening of these polymorphisms may enable early revealing of population groups with increased risk of MS.

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PRION FORM OF THE SUP35 PROTEIN [PSI+] MAY HAVE A ROLE IN CONTROL OF GENOME STABILITY IN YEAST *SACCHAROMYCES CEREVISIAE*

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Prions are the infectious forms of normal proteins which have modified tertiary structure. They have the ability to self-propagationthrough converting the normal protein molecules into the prion form. The prions are responsible for many neurodegenerative diseases such as Alzheimer's (AD), Parkinson's, Huntington's and Lou Gehrig's. There were also noted the increased frequency of genome instability in the neurons from the patients suffered from the neuromental diseases caused by prions. In the case of AD, a tenfold increase was observed in the level of aneuploidy for chromosome 21 in brain sections subjected to neurodegeneration [1]. In yeast *Saccoromyces cerevisiae* the prion [PSI+], the research model of mammal prions, is the prion form of translation termination factor Sup35. The sup35 mutants were obtained and investigated. The majority of the mutants showed chromosome instability [2]. It could be the prions may cause neurodegenerative symptoms by increasing genome instability. But the association of the prion formation and the mutagenesis haven't been investigated yet.

Material and Methods

The strains with prion [PSI+] and with the normal conformation of the Sup35 were investigated in the alpha-test. The alpha-test is a convenient test-system in yeast *Saccharomyces cerevisiae* allowing calculation the frequency of high range of genetic changes in one experiment. In the alpha-test the following genetical events could be counted: the loss of chromosome, gene mutations, gene conversion, loss of the chromosome arm and recombination. The model of the alpha-test is based on the mechanism of mating type switching in heterothallic strains *S.cerevisiae*[3].The mating type is regulated by the *MAT* locus located on the chromosome III and represented by two allels - *MATa* and *MATalpha*, that determinate the mating type a and alpha correspondently. Only cells with opposite mating type can mate. The changes in the genetic material interfering the expression of the MATalpha result in switching of the mating type α→a. It allows hybridization with other cells having mating typealpha. That's why any appearance of the hybrids in the mixture of two yeast strains with the same alpha-mating type evidence, that one of the parents of the hybrids have acquired a-mating type. Using special strains in the alpha-test we can score the general level of genome instability as well as molecular nature of genetic changes caused by different mutagens.

Results

Yeast strain with the prion form of the Sup35 protein showed two-fold decrease in the frequency of "illegitimate" hybridization. Prionization of the Sup35 protein does not affect normal mating between strains of opposite mating type.

Table 1. The frequency of "illegitimate" and "legitimate" hybridization.

Strain	The frequency of "illegitimate" hybridization (*10^{-6}) (median an conf. interval)	The frequency of "legitimate" hybridization (*10^{-2})(median an conf. interval)
[PSI+]	3,06 (2,63-3,59)	7,6 (5,1-10,4)
[PSI-]	6,1 (5,76-7,2)	6,1 (4,5-8,8)

We also investigate the hybrids phenotype. The [PSI+] strain represents the 2-fold lower frequency of chromosome loss and gene mutations, and 5-fold increased frequency of gene conversions. The canavanine test also showed double decrease of mutation frequency in the strain carrying the prion.

Conclusions

We investigated the effect of the [PSI+] prion on the genome stability. Surprisingly the [PSI+] reduces the frequencies of both mutations and chromosome loss, it also increases the frequency of gene conversions. The mechanism of the influence remains unknown. Such a complex effect might be caused by proteome changes due to translation termination failing and reading through stop-codons. There is also evidence that Sup35 participates in chromosome segregation [1]. Our results are supported by previous findings. The role of prions in genome stability needs further investigation.

This investigation was supported by the RFBR grants of #15-04-08625.

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INDUCTION OF GENOMIC INSTABILITY ON THREE GENERATIONS OF MICE IRRADIATED BY INFRARED LIGHT

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In the last time, the phenomenon of adaptive response (AR) has attracted considerable attention of investigators. It is considered as a form of cell defense from mutagenic action of different factors. Therefore the search for adaptogens of physical and chemical nature which are able to transform the organisms to a new adapted state similarly as low doses is an actual problem. Various devices, based on the action of electromagnetic waves of the infrared subspectrum are currently used in clinical practice. Previously, in our experiments it was shown that exposure of mice to infrared light (IRL) as well as low doses of X- and γ-rays, induced AR in bone marrow cells, remained unchanged thymus weight after irradiation with a challenging dose (1.5 Gy) and decreased tumor growth rate. One more feature of the effect of ionizing radiation small doses is the genetic instability in offspring. This phenomenon consists essentially in changes in the properties of the descendants of irradiated parents. Genetic instability has been carefully studied as on cultures of cells in vitro and as on animals in vivo. However, we have insufficient experimental evidence on this phenomenon in descendants whose parents were exposed to non-ionizing radiation in vivo.

In view of this, the aim of the present work was to investigate the biological action of IRL (850 nm, 101 Hz, 22 mW/cm^2) on the induction of adaptive response in hemopoietic organs (the bone marrow and thymus) and the rate of Ehrlich carcinoma growth on the mice offspring (F_1, F_2 and F_3).

Materials and methods

In our investigations we used three generation of the white mongrel SHK male mice exposed to ionizing or non-ionizing radiations. Parents were exposed to infrared light from a light therapy device at wavelengths 850 nm modulated by a frequency of 101 Hz for 10 min or to a dose of 0.1 Gy of X-rays. To obtain the first-generation offspring (F1), irradiated male mice were mated with non-exposed females 15 days post-irradiation. F2 and F3 offspring of male mice were produced from the random mating of male F1 and F2 mice with control females. Two- to three-month-old male offspring of irradiated and unirradiated parents were additionally irradiated with a dose of 1.5 Gy of X-rays. Another group of male offspring of irradiated and unirradiated parents were exposed to X-rays by the scheme of adaptive response: an adapting dose of 0.1 Gy followed a day later by a challenging dose of 1.5 Gy. Each experimental point was obtained using no less than five mice. The level of cytogenetic damage was assessed in bone marrow cells using a micronucleus test. The weight of the thymus was determined from the ratio of the average weight of the organ to the average weight of animals in the group. The influence of the adaptive exposures on the tumor growth was estimated by measuring the size of the tumor at different times after the inoculation of ascitic cells into the femur.

Results and Discussion

As can be seen from fig.1, in F1, F2 and F3 generation of mice from irradiated males, the radiosensitivity lowered, and the induction of adaptive response did not took place. Thus, the level of spontaneous damage was identical in descendants from both irradiated and unirradiated males.

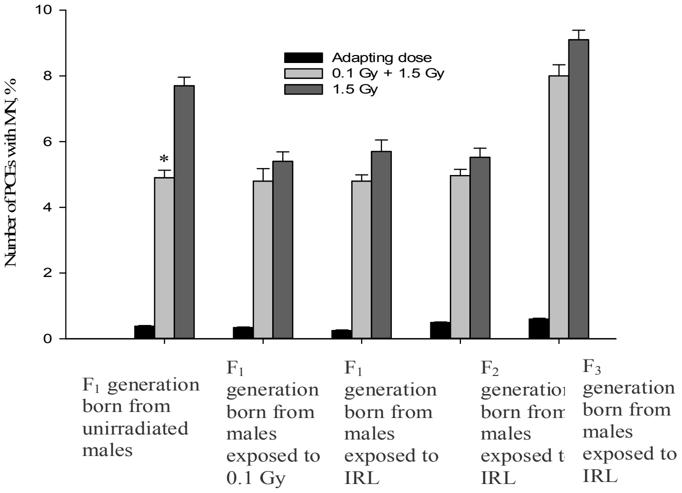

Fig. 1. Yield of polychromatophil erythrocytes (PCEs) with micronuclei (MN) in bone marrow cells in F_1, F_2 and F_3 generation born from male mice exposed to IRL or 0.1 Gy and subsequently irradiated by the scheme of adaptive response (0.1 Gy + 1.5 Gy of X-rays)

The fig.2 shows the dependence of the thymus weight in F_1, F_2 and F_3 generation of mice born from males exposed to infrared light or 0.1 Gy and subsequently irradiated by the scheme of adaptive response. It can be seen that the thymus weight in generations decreased to that in mice exposed only to a dose of 1.5 Gy. I.e., this criterion is not observed induction of adaptive response, in contrast to generation from unirradiated animals.

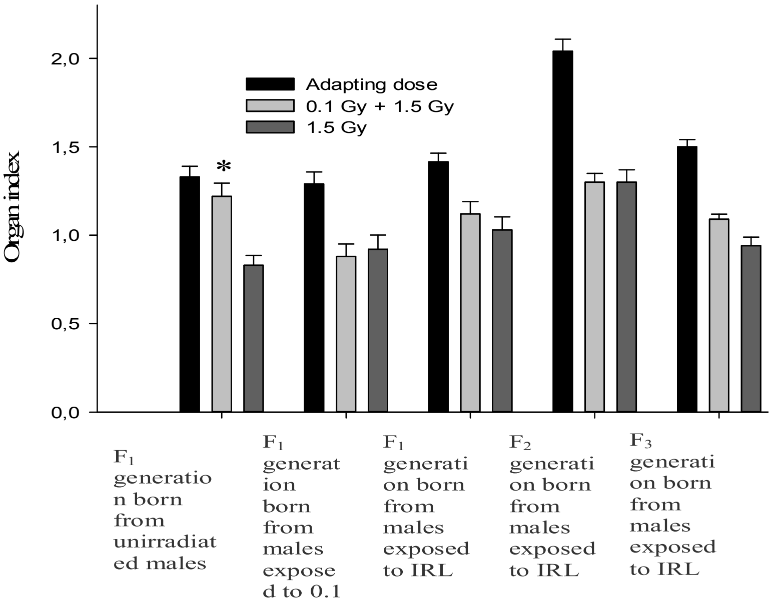

Fig. 2. Dependence of the thymus weight in F_1, F_2 and F_3 generation of mice born from males exposed to infrared light or 0.1 Gy and subsequently irradiated by the scheme of adaptive response

In fig.3, the results on the dynamics of the growth of Ehrlich carcinoma in F_1, F_2 and F_3 generation from male mice exposed to infrared light or 10 cGy of X-rays. The growth rate of a tumor in all generations did not differ from that in control mice.

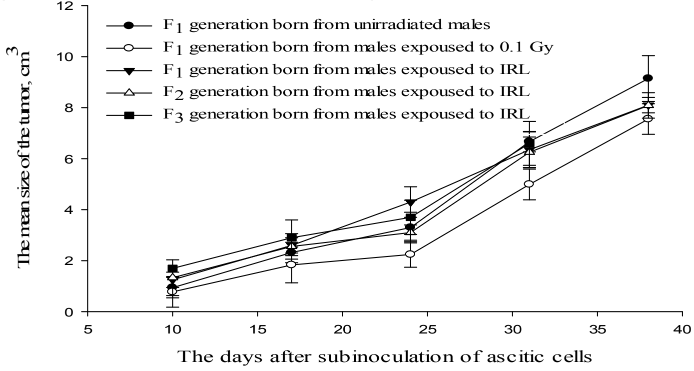

Fig. 3. Dynamics of the growth of Ehrlich carcinoma in F_1, F_2 and F_3 generation born from male mice exposed to infrared light or 0.1 Gy of X-rays

Conclusions

Our investigation of three generations from males irradiated by IRL or X-rays demonstrated that: the level of spontaneous cytogenetic damages did not differ from that of unirradiated mice, the radiosensitivity decreased, no AR takes place, the thymus weight decreased and the tumor growth rate did not differ from that of the unirradiated males offspring. So our experimental data demonstrate the genomic instability on offspring from mice exposed to the low dose ionizing and non-ionizing radiations in at least three generation. For detection of genomic instability in descendants it is necessary to use different tests.

Acknowledgements

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DISPLAY OF GENETIC INSTABILITY OF CELLS IN THE POPULATION OF *CHLORELLA VULGARIS* AFTER SPARSELY AND DENSELY RADIATION EXPOSURE

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The character of gamma-radiation impact depends on the energy of the gamma-ray irradiation and the spatial characteristics of exposure both external and internal. Densely radiation, characterized by higher values of linear energy transfer (LET) is more effective in many respects [3, 7]. Cells survived after irradiation generate defective offspring which is the cell clones with altered heredity, increased mortality and violation of the vital functions. Delayed effects of colonies formation are well studied in different cell lines, but there's few data concerning genetic instability after exposure to ionizing radiation on plants.

That is why it was interesting to explore the viability of Chlorella cells irradiated in various stages of growth with ^{60}Co gamma-rays (LET = 0,2 keV/m) and ^{239}Pu alpha-particles (LET = 125 keV/m) and to study the delayed effects of colonies formation that determine the genetic instability of the studied cells.

Materials and Methods

Test organism and culture conditions. Chlorella vulgaris has been chosen as an experimental organism due to the advantages of this unicellular green alga: 2-10 microns size in diameter makes it easy to observe this object by light microscopy. Chlorella multiplies rapidly through autospores 1-6 times per day [1]. Chlorella is a convenient object for biological monitoring of natural ecosystems [4, 5], since it has a wide habitat and is present both in water and soil.

Chlorella cells are characterized by several types of inactivation: 1) death of the young cell without growth stage immediatly after irradiation; 2) death after increasing of cell volume up to the volume of mother cells and even more - in this case the outlines of autospores could be visible in the cells. [6]; 3) the cell can demonstrate several cycles of reduplication with producing of pathological microcolony. Microcolony method helps to estimate the dose-rate dependence on development of different types of inactivation of Chlorella sells [2].

Cultivation of Chlorella was carried out on the liquid Tamiya medium (50%) which contains KNO3 – 5.0; MgSO4 x 7H2O – 2.5; KH2PO4 – 1.25, FeSO4 – 0.003 g/l. It is known that this nutrient medium is more suitable for protococcal algae, such as Chlorella [3].

Under optimum conditions, cell culture reaches the stationary growth phase on the 8th day, followed by gradual deceleration of the growth efficiency.

Cells were irradiated with ^{60}Co gamma-rays (LET = 0,2 keV/m) and ^{239}Pu alpha-particles (LET = 125 keV/m) in the following manner: one drop of the suspension (0.1 ml) in concentration of 106 cells/ml (number of cells was calculated in the Goryaev chamber) was placed on the nonnutrient agar surface with the following evaporation of the liquid part of the medium, and after that the remaining cell monolayer was exposed to radiation.

Effect of radiation was evaluated by survival rate and by cell inactivation types. The survival rate was determined through estimation of number of cells with retained reproduction ability in comparison with control sample.

Research results

Fig. 1 represents dose-survival curves of Chlorella cells irradiated in the logarithmic phase of growth with gamma rays (curve 1) and alpha particles (curve 2). Evidently that the survival of chlorella irradiated by alpha particles is lower than the survival of cells exposed to the same dose of gamma rays. Since the survival curves after both types of radiation are exponential, we can conclude that the relative biological effectiveness (RBE) does not have any dependence on the survival rate at which it was calculated. In this case, the relative biological effectiveness of alpha radiation is 3.

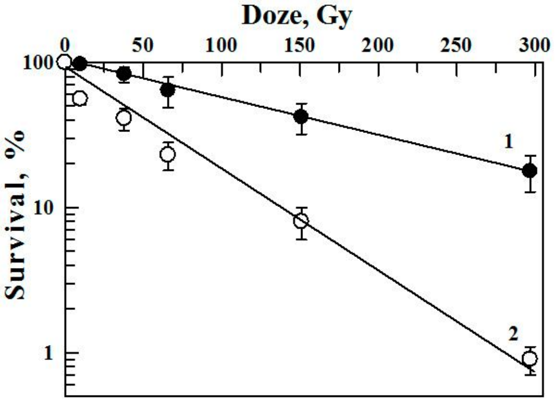

Fig. 1. Chlorella cells survival after irradiation by gamma rays (curve 1) and alpha particles (curve 2). X-axis – dose (Gy), Y-axis – survival (%).

Furthermore, different types of cell death were found – without division, and after the first or second division. The proportion of inactivation types varied with irradiation dose increasing. Thus, cell death after the second division dominated at the dose range of 10-50 Gy while without division death was generally observed at doses of 100 to 300 Gy.

At the next step the study of the delayed effects of colonies formation was conducted. Fig. 2 demonstrates the dependence of the delayed effect of colonies formation of chlorella cells after gamma irradiation. The number of colonies was counted right after 24, 48, 72, 96, 120, 144 hours after irradiation. We can see that the number of later formed colonies increases with increasing dose (Fig. 2, left).

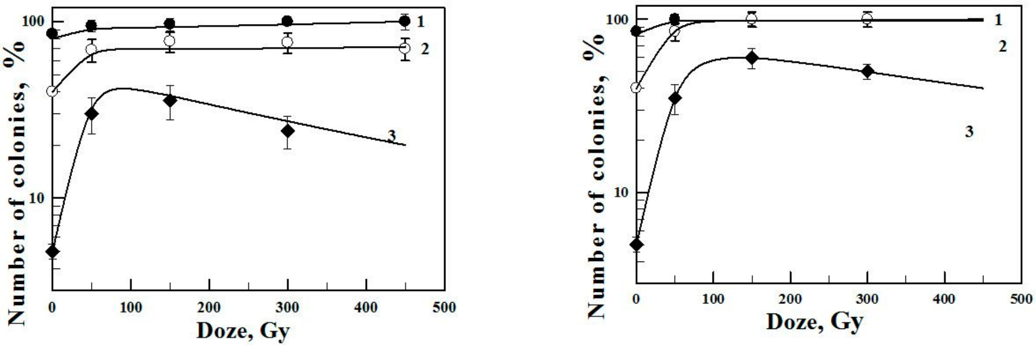

Fig. 2. Dependence of the delayed effects of colonies formation of chlorella cells of gamma-irradiation (left) and alfa-irradiation (right). Curve 1 – the number of colonies obtained after 36 hours of growth, curve 2 – the number of colonies obtained after 48 hours of growth, curve 3 - the number of colonies obtained after 96 hours of growth.

Fig. 3 (right) shows that the doses ranging from 50 Gy to 100 Gy do not reduce the survival of the unicellular algae population by 50%, but induce a large number of sublethal injuries. As a result, the number of growing colonies is significantly different from number of control cells, especially in the later stages. The doses ranging from 350 to 450 Gy generate so mass injuries that the growth of cells is almost completely inhibited within two days after exposure.

Taking into account the time required to repair cells from sublethal injuries, it may be noted here that after 48 hours delayed effect of colonies formation is most intense, hence the cells need at least two days to activate the repair and error-correcting systems. However, after 72 hours the cells grown intensity decreases again, which means the heterogeneity of cell population: the same cells require different recovery time.

Thus, the duration of the cell recovery after sparsely irradiation is equal to the duration of the cell recovery after densely irradiation and requires 48 hours.

After 72 hours the colonies growth decreases linearly with time and is the lowest after 96 hours, whereas under the action of gamma radiation colonies formation was observed even after 72 hours. So, densely radiation produces more injuries per dose unit.

After densely radiation exposure the number of cells which are able to colonization is reduced due to the large number of cells dying "under the beam".

Thus we have shown that RBE of densely radiation for Chlorella is equal to 3. After irradiation with alpha particles the number of cells dying without division, increases sharply with increasing dose, and it is higher than after gamma-rays irradiation.

Delayed effects of colonies formation, characterizing genetic instability, are observed both after sparsely and densely irradiation, but with different doses that induce the greatest damage: it is within the range of 50 - 100 Gy for gamma-irradiation and 20 - 50 Gy for alpha-irradiation. Minimal duration of the cell recovery is the same and requires around 48 hours. At the same time densely radiation causes more injuries per dose unit, so the cells which are capable of restoring demonstrate the colony-formation within 48 hours after irradiation.

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THE RESEARCH OF THE PHENOMEN OF CO-MUTAGENESIS UNDER IONIZING RADIATION

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The impact of co-mutagens on the realization of radiation-induced genetic damage in human cells is an important research topic in radiobiology nowadays. A phenomenon of co-mutagenesis can be observed when the substances without an own mutagenic activity are able to significantly modify, namely amplify, the effects of the environmental mutagens [1, 2]. Some of the medical compounds, such for instance, ascorbic acid (AA), which is designated as "signal molecule causing specific activity in cells" [3], verapamil (V) being blocker of calcium channels [4] etc were recently shown to be dangerous co-mutagens.

Materials and Methods

Venous blood donors has been cultivated by semi-micro method with some modifications during 52 hrs [5]. Peripheral blood lymphocytes (PBL) culture has been exposed to radiation in G_0- period of cellular cycle on X-ray unit "RUM-17", range of studied doses 0,3 and 2,0 Gy. As modifier of radiation effect, AA has been used, which was introduced in PBL culture right after exposure to radiation in the range of concentrations 20,0-80,0 µg/ml of blood, V - in the range of concentrations 1,5-4,0 mg/ml). Metaphase analysis of cells has been carried out in the first postradiation mitosis.

Results and Discussion

Our studies for the first time showed the effect of co-mutagens AA and V on the formation of radiation-induced chromosomal rearrangements in human nonmalignant somatic cells and the dependence of co-mutagenesis on the ionizing radiation (IR) dosage and concentration of co-mutagenes. In Fig.1 formation of co-mutagenic effect of AA and V depending on radiation dose, concentration of co-mutagense is showed most illustratively. The obtained data indicates that V (4,0 mg/ml) exhibits co-mutagenic effect with low doses of IR (0.3 Gy) potentiates damaging effect of radiation due to increase of overall frequency of chromosome aberrations in ~ 1.5 times compared with effect of exposure to radiation. Co-mutagenic effect of V has formed due to radial markers.

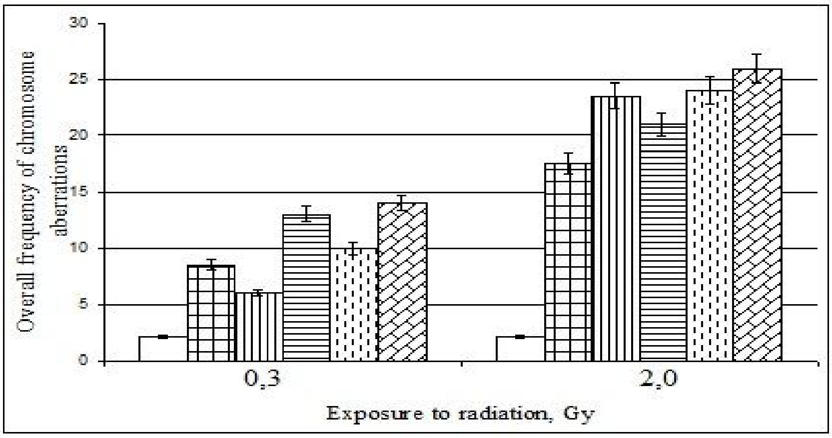

Fig.1. Overall frequency of chromosome aberrations in PBL culture under combined effect of IR (0,3-2,0 Gy) and co-mutagens (AA (20,0-80,0 µg/ml) and V (1,5-4,0 µg/ml). ☐ – control, ▦ - exposure to radiation, ▥ - exposure to radiation + AA 20,0 µg/ml of blood, ▤ - exposure to radiation + AA 80,0 µg/ml of blood, ⬚- exposure to radiation + V 1,0 мg/ml of blood, ▨- exposure to radiation + V 4,0 мg/ml

At exposure to radiation of PBL in low dose (0,3 Gy), AA in concentration (20,0 µg/ml of blood) shows radioprotective effect, which becomes apparent in decrease of overall frequency of chromosome aberrations compared with effect of radiation alone(Fig.1). AA in concentration (80,0 µg/ml of blood), increases overall frequency of chromosome aberrations compared with effect of exposure to radiation in low dose (0,3 Gy) in 1,4 times. At exposure of cells to radiation in relatively high dose (2,0 Gy), co-mutagenic effect of AA and V is kept in the range of used concentrations, increasing on average frequency of chromosomal aberrations rearrangements of chromosome type. Since exposure to radiation along with chromosome breaks can induce pre-mutative potential changes in them, additional effect of co-mutagens in high concentration may contribute to their realization in structural rearrangement of chromosomes, including due to suppression of reparation enzymes [6].

Conclusion

Formation of co-mutagenic effects of some drugs in irradiated human cells depends on their concentration and radiation dose. On chromosomal level human somatic cells established phenomenon of co-mutagenesis by the combined action of radiation and co-mutagenes verapamil, ascorbic acid *in vitro*. The obtained results should be taken into account during the development of medical prescriptions containing co-mutagene compounds for individuals occupationally exposed to IR.

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TOXICITY ASSESSMENT OF NATURAL WATERS NEAR THE LOCATION OF RADIOACTIVE WASTE DISPOSAL BY THE METHOD OF ALLIUM-TEST

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Currently, nuclear energy is one of the most promising sources of energy. Lately sharply increased not only scales, but also the sphere of use of sources of ionizing radiation. In this regard, the problem of radiation safety attracts attention of many people and creates the need for radiation monitoring in the vicinity of the nuclear industry.

Monitoring - a process of systematic or continuous monitoring and gathering information about processes, objects, phenomena, with a view to further evaluation and monitoring. The tasks of the radiation monitoring includes monitoring the state of the environment, identification and prediction of adverse changes, environmental security, and a socially acceptable level of radiation effects on people and the environment in the areas of influence of the enterprises and organizations of the nuclear-industrial complex (NPC) [1]. There are various approaches to solving such problems. In addition to traditional physical and chemical methods for environmental assessment are very popular biological control methods, based on the response of living organisms.

One of these methods is Allium - a test that allows to determine the toxicity of the environment on biological indicators onion (Allium cepa) [2]. This technique is widely used in European countries to assess the toxicity of chemicals and complex wastewater pollution. It is known that the method Allium - test was used to assess the toxicity of the soil from the area of the accident at the Chernobyl nuclear power plant, as well as to assess the cyto - and genotoxicity of surface water in the area of radionuclide anomalies, formed as a result of an underground nuclear explosion in the north of the Perm region [3]. This line of research is a priority and recommended by the International Committee on Radiological Protection.

The aim of our work was the study of the response of biological systems to radiation exposure and assessment of the applicability of the methodology Allium - the test in practice, radiation monitoring.

Materials and Methods

The studies were conducted on the basis of teaching and research in the area of a polygon placement of radioactive waste (RW) SSC RF - IPPE [6, 7].

Water sampling for biological testing was conducted in accordance c landscape-geochemical features of the terrain. To assess the potential biohazard water samples from two control wells in store: well №4, №7 wells and wells №10, as well as a stream originating in the territory of the repository. A control sample was used to defend the tap water. Testing was conducted in natural waters triplicate. Water samples were taken for testing in May, July and October 2013.

Radiochemical analysis data indicate the presence of the tested water samples β-radionuclide 90Sr. The highest content of strontium observed in the water from the well №4 (from 22 to 40 Bq / l). The content of radionuclides in natural waters outside the repository (the creek and swamp) varies seasonally (ranging from 3 to 16 Bq / l). The level of radioactivity in the water from the well №7 is not significant (less than 0.15 Bq / l) at all times sampling.

Test system for studying the biological effects induced component composition of water samples were selected root meristem cells of onion (Allium cepa, grade

Shtutdgarter Risen). The bulbs are approximately the same weight (2.5-3 g) and size (1.8-2.2 cm) was placed in a plastic cuvette with the test water for 72 hours for germination, so that water is only concerned collum bulbs. This time is sufficient to start the growth of adventitious roots and start the process of active cell division. At the end of the test roots 1.5-2.0 cm long were fixed in acetoacetyl alcohol. Common methods used cooking squashed preparations, cell staining was performed atsetoorseinom. In each embodiment 15 bulbs used [8].

As analyzed indicators were selected mitotic index of root meristem cells and accounting with chromosomal aberrations at the stage of ana-telophase [9].

Results and Discussion

According to the results of bioassay toxicity was evaluated in natural waters. The cytotoxicity of water (Figure 1) was characterized in terms of the mitotic activity of the cells of the root meristem. Genotoxicity - in terms of frequency of aberrant cells (Figure 2).

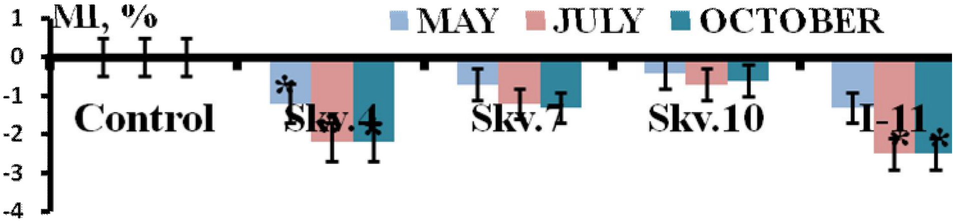

Figure 1 Results of the cytotoxicity of water samples from the area of regional radioactive waste storage Obninsk. The abscissa indicated sampling time, and the ordinate - mitotic index%.

Presented in Figure 1 data show that water samples from monitoring wells storage, as well as surface water in close proximity to it, inhibit the activity of cell division in the root meristem. However, a significant decrease in the value significantly mitotic index in onion rootlets recorded using water from wells 4 and surface runoff. These data are consistent with the results of radiological monitoring.

When considering the distribution of dividing cells on the main phases of mitosis, we have not found significant differences between the control and experimental options. Therefore, this indicator is not informative.

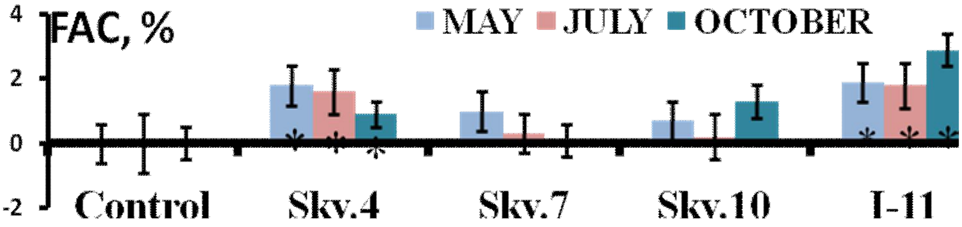

Figure 2 Results of the genotoxicity of water samples from the area of regional radioactive waste storage Obninsk. The abscissa indicated sampling time, the vertical axis - the frequency of aberrant cells%.

Percentage of formation of aberrant cells for testing water from wells 4 and surface runoff is 2 times higher than in the controls, and other water samples. This confirms and genotoxic effect. This result is recorded in different periods of sampling.

A more detailed analysis of the results of the evaluation of genotoxicity of water we have characterized the contribution of different types of fixed aberrations. The results of the analysis are shown in Figure 3.

The spectrum observed chromosomal aberrations represented mainly chromatid forms of impairment (bridges and fragments), the presence of genomic disorders (lagging chromosomes) is insignificant [12]. A large proportion of the changes observed at the level of chromosomes in interphase is repariruemoy during the mitotic cycle. Therefore, the potential biological risk to the ecosystem can be considered negligible.

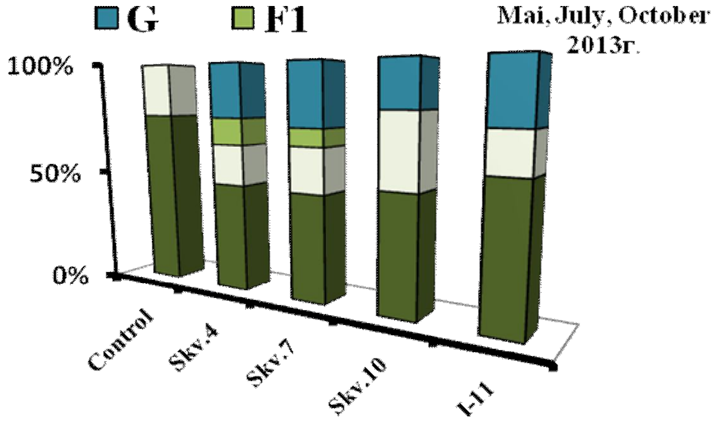

Figure 3 The spectrum of chromosomal aberrations observed in testing water samples from the area of waste facilities Obninsk.

Conclusion

Thus, the results of cytogenetic analysis in testing water samples from the area of the waste facilities permit the following conclusions:

- Allium - the test is a very convenient method of assessing the quality of the environment, characterized by high sensitivity, informative, efficiency, reproducibility of results;
- Biotesting natural waters from the territory of the storage of radioactive substances has shown that the negative biological effects are influenced by water from wells 4 and surface runoff;
- The most informative indicator bioassay can be considered as a test for genotoxicity water.

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EFFECTS OF DOUBLE-STRAND BREAKS DNA REPAIR GENE SPN-B ON LIFESPAN AND RADIORESISTANCE IN *DROSOPHILA MELANOGASTER*

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DNA double-strand breaks (DSBs) induced by ionizing radiation are considered the most relevant lesion for mutations and carcinogenesis, and unrepaired or misrepaired DSBs are a serious threat to genomic integrity [1, 2]. DNA repair is an essential mechanism of cellular response to different stress impacts including ionizing irradiation. It is a topical issue to disclose the role of DNA repair genes in the stress-response regulation and integration in the whole-organism level. In this study, we investigated the role of *Drosophila's spn-B* gene in lifespan regulation under in vivo ionizing radiation exposure. The s*pn-B* gene is a homolog protein of mammals DNA double strand breaks repair gene *XRCC3*, which is responsible for homologous recombination and non-homologous DNA end joining [3].

Materials and Methods

To study radioadaptive response, we used flies with mutations in the *spn-B* gene (genotype: $Dp(1;Y)B^S$, B^+; ru^1 st^1 $spn\text{-}B^1$ e^1 $ca^1/TM3$, Sb^1). Flies were exposed by gamma-radiation under different irradiation conditions: 1) without treatment; 2) chronic irradiation at 40 cGy dose rate induced by Ra-226 source during preimaginal developmental stages (12 days); 3) acute irradiation at 30 Gy dose rate induced by Co-60 source after imago hatching (50 min); 4) successive exposure by both doses. Age-dependent changes of *spn-B* gene expression were studied in irradiated (40 cGy) and non-irradiated flies of the wild type strain *Canton-S* at 1, 14, 28, 42 and 56 days after imago hatching. For investigation of changes in lifespan in individuals with ubiquitous and neuronal conditional overexpression in response to acute exposure to γ- radiation at a dose rate of 30 Gy, the RU486-activatable GeneSwitch system were used [4, 5]. Flies were obtained due to crossing of females with additional copy of the *spn-B* gene under UAS-promoter (genotype: w^{1118}, *UAS-spn-B*) and males with either da-GeneSwitch-Gal4 (ubiquitous) or elav-GeneSwitch-Gal4 (neuronal) driver. Flies were exposed by gamma-radiation under different irradiation conditions: 1) without overexpression and without treatment; 2) without overexpression and with acute dose 3) with overexpression and without treatment 4) with overexpression and with acute hatching.

Results and Discussion

Actual direction of modern radiobiology is the study of the molecular mechanisms of radioadaptive response. However, it remained unclear that how do the individual cellular processes integrate in variation of parameters of the whole organism's lifespan? Lifespan assay showed that chronic low-dose irradiation induces the radiation hormesis and adaptive response in the *Canton-S* wild-type flies. These effects were less expressed in flies with mutations in the *spn-B* (XRCC3) gene. It is known that mutants *spnB*^{1} are sensitive to X-ray radiation between 24 and 72 hours after the oviposition [6]. *Drosophila spnB*^{BU} mutants are sensitive to irradiation with 25 Gy, with only 19% of *spnB*^{BU} mutants surviving [7]. Changes of gene expression with age have a big effect on the aging process [8-10], the development of diseases [11-13] and as a consequence of the process of adaptation to damaging environmental factors and lifespan. For this purpose, we estimated age-dependent changes in *spn-B* gene expression. Transcriptional activities of the *spn-B* gene was increased by 1.6-2.0 times compared with non-irradiated animals ($p<0.05$). We supposed that *spn-B* (XRCC3) overexpression might have resulted in more efficient DNA repair and increased organism radioresistance same as previous low-dose exposure. However, an increased resistance to gamma-irradiation exposure at 30 Gy dose rate was not revealed in flies with ubiquitous and neuronal conditional overexpression of the *spn-B* gene. The reason for the lack of stimulation of radio resistance may be insufficient of epigenetic regulation of DNA repair processes [14]. Another reason for the decline of the lifespan may be an imbalance between the different intracellular pathways and energy depletion, because DNA repair is a process that requires large amounts of energy [15]. Also, our data are consistent with the Mikhail Blagosklonny's theory, according to which aging and age-related diseases start with cells hyper functions [16].

Conclusion

Our analysis has shown that radioadaptive response and effect of radiation hormesis are absent or evident to a lesser extent in individuals with mutations in the *spn-B* (XRCC3) gene compared with the wild type *Canton-S* species. Chronic exposure of ionizing γ-radiation at low dose on before imago stages of development leads to an increase in the expression of the *spn-B* gene, which is maintained throughout the lifespan of fruit flies. The ubiquitous and neuronal conditional overexpression of the *spn-B* gene did not induce resistance to acute exposure to γ-radiation, but rather reinforces the negative impact of acute exposure at a dose of 30 Gy to the lifespan. Thus, obtained data demonstrate an essential role of the DNA double-strand breaks repair gene *spn-B* (XRCC3) in gamma-irradiation biological effects.

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COMBINED ACTION OF IONIZING RADIATION AND FOOD SUPPLEMENTS ON THE INDUCTION OF ADAPTIVE RESPONSE AND TUMOR GROWTH ON MICE *IN VIVO*

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In recent years one of the major problems of modern radiobiology is the study of radiation protective mechanisms with the help of different substances as well as activation of internal resources of the organism. Internal resources mean such phenomena as hormesis and adaptive response which represent cell or body reaction on low doses of inducing factors and predetermine their further high dose effect resistance. Since natural biologically active substances have low toxicity and are capable of affecting physiological processes taking place in human's organism and increasing organism's natural defense system, the interest to protective means of vegetal origin and search of special food supplements intensifies every year. The purpose of this study is to investigate the combined action low dose rate high-LET and X-ray radiations and food supplement on sensitivity, induction of adaptive response (AR) and tumor growth on mice in vivo.

Materials and methods

Males of SHK mice at the age of two months were used for all experiments. The animals were being irradiated with 11.6 cGy (0.5 cGy/day) of low-dose-rate high-LET radiation behind the concrete shield of the 70 GeV protons accelerator. The X-ray irradiation was carried out using the RTH device (1 Gy/min).

The diet composition included products containing big amount of biologically active substances, such as: soybean meat, buckwheat, lettuce leaves and drug of fish oil. Four groups of mice were fed with selected products mentioned above during the whole irradiation period of 22 days. The control groups received the same food without irradiation. In order to determine the level of radiosensitivity, all groups of mice were subjected to X-radiation with the dose of 1.5 Gy and for induction of AR the animals were irradiated according to the standard scheme of radiation adaptive response (10 cGy+1.5 Gy). The percent of polychromatic erythrocytes (PCE) with micronucleus (MN) in bone marrow served as definition criteria of cytogenetic level of damage.

Results and Discussion

The left part of fig.1 shows the dependence of the number of PCEs with MN in the bone marrow of mice exposed to combined action of the diet and the dose of 1.5 Gy of X-rays. As can be seen the diet containing huge amount of biologically active substances, such as soybean meat and buckwheat led to the decrease of cytogenetic damage in mice after exposure to 1.5 Gy of X-rays. However, the effects of lettuce leaves were not statistically relevant, whereas drug of fish oil had no influence on the damage level. On the right part - the number of micronucleated PCE in mice exposed to the diet and irradiation by the scheme of AR. In mice exposed to the combined action of the diet and irradiation by the scheme of AR the number of PCE with MN did not differ from that of the control mice. So investigated diet composition did not change the level of AR.

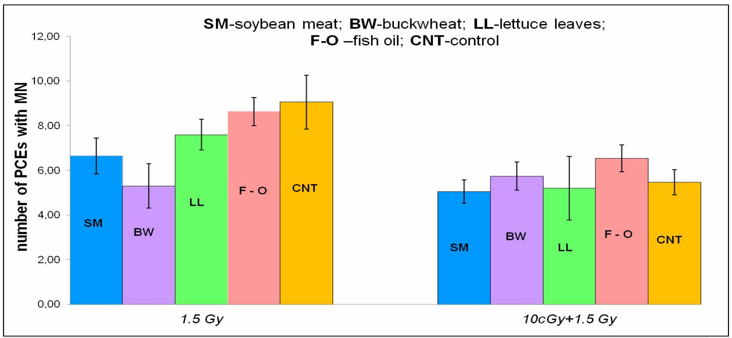

Fig.1. Number of PCEs with MN in bone marrow cells of mice combined exposed to food supplements and subsequently irradiated with the dose of 1.5 Gy of X – rays and by the scheme of adaptive response (10 cGy + 1.5 Gy)

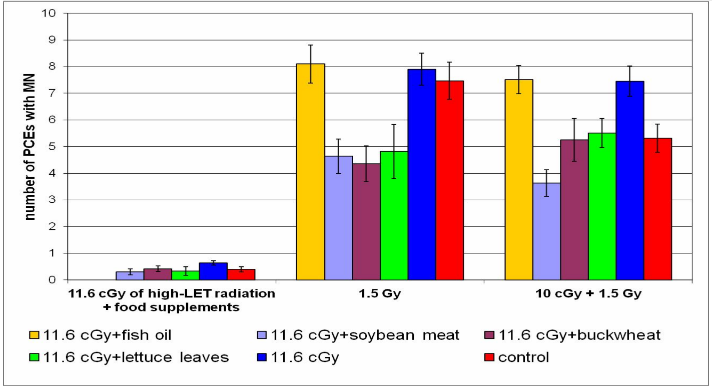

Fig. 2. Number of PCEs with MN in bone marrow cells in mice exposed to 11.6 cGy of high-LET radiation in presence food supplements and subsequently irradiated with the dose of 1.5 Gy of X – rays and by the scheme of adaptive response

The fig. 2 shows the level of cytogenetic damage in bone marrow of mice exposed to the combined effect of 11.6 cGy of the high-LET radiation and the food supplements followed by 1.5 Gy X-ray irradiation and by the scheme of AR. As can be seen from this figure in mice irradiated with low dose of high-LET radiation and having dietary supplement the decrease of PCE with MN to the level of natural background radiation was found as compared to the mice that were fed with the standard food only. In the middle part of the figure shows the radiosensitivity to the dose of 1.5 Gy of X-rays in mice exposed to 11.6 cGy of high-LET radiation in the presence or absence of food supplements. It can be seen that the drug of fish oil diet as well as the high-LET radiation without any food supplements did not influence the level of the cytogenetic damage. At the same time, the diet containing soybean meat, buckwheat and lettuce leaves significantly decreased the number of damage, i.e. ARs took place. The data on combined effect of the diet and low dose high-LET radiation followed by additional irradiation with the AR scheme (10 cGy + 1.5 Gy) are shown in the right part of the picture. It can be seen that the combined action of food supplement, with the exception of the drug of fish oil, and high-LET radiation led to decrease the cytogenetic level of damage in mice irradiated with the scheme of AR compared with the level of damage under standard AR.

In the next set of experiments it was found that diet containing soybean, buckwheat or greens unlike fish oil caused significant slowdown in the growth of tumor as well as combined action of the diet and high-LET radiation in contrast to the mice irradiated only with 11.6 cGy of high-LET radiation.

Conclusions

The results of the study indicate that: due to influence of high-LET radiation with the dose of 11,6 Gy, mice who had dietary supplement demonstrated reduction of PCE with MN to the level of natural background radiation comparing with mice who had only standard food, reduces the sensitivity of mice to X-radiation with the dose of 1,5 Gy and causes significant slowdown in growth of tumor; the combined effect of high-LET radiation and the food supplements (except for cod-liver oil) reduces the sensitivity of mice to irradiation with the dose of 1.5 Gy, which demonstrate ability of

AR induction and did not action on the AR level and causes the slowdown in growth rate of tumor in contrast to the mice only irradiated with high-LET with the dose of 11.6 Gy. Received data provide evidence for the protective effects of the investigated oral supplementation that appears to be an effective approach radioprotection after low dose of space radiation.

MOLECULAR NATURE OF PRIMARY DNA LESIONS DETECTED IN THE ALPHA-TEST

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Most heritable alterations in the genetic material are caused by the error-prone repair of spontaneous and induced primary DNA lesions. The genetic consequences of primary DNA lesions that were processed into genetic endpoints are well established. Mutations or chromosomal aberrations alter cellular phenotype, increase the risk of cancer and genetic diseases[1]. However, little is known if primary DNA lesions affect somehow cellular phenotype before lesions are eliminated by repair. Our aim is to study the ratio between correct and error-prone processing of primary DNA lesions as well as possibility of phenotypic expression of primary DNA lesions before they are fixed by repair. We use an yeast-based assay that is called the alpha-test.

Materials and Methods

The alpha-test is based on mating type switch α (alpha) to a in heterothallic yeast *Saccharomyces cerevisiae.* Haploid yeast cells express one of two mating types: a or α. Normally, haploid cells are able to mate exclusively with haploid cells of the opposite mating type to form a/α diploids, that are unable to mate [2]. The mating type of haploid cells (a or α) is determined by two different alleles of the *MAT* locus: *MAT a* and *MATα*, which is mapped on chromosome III [2]. In addition to the *MAT* locus there are two cassettes, *HMR*a and *HMLα* on the same chromosome, where a and α information, is stored but not expressed [2]. In homothallic yeast strains mating type switch occurs as often as every cell division is accomplished by an intrachromosomal gene conversion mechanism between cassettes (*HMR*a or *HMR*α) and the *MAT* locus initiated by *HO* endonuclease [2]. In heterothallic yeast the mating type switch is a rare event (10^{-6} to 10^{-7}), because of defective the *HO* gene *(ho* allele) [2]. Mating type switch in heterothallic strains can be induced by DNA damaging agents due to disturbance of the *MATα* locus expression. When *MATα* expression is broken, heterothallic haploid cells switch their mating types from α to a, have a-like mating behaviors and mate with other α cells.

In the alpha-test we use two strains of the same mating type α which have complementary genetic markers. One of the yeast strains is treated with the various agents, after that we incubate both strains on media for selective growth of hybrids arising from illegitimate mating between two strains [3]. Our model suggests that in the treated strain primary DNA lesion breaks the *MATα* locus expression, that leads to temporary or permanent mating type switch α to a. Such mating type switch allows mating between two α cells. After the hybrid formation repair may take a place. Some primary DNA lesions are transformed through inaccurate repair into gene mutations, or induce chromosome aberrations, gene conversion and recombination. Most of primary DNA lesions are fixed in the error-free manner. Before repair takes a place DNA lesions may cause phenotypic changes in yeast cells that results in a temporary mating type switch α →a [3]. Thereby, in the alpha-test the frequency of illegitimate mating reflects the level of DNA instability and allows us to estimate ratio between correct and error-prone processing of primary DNA lesions by analysis of the phenotypes of illegitimate hybrids.

Results and Discussion

To identify the nature of primary lesions that are able to affect phenotype we used several specific mutagens in combination with different repair systems defects.

To study phenotypic expression of double-strand breaks, we quantified the effect of camptothecin (CPT) in the alpha-test. We have shown that camptothecin-induced double-strand breaks significantly increase the frequency of inheritable and nonheritable genetics changes in yeast cells (figure 1).

To evaluate the phenotypic expression of unpaired nucleotides, we studied the effects of the inactivation of mismatch repair by disruption of the *PMS1* gene in the alpha-test. Our results show that disruption of the *PMS1* gene increases the frequency of mating type switch on account of only inheritable genetics changes (figure 1). Unpaired nucleotides did not induce gene conversion and temporary lesions (figure 1).

To study phenotypic expression of base modifications, we investigated analogs of purine bases such as 6-Nhydroxylaminopurine (HAP) and 8-oxoguanine (8-oxoG) in the alpha-test. HAP increases the frequency of illegitimate mating in the alpha-test by both inheritable and nonheritable genetics changes especially raises frequency of gene mutations for about 139-fold (figure 1). 8-oxoG accumulated in yeast strain defective in the 8-oxoG DNA glycosylase *(ogg1)* increases the frequency of mating type switch and induces gene conversion and temporary lesions (figure 1).

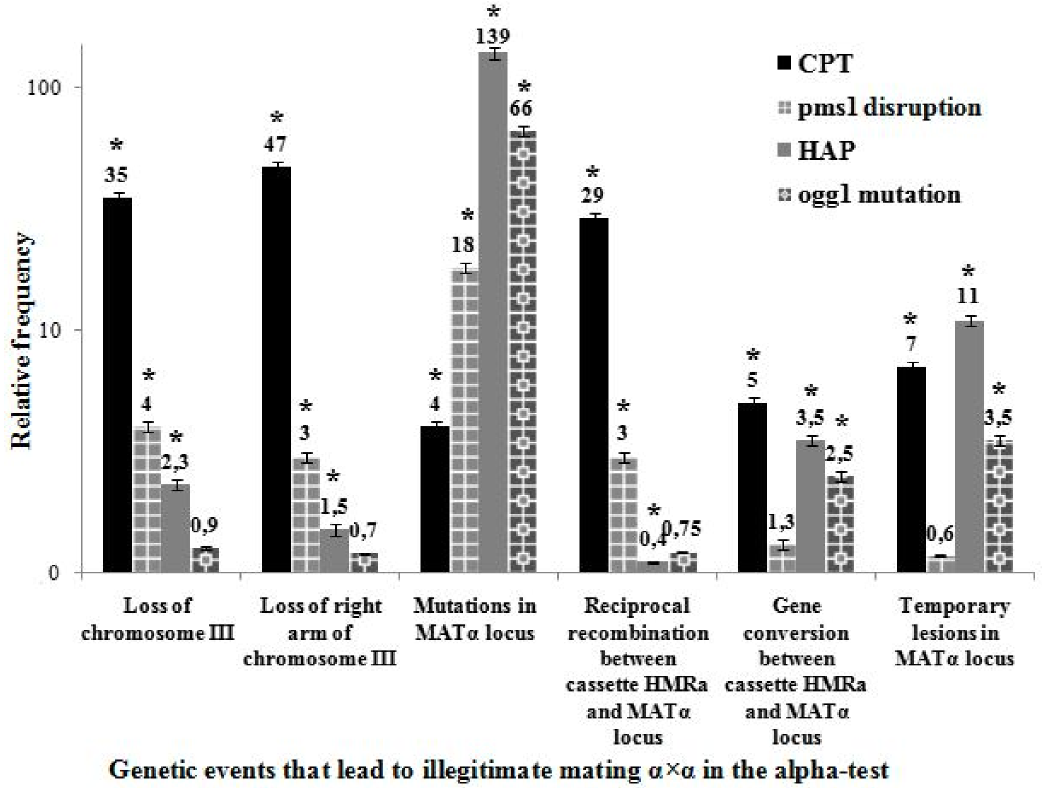

Figure 1. Relative frequency of inheritable and nonheritable genetics changes detected in the alpha-test. Relative frequency is ratio between frequencies obtained from experiments with and without treatment or wild type and mutants. * - significance difference between the treatment and control variants was estimated using Mann–Whitney test.

Conclusion

We demonstrate here the successful application of the alpha-test to identify phenotypic expression of double-strand breaks and base modifications before they are vanished by repair. Unpaired nucleotides are detected in the alpha-test after they were transformed into inherited genetic changes. Our data indicate that the alpha-test allows to score phenotypic expression of primary lesions that occur mostly during G1 stage of the cell cycle.

Acknowledgements

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EFFECT OF HYPOXIA ON *HIF1A*, *MTHFR*, AND *UCP2* GENES EXPRESSION

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Exercise-induced hypoxia is a key factor influencing the athlete's performance. Hypoxic training, involves exercising in, living in or breathing oxygen-reduced air is used for the purpose to improve athletic performance. Brief exposure to hypoxia is sufficient to induce beneficial adaptations: increased expression of genes involved in angiogenesis, genes encoding glycolysis enzymes, and genes important for lactate shuttling, glucose transport, capillary density augmentation and muscle oxidative capacity [1]. However, despite a good deal of research into the topic, its true effects and a recommended approach are still not well established. In addition, athletes respond to hypoxia with a marked inter-individual variability due to their genetics. Adaptation to hypoxia depends mostly on changes in the expression of various genes. The objective of our work was to determine the impact of hypoxic training on *HIF1A* (hypoxia-inducible factor), *UCP2* (uncoupling protein 2) and *MTHFR* (methyl-tetrahydrofolate reductase) genes expression.

Materials and Methods

Twenty-seven healthy endurance-trained athletes participated in the study. A total of 3 ml blood sample was collected for total leukocyte RNA extraction. Blood samples were taken at rest prior the training protocol and one day after the last training session.

TRIzol® reagent was used for the isolation of high-quality total RNA (Ambion, USA). A total of 1 mg of total RNA was reverse transcribed in a total volume of 20 µl. Level of mRNA for genes was quantified using the CFX 96 Bio-Rad Real-Time PCR System with Applied Biosystems TaqMan Gene Expression Assays and Gene Expression Master Mix following manufacturer's protocol. The mRNA contents were normalized to GAPDH mRNA levels. PCR assays were performed at least in duplicate for each sample, and the results were averaged. Data are presented as mean ± SEM. Exercise-induced changes in mRNA levels of *HIF1A*, *MTHFR* and *UCP2* were analysed with the Wilcoxon matched-pairs test. Comparisons between two groups were analyzed with Mann-Whitney rank sum test. The Spearman's rank correlation coefficient was used as the measure of statistical dependence of the variables. Differences were considered significant at $P<0.05$.

Results and Discussion

The results revealed interindividual variability in expression of *HIF1A*, *MTHFR* and *UCP2* genes at rest and in response to hypoxia. In general, it was shown that level of *MTHFR* and *UCP2* mRNA increased significantly in response to strenuous exercises (from 0.21±0.02 to 0.44±0.07 a.u. for *MTHFR* gene, $P=0.012$ and from 0.66±0.025 to 0.94±0.08 a.u. for *UCP2* gene; $P=0.036$). We have also shown that the expression of *UCP2* gene was 1.4-fold greater for athletes with *Val/Val* genotype than those with either the *Val/Ala* or *Ala/Ala* genotypes. In addition, carriers of *Val/Val* genotype were characterized by higher level of athletic performance.

Most importantly, the amount of *HIF1A* mRNA in leukocytes after 2 weeks of hypoxic training decreased from 3.04±0.25 to 1.61±0.13 a.u. (P=0.001), whereas the level of *UCP2* increased significantly after training from 0.39±0.05 to 1.55±0.09 a.u. (P=0.0006) and *MTHFR* mRNA level – from 0.20±0.02 to 0.66±0.05 a.u. (P=0.0007, Figure 1). A study performed by Mounier *et al.* also showed significant decrease in *HIF1A* mRNA after hypoxic training [2]. Lundby *et al.* demonstrated that *HIF1A* mRNA level is transiently increased in untrained human skeletal muscle in response to an acute exercise bout, but this response is blunted after exercise training [3]. It is known that transcription factor *HIF1A* plays an essential role in adaptation to low oxygen pressure. Under hypoxic conditions, *HIF1A* is responsible for increased expression of over 70 genes involved into various physiological processes such as erythropoiesis, angiogenesis and glucose metabolism [4]. Therefore, we suppose that reduced *HIF1A* expression indicates improving of athlete’s adaptation to hypoxia.

Interestingly, the expression of *MTHFR* positively correlated with the expression of *UCP2* in baseline (r=0.81, P<0.05) and after hypoxic training (r=0.73, P<0.05), and with mRNA level of *HIF1A* gene (r=0.71, P<0.05) but only after training.

MTHFR gene encodes an enzyme that is responsible for methylation. DNA methylation has recently been demonstrated to be an important factor in the exercise-induced adaptation in skeletal muscles. It is one of the regulatory mechanisms controlling genes involved in muscle hypertrophy [5] and mitochondrial biogenesis [6]. According to this knowledge, we can assume that increase of *MTHFR* gene expression is an important factor for hypoxia adaptation.

Esteves *et al.* showed that overexpression of *UCP2* gene generates a mitochondrial retrograde signaling that modifies expression of glycolytic and oxidative enzymes, leading to enhanced oxidative phosphorylation [7]. Consequently, increase of *UCP2* gene expression after 2 weeks of hypoxic training indicates improving of athlete’s aerobic endurance.

Conclusion

According to all the above-mentioned results, we propose that expression of *UCP2*, *MTHFR* and *HIF1A* genes is one of the most important indicator of athlete’s adaptation to hypoxia that will be useful for developing a training program to help athletes maximize their athletic performance.

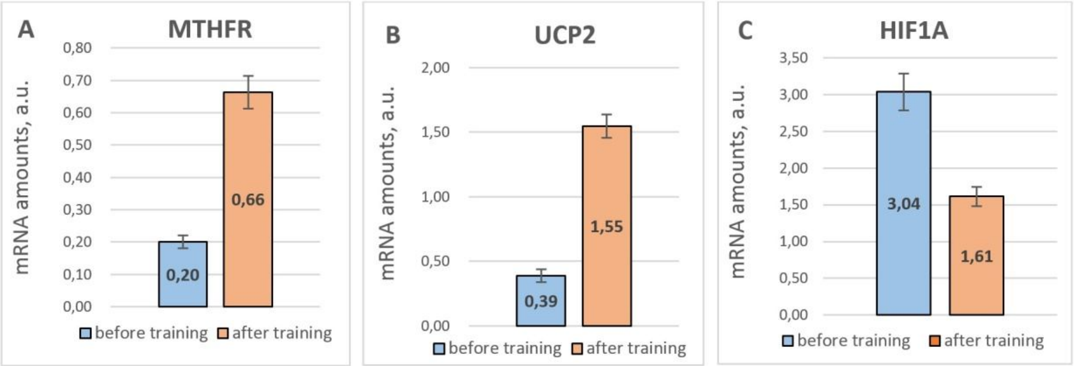

Figure 1 MTHFR (A), UCP2 (B) and HIF1A (C) mRNA amounts in leukocytes before and after hypoxic training period. Values are presented as mean ± SEM. a.u.: arbitrary

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ABSTRACTS & PAPERS
about
N.W. Timofeeff-Ressovsky

PERSONAL RECOLLECTIONS ABOUT N.W. TIMOFÉEFF-RESSOVSKY AND HIS ACTION FOR RADIATION BIOPHYSICS IN BERLIN-BUCH AND DUBNA

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To meet Timoféeff-Ressovsky in person was an exceptional experience that has left memorable impressions. His fate was interlinked with barriers that made personal contacts almost impossible. It was thanks to the German physicist Robert Rompe and the Russian geneticist Dubinin that the authors had the opportunity to get to know Timoféeff-Ressovsky.

A first encounter between Timoféeff-Ressovsky and Hemut Abel took place in Obninsk in 1966. On this occasion cooperation between Obninsk and Rossendorf was agreed upon to facilitate the study of radiation induced mutations of Drosophila and Arabidopsis as well as the analysis of radiation induced DNA damages, their possible intracellular repair, and their biological consequences. The findings led to numerous publications.

In 1967 Gudrun Erzgräber met Timoféeff-Ressovsky in person in Obninsk. Both authors were deeply impressed by Timoféeff-Ressovsky's amicable, fatherly and humorous approach to work with young scientists. For him, our scientific cooperation represented a reconnecting to Berlin-Buch, where he had worked for almost two decades.

The cooperation with Timoféeff-Ressovsky led to a significant expansion of radiation biophysics in the GDR. A department for radiation biophysics was founded in Berlin-Buch's Institute for Biophysics and headed by Abel. As its branch, a department for biophysics was built in Dubna under the leadership of Erzgräber.

In 1987 the Soviet military court requested the GDR's legal aid in connection with the judicial rehabilitation of Timoféeff-Ressovsky. The Academy of Sciences of the GDR accepted this request and carried out a thorough investigation into the available documents of oral presentations and publications authored by Timoféeff-Ressovsky. The investigation, that was assisted by Abel among others, found that Timoféeff-Ressovsky's research at no point supported the fascist racial ideology or Germany's war activities.

TIMOFÉEFF-RESSOVSKY'S SCIENTIFIC NETWORK IN THE 1920s-1940s AND THE DAWN OF THE EVOLUTIONARY SYNTHESIS

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Ernst Mayr already pointed to important developments in Germany towards an Evolutionary Synthesis from the 1920s onwards: „Simultaneously, there was a parallel synthesis in Germany, led by Timoféeff-Ressovsky, a student of Chetverikov"(Mayr 1997: 193)

We here show that the efforts towards a Synthesis in Germany began surprisingly early, i.e., in the 1920s in a scientific network that is widely unnoticed by Historians of Science. Centre of the network is, as said by Mayr, Nikolai W. Timoféeff-Ressovsky who was employed by Oskar Vogt in 1925. Vogt, at that time head of the "Kaiser-Wilhelm-Institut-für-Hirnforschung", had extensive contacts to the Russian scientific community and had been looking for young geneticists to do entomological variation studies. Timoféeff-Ressovsky rapidly established himself in the scientific community of Berlin and cultivated contacts to the most important scientists of the time. Timoféeff-Ressovsky introduced a highly interdisciplinary "Genetical Colloquium" bringing together biologists and physicists of various sub-disciplines discussing topics of genetics, molecular biology, and evolution. An outcome of these colloquia was a series of monographs called "Problems of theoretical and applied genetics and its adjacent areas" by several authors. Preannouncements in the books tell us that there have been further volumes in planning; however, the publication was stopped by World War II. Topics of the planned volumes were, e.g., *Mutation and its importance for selective breeding* (Hans Stubbe), *Genetics of Natural Selection* (Nikolai Timoféeff-Ressovsky), *Geographical and Individual variability* (William F. Reinig), *Genetics and Animal Systematics* (William F. Reinig & Nikolai Timoféeff-Ressovsky), *Genetical interpretation of paleontological facts* (Otto Heinrich Schindewolf). Given the fact that those preannouncements are from 1937 – the publication year of Dobzhanskys *Genetics and the Origin of Species* and five years ahead of Mayrs *Systematics and the Origin of Species* – these plans seems remarkably ahead of their time.

Furthermore the participants of Timoféeff-Ressovsky's colloquia intended to establish a "Central Department for experimental and biogeographical evolutionary research"– actually, the first and only attempt to institutionalize the Evolutionary Synthesis. Unfortunately, those plans got terminated by the outbreak of World War II. Hence we can not only speak of a parallel synthesis as postulated by Mayr, but it might be that the dawn of the Synthesis was even earlier than in Anglo-American scientific communities, and that Berlin's scientific infrastructure at that time was an optimal breeding ground for such an interdisciplinary endeavor.

В ПАМЯТИ:
ДМИТРИЙ НИКОЛАЕВИЧ ТИМОФЕЕВ-РЕСОВСКИЙ † 1/2 мая 1945
АНДРЕЙ НИКОЛАЕВИЧ ТИМОФЕЕВ † 9 сентября 2014
НИНА АЛЕКСЕЕВНА ТИМОФЕЕВА † 28 января 2014

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Научное сообщество биологов, физиков и биофизиков мира и общественность России и Германии потеряло в прошлом году сына выдающихся генетиков-супругов Елены Александровны и Николая Владимировича Тимофеевых-Ресовских, Андрея Николаевича и его жены Нины Алексеевны. Среди биологов-генетиков тяжелая судьба семьи-ученых и обоих их сыновей сегодня общеизвестно (благодаря роману Д. Гранина «Зубр», биографии В.В. Бабкова и Е.С. Саканяна и кинотрилогии последней, а также переизданным воспоминаниям Н.В. Тимофеева-Ресовского и его учеников). Однако жизненная судьба старшего сына, ученика Французской гимназии в Берлине (1933-1943) и студента Берлинского университета (с апреля 1943 г.), прояснилась намного позже: он активно участвовал в сопротивлении нацистскому режиму в Германии, в результате чего он был арестован в конце июня 1943 гестапо, осужден и убит в концлагере Эбензее/Маутгаузен (Австрия) в мае 1945 г. В связи с его личной судьбой Андрей Николаевич многократно подавал на розыск (в том числе с помощью автора данного доклада), каким образом его старший брат оказался в концлагере и какова была его дальнейшая судьба. Благодаря тому, что в ноябре 2011 г. в Эбензее был открыт Мемориал, в котором имя Димитрия Тимофеева значится среди тысяч погибших узников, была опубликована книга об истории концлагеря Эбензее, включая список всех погибших узников. В мае 2014 по просьбе Андрея Николаевича была установлена табличка его памяти с фотографией и с текстом. (полный текст см. Dimitrij Timoféeff-Ressovsky, genannt Foma. Winkler & Nikišanova http://www.leibnizsozietaet.de/wp-content/uploads/2015/02/WinklerNikišanova.pdf Leibniz Online 2015: 17)

Автор освещает длинный путь розыска следов, представляет документы и переписку Димитрия (Фомы) с матерью, пытается нарисовать живую картину памяти этого смелого юноши

Фото мемориал: КЦ Маутгаузен/Эбензее. См. www.memorial –ebensee.at

ВОСПОМИНАНИЯ О НИКОЛАЕ ВЛАДИМИРОВИЧЕ ТИМОФЕЕВЕ-РЕСОВСКОМ

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Мне посчастливилось знать Николая Владимировича Тимофеева-Ресовского и работать в его отделе лаборатории «Б» на протяжении почти 1,5 лет. Он был, несомненно, выдающейся личностью, а Сунгуль был кусочком рая: природа, коллектив, работа, общий творческий поиск, отдых – заплывы на лодках и яхте по системе озёр - всё было впервые и какое! Спустя 60 лет аура Сунгуля жива в нас, о Сунгуле мы слагали стихи.

По окончании биологического факультета Уральского госуниверситета им.А.М.Горького в 1953г. двое с нашего курса были направлены на работу в лабораторию «Б»: микрозоолог Мошкина Людмила Викторовна и я – физиолог человека и животных. Мой маршрут на место будущей работы таков: Свердловск – Москва – Свердловск - ст. Маук ЮУр ж.д. – пос.Сунгуль (или Касли 33/6). Сойдя с поезда на ст. Маук, я, бросив чемодан в домике для приезжих, тут же полезла на ближайшую гору, вечерело, солнце заходило, с вершины открывался прекрасный вид на окрестные горы, я насчитала до 20 озер. Южный Урал поразил меня своими красотами и на следующий день, когда на газике в 5 часов утра мы ехали в Сунгуль: лес в розовых лучах солнца (был конец августа), зеленые сосны, желтые березы, красные осины и рябинки, голубизна озёр поражали красками, особенно красивой была узкая дорога между озерами Киреты и Большие Касли.

Миновав два КПП, приехали в поселок. На следующее утро я посетила спец. отдел, где мне оформили пропуск в основную 3-ю зону и проинструктировали как себя вести: запрещалось разглашать сведения, фотографировать объект и, в частности, рекомендовали не вступать в разговоры с Тимофеевым-Ресовским на политические, исторические и философские темы, «так как он вас, несмотря на ваши дипломы с отличием, за пояс заткнет».

Был ещё период отпусков, в лаборатории меня встретил заместитель Тимофеева-Ресовского – Кач Александр Сергеевич. Когда мы с ним беседовали, шествуя по ковровой дорожке 2 –го этажа, я невпопад заметила вслух, что у него такой же прямоугольный перстень, как у расконвоированных пленных немецких офицеров, с которыми часто встречалась в трамвае, когда по утрам ехала в университет. Александр Сергеевич вдруг остановился, внимательно посмотрел на меня и спросил: «А разве Вас не предупредили, что я немец?». «Нет», – растерянно пролепетала я. «Настоящее моё имя –Александр Зигфридович» - сказал он доверительно. Затем он пристроил меня за свободный стол с микроскопом, вручил том Кассирского, какие-то крашеные мазки и велел мне изучать клетки костного мозга. Впоследствии я узнала, что он один из немецких евреев, которых Н.В.Тимофеев-Ресовский спас в своей лаборатории под Берлином.

В возглавляемом Тимофеевым-Ресовским биофизическом отделе было 2 лаборатории: 1-я собственно Тимофеева-Ресовского, куда была направлена моя однокурсница, и 2-я – радиотоксикологическая Юрия Ивановича Москалёва, куда была направлена я. Юрий Иванович в 1948г. защитил кандидатскую диссертацию в Ленинграде у академика Гинецинского по нейрофизиологии и был направлен в лабораторию «Б». Юрий Иванович был основателем отечественной радиотоксикологии, за 6 лет работы он выдал докторскую диссертацию в 2-х томах по радиотоксикологии всех радиоизотопов, которые только смогли выделить из реакторной «юшки» сотрудники радиохимического отдела профессора Сергея Александровича Вознесенского (побывавшего в «Бутырке»).

Через некоторое время в коридоре 2-го этажа появился крепко скроенный среднего роста мужчина «в годах» с выразительными чертами лица, и повсюду раздавался его гудящий баритон. Я догадалась, что это Тимофеев-Ресовский. Увидав меня, пригласил зайти к нему. Первым делом он спросил у меня, какие предметы лучше всего преподавали в университете. «Марксизм-ленинизм» – отчеканила я. «А радиобиология у Вас была?» – «Нет…».

В результате такого прощупывания меня и, вероятно, работавшей у него Людмилы, он решил прочитать нам несколько лекций, главным образом о взаимодействии энергии с веществом, с клеткой. Занятия проходили в его кабинете, правую половину которого занимал огромный письменный стол, позади него на стене, как в классе, висела черная доска, в левой половине стоял круглый светлый стол с двумя большими мягкими креслами в полотняных чехлах. Направо от двери во всю стену был «иконостас»: фотографии выдающихся ученых с мировым именем, среди них оказалась дама в модной шляпке и перекинутой через плечо чернобурой лисой по моде 30-40 г.г. Николай Владимирович предложил нам с Милой назвать имена ученых, мы отгадали лишь некоторых. На наш вопрос о даме он ответил, что это знаменитая немецкая балерина. «Иконы» были явно самодельные: фотографии были под стеклом и скреплялись по краям черной изоляционной лентой. На одном из таких занятий Николай Владимирович, объясняя Комптон-эффект, энергично взмахнул правой рукой с мелом, начертив орбиту электрона, и вдруг лицо его онемело, левой рукой он схватился за правое плечо и попросил: «Позовите скорее Дмитрия Ивановича». Мила побежала искать Семенова, а я осталась растерянная, не зная как помочь. По-видимому, видя мою растерянность, Николай Владимирович успокаивая меня, сказал, что скоро все пройдет, что привычный вывих плеча у него издавна, со дня венчания, когда так же энергично он распахнул дверцу кареты невесте для поездки в церковь. «Священник и гости ждали меня целый час, пока нашли врача, чтобы вправил сустав», - уже почти улыбаясь, вспоминал Николай Владимирович. Чтобы продлить приятные воспоминания он сказал, что его невеста была высокой стройной блондинкой, наездницей, прекрасно держалась в седле. Елена Александровна была выше мужа, курила, имела грубый, прокуренный голос, была очень приветливым и очень воспитанным человеком, по-видимому, дореволюционного еще воспитания. Рассказывали, что при защите кандидатской диссертации она в смущении обратилась к слушателям не «уважаемые товарищи», как было принято в советские времена, а «уважаемые дамы и господа». Она в связи с потерей мужем зрения в ГУЛАГе читала ему статьи на немецком, французском, английском и русском языках. Он же мог читать только с помощью лупы. Все прочитанное вечерами обсуждалось днем. Ежедневно часов в десять утра в кабинет к Елене Александровне на кофе собирались, как говорил Николай Владимирович, на «малый треп» он и его ближайший помощник Николай Викторович Лучник, а также Дмитрий Иванович Семенов, т.е. все «гулаговцы», ставшие ими по разным причинам: Н.В.Лучник, будучи студентом второго курса биофака МГУ в 1942 году попал на летнюю практику на Кавказ и остался там при немцах, Д.И. Семенов был захвачен при освобождении Вены, куда переехали его родители еще до войны и где он окончил медицинский факультет университета. На этих «трепах», т.е. ежедневных коллоквиумах, обсуждались научные проблемы. Помню, как всем не давал покоя вопрос о причинах терапевтического эффекта селезеночных бесклеточных экстрактов при введении их облученным мышам, о котором сообщил Эллингер. Аналитический ум Тимофеева исследовал все, На этих «трепах», несомненно, были обсуждены вопросы, поднятые в одной из первых публикаций в Трудах Института биологии Уральского филиала АН СССР за 1957 год, где совместно с Н.В.Лучником они дали классификацию лучевых поражений, все возможные варианты воздействия радиации на организм, обсудили возможные пути перехвата энергии, возможные типы защиты и терапии. Еще ранее Н.В.Тимофеев-Ресовский сформулировал «теорию мишени», определив теоретически чувствительные точки приложения энергии в структуре клетки, что было близко к истине, независимо от значимости преимущественного поражения в клетке наследственных структур (ДНК) или энергетических (митохондрии). После того, когда Уотсот и Крик создали теорию пространственной структуры ДНК и стали нобелевскими лауреатами, Николай Владимирович иронизировал: «Ну, теперь все заДНКкакали». Это его выражение привезла в Озерск мой научный руководитель Рахиль Евельевна Либинзон, для знакомства с Тимофеевым ездившая в Миассово с докладом о радиочувствительности нуклеиновых кислот. Материалы ее исследований были с интересом восприняты и одобрены. Помимо теоретических вопросов Николай Владимирович вел практически важные эксперименты по биоочистке радиационно загрязненных вод. На склоне холма была построена система из семи соединяющихся прудков, в верхний из которых загружали десятки кюри радиоактивных отходов реактора. Моя однокурсница смотрела, насколько эта эко система очищает воду.

По моему глубокому убеждению, истинным наслаждением для Николая Владимировича было общение с молодежью. Завлекать молодых людей в науку, щедро делиться со всеми накопленными им знаниями было отрадой для его души. В этом я убедилась, скажу о двух случаях. Вскоре, после приезда в Сунгуль, месяца через три, у меня должен был быть день рождения, исполнялось 23 и это следовало отметить. Наше женское общежитие, размещавшееся в трехкомнатной квартире первого этажа дома, решило пригласить мужское общежитие из такой же квартиры на третьем этаже. Все хотели танцевать, но где взять музыку? Людмила предложила взять проигрыватель у Тимофеевых. «Но тогда нужно их приглашать» - возразила я, - «Ну и приглашай». Мы отправились в коттедж, двери тогда никто не запирал, на пороге нас встретил сам хозяин. Мы пригласили его и Елену Александровну и попросили проигрыватель. «Конечно, берите» - сказал Николай Владимирович, «у вас ведь верно есть адъютанты? Леля, ты пойдешь?» - обратился он к лежавшей на кушетке Елене Александровне. «Нет, я лучше отдохну, иди один» ответила та. К назначенному часу собралось человек 25, всех рассадили за три сдвинутых стола, Николай Владимирович сидел на почетном месте. Вдруг он в середине застолья поднялся и провозгласил тост «за юмористическое отношение к жизни». Настроение тогда было еще послевоенное, 27 миллионов жертв застряли в подкорке, какой юмор? Я, как хозяйка, к тому же рьяная комсомолка, насторожилась, какую еще аполитичную вещь ждать? Что делать? Хорошо, что сидевшие рядом ребята схватили меня за кисти рук и приказали не высовываться. После застолья Николай Владимирович вышел в прихожую покурить и за ним все наши кавалеры, окружили его плотным кольцом, и он начал рассказывать. Это продолжалось до трех часов ночи, потом все пошли его провожать. Знаю я эти рассказы о том, что Европа мала: «завтракаешь со шведским королем, а обедаешь уже с норвежским», обо всех музеях, художниках, течениях в живописи и т.п. О ГУЛАГе ни слова и о своей трагедии. О ней я узнала случайно, когда через год после выезда из Сунгуля приехала в Свердловск и решила без приглашения навестить Тимофеевых. Дома застала их сноху Нину, жену сына Андрея. Она то и поведала мне под большим секретом, что «старики» уехали в центр за подарком для Андрея, хотя это и не его день рождения, а день рождения его старшего брата, которого дома называли Фомой и который во время войны погиб в одной из тюрем Берлина, т.к.входил в подпольную молодежную организацию, ставившую целью убрать Гитлера, и был выдан. Отцу намекали, что он мог бы обратиться за помилованием, если бы согласился принять участие в Проекте, который должен был доказать превосходство арийской расы на генетическом уровне, но он отказался. Это тяжелый груз, и не о том ли он исповедовался Меню перед смертью?.И второй пример. В начале 70-х г. я, как секретарь парторганизации нашего института, была на совещании в Озерском Горкоме партии, где А.Ф.Разжигаев, член Горкома, приехавший с идеологического совещания в Москве, рассказал интересную историю. Оказалось, что секретарь комсомольской организации Обнинска написал в ЦК ВЛКСМ письмо, в котором утверждал, что комсомол не нужен, а молодежь должна заниматься только наукой. Откуда дул ветер сразу стало ясно (Тимофеев в то время работал в Обнинске). В ЦК КПСС решили обследовать три вузовских города (в т.ч.Обнинск и Воронеж), чтобы найти среди профессуры того, кто мог бы противостоять Тимофееву по влиянию на молодежь. Такого не нашлось. После совещания я, обеспокоенная за судьбу Николая Владимировича, спросила у А.Ф.Разжигаева, что же с ним решили делать. Усмехнувшись, он ответил, что надеются лишь на его преклонный возраст. Приобщать молодежь к науке – это сокровенное желание Тимофеева, его убеждение, что только это может принести пользу и стране, и всему человечеству.

Николай Владимирович был очень открытым и эмоциональным человеком. Помню рассказ Веры Николаевны Стрельцовой, жены Ю.И.Москалева, тоже кандидата мед. наук. Тогда она была еще и секретарем парторганизации лаборатории «Б». В декабре 1953 года она встретила Николая Владимировича на узкой протоптанной в снегу дорожке, когда он возвращался домой с только что впервые после войны полученным советским паспортом. Он был очень взволнован и тотчас поделился с ней этой радостью. Она тоже расчувствовалась до слез, поздравила его и они обнялись. Кто то их видел, и на следующий день ее вызвали для объяснений в спецотдел.

Отчеты нашего отдела должен был утверждать начальник лаборатории «Б», тогда им был Г.А.Середа, химик. В суть биологических проблем он не вникал, чтобы не тратить зря времени, он проводил обсуждение отчетов в своем кабинете, присутствуя формально. Обсуждали мы, а он демонстративно занимался своими делами – на логарифмической линейке обсчитывал собственные данные. Это уже давно вызывало у всех глухой протест. В.Н.Стрельцова решила его поддеть; однажды, во время бурных дебатов, она бросила фразу: «медицина-это не химия, где перелил из пробирки в пробирку…». Ее слова заглушил взрыв хохота, Глеб Аркадьевич, наконец, поднял голову и непонимающе всех оглядел. Николай Владимирович, сидевший в кресле-качалке, хохотал, раскачиваясь и поднимая ноги чуть не выше головы.

Относились к Николаю Владимировичу все очень тепло, многие сочувственно, даже службисты НКВД, об этом хорошо написал Д.Гранин.

Когда я узнала, что в радиохимическом отделе открывается аспирантура, я заглянула в кабинет Николая Владимировича, чтобы узнать, будет ли аспирантура в нашем отделе. По тому, как он сперва взглянул в окно, я поняла, что он думает, как бы мне популярней все объяснить. «Вы хотите разрабатывать чужие мысли?» - спросил он. «Нет» - ответила я. «А свои есть?» - «Нет». «Тогда читайте, ищите и поверьте, когда у Вас появится собственный интерес, сил будет гораздо больше, все пойдет быстро, на интересе». Как в воду глядел, так у меня все и сложилось. Сперва в лаборатории «Б» я занималась радиотоксикологией, потом, после переезда в 1955 году в г.Озерск, в Филиале №1 Института биофизики АМН СССР – разработкой в эксперименте моделей хронического радиационного поражения, при этом очень хотела заниматься экспериментальной терапией и когда появилась такая возможность работать стало очень интересно, с нетерпением ждали результатов каждого эксперимента. Для лечения острой лучевой болезни в эксперименте на мелких и крупных лабораторных животных мы применяли различные стимулирующие и замещающие средства: клетки костного мозга, селезенки, печени здоровых доноров, нуклеиновые кислоты: ДНК и РНК, ДНКазу. Проводили очищение крови от радиотоксинов с помощью гемосорбции, а также использовали биосинтетические регуляторы кроветворения: Г- КСФ и интерлейкины (ИЛ-2, ИЛ-1β). Все это стало предметом моих мыслей и интересов на многие годы. Совет Николая Владимировича помню всегда. Светлая ему память.

◆

О, Сунгуль! Ты последнее звено в цепи озер
У подножия седых Уральских гор,
В стороне от всех дорог и деревень,
В старину бродил здесь только дикий зверь.
Красота твоя неброска и мила,
Ты, как дочь меньшая батюшки-купца
В русской сказке, что всегда о доброте,
И о верности, любви и о мечте.
О, Сунгуль! Солнце и вода!
Гладь сверкает, словно зеркала!
После долгих-долгих лет
Снова шлю тебе привет,
Не забыть тебя мне никогда:
Чашу светлых твоих вод
В окружении лесов,
В ожерелье изумрудных берегов.
О, Сунгуль! Здесь бродили с тобой,
Любовь, не ставшая, увы, моей судьбой.
Моя юность здесь осталась навсегда,
Хоть давно уже прошла ее пора.
Вскоре же после Великой войны
Народец ученый сюда привезли
Из ГУЛАГов, заграниц и из ВУЗов всех столиц
Делать щит против Третьей войны.
О, Сунгуль! Ты прости! Загубили частицу земли:
Где стоял институт – лишь плита,
И народ никогда
Не вернется сюда…
Создан атомный щит для страны –
Города вдоль Уральской гряды,
Неизвестными были вчера,
Но теперь знают их имена.
И сейчас важен их арсенал
Для России и мира всего!
А потери? Ведь жертв не считал
Никогда и никто…
О, Сунгуль! Озеро мое у Вишневых гор,
Бирюза воды и лугов простор,
Нежная и хрупкая милая краса
Скрыта за лесами от людей не зря…

Addendum to the Cancer genetics & Cancer therapy

ACUTE MYELOID LEUKEMIA LEADS THE WAY IN MOLECULAR CANCER GENETICS: PRECISION MEDICINE AT REACH?

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Acute myeloid leukemia (AML) is a prime model disease for understanding the genomic aberrations underlying cancer as it has a long-lasting history of being first. Unraveling the molecular basis of AML started with the invention of chromosome banding analysis, allowing for the first time the detection of recurrent translocation such as t(15;17) in acute promyelocytic leukemia (APL), which then also became the first human leukemia to be successfully treated by molecularly targeted therapy. Using all-trans retinoic acid (ATRA), which targets the rearranged retinoic acid receptor alpha (RARA), one was able to overcome the transformation potential of the fusion gene PML-RARA.

Thus, in the past cytogenetic markers have significantly improved the risk stratification of AML, and recently the development of genomics technologies, such as DNA microarray analysis and next generation sequencing (NGS), has tremendously contributed to decipher the AML associated molecular changes. Especially, as it was again in AML that first gene expression profiling studies demonstrated their power and the first human tumor genome to be sequenced in 2008 was unsurprisingly an AML case. In accordance, a growing number of genomic aberrations and gene mutations have been identified in AML, which are associated with epigenetic changes and deregulated gene expression. These findings further highlight the molecular heterogeneity of AML (and cancer in general) and show that individual patients present with a distinct and almost unique combination of somatically acquired genetic aberrations.

Importantly, this growing genetic information has started to translate into the clinical routine, and AML cases are already characterized on the basis of the underlying genetic defects that define distinct entities of clinical importance. First, cytogenetic and molecular genetic changes represent powerful prognostic markers, and second some genetic and epigenetic aberrations can be targeted by novel therapeutic approaches, such as tyrosine kinase inhibitors and demethylating agents. However, there are still limitations regarding the use of prognostic biomarkers in clinical practice as for many novel markers the prognostic impact so far has only been evaluated in retrospective studies, and thus several new markers still need to be interpreted cautiously. Furthermore, for an improved clinical decision making there is an unmet need for predictive markers that can be attributed to the clinical benefit of novel treatment approaches.

FROM CANCER GENETICS TO TARGETED THERAPIES – MODELING HUMAN LYMPHOMA PATHOGENESIS IN MICE

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The systematic description of aberrations in tumors has dramatically broadened our knowledge about the genetic and epigenetic mutations in cancer. However, the distinction in tumor promoting (or driver) and bystander (or passenger) aberrations is still challenging and hinders the design of new drugs that are the basis for tailored therapies.

By targeting presumed driver mutations into the progenitor cells from which the tumors supposedly arise we are aiming to model distinct classes of human B cell lymphomas in mice. These faithful preclinical models of human lymphomas are used to investigate the functional role of both the oncogenic mutations intentionally incorporated into the models as well as of additional aberrations accumulating in the tumors during their progression in the animal. Our work to date has revealed that such animal models can reproduce mutational signatures seen in the corresponding human lymphoma entities, as well as clinically relevant patterns of tumor dissemination. We provide evidence that tailored mouse models of human lymphomas are valuable tools to investigate lymphoma pathogenesis mechanistically and identify relevant therapeutic strategies for improved patient management.

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