ABSTRACT&REFERENCES

DOI: 10.15587/2519-8025.2018.143734

SIZE AND FUNCTIONAL STATE DISTRIBUTION OF CHROMATIN LOOP DOMAINS AND ITS REORGANIZATION UPON CELL ACTIVATION: HI-C DATA ANALYSIS

p. 4-9

Katerina Afanasieva, PhD, Associate Professor, Educational and Scientific Center "Institute of Biology and Medicine" Taras Shevchenko National University of Kyiv, Volodymyrska str., 64/13, Kyiv, Ukraine, 01601 E-mail: aphon@ukr.net

ORCID: http://orcid.org/0000-0002-1349-2767

Andrei Sivolob, Doctor of Biological Sciences, Professor, Educational and Scientific Center "Institute of Biology and Medicine" Taras Shevchenko National University of Kyiv, Volodymyrska str., 64/13, Kyiv, Ukraine, 01601 E-mail: sivolob@univ.kiev.ua ORCID: http://orcid.org/0000-0002-7306-0763

Chromatin structure at high levels of its organization, which remains not to be completely understood, attracts much attention because it is the basis of regulation of functional processes in nuclei of eukaryotic cells. An important aspect of this organization is the existence of relatively autonomic structural elements, the chromatin loop domains. Hi-C is one of the most effective methods to study the three-dimensional structure of chromatin. The bioinformatic databases contain much Hi-C data that have not been examined completely. In particular, a detailed analysis of the loop sizes and regularities of their location in defined chromatin regions (transcriptionally active or inactive) has not been performed, it remains to be seen how the loop density and sizes change, if there is any change, depending on the functional activity of chromatin regions.

The aim of the study was to figure out the peculiarities of the size and functional state distribution of the chromatin loop domains in cells with different functional activity.

Materials and methods: bioinformatic analysis of the Hi-C data deposited in databases of open access.

Results: the size distributions of the chromatin loop domains in cells of different types, the distribution of the loop domains among different chromatin compartments in lymphoblastoid GM12878 cells and the size distributions within these compartments have been obtained, the changes in the loop size distribution under mouse lymphocyte activation have been analyzed.

Conclusions: the contour length of the loop domains is distributed exponentially, the distribution parameters are cell-specific, the majority of the loops are located in euchromatin regions, and the cell activation is accompanied by an increase in both the number of loops and their contour length **Keywords**: chromatin, loop domains, chromatin compartments, Hi-C method, cell activation, bioinformatics

References

1. Dekker, J., Mirny, L. (2016). The 3D Genome as Moderator of Chromosomal Communication. Cell, 164 (6), 1110– 1121. doi: http://doi.org/10.1016/j.cell.2016.02.007 2. Dixon, J. R., Gorkin, D. U., Ren, B. (2016). Chromatin Domains: The Unit of Chromosome Organization. Molecular Cell, 62 (5), 668–680. doi: http://doi.org/10.1016/j.molcel.2016.05.018

3. Rao, S. S. P., Huntley, M. H., Durand, N. C., Stamenova, E. K., Bochkov, I. D., Robinson, J. T. et. al. (2014). A 3D Map of the Human Genome at Kilobase Resolution Reveals Principles of Chromatin Looping. Cell, 159 (7), 1665–1680. doi: http://doi.org/10.1016/j.cell.2014.11.021

4. Vian, L., Pekowska, A., Rao, S. S. P., Kieffer-Kwon, K.-R., Jung, S., Baranello, L. et. al. (2018). The Energetics and Physiological Impact of Cohesin Extrusion. Cell, 173 (5), 1165–1178. doi: http://doi.org/10.1016/j.cell.2018.03.072

5. Lieberman-Aiden, E., van Berkum, N. L., Williams, L., Imakaev, M., Ragoczy, T., Telling, A. et. al. (2009). Comprehensive Mapping of Long-Range Interactions Reveals Folding Principles of the Human Genome. Science, 326 (5950), 289–293. doi: http://doi.org/10.1126/science.1181369

6. Kieffer-Kwon, K.-R., Nimura, K., Rao, S. S. P., Xu, J., Jung, S., Pekowska, A. et. al. (2017). Myc Regulates Chromatin Decompaction and Nuclear Architecture during B Cell Activation. Molecular Cell, 67 (4), 566–578. doi: http://doi.org/ 10.1016/j.molcel.2017.07.013

7. Gene Expression omnibus. URL: https://www.ncbi. nlm.nih.gov/geo/

8. Sanborn, A. L., Rao, S. S. P., Huang, S.-C., Durand, N. C., Huntley, M. H., Jewett, A. I. et. al. (2015). Chromatin extrusion explains key features of loop and domain formation in wild-type and engineered genomes. Proceedings of the National Academy of Sciences, 112 (47), 6456–6465. doi: http://doi.org/10.1073/ pnas.1518552112

9. Fudenberg, G., Imakaev, M., Lu, C., Goloborodko, A., Abdennur, N., Mirny, L. A. (2016). Formation of Chromosomal Domains by Loop Extrusion. Cell Reports, 15 (9), 2038–2049. doi: http://doi.org/10.1016/j.celrep.2016.04.085

10. McGhee, J. D., von Hippel, P. H. (1974). Theoretical aspects of DNA-protein interactions: Co-operative and non-co-operative binding of large ligands to a one-dimensional homogeneous lattice. Journal of Molecular Biology, 86 (2), 469–489. doi: http://doi.org/10.1016/0022-2836(74) 90031-x

11. Afanasieva, K., Chopei, M., Lozovik, A., Semenova, A., Lukash, L., Sivolob, A. (2017). DNA loop domain organization in nucleoids from cells of different types. Biochemical and Biophysical Research Communications, 483 (1), 142–146. doi: http://doi.org/10.1016/j.bbrc.2016.12.177

DOI: 10.15587/2519-8025.2018.146274

SEASONAL DYNAMICS OF MANGANESE AND IRON COMPOUNDS IN THE SUPERFICIAL WATERS OF VIDSICHNE WATER INTAKE OF TETERIV RIVER

p. 10-14

Ella Arystarkhova, PhD, Associate Professor, Department of Environmental Safety and Economy of Natural Management, Zhytomyr National Agroecological University, Staryi blvd., 7, Zhytomyr, Ukraine, 10008 E-mail: ella.aryst@gmail.com ORCID: http://orcid.org/0000-0002-7523-4608 **Research aim** – to determine features of the season dynamics of concentrations of manganese (Mn) and iron (Fe) in the surface waters of Vidsichne water intake, Teteriv river in 2012-2014 and clarification of their correlations with the water temperature, hydrogen index (pH), content of dissolved oxygen (DO), and also by the number of dominating associations of planktonic algae.

Methods. Water samples (1 dm^3) were taken from the water intake (at realizing arrangements for cleaning and deepening its bottom part), and Mn and Fe compounds concentrations were determined in them by colorimetric methods, DO - by DO 4000 measurer, hydrogen index – by pH-meter, temperature – by the mercury thermometer. For studying the phytoplankton content, there was realized the hydrobiological analysis. The statistical processing of data was realized by MO Excel 2003 program.

Research results. Mn compounds concentration in water exceeded MPC_w and had two peak values in summer. Fe compounds were also observed in increased amounts, but their peak was in another season every year. There were revealed reliable correlations of strong and middle Mn concentrations in water with a temperature and DO. The tendency to strengthening correlations of concentrations of these compounds with blue-green algae and weakening – with green ones was demonstrated. Mutual connections of Fe with these parameters were in whole weaker comparing with Mn, especially with pH and planktonic algae. And only in 2014 coefficient values of correlation between iron and temperature and DO essentially grew.

Conclusions. It was established, that concentrations of Mn and Fe compounds in water of the water intake exceeded MPC during most seasons (0,1 and 0,3 mg/dm³ respectively) in 2–8 times. The most content of Mn was observed especially in summer months, and Fe – in different seasons. Changes of Mn concentrations were much stronger connected with the water temperature (0,7029, $p \le 0.01 - in 2012$ and 0,6702, $p \le 0.05 - 2013$ years) and DO (-0,6272, $p \le 0.05 - 2013$) in 2012, -0.8752, $p \le 0.0001 - 2013$ and -0.6349, $p \le 0.05 - 2013$ 2014 years), than ones of Fe concentrations. Correlations of Fe compounds with these parameters reaches reliability only in 2014 year (0,7326 and -0,7469 respectively, $p \le 0,01$). Mn and Fe compounds had reliable connections only with blue-green algae (cyanogen bacteria) among all phytoplankton associations: Mn (0,6808, $p \le 0,05$) – in 2014 and Fe (0,7410, $p \le 0.01$) – in 2012. During the three year period of the studies there was fixed weakening connections between Mn and water temperature (by 28,54 %) and amounts of green algae (by 65,63 %) and strengthening – with amounts of blue-green ones (by 77,95 %), and also the growing dependence of Fe compounds concentrations on the temperature (by 79,12%) and DO (by 95,77%). Most revealed tendencies (except season dynamics of Mn and its correlations with the temperature, DO and amounts of blue-green ones) were atypical for the water intake and appeared, most probably, as a result of arrangements for cleaning the bottom part of the water body and its deepening that resulted in disorders in the condition of the water environment, including the abnormal increase of blue-green algae amounts in December of 2012 (up to 91,06 thousand cl/dm³)

Keywords: Mn, Fe, season variations, abiotic parameters, biological parameters, correlations

References

1. Zapolskyi, A. K., Shumigay, I. V. (2015). Okhorona vod vid vysnazhennia i sabrudnennia. Agroecologichnyi zhurnal, 3, 6–15.

2. Lur'ie, U. U. (Ed.) (1973). Unifizyrovannyie metody analisa vod. Moscow: Isdatiel'stvo Chimia, 376.

3. Snizhko, S. I. (2001). Otsinka ta prognosuvannia iakosti pryrodnykh vod. Kyiv: Nika-Tsentr, 264.

4. Bren', N. V. (1999). Ispol'sovanie besposvonochnykh dlia monitoringa sagriasneniia vodnyh ekosystem tiazholymi metallami. Hydrobiologicheskiy zhurnal, 35, 75–88.

5. Pinkina, T. V. (2007). Dzherela nadkhodzhennia vazhkykh metaliv u prisni vodoymy ta yikh risnjbichnyy vplyv na hidrobiontiv. Voda: problemy ta shliakhy vyrishennia. Zhytomyr, 80–84.

6. Kot, I. S., Trokhymenko, I. A., Dyka, I. O., Myslyva, T. M. (2012). Vazhki metaly u vodakh i torfakh Zhytomyrs'koho Polissia. Nauka. Molod'. Ekologia-2012. Zhytomyr, 181–186.

7. Arunakumara, K. K. I. U., Zhang, X. (2008). Heavy metal bioaccumulation and toxicity with special reference to microalgae. Journal of Ocean University of China, 7 (1), 60–64. doi: http://doi.org/10.1007/s11802-008-0060-y

8. Bergkemper, V., Weisse, T. (2017). Phytoplankton response to the summer 2015 heat wave – a case study from prealpine Lake Mondsee, Austria. Inland Waters, 7 (1), 88–99. doi: http://doi.org/10.1080/20442041.2017.1294352

9. Dudnik, S. V. (2014). Vodna toksykologia. P. 2: Ichtiotoksykologia. Kyiv, 108.

10. Malik, A., Grohmann, E., Akhtar, R. (Eds.) (2014). Environmental Deterioration and Human Health: Natural and anthropogenic determinants. Dordrecht: Springer, 8–16. doi: https://doi.org/10.1007/978-94-007-7890-0

11. River watch. Manual for public environmental monitoring (2015). Saint Petersburg: Friends of the Baltics. Coalition Clean Baltics, 32.

12. Biliavskiy, H. O., Butchenko, L. I. (2006). Osnovy ekolohii: teoria ta praktykum. Kyiv: Libra, 368.

DOI: 10.15587/2519-8025.2018.146337

CHROMOSOME TYPE ABERRATIONS OUTCOME IN ONCOGYNECOLOGICAL PATIENTS DUE TO RADIATION THERAPY ON ROCUS-AM AND LINEAR ACCELERATOR CLINAC 600C

p. 15-21

Maznyk Nataliya, Doctor of Biological Sciences, Head of Laboratory, Laboratory of Radiation Cytogenetics, State Institution "Grigoriev Institute for medical Radiology NAMS of Ukraine", Pushkinska str., 82, Kharkiv, Ukraine, 61024

Sypko Tetiana, Researcher, Laboratory of Radiation Cytogenetics, State Institution "Grigoriev Institute for medical Radiology NAMS of Ukraine", Pushkinska str., 82, Kharkiv, Ukraine, 61024

Pshenichna Nataliya, Junior Researcher, Laboratory of Radiation Cytogenetics, State Institution "Grigoriev Institute for medical Radiology NAMS of Ukraine", Pushkinska str., 82, Kharkiv, Ukraine, 61024 **Starenkiy Viktor,** MD, Senior Researcher, Head of Department, Department of Radiotherapy, State Institution "Grigoriev Institute for medical Radiology NAMS of Ukraine", Pushkinska str., 82, Kharkiv, Ukraine, 61024

Sukhina Olena, MD, Professor, Chief Researcher, Department of Radiotherapy, State Institution "Grigoriev Institute for medical Radiology NAMS of Ukraine", Pushkinska str., 82, Kharkiv, Ukraine, 61024

Krugova Iryna, PhD, Senior Researcher, Department of Oncogynecology, State Institution "Grigoriev Institute for medical Radiology NAMS of Ukraine", Pushkinska str., 82, Kharkiv, Ukraine, 61024

Aims: The detection of chromosome type aberrations outcome in oncogynecological patients during radiation therapy depending on the irradiation regime.

Methods: The group of 36 oncogynecological patients was examined before treatment, in the middle and at the end of external gamma-radiotherapy ⁶⁰Co on ROCUS-AM and megavolt therapy on linear accelerator Clinac 600C. Lymphocytes were cultivated by conventional technique during 50–54 hours. Chromosome type aberrations were detected with the classical cytogenetic analysis.

Results of research: The chromosome type aberrations changes in lymphocytes of oncogynecological patients during external gamma-radiotherapy 60Co on ROCUS-AM and megavolt therapy on linear accelerator Clinac 600C were demonstrated. The excess of chromosome type cytogenetic damage over spontaneous level was shown in patients before treatment. Quite monotonic increase of chromosome type aberrations frequency from the start to the end of radiotherapy course in both groups was found. However the pace of chromosome type aberrations increase was different depending on the irradiation regime and more pronounced in oncogynecological patients undergoing gamma-therapy ⁶⁰Co. The range of cells with unstable chromosome aberrations expanded during the radiotherapy course. In the middle of the radiotherapy cells with 1–7 aberrations per cell in both groups were observed. At the end the number of damages per aberrant cell varied from 1 to 11 in ROCUS-AM patients and from 1–9 in patients after megavolt therapy on a linear accelerator. The distribution of the chromosome type aberrations among cells was found to be over-dispersed according to Poisson statistic in both studied groups at the middle and at the end of the radiotherapy course.

Conclusion: The study of the radiation-induced aberrations revealed the similar and different features of cytogenetic damages accumulation in patient groups depending on the regime of irradiation. The study results revealed the absence of the expected larger genotoxic effect on the patients' lymphocytes due to treatment on a linear accelerator in comparison with the ROCUS-AM, despite of the difference in the exposure energy. The data obtained are particularly important for a correct assessment of the local fractionated irradiation effects in the non-tumor patient cells.

Keywords: chromosome type aberrations, lymphocytes, oncogynecological patients, external radiation therapy.

References

1. Hudkov, I. M. (2016). Radiobiolohiya. Kyiv: NUBiP Ukrainy, 485.

2. Ivchuk, V. P., Vincevich, L. V. (2011). Osobennosti luchevogo lecheniya na lineynom uskoritele bol'nyh rakom molochnoy zhelezy I-II stadiy posle organosohranyayushchih operaciy. Radiolohichnyi visnyk, 4, 25–27.

3. Matyakin, G. G., Chuprik-Malinovskaya, T. P., Nasnikova, I. Yu., Emel'yanov, I. V. (2011). Sovremennye vozmozhnosti luchevoy terapii v onkologii. Kremlevskaya medicina. Klinicheskiy vestnik, 1, 47–51.

4. González Ferreira, J. A., Jaén Olasolo, J., Azinovic, I., Jeremic, B. (2015). Effect of radiotherapy delay in overall treatment time on local control and survival in head and neck cancer: Review of the literature. Reports of Practical Oncology & Radiotherapy, 20 (5), 328–339. doi: https://doi.org/10.1016/j.rpor.2015.05.010

5. Magnata, S. P., Serafim, I., Netto, J., Gomes, P., Netto, A. M., Amaral, A. (2002). Unstable chromosome aberrations in peripheral blood lymphocytes from patients with cervical uterine cancer following radiotherapy. Cellular and Molecular Biology (Noisy-le-grand), 48 (7), 809–811.

6. Brandan, M. E., Perez-Pastenes, M. A., Ostrosky-Wegman, P., Gonsebatt, M. E., Diaz-Perches, R. (1994). Mean Dose to Lymphocytes During Radiotherapy Treatments. Health Physics, 67 (4), 326–329. doi: https://doi.org/10.1097/00004032-199410000-00002

7. Vuckovic-Dekic, L., Spremo, B., Stanojevic-Bakic, N., Garzicic, B., Durbaba, M. (1994). Immunosuppressive and cytogenetic effects of pelvic irradiation on the peripheral lymphocytes of patients with cervical cancer. One year follow-up. Archivum Immunologiae et Therapiae Experimentalis, 42 (1), 63–66.

8. Gershkevitsh, E., Hildebrandt, G., Wolf, U., Kamprad, F., Realo, E., Trott, K.-R. (2002). Chromosomal Aberration in Peripheral Lymphocytes and Doses to the Active Bone Marrow in Radiotherapy of Prostate Cancer. Strahlentherapie Und Onkologie, 178 (1), 36–42. doi: https://doi.org/10.1007/ s00066-002-0886-y

9. Cytogenetic Dosimetry: Applications in Preparedness for and Response to Radiation Emergencies (2011). Vienna: International Atomic Energy Agency, 247.

10. Sypko, T. S., Pshenichna, N. D., Maznyk, N. O. (2015). Mitotychna aktyvnist kultur limfotsytiv krovi onkolohichnykh khvorykh na riznykh etapakh promenevoi terapiyi na liniynomu pryskoriuvachi. Materialy VI zizdu radiobiolohichnoho tovarystva Ukrainy. Kyiv, 118–119.

11. Sypko, T. S., Pshenichna, N. D., Maznyk, N. O. (2015). Mitotychna aktyvnist v kulturakh limfotsytiv krovi onkolohichnykh khvorykh pid chas hamma-terapiyi 60Co na aparati Rokus-AM. Materialy naukovo-praktychnoi konferentsiyi z uchastiu mizhnarodnykh spetsialistiv. Kharkiv, 81–82.

12. Higueras, M., González, J. E., Di Giorgio, M., Barquinero, J. F. (2018). A note on Poisson goodness-of-fit tests for ionizing radiation induced chromosomal aberration samples. International Journal of Radiation Biology, 94 (7), 656–663. doi: https://doi.org/1 0.1080/09553002.2018.1478012

13. Atramentova, L. A., Utevskaya, O. M. (2008). Statisticheskie metody v biologii. Gorlovka: «Vidavnictvo Lihtar», 248.

14. Semenov, A. V., Vorobcova, I. E. (2016). Chastota hromosomnyh aberraciy v limfocitah perifericheskoy krovi bol'nyh s solidnymi opuholyami. Voprosy onkologii, 62 (3), 485–489.

15. Mel'nikov, A. A., Vasil'ev, S. A., Smol'nikova, E. V., Urazova, L. N., Musabaeva, L. I., Velikaya, V. V. et. al. (2012). Dynamics chromosomal aberrations and micronuclei in lymphocytes of patients with malignant neoplasms in neutron therapy. Sibirskiy onkologicheskiy zhurnal, 52 (4), 52–56. 16. Roch-Lefevre, S., Pouzoulet, F., Giraudet, A. L., Voisin, P., Vaurijoux, A., Gruel, G. et. al. (2010). Cytogenetic assessment of heterogeneous radiation doses in cancer patients treated with fractionated radiotherapy. British Journal of Radiology, 83 (993), 759–766. doi: https://doi.org/10.1259/bjr/21022597

17. Xunclà, M., Barquinero, J. F., Caballín, M. R., Craven-Bartle, J., Ribas, M., de Vega, J. M., Barrios, L. (2008). Cytogenetic damage induced by radiotherapy. Evaluation of protection by amifostine and analysis of chromosome aberrations persistence. International Journal of Radiation Biology, 84 (3), 243–251. doi: https://doi.org/10.1080/09553000801902141

DOI: 10.15587/2519-8025.2018.146930

DYNAMICS OF ANXIETY OF PARTICIPANTS OF UNITED FORCES OPERATION

p. 22-26

Zoryna Boiarska, PhD, Associate Professor, Department of Biophysics, Vasyl' Stus Donetsk National University, 600-richchia str., 21, Vinnytsia, Ukraine, 21021 E-mail: z.boiarska@gmail.com ORCID: http://orcid.org/0000-0002-6722-2498

Roman Pinchuk, Vasyl' Stus Donetsk National University, 600-richchia str., 21, Vinnytsia, Ukraine, 21021, Lance Sergeant, The chief of the ground faulting of the radiolocation station of military unit A4610, Bohoniki, Vinnytsia region, Ukraine, 23233

E-mail: romans.pinchuk@gmail.com ORCID: http://orcid.org/0000-0001-5143-6494

The aim of the work- to investigate features of a psychological state of the participants in the united forces operation that were in the east of our state on the second line of defense for four months.

Materials and research methods. Questionnaires of fighters-contractors according to the methods: "Scale of reactive and personal anxiety Ch. D. Spielberger – Yu. L. Khanina "and the Beck Depression Inventory (BDI) questionnaire. The study was conducted in the first days after arriving at the location site, two months in the zone of the united forces operation and two weeks after returning from the war zone. The study was conducted on the basis of 177 separate radar platoon (Lisichansk, Lugansk region) with combatants-volunteers from April to August 2018.

Simulation Results. As a result of the study, there were established a predominantly moderate level of reactive and personal anxiety and the absence of signs of depression at the beginning of the assignment and during the stay in the area of the operation. There was an increase in the level of anxiety and the appearance of signs of depression after returning from the combat zone. The analysis of the main problems of the participants of the operation of the combined forces arising from the return to the conditions of peaceful life (violation of the rights to social guarantees, bureaucratic problems when applying for benefits) has been carried out.

Conclusions. Thus, in the first days of arrival in the combat zone, the combatants are dominated by the average level of reactive and personal anxiety, and there are no signs of depression. After two months of performing combat missions, the level of reactive and situational anxiety among combatants remains within the average indicators, the participants of the study have no signs of depression, which allows to conclude that a high adaptive level is achieved. Two weeks after returning from the combat zone, most combatants increase the level of reactive anxiety and show signs of mild depression. The prospect of further research is seen in the development of effective methods for the physical and psychological rehabilitation of combatants in order to increase their adaptive capabilities upon returning from the environment

Keywords: diagnosis of posttraumatic syndrome, reactive anxiety, personality anxiety, depression, combatant, united forces operation

References

1. Timchenko, V. O. (2017). Psykholohichni naslidky perebuvannia riatuvalnykiv u zoni provedennia antyterorystychnoi operatsii. Kharkiv, 81.

2. Shvets, A. V., Khoroshun, E. M., Koval, O. V., Lukianchuk, I. A., Chaikovskyi, A. R. (2016). Medychni zakhody z poperedzhennia presuitsydalnykh form povedinky viiskovosluzhbovtsiv v umovakh voiennoho konfliktu ta pislia yoho zavershennia. Kyiv, 59.

3. Timchenko, V. O. (2015). Refleks prydushennia abo shcho zavazhaie veteranam ATO povernutysia do zvychainoho myrnoho zhyttia. Problemy ekstremalnoi ta kryzovoi psykholohii, 18, 234–243.

4. Leskov, V. O. (2006). Psykholohichna reabilitatsiia viiskovosluzhbovtsiv zapasu v systemi minimizatsii vyiaviv nehatyvnykh psykholohichnykh naslidkiv lokalnykh voiennykh konfliktiv. Zbirnyk naukovykh prats instytutu psykholohii im. H. S. Kostiuka APN Ukrainy, VIII (3), 191–197.

5. Paroniants, T. P. (2004). Vynyknennia i proiav pisliatravmatychnykh stresovykh rozladiv u pratsivnykiv orhaniv vnutrishnikh sprav v umovakh vykonannia myrotvorchoi misii OON (na prykladi kolyshnoi Yuhoslavii). Kharkiv, 18.

6. Mushkevych, M. (2015). Volyn: yak dopomohty viiskovomu ta yoho simi reabilituvatysia. Available at: http://www. volynnews.com/news/vidsichagresoruukrayinayedina/volynski-atoshnyky-ne-skhylni-do-suyitsydu-ale-yim-potribna-dopomoha/

7. Popeliushko, R. P. (2017). Rezultaty doslidzhennia psykholohichnykh osoblyvostei kombatantiv do ta pislia uchasti u boiovykh diiakh. Innovative solutions in modern science, 5 (14), 78–91.

8. Kharchenko, O., Mramornova, O. (2016). Problemy veteraniv antyterorystychnoi operatsii na skhodi Ukrainy. Visnyk KhNU imeni V. N. Karazina. Seriia «Sotsiolohichni doslidzhennia suchasnoho suspilstva: metodolohiia, teoriia, metody», 37, 115–124.

9. Bukovska, O. O. (2015). Psykholohichna dopomoha simiam viiskovosluzhbovtsiv, yaki povertaiutsia iz zony boiovykh dii. Visnyk Chernihivskoho natsionalnoho pedahohichnoho universytetu im. T. H. Shevchenka, 128, 29–32.

10. Ahaiev, N. A., Kokun, O. M., Pishko, I. O., Lozinska, N. S., Ostapchuk, V. V., Tkachenko, V. V. (2016). Zbirnyk metodyk dlia diahnostyky nehatyvnykh psykhichnykh staniv viiskovosluzhbovtsiv. Kyiv: NDTs HP ZSU, 234.

DOI: 10.15587/2519-8025.2018.146936

CONTENT OF SOME BIOELEMENTS IN BODIES AND TISSUES OF EXPERIMENTAL ANIMALS UNDER CONDITIONS OF NITROGEN INTOXICATION

p. 27-30

Larisa Nechytaylo, Assistant, Department of Biological and Medical Chemistry, Ivano-Frankivsk National Medical University, Halytska str., 2, Ivano-Frankivsk, Ukraine, 76018 E-mail: larysa.nechytailo@gmail.com

Anna Yerstenyuk, Doctor of Biological Sciences, Professor, Department of Biological and Medical Chemistry, Ivano-Frankivsk National Medical University, Halytska str., 2, Ivano-Frankivsk, Ukraine, 76018 E-mail: erst@ukr.net

E-man: cist@uki.net

The aim of the study. Analyze the content of some bioelements and cumulative properties of heavy metal ions (on an example of cadmium) for nitrate intoxication.

Materials and methods. The object of the study was white rats, which were divided into two groups: I - control, II research (receiving aqueous NaNO₃ solution with drinking water at a dose of 1/10 DL_{s0}). Intoxication was carried out for 10 days. The material was collected (renal tissue, liver and spleen) on 1st, 14th and 28th days after the completion of the administration of the toxicant. The level of macro- and micronutrients was determined by the atomic absorption spectrophotometer C-115PK. The obtained results were statistically processed using the computer program Statistics.

Results. Under the influence of NaNO₃, an increase in the calcium level in the renal tissue, liver and spleen was noted compared with the control group of animals. At the same time, the Mg content in the liver was declined throughout the observation period, whereas in the kidneys and spleen - on the first day of the experiment. The research of essential trace elements, such as Zn and Cu, allowed to establish the following changes: enhance of Zn level in the liver on the 1st and 14th day and its decrease on the 28th day; in the renal tissue and spleen the value of this index was increased on the 28th day in comparison with the control group of animals. The content of Cu was increased on the 28th day in the spleen and liver, whereas in the renal tissue the value of this index was lower than the control group values. Te analysis of the cadmium level showed that Cd content in the spleen, the liver and the renal tissue of the animals after influence of NaNO₃ exceeded the control values in 3–3,8 times.

Conclusions. It was established that the organisms of experimental animals under the condition of nitrate intoxicationare characterizes by the development of dysmicroelementosis, which is featured by the changes in the levels of vital macroand trace elements in organs and tissues, which is important for the regulation of metabolic processes. An increase in the ability of cadmium ions to accumulate in the studied organs and tissues is also shown

*Keywords:*macroelements, trace elements, sodium nitrate, liver, kidneys, spleen, white rats

References

1. Panasenko, T., Krasnorutskaya, K. I. (2016). Content of nitrate ions in food products of vegetable origin. Current issues of biology, ecology and chemistry, 12 (2), 103–112.

2. Khomenko, Yu. G., Bondarenko, I. V., Bilik, L. I., Dzhulai, O. S. (2011). Medico-ecological problem of human's total nitrates contamination by drinking water and food products and ways of its solution. Actual problems of transport medicine, 23 (1), 82–86.

3. Nechyatilo, L. Ya., Erstenyuk, A. M. (2011). Comparative analysis of the chemical composition of the water of the plain zone of the Precarpathian Region. Bulletin of the National University «Lviv Polytechnic». Chemistry series, technology of substances and their application, 700, 282–286. 4. Nechytaylo, L. Ya. (2014). Dynamics of Changes in the Content of Nitratesin the Drinking Water of the Precarpathian Region and Study of the Effect of Nitrate intoxication on the Micro- and Macro-Elemental Structure of the Liver of Experimental Animals. Biology of Animals, 16 (4), 200.

5. Wimalawansa, S. J. (2010). Nitric oxide and bone. Annals of the New York Academy of Sciences, 1192 (1), 391–403. doi: http://doi.org/10.1111/j.1749-6632.2009.05230.x

6. Belenichev, I. F., Zhernova, G. A. (2009). Free radical damage mechanisms mitochondria when exposed to excess NO. Actual nutrition of the pharmaceutical and medical science and practice, 2 (XXII), 38–40.

7. Gubsky, Yu. I., Levitsky, E. L., Olar, V. V. (2010). Molecular Mechanisms of Klitini for the Day of Biocidal Xenobiotics: The radicals, necrosis, apoptosis. Ukrainian Biochemical Journal, 82 (4 (2)), 9–11.

8. Stakhurska, I. O., Prishlyak, A. M. (2014). Intensyvnist methemohlobin utvorennia u shchuriv riznoi stati za umovy toksychnoho urazhennia natriiu nitrytom. Medical chemistry, 16 (3), 128.

9. Korda, M. M., Yaroshenko, T. Ya. (2005). Rol oksydu azotu v patohenezi urazhennia pechinky ksenobiotykamy. Medical chemistry, 3,74–79.

10. Marushko, Yu. V., Tarynska, O. L., Olefir, T. I., Asonov, A. O. (2010). Nakopychennia kadmiiu ta yoho vplyv na orhanizm dytyny. Klinichna pediatriia, 5 (26), 49–52.

11. Pustovit, S. V. (2010). Biological principle and mechanisms of regulation of medical and biological development. Modern problems of toxicology, 4, 5–9.

12. Pykhteeva, E. G., Potapov, E. A., Bol'shoy, D. V., Pykhteeva, E. D. (2011). In vitro modelirovanie deystviya kadmiya na epitelial'nye kletki pri predvaritel'noy induktsii metallotioneina in vivo. Aktual'nye problemy transportnoy meditsiny, 2 (24), 88–93.

DOI: 10.15587/2519-8025.2018.147090

METABOLIC CHANGES IN THE BONE TISSUE OF ANIMALS IN CONDITIONS OF EXPERIMENTAL CADMIUM INTOXICATION

p. 31-35

Nadiia Khopta, PhD, Associate Professor, Department of Biological and Medical Chemistry named after academician Babenko H. O., Ivano-Frankivsk National Medical University, Halytska str., 2, Ivano-Frankivsk, Ukraine, 76018 E-mail: khopta31@ukr.net

Anna Ersteniuk, Doctor of Biological Sciences, Professor, Department of Biological and Medical Chemistry named after academician Babenko H. O., Ivano-Frankivsk National Medical University, Halytska str., 2, Ivano-Frankivsk, Ukraine, 76018 E-mail: erst@ukr.net

Objective: to investigate the features of metabolic processes, bioelement composition and mineral density of the bone tissue of white rats (sexually mature males) in conditions of defeat by cadmium ions.

Materials and methods. The toxicant (Cadmium chloride, CdCl₂, 1,2 mg/kg) was administered to animals for 10 days, and then removed from the experiment on days 1, 14 and 28. The blood and femurs were investigated. Blood levels of calcium-phosphorus metabolism, acidi and alkaline phosphatases, magnesium,

Hydroxyproline concentrations were studied by standardized methods using reagent kits, as well as the level of Parathyroid hormone and Calcitonin in the development of intoxication. In the ash of the femurs, the content of osteotropic bioelements and toxic cadmium was determined. The bone mineral density (BMD)was investigated using standard x-ray densitometry.

Results. An increase in the concentration of total and ionized calcium on the background of increased secretion of Parathyroid hormone and reduced Calcitonin has been established; decreased activity of alkaline phosphatase, increased acidi phosphatase, especially on the 14-th day. In animals, an increase in the concentration of Hydroxyproline was observed in the blood (2,5-3,5 times) and a decrease in magnesium. When determining the content of osteotropic bioelements in the ash of the femoral bones of rats under conditions of CdCl₂ exposure, a decrease in the content of Calcium, Magnesium, Copper and Zinc in the femoral bones (by 13–45 %) against the background of a significant increase in the content of Cadmium (9,8 times) was found. Also, there is a decrease in BMD, especially low values recorded on the 14th day.

Conclusions. The results of complex studies show that under conditions of introduction of $CdCl_2$ into animals, metabolic processes in bone tissue are disturbed, dismicroelementosis develops, the mineral phase of the bone is demineralized, its collagen matrix is destroyed, and resorption dominates over osteosynthesis.

Keywords: Cadmium, bone tissue, toxic effects, markers of bone metabolism, osteotropic bioelements, mineral density of bone tissue.

References

1. Overview of the problem of cadmium, lead and mercury pollution in the environment in Russia and Ukraine (2008). Integrovermental Forum on Chemical Safety Global Partnerships for Chemical Safety Contributing to the 2020 Goal., 60.

2. Paraniak, R. P., Vasyltseva, L. P., Makuh, Kh. I. (2007). Ways of the receipt of heavy metals in the environment and their impact on living organisms. Biology of animals, 9 (3), 83–89.

3. Moulis, J.-M. (2010). Cellular mechanisms of cadmium toxicity related to the homeostasis of essential metals. BioMetals, 23 (5), 877–896. doi: http://doi.org/10.1007/s10534-010-9336-y

4. Thévenod, F., Lee, W.-K. (2013). Toxicology of Cadmium and Its Damage to Mammalian Organs. Metal Ions in Life Sciences, 11, 415–490. doi: http://doi.org/10.1007/978-94-007-5179-8 14

5. Antonyak, H. L., Biletska, L. P., Babych, N. O., Panas, N. E. et. al. (2010). Cadmium in human and animal organism. I. Intake and accumulation in cells. Studia Biologica, 4 (2), 127–140. doi: http://doi.org/10.30970/sbi.0402.088

6. Ersteniuk, A. M., Khopta, N. S., Bazalytska, I. S. (2013). Correction of bone tissue alteration by artichoke extract in conditions of itai-itai disease. Lviv-Lublin conference of Experimental and Clinical Biochemistry. Lviv-Lublin, 38.

7. Valko, M., Morris, H., Cronin, M. (2005). Metals, Toxicity and Oxidative Stress. Current Medicinal Chemistry, 12 (10), 1161–1208. doi: http://doi.org/10.2174/0929867053764635

8. Bernard, A. (2008). Cadmium and its adverse effects on human health. Indian Journal of Medical Research, 128 (4), 557–564.

9. Vasko, L. V., Kiptenko, L. I., Gortynska, O. M. (2011). Ultrasonstructure of bone cells under conditions of irradiation

and consumption of heavy metal salts. World of Medicine and Biology, 4, 23–26.

10. Extract from the Law of Ukraine «On the Protection of Animals from Cruel Treatment» (2010). Morphology, IV (2), 73–75.

11. Andrusyshyna, I. M., Lampeka, O. G., Golub, I. O. et. al. (2010). Atomic absorption methods for the determination of macro and microelements in biological environments in violation of their metabolism in the human body. Kyiv: VD «Avitsena», 60.

DOI: 10.15587/2519-4984.2018.148075

AMPHIBIAN SKIN GLANDS SECRETIONS AFFECT PLASMA COAGULATION TESTS

p. 36-41

Iryna Udovychenko, Postgraduate Student, Department of Biochemistry, Educational and Scientific C entre «Institute of Biology and Medicine» of Taras Shevchenko National University of Kyiv, Volodymyrska str., 64/13, Kyiv, Ukraine, 01601

E-mail: irisha.nikolaeva@gmail.com ORCID: http://orcid.org/0000-0002-4586-1424

Yuliia Dudkina, Educational and Scientific Centre «Institute of Biology and Medicine» of Taras Shevchenko National University of Kyiv, Volodymyrska str., 64/13, Kyiv, Ukraine, 01601

E-mail: yuliiadudkina@gmail.com

ORCID: *http://orcid.org/0000-0002-4636-6230*

Denys Oliinyk, Educational and Scientific Centre «Institute of Biology and Medicine» of Taras Shevchenko National University of Kyiv, Volodymyrska str., 64/13, Kyiv, Ukraine, 01601

E-mail: oleynikdenis3007@gmail.com ORCID: http://orcid.org/0000-0002-2814-460X

Oleksandra Oskyrko, Educational and Scientific Centre «Institute of Biology and Medicine» of Taras Shevchenko National University of Kyiv, Volodymyrska str., 64/13, Kyiv, Ukraine, 01601

E-mail: sashaoskirko@gmail.com ORCID: http://orcid.org/0000-0003-0092-4193

Oleksii Marushchak, Postgraduate student, Department of Animal monitoring and Conservation, I. I. Schmalhausen Institute of Zoology of National Academy of Sciences of Ukraine, B. Khmelnytskogo str., 15, Kyiv, Ukraine, 01030 E-mail: vse_okei@bigmir.net ORCID: http://orcid.org/0000-0001-9380-5593

Tetiana Halenova, PhD, Seniour researcher, Educational and experimental laboratory «Physical and chemical biology», Educational and Scientific Centre «Institute of Biology and Medicine» of Taras Shevchenko National University of Kyiv, Volodymyrska str., 64/13, Kyiv, Ukraine, 01601 ORCID: http://orcid.org/0000-0003-2973-2646

According to the extremely high mortality and disability rates associated with the abnormal functioning of the hemostasis system, the search for new approaches for the prevention

and treatment of these conditions is one of the most acute problems of modern biochemistry. The active components of reptile poisons are actively used in the treatment of these diseases, but the study of the effects of amphibians' skin glands secretion on the functioning of hemostasis system has not yet been carried out. So, the aim of this work was to assess the effects of the components of amphibian skin secretions on the functioning of the coagulation link of the hemostasis system. Methods. In this study the skin secretions of ten Ukrainian species of amphibians were collected: B. bombina, B. variegata, B. bufo, B. viridis, R. temporaria, P. ridibundus, P. esculentus, P. fuscus, S. salamandra and the hybrid of B. bombina and B. variegata. The samples of crude skin secretions were prepared. The activated partial thromboplastin time (aPTT), thrombin time (TT) and prothrombin time (PT) tests were conducted in vitro using the coagulation analyzer (Rayto RT-2201C, China) and the standard set of reagents (RE-NAM, Russian Federation).

Results. It was established that the components of crude skin secretions of B. bombina, B. variegata, their hybrid, R. temporaria and P. ridibundus prolonged the aPTT of clotting plug formation. The components of skin secretions of B. viridis, P. esculentus, P. fuscus and S. salamandra prolonged the TT of clotting plug formation.

Conclusions. The fact that some amphibian species prolonged the aPTT and TT of clotting plug formation could be the indicator of the presence of inhibitors of certain factors of coagulation hemostasis or be the reason of the degradation of the components of coagulation hemostasis by active components of skin secretion. Such results prove that the amphibian crude skin secretions are a potential source of the compounds that can affect the hemostasis system. The identification of an active component and the elaboration of its mechanism of action are required in further investigations

Keywords: amphibians, skin gland secretions, skin poisons, plasma coagulation tests, coagulation hemostasis

References

1. Piepoli, M. F., Corrà, U., Abreu, A., Cupples, M., Davos, C., Doherty, P. et. al. (2015). Challenges in secondary prevention of cardiovascular diseases. International Journal of Cardiology, 180, 114–119. doi: http://doi.org/10.1016/j.ijcard.2014.11.107

2. Yusuf, S. (2018). Improving worldwide access to inexpensive and effective treatments for common cardiovascular diseases. European Heart Journal Supplements, 20, 18–22. doi: http://doi.org/10.1093/eurheartj/suy005

3. Clarke, B. T. (2007). The natural history of amphibian skin secretions, their normal functioning and potential medical applications. Biological Reviews, 72 (3), 365–379. doi: http://doi.org/10.1111/j.1469-185x.1997.tb00018.x

4. Xu, X., Lai, R. (2015). The Chemistry and Biological Activities of Peptides from Amphibian Skin Secretions. Chemical Reviews, 115 (4), 1760–1846. doi: http://doi.org/10.1021/cr4006704

5. Montecucchi, P. C., Gozzini, L., Erspamer, V., Melchiorri, P. (2009). Primary structure of tryptophan-containing peptides from skin extracts of Phyllomedusa rhodei (tryptophyllins). International Journal of Peptide and Protein Research, 23 (3), 276–281. doi: http://doi.org/10.1111/j.1399-3011.1984. tb02720.x 6. Barberio, C., Delfino, G., Mastromei, G. (1987). A low molecular weight protein with antimicrobial activity in the cutaneous "venom" of the yellow-bellied toad (Bombina varie-gata pachypus). Toxicon, 25 (8), 899–909. doi: http://doi.org/10.1016/0041-0101(87)90250-9

7. Gomes, A., Giri, B., Saha, A., Mishra, R., Dasgupta, S., Debnath, A. (2007). Bioactive molecules from amphibian skin: Their biological activities with reference to therapeutic potentials for possible drug development. Indian Journal of Experimental Biology, 45 (71), 579–590.

8. Erspamer, V. (1999). Biogenic amines and active polypeptides of amphibian skin. Biological reviews of the Cambridge Physiological Society, 172 (3), 211–220.

9. Vigerelli, H., Sciani, J. M., Eula, M. A. C., Sato, L. A., Antoniazzi, M. M., Jared, C., Pimenta, D. C. (2018). Biological Effects and Biodistribution of Bufotenine on Mice. BioMed Research International, 2018, 1–10. doi: http://doi.org/ 10.1155/2018/1032638

10. Cei, J. M., Erspamer, V., Roseghini, M. (1967). Taxonomic and Evolutionary Significance of Biogenic Amines and Polypeptides Occurring in Amphibian Skin. I. Neotropical Leptodactylid Frogs. Systematic Zoology, 16 (4), 328–342. doi: http://doi.org/10.2307/2412152

11. Cunha Filho, G. A., Schwartz, C. A., Resck, I. S., Murta, M. M., Lemos, S. S., Castro, M. S. et. al. (2005). Antimicrobial activity of the bufadienolides marinobufagin and telocinobufagin isolated as major components from skin secretion of the toad Bufo rubescens. Toxicon, 45 (6), 777–782. doi: http:// doi.org/10.1016/j.toxicon.2005.01.017

12. Daly, J. W., Highet, R. J., Myers, C. W. (1984). Occurrence of skin alkaloids in non-dendrobatid frogs from Brazil (Bufonidae), Australia (Myobatrachidae) and Madagascar (Mantellinae). Toxicon, 22 (6), 905–919. doi: http://doi.org/ 10.1016/0041-0101(84)90182-x

13. Azevedo, A. P. S., Farias, J. C., Costa, G. C., Ferreira, S. C. P., Aragão-Filho, W. C., Sousa, P. R. A. et. al. (2007). Anti-thrombotic effect of chronic oral treatment with Orbignya phalerata Mart. Journal of Ethnopharmacology, 111 (1), 155– 159. doi: http://doi.org/10.1016/j.jep.2006.11.005

14. Koch, E., Biber, A. (2007). Treatment of rats with the Pelargonium sidoides extract EPs® 7630 has no effect on blood coagulation parameters or on the pharmacokinetics of warfarin. Phytomedicine, 14, 40–45. doi: http://doi.org/10.1016/j.phymed. 2006.11.026

15. Nikolaieva, I., Dudkina, Yu., Oliinyk, D., Oskyrko, O., Marushchak, O., Halenova, T., Savchuk, O. (2018). Amphibian skin secretions: a potential source of proteolytic enzymes. Biotechnologia Acta. In press.

DOI: 10.15587/2519-8025.2018.148330

QUANTITATIVE AND QUALITATIVE CHARACTERISTICS OF POLYPEPTIDE POOL IN PATIENTS WITH BLADDER CANCER

p. 42-47

Viktor Dmytryk, Postgraduate student, Department of Biochemistry, ESC "Institute of Biology and Medicine", Taras Shevchenko National University of Kyiv, Akademika Hlushkova ave., 2, Kyiv, Ukraine, 03127

ORCID: http://orcid.org/0000-0002-4430-4511

Daryna Krenytska, Department of Biochemistry, ESC "Institute of Biology and Medicine", Taras Shevchenko National University of Kyiv, Akademika Hlushkova ave., 2, Kyiv, Ukraine, 03127

ORCID: http://orcid.org/0000-0002-6693-5904

Tetiana Luhovska, PhD, Department of Biochemistry, ESC "Institute of Biology and Medicine", Taras Shevchenko National University of Kyiv, Akademika Hlushkova ave., 2, Kyiv, Ukraine, 03127

ORCID: http://orcid.org/0000-0001-5068-5106

Pavel Yakovlev, PhD, Department of Urology, O. O. Bogomolets National Medical University, T. Shevchenko blvd., 13, Kyiv, Ukraine, 01601

ORCID: http://orcid.org/0000-0002-1767-3231

Aim: investigate and characterize the presence of polypeptide pool in blood plasma and tumor tissues in patients with bladder cancer at different stages of the disease.

Materials and Methods: Patients with bladder cancer at different stages participated in the trial. The diagnosis was based on X-ray, endoscopic, clinical research methods with morphological verification. None of the patients treated the oncological diseases for a preliminary study. Plasma blood was taken in the preoperative period. Cancer and healthy tissues of the bladder were selected for biopsy, immediately after surgery. Isolation of polypeptide pool in blood plasma and tissue homogenates was carried out using the Nikolaichuk method. The qualitative composition of the protein component of polypeptide pool fraction was investigated using chromatography, using a column with Sephadex G 15.

Results: In the course of the study, reliable changes in the content of medium molecules in blood plasma and tumor homogenates in patients with bladder cancer have been shown. The changes correlate with the stage of the disease. A qualitative analysis of the composition of the protein component of medium mass molecules was carried out, using chromatography.

Conclusions: The fraction of the medium mass molecules from the blood plasma and tumor tissues of patients with various stages of bladder cancer was obtained. The quantitative and qualitative content of the fraction of polypeptide pool in blood plasma and tumor homogenates has been investigated. The content of polypeptide pool in the blood plasma and tumor tissues of patients with bladder cancer is significantly increased compared with the blood plasma of healthy men and compared to healthy tissues of the bladder. The qualitative composition of the polypeptide pool in blood plasma and tumor homogenates differs from that in the plasma of healthy patients or in healthy tissues of the bladder

Keywords: polypeptide pool, bladder cancer, tumor marker, molecules of average molecular weight

References

1. Ploeg, M., Aben, K. K. H., Kiemeney, L. A. (2009). The present and future burden of urinary bladder cancer in the world. World Journal of Urology, 27 (3), 289–293. doi: http://doi.org/10.1007/s00345-009-0383-3

2. Murta-Nascimento, C., Schmitz-Dräger, B. J., Zeegers, M. P., Steineck, G., Kogevinas, M., Real, F. X., Malats, N. (2007). Epidemiology of urinary bladder cancer: from tumor development to patient's death. World Journal of Urology, 25 (3), 285–295. doi: http://doi.org/10.1007/s00345-007-0168-5

3. Ishchuk, T., Glavachek, D., Savchuk, O., Yakovlev, P., Falaleeva, T., Beregova, T., Ostapchenko, L. (2018). Plasma levels of MMPs and TIMP-1 in urinary bladder cancer patients. Biomedical Research and Therapy, 5 (1), 1931–1940. doi: http:// doi.org/10.15419/bmrat.v5i1.407

4. Lopukhin, Yu. M., Dobretsov, G. E., Gryzunov, Yu. A. (2000). The conformational change of the molecule of albumin; a new type of reaction to the disease process. Byulleten' eksperimental'noybiologiiimeditsiny, 130 (7), 4–9.

5. Malakhova, M. Ya. (2000). Endogenous intoxication as a reflection of compensatory adjustment of metabolic processes in the body. Efferentnaya terapiya, 6 (4), 3–14.

6. Afanas'eva, A. N., Evtushenko, V. A. (2005). Endogenous intoxication in patients with gastric cancer in the early postoperative period. Klinicheskaya laboratornaya diagnostika, 2, 18–21.

7. Karelin, A., Filippova, M., Ivanov, V. (1997). Biologically active proteolytic fragments of functional proteins produced in vitro. Bioorganic chemistry, 23 (5), 388–409.

8. Khavinson, V. Kh., Ryzhak, G. A. (2010). Peptide regulation of basic body functions. Vestnnik Roszdravnadzora, 6, 58–62.

9. Nikolaychuk, B. V., Korkovsky, G. A., Lobycheva, G. A. (1989). Molecules of average molecular weight – study and methods of determination. Laboratornoe Delo, 8, 31–33.

10. Chalenko, V. V. (1998). Possible reasons for the increase in the concentration of molecules of average weight in pathology. Pathological physiology, 4, 13–15.

11. Nikol'skaya, V. A., Danil'chenko, Yu. D., Memetova, Z. N. (2013). Biochemical aspects of the consideration of the role of high molecular mass in the body. Uchenye zapiski Tavricheskogo natsional'nogo universiteta im. V. I. Vernadskogo. Seriya «Biologiya, khimiya», 26 (1 (65)), 139–145.

12. Lin'kova, N. S., Tarnovskaya, S. I., Kostylev, A. V., Elashkina, E. V., Nichik, T. E., Morozova, E. A. et. al. (2013). Stem cells and short peptides: application prospects in gerontology. Gerontology, 2, 12–18.

13. Yackin, O. (2005). Isolation of functional fragments of proteins and quantitative determination their content in the cells and tissues of human and rat. Expert Review of Molecular Diagnostics, 5, 145–157.

14. Astashova, T. A., Astashov, V. V., Morozov, S. V. (1998). Chromato-mass spectrophotometric analysis of the products of POL in organs and tissues under the conditions of the toxicosis model. Questions biological. medicine and pharmacological chemistry, 4, 52–55.

15. Prinkova, T. Yu., Prokhorova, V. I., Khotko, E. A., Tsyrus, T. P., Shishlo, L. M., Taganovich, A. D. (2012). Laboratory indices of endogenous intoxication in uterine cancer and the significance of their determination to assess the stage and degree of differentiation of the tumor. Laboratory Diagnostics. Eastern Europe, 4, 79–87.

16. Lowenthal, M. S. (2005). Analysis of Albumin-Associated Peptides and Proteins from Ovarian Cancer Patients. Clinical Chemistry, 51 (10), 1933–1945. doi: http://doi.org/10.1373/ clinchem.2005.052944