https://doi.org/10.29326/2304-196X-2024-13-4-382-386

Change in hepatocyte nuclear-cytoplasmic ratio at nontuberculosis mycobacteria infection against the background of immunomodulator action

Evgeny A. Kosobokov, Tatyana S. Dudoladova
Omsk Agrarian Scientific Center, 26 Korolev avenue, Omsk 644012, Russia

ABSTRACT
The study was targeted at the examination of the effect of the specific immunomodulator KIM-M2 on the morphostructure of liver cells of guinea pigs infected with nontuberculosis mycobacteria. The research was carried out in 15 guinea pigs selected by gender at the Diagnostic Research and Biotechnology Laboratory of the Department of Veterinary Medicine of the Omsk Agrarian Scientific Center. All animals were kept in a specialized animal keeping facilities according to standard housing and feeding regime. The experimental animals were subdivided into three groups of five animals in each: group 1 – challenge group (*Mycobacterium scrofulaceum*), group 2 – experimental group (*Mycobacterium scrofulaceum* and KIM-M2), group 3 – pure control group (saline solution). On day 30 after the start of the experiment, the animals were removed from the experiment, liver biopsy samples were collected and histologic specimens were prepared according to the classical method. During the experiment, it was found that KIM-M2 had a regenerative effect on the liver tissue of the guinea pigs infected with nontuberculosis mycobacteria, which was associated with 1.5-fold increase in the number of mononuclear hepatocytes, 3-fold increase in binuclear cells and 4.3-fold decrease in anucleate hepatocytes thus indicating the manifestation of compensatory reactions in the organ and increase in the depth of regenerative processes. As for animals in group 1; 1.8- and 1.3-fold increase in the area of the nucleus and cytoplasm as compared with the individuals in group 2, and 2.7- and 2-fold increase as compared with the animals in the control group, respectively, indicated the launch of the accumulation mechanisms of the potential reparative reserves and increase in their depth in the liver tissues.

Keywords: nontuberculosis mycobacteria, *Mycobacterium scrofulaceum*, guinea pig, liver, hepatocytes, immunomodulator

Acknowledgements: The authors express their gratitude to the staff of the Laboratory of Epizootology and Tuberculosis Control of the Department of Veterinary Medicine of the Omsk Agrarian Scientific Center for the opportunity to use the author's specific immunomodulator KIM-M2 for research purposes.

For citation: Kosobokov E. A., Dudoladova T. S. Change in hepatocyte nuclear-cytoplasmic ratio at nontuberculosis mycobacteria infection against the background of immunomodulator action. *Veterinary Science Today.* 2024; 13 (4): 382–386. https://doi.org/10.29326/2304-196X-2024-13-4-382-386

Conflict of interests: The authors declare no conflict of interests.

For correspondence: Evgeny A. Kosobokov, Cand. Sci. (Veterinary Medicine), Senior Researcher, Diagnostic Research and Biotechnology Laboratory, Department of Veterinary Medicine, Omsk Agrarian Scientific Center, 93 Lermontova str., Omsk 644001, Russia, *vet_nauka@mail.ru*

УДК 619:616.36:611-018:579.873.2:615.37

Изменение ядерно-цитоплазматического соотношения гепатоцитов при заражении нетуберкулезными микобактериями на фоне действия иммуномодулятора

Е. А. Кособоков, Т. С. Дудоладова
ФГБНУ «Омский аграрный научный центр» (ФГБНУ «Омский АНЦ»), проспект Королёва, 26, г. Омск, 644012, Россия

РЕЗЮМЕ
Целью исследования явилось изучение влияния специфического иммуномодулятора КИМ-М2 на морфоструктуру клеток печени морских свинок, зараженных нетуберкулезными микобактериями. Работа проведена в лаборатории диагностических исследований и биотехнологии отдела ветеринарии ФГБНУ «Омский аграрный научный центр» на поголовье из 15 морских свинок, отобранных по гендерному признаку. Все животные находились в условиях специализированного вивария со стандартным режимом содержания и кормления. Опытных животных разделили на 3 группы по 5 гол. в каждой: 1-я – контроль заражения (*Mycobacterium scrofulaceum*), 2-я – экспериментальная (*Mycobacterium scrofulaceum* и КИМ-М2), 3-я – чистый контроль (физиологический раствор). На 30-е сут после начала эксперимента животных выводили из опыта, отбирали биоптаты печени и готовили гистологические препараты по классической методике. В ходе эксперимента установлено, что КИМ-М2 оказывает регенеративное действие на печеночную ткань зараженных нетуберкулезными микобактериями морских свинок, обусловленное увеличением в 1,5 раза количества одноядерных гепатоцитов, увеличением в 3 раза двухъядерных клеток и уменьшением в 4,3 раза безъядерных гепатоцитов, что указывает на проявление компенсаторных реакций в органе и увеличение глубины регенеративных процессов. У животных 1-й группы увеличение площади ядра и цитоплазмы в 1,8 и 1,3 раза в сравнении с особями 2-й группы

и увеличение соответственно в 2,7 и 2 раза по сравнению с животными из контрольной группы свидетельствует о запуске механизмов накопления потенциальных репаративных резервов и увеличении их глубины в тканях печени.

Ключевые слова: нетуберкулезные микобактерии, *Mycobacterium scrofulaceum*, морская свинка, печень, гепатоциты, иммуномодулятор

Благодарности: Авторы статьи выражают благодарность сотрудникам лаборатории эпизоотологии и мер борьбы с туберкулезом отдела ветеринарии ФГБНУ «Омский АНЦ» за предоставленную возможность использования авторского специфического иммуномодулятора КИМ-М2 для научных исследований.

Для цитирования: Кособоков Е. А., Дудоладова Т. С. Изменение ядерно-цитоплазматического соотношения гепатоцитов при заражении нетуберкулезными микобактериями на фоне действия иммуномодулятора. *Ветеринария сегодня*. 2024; 13 (4): 382–386. https://doi.org/10.29326/2304-196X-2024-13-4-382-386

Конфликт интересов: Авторы заявляют об отсутствии конфликта интересов.

Для корреспонденции: Кособоков Евгений Андреевич, канд. вет. наук, старший научный сотрудник лаборатории диагностических исследований и биотехнологий отдела ветеринарии ФГБНУ «Омский АНЦ», ул. Лермонтова, 93, г. Омск, 644001, Россия, *vet_nauka@mail.ru*

INTRODUCTION

Currently, the role of non-tuberculosis mycobacteria has significantly increased globally. Mycobacterioses cause notable economic damage to animal production holdings, which is associated with a decreased performance, as well as with early culling of animals and their emergency slaughter [1, 2, 3]. High financial costs and lack of effective antiepidemic measures are a threat not only to the holding where mycobacteriosis has been detected, but also to the whole country [4, 5, 6, 7]. This issue has not been studied in depth enough and requires increased attention of the scientific and industrial organizations [8, 9, 10].

Scientists from Russia and many foreign countries have proved that nontuberculosis mycobacteria have not only sensitizing capacities, but they can also localize inducing specific changes in the animal body and cross-immune reactions to the PPD-tuberculin administration [11, 12, 13].

Toxins released by mycobacteria during their vital activity in the macroorganism affect the enzymatic activity of the liver, thus causing pathological changes in the liver tissue, which leads to a decrease in the level of the blood-bile barrier [14, 15, 16, 17].

One of the main functions of the liver is transformation of carbohydrates into glycogen, which is the most important energy resource of the body as a whole [18, 19]. Moreover, stellate reticulum endotheliocytes have a phagocytic effect that neutralizes the accumulation and transport of toxic substances in the animal's body [10, 20, 21].

According to the scientific data of many authors, one of the more effective methods of infectious pathogen control involves the use of immunoprophylaxis drugs [2, 22]. Currently, many modern immunomodulators do not demonstrate a sufficiently high ability to stimulate the effectiveness of the immune response to the infectious agents and their toxins in the organism.

Development of modern immunocorrecting agents and their use makes it possible to increase the body's resistance to the infectious pathogens. An increase in the immune response with the help of a specific immunomodulator enhances the regenerative properties of the cells, tissue and organ as a whole [23, 24, 25].

In view of the above material, the goal was set to study the effect of a specific immunomodulator on liver tissue under the laboratory infection with nontuberculosis mycobacteria.

MATERIALS AND METHODS

The research was carried out in a specialized animal keeping facility. Fifteen adult outbred guinea pigs of tortoiseshell color were used in the study. The animals demonstrated negative PPD test results.

A specific complex immunomodulator KIM-M2 was produced by cultivating BCG vaccine strain in a liquid synthetic Sauton medium, then the grown bacterial mass was destructed with an ultrasonic disperser UZDN-1 (Russia) and the resulting suspension was centrifuged at 15,000 rpm. The protein amount was determined in the collected supernatant after its incubation with formalin using bromophenol blue. Hereafter, the protein concentration was brought up to 1 mg/mL with saline solution. The resulting BCG antigen complex was conjugated with polyvinylpyrrolidone (PVP) and polyethylene glycol (PEG) [26].

The designed KIM-M2 series contained 320 mg of PVP and 80 mg of PEG polyions per 1 mg/mL of the protein. A 200 mL sample of the drug was prepared.

The animals were subdivided into three groups of five animals in each. The animals in group 1 (infection control) and group 2 (experimental) were inoculated with *Mycobacterium scrofulaceum* into the groin area at a dose of 0.001 mg/mL. In 2 weeks, the animals in the experimental group were subcutaneously injected with KIM-M2 immunomodulator into the inner thigh at a dose of 500 mg/mL of the protein. The animals in group 3 (pure control) were injected with a sterile 0.9% saline solution. The microorganisms of pathogenicity groups III–IV were handled in accordance with the sanitary rules and regulations (SanPiN 3.3686-21[1]). The specific immunomodulator is based on the antigenic complex of BCG vaccine strain. On day 30 after the start of the experiment, the animals were euthanized under ether anesthesia and bled. Pieces

[1] https://docs.cntd.ru/document/573660140?ysclid=lzck1dxyyc979388926 (in Russ.)

Table 1
Hepatocyte ratio in liver tissues of the experimental animals

Indicator	Group 1	Group 2	Group 3
Number of mononucleate hepatocytes	41.8%	63.5%	74.5%
Number of binucleate hepatocytes	8.3%	25.0%	18.0%
Number of anucleate hepatocytes	49.9%	11.5%	7.5%

of liver were extracted and fixed in 10% neutral formalin for further work. Further preparation was carried out at STP-120 automatic tissue processor (carousel type; Germany), paraffin blocks were embedded using EC 350 embedding center (Germany). Serial semi-thin sections (5–7 μm) were made using HM-340E microtome (Germany). Histological sections were stained with hematoxylin and eosin according to the generally accepted routine technique.

The work was carried out in compliance with the international principles set out in the Declaration of Helsinki for animals, Directive 2010/63/EU of the European Parliament and of the Council on the protection of animals used for scientific purposes, as well as in accordance with the Guidelines for regulating the use of experimental animals.

Computer morphometry and digital images of micropreparations were performed in 10 fields using Axio Imager A1 (Zeiss, Germany) light microscope (ocular lens 10×, objective 40×), the area of hepatocytes and their nuclei was measured in micrometers (μm^2) using a software package and the AxioVision version 4.8 archiving system.

Statistical processing of the digital data was carried out using Microsoft Office 2010 and involved determination of the arithmetic averages (*M*) and calculation of the errors of arithmetic averages (*m*). The significance was determined by the Student's *t*-test and differences were considered significant at $p < 0.05$.

RESULTS AND DISCUSSION

The results of morphological examination demonstrated that in animals of group 1, the liver was visually enlarged and blood-filled, the edges did not converge along the incision, the organ was of loose consistency, dark brown color with large spilled gray lesions, the capsule was edematous and thickened. Beam structure was preserved. The hepatocytes were partially rounded. A large number of non-nuclear hepatocytes were observed. In 50% of the cases, nuclear karyopycnosis was reported, the cell wall was deformed, the cytoplasm was vacuolated and infiltrated into the intercellular space. Kupfer cells were not differentiated due to extensive overgrowth of loose connective tissue. The subendothelial space was expanded.

In KIM-M2 immunized animals in the experimental group, the liver was slightly enlarged, red in color, the capsule was within normal size, the liver lobules were clearly visible, the beam-radial structure was preserved. The centrilobular veins were varicosed. Small single focal hemorrhages were visible on the periphery of the hepatic lobes. Necrotic and dystrophic foci were not detected. There was a moderate connective tissue growth around the triads. The hepatocytes were identified, cell structure was determined, cytoplasm did not infiltrate into the intercellular space, karyopycnotic changes in the nucleus were not detected. Kupfer cells located in the periportal zone of the hepatic lobules were discernible in the sinusoids. No pathological lesions were detected in the intact animals.

The histological test results demonstrated that in the KIM-M2 immunized guinea pigs, the number of mononuclear hepatocytes was 63.5% of the total number of hepatocytes, which was 21.7% higher than in the infected control animals, and 11.0% less than in pure control animals. The proportion of binucleated hepatocytes from the total number of cells was 25.0%, which was 16.7% higher than in case of infection without the use of KIM-M2, and 7.0% higher than in the healthy animals. The number of anucleate hepatocytes was 11.5%, which was 38.4% less compared to infection controls and 4.0% higher compared to pure controls (Table 1).

Based on the data obtained, it can be seen that the specific immunomodulator of microbial origin KIM-M2 enhances the immune response owing to a significant increase in the number of binucleate hepatocytes during intensive mitotic division in animals of the experimental group. The number of mononucleate hepatocytes was lower in comparison with the pure controls, which can be explained by the abundant formation of binucleate hepatocytes. The number of anucleate hepatocytes increased insignificantly.

According to the morphometric study results, the average total area of mononucleate hepatocytes in animals in group 2 was established, which was 2,721.10 μm^2, which was 53.6% more than in the intact guinea pigs, and 22.8% less than in the infected animals in group 1. The average core area of mononucleated hepatocytes in animals inoculated with KIM-M2 was 289.83 μm^2, which was 47.6% more than in the intact guinea pigs and 45.0% less than in the animals in the infection control group. In animals in group 1, the average total area of mononucleate hepatocytes was 3,526.94 μm^2, the average core area of mononucleate hepatocytes was 526.76 μm^2. In intact animals, the average total area of mononucleate hepatocytes was 1,772.14 μm^2, the average core area of mononucleate hepatocytes was 196.35 μm^2 (Table 2).

Based on the results obtained, it can be concluded that the animals in group 2 accumulated potential restorative reserves and polyploidization reserves when exposed to the specific immunomodulator KIM-M2. In guinea pigs from the infection control group, a disturbed hepatocyte mitotic division was observed and the liver destruction process was reported, which slows down the recovery process.

According to the results of calculating the area of liver cells and their nuclei, the intracellular regeneration

Table 2
Morphometric characteristics of the hepatocytes

Groups	Hepatocyte cytoplasm area, μm^2 ($M \pm m$)	Area of hepatocyte nuclei, μm^2 ($M \pm m$)	Nuclear-cytoplasmic ratio
1	3,526.94 ± 243.200*	526.76 ± 28.147*	14.9
2	2,721.10 ± 44.757*	289.83 ± 15.474*	10.7
3	1,772.14 ± 45.124	196.35 ± 16.489	11.1

* differences are statistically significant as compared to group 3 (control), with $p \leq 0.01$

of the organ was determined by calculating the group nuclear-cytoplasmic ratio, which makes it possible to determine the level of metabolism and compensatory reactions in the body of laboratory animals.

CONCLUSION

Thus, in the animal experiment, it was established that a specific immunomodulator of microbial origin triggers and enhances the process of the liver cellular and intracellular regeneration, which stimulates the body to resist the mycobacterium toxins. In guinea pigs infected with nontuberculous mycobacteria, the destructive processes developed when KIM-M2 was not used, and the mechanism of liver tissue repair was underdeveloped.

REFERENCES

1. Baratov M. O. Nontuberculous mycobacterium occurrence in biological material and environmental samples covered by epidemiological surveillance in the Republic of Dagestan. *Veterinary Science Today*. 2023; 12 (2): 140–146. https://doi.org/10.29326/2304-196X-2023-12-2-140-146

2. Vlasenko V. S., Kosobokov Ye. A., Dudoladova T. S., Gulyaeva Ye. A. Morphometric parameters of guinea pig liver under the infuence of KIM-M2 drug in the model of experimental tuberculosis. *Morphology*. 2019; 155 (2): 61. https://elibrary.ru/nmsrwi (in Russ.)

3. Novikov A. N., Boganets N. S. The differential diagnosis of allergic reactions to PPD-tuberculin at cattle in the long-term tuberculosis favorable farms. *Nauchno-tekhnicheskii progress v sel'skokhozyaistvennom proizvodstve. Agrarnaya nauka – sel'skokhozyaistvennomu proizvodstvu Sibiri, Kazakhstana, Mongolii, Belarusi i Bolgarii: materialy Mezhdunarodnoi nauchno-tekhnicheskoi konferentsii (Minsk, 19–21 oktyabrya 2016 g.). V 2 t. T. 2 = Scientific and technical progress in agricultural production. Agrarian science to agricultural production of Siberia, Kazakhstan, Mongolia, Belarus and Bulgaria: proceedings of the International research-to-practice conference (Minsk, 19–21 October 2016). In 2 vol. Vol. 2*. Minsk: Scientific and practical Center of the National of Academy of Sciences of Belarus of Agriculture Mechanization; 2016; 117–120. https://elibrary.ru/ynsbdf (in Russ.)

4. Vlasenko V. S., Bazhin M. A., Novikov A. N., Petrov S. J., Shuliko E. M., Nazarova V. A. The specific immunomodulating agents for tuberculosis prevention and mycobacteriosis of cattle. *Dostizheniya nauki i tekhniki APK*. 2011; (9): 75–78. https://elibrary.ru/ogbtcr (in Russ.)

5. Vlasenko V. S., Gichev Yu. M., Dudoladova T. S., Kosobokov E. A., Koshkin I. N. Histopatomorphological changes of internal organs of guinea pigs during the introduction of antituberculosis preparation KIM-M2. *Bulletin of KSAU*. 2019; (8): 97–102. https://elibrary.ru/lrfywq (in Russ.)

6. Gong Q. L., Chen Y., Tian T., Wen X., Li D., Song Y. H., et al. Prevalence of bovine tuberculosis in dairy cattle in China during 2010–2019: A systematic review and meta-analysis. *PLoS Neglected Tropical Diseases*. 2021; 15 (6):e0009502. https://doi.org/10.1371/journal.pntd.0009502

7. Islam M. N., Khan M. K., Khan M. F. R., Kostoulas P., Rahman A. K. M. A., Alam M. M. Risk factors and true prevalence of bovine tuberculosis in Bangladesh. *PLoS ONE*. 2021; 16 (2):e0247838. https://doi.org/10.1371/journal.pone.0247838

8. Kamalieva Yu. R., Mingaleev D. N., Ravilov R. Kh. Identification of non-tuberculosis mycobacteria isolated from cattle in the Republic of Tatarstan. *Agrarian Science*. 2021; (11–12): 32–35. https://doi.org/10.32634/0869-8155-2021-354-11-12-32-35 (in Russ.)

9. Koshkin I. N., Vlasenko V. S., Dudoladova T. S. Morphological changes in liver tissue under the action of conjugates of BCG antigens and betulin derivatives in experimental tuberculosis. *Perm Agrarian Journal*. 2021; (3): 100–109. https://doi.org/10.47737/2307-2873_2021_35_100 (in Russ.)

10. Myasoedov Yu. M., Najmanov A. H. The study of the sensitizing properties of atypical mycobacteria of different groups according to the Ranyon classification. *Veterinaria i kormlenie*. 2019; (4): 6–8. https://doi.org/10.30917/ATT-VK-1814-9588-2019-4-1 (in Russ.)

11. Travenko E. N., Porodenko V. A. Evaluation of the morphofunctional state of the liver by morphometric methods. *Russian Journal of Forensic Medicine*. 2019; 5 (3): 19–23. https://doi.org/10.19048/2411-8729-2019-5-3-19-23 (in Russ.)

12. Myadelets O. D., Lebedeva E. I. Degenerative and regenerative processes in the liver of white rats during the modeling of toxic cirrhosis. Changes of oval cells. *Journal of the Grodno State Medical University*. 2017; 15 (3): 294–300. https://doi.org/10.25298/2221-8785-2017-15-3-294-300 (in Russ.)

13. Naymanov A. H., Ustinova G. I., Tolstenko N. G., Vangeli E. P., Kucheruk O. D. Non-tuberculous (atypical) mycobacteria and their sensitizing significance. *Veterinaria i kormlenie*. 2015; (1): 19–22. https://elibrary.ru/tgucfr (in Russ.)

14. Naymanov A. H., Ustinova G. I., Tolstenko N. G., Vangeli E. P., Kucheruk O. D. Sensitizing properties of fast-growing non-tuberculous mycobacteria fourth group according to the classification of Runyon. *Veterinariya*. 2015; (2): 23–27. https://elibrary.ru/tjrdqp (in Russ.)

15. Dengis N. A., Vlasenko V. S., Borisov E. S. Epizootic situation on cattle tuberculosis in the Omsk region. *Bulletin of KSAU*. 2024; (3): 108–114. https://doi.org/10.36718/1819-4036-2024-3-108-114 (in Russ.)

16. Koshkin I. N., Vlasenko V. S., Kulakov I. V. The effect of experimental BCG antigen–betulin-derived conjugates on the guinea pig immunological response. *Russian Journal of Bioorganic Chemistry*. 2021; 47 (4): 837–844. https://doi.org/10.1134/S1068162021040142

17. Balseiro A., González-Quirós P., Rodríguez Ó., Francisca Copano M., Merediz I., de Juan L., et al. Spatial relationships between Eurasian badgers (*Meles meles*) and cattle infected with *Mycobacterium bovis* in Northern Spain. *The Veterinary Journal*. 2013; 197 (3): 739–745. https://doi.org/10.1016/j.tvjl.2013.03.017

18. Allen A. R., Skuce R. A., Byrne A. W. Bovine tuberculosis in Britain and Ireland – A perfect storm? the confluence of potential ecological and epidemiological impediments to controlling a chronic infectious disease. *Frontiers in Veterinary Science*. 2018; 5:109. https://doi.org/10.3389/fvets.2018.00109

19. Ionina S. V., Donchenko N. A., Donchenko V. N. Relationship between circulations of mycobacteria in the environment and tuberculin responses in animals. *Siberian Herald of Agricultural Science*. 2016; (2): 61–66. https://elibrary.ru/vxvylj (in Russ.)

20. Protodyakonova G. P. Complex research results on a tubercular infection. *Scientific notes Kazan Bauman State Academy of Veterinary Medicine*. 2019; 237 (1): 151–155.

https://doi.org/10.31588/2413-4201-1883-237-1-151-155 (in Russ.)

21. Kamalieva Y. R., Mingaleev D. N., Ravilov R. Kh. Identification of non-tuberculosis mycobacteria isolated from environmental objects in the Republic of Tatarstan. *Scientific notes Kazan Bauman State Academy of Veterinary Medicine*. 2021; 248 (4): 100–105. https://doi.org/10.31588/2413-4201-1883-248-4-100-105 (in Russ.)

22. Turgenbayev K. A., Borsynbayeva A. M., Plazun A. A., Turgenbayev R. K. Tuberculosis prevalence in animals and humans in the Republic of Kazakhstan. *Veterinary World*. 2021; 14 (9): 2362–2370. https://doi.org/10.14202/vetworld.2021.2362-2370

23. Bazhin M. A., Vlasenko V. S., Nevorotova G. P., Kosobokov E. A., Ivanov A. A., Pelik V. A. The assessment of immunogenic properties of antituberculosis preparations on laboratory animals and cattle. *Vestnik of Omsk SAU*. 2016; (2): 147–152. https://elibrary.ru/wjterx (in Russ.)

24. Payne A., Boschiroli M. L., Gueneau E., Moyen J. L., Rambaud T., Dufour B., et al. Bovine tuberculosis in "Eurasian" badgers (*Meles meles*) in France. *European Journal of Wildlife Research*. 2013; 59 (3): 331–339. https://doi.org/10.1007/s10344-012-0678-3

25. Taller L. A., Dyusenova G. M., Janchenko T. A. Isolation of atypical mycobacteria from biomaterial from laboratory animals on modified nutrient medium. *Dostizheniya nauki i tekhniki APK*. 2015; (4): 56–57. https://elibrary.ru/trmvmd (in Russ.)

26. Bazhin M. A., Vlasenko V. S., Novikov A. N., Nevorotova G. P., Shuliko E. M., Reutova T. S. Sposob polucheniya spetsificheskogo immunomodulyatora = Method for producing specific immunomodulator. *Intellectual Property. Industrial Property*. 2010; (5): 67. https://elibrary.ru/tcoadv (in Russ.)

Received 31.05.2024
Revised 15.07.2024
Accepted 11.09.2024

INFORMATION ABOUT THE AUTHORS / ИНФОРМАЦИЯ ОБ АВТОРАХ

Evgeny A. Kosobokov, Cand. Sci. (Veterinary Medicine), Senior Researcher, Diagnostic Research and Biotechnology Laboratory, Department of Veterinary Medicine, Omsk Agrarian Scientific Center, Omsk, Russia; *https://orcid.org/0009-0007-4383-0038, vet_nauka@mail.ru*

Tatyana S. Dudoladova, Cand. Sci. (Biology), Leading Researcher, Diagnostic Research and Biotechnology Laboratory, Department of Veterinary Medicine, Omsk Agrarian Scientific Center, Omsk, Russia; *https://orcid.org/0009-0006-8307-9472, dud.08@mail.ru*

Кособоков Евгений Андреевич, канд. вет. наук, старший научный сотрудник лаборатории диагностических исследований и биотехнологий отдела ветеринарии ФГБНУ «Омский АНЦ», г. Омск, Россия; *https://orcid.org/0009-0007-4383-0038, vet_nauka@mail.ru*

Дудоладова Татьяна Сергеевна, канд. биол. наук, ведущий научный сотрудник лаборатории диагностических исследований и биотехнологий отдела ветеринарии ФГБНУ «Омский АНЦ», г. Омск, Россия; *https://orcid.org/0009-0006-8307-9472, dud.08@mail.ru*

Contribution: The authors have made equal contribution to the study: data collection and analysis; determination of goals and objectives, methods of the study; formulation and scientific justification of conclusions, documentation of key outputs from the study in the paper.

Вклад авторов: Авторы внесли равный вклад в проведение исследования: сбор и анализ материала; определение целей и задач, методов исследования; формулирование и научное обоснование выводов, оформление ключевых результатов исследования в виде статьи.