EFFECT OF THE ORGANOSELENIUM COMPOUND 974ZH ON THE *TLR2* AND *TLR4* GENE EXPRESSION IN BLOOD AND SPLEEN CELLS OF EXPERIMENTAL ANIMALS WHEN CO-ADMINISTERED WITH *YERSINIA PESTIS* EV

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ABSTRACT

One of the important directions for increasing the immunogenic properties of vaccine strains against highly dangerous infections is the search for adjuvants that not only stimulate the immunological effectiveness of vaccination, but can also provide a metabolic correction of the vaccination process. Organoselenium compounds have immunotropic properties and an antioxidant effect, and therefore, the study of the effect of the organoselenium compound 2,6-dipyridinium-9-selenabicyclo[3.3.1]nonane dibromide (974zh) on the activity of the TLR2 and TLR4 gene expression by macroorganism cells of experimental animals immunized with Yersinia pestis EV NIIEG vaccine strain, is a current area of research.

The aim of the work. *To assess the TLR2 and TLR4 gene expression by cells of the immune phagocyte system of experimental animals immunized with the Y. pestis EV vaccine strain against the background of immunomodulation with the organoselenium compound 974zh.*

Materials and methods. *The study was carried out on 125 certified outbred white mice. Biological material (blood, spleen) was disinfected, and the spleen was homogenized. RNA isolation and reverse transcription were performed using commercial reagent kits. The expression level of the TLR2 and TLR4 genes was determined using real-time polymerase chain reaction with specific primers.*

Results. *When assessing innate immunity using the example of blood and spleen cells of animal models, features of the TLR2 and TLR4 gene expression were revealed in response to the introduction of the Y. pestis EV vaccine strain against the background of immunomodulation with the 974zh. It was found that 974zh induces a statistically significant increase in TLR2 gene expression when co-administered with Y. pestis EV at a dose of both 10^4 CFU and 10^3 CFU.*

Conclusion. *Y. pestis EV against the background of immunomodulation with 974zh, stimulates the expression of the TLR2 and TLR4 genes, which may indicate an increase in the immunogenic properties of the Y. pestis EV vaccine strain under the influence of this preparation.*

Key words: *gene expression, TLR, organoselenium compound, immunity*

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ВЛИЯНИЕ СЕЛЕНОРГАНИЧЕСКОГО СОЕДИНЕНИЯ 974ZH НА ЭКСПРЕССИЮ ГЕНОВ *TLR2* И *TLR4* В КЛЕТКАХ КРОВИ И СЕЛЕЗЁНКИ ЭКСПЕРИМЕНТАЛЬНЫХ ЖИВОТНЫХ ПРИ СОВМЕСТНОМ ВВЕДЕНИИ С *YERSINIA PESTIS* EV

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РЕЗЮМЕ

Одним из важных направлений повышения иммуногенных свойств вакцинных штаммов против особо опасных инфекций является поиск адъювантов, которые не только стимулируют иммунологическую эффективность вакцинации, но и могут оказывать метаболическую коррекцию вакцинального процесса. Селенорганические соединения обладают иммунотропными свойствами и антиоксидантным эффектом, в связи с чем изучение влияния селенорганического соединения 2,6-дипиридиний-9-селенабицикло[3.3.1]нонан дибромида (974zh) на активность экспрессии генов TLR2 и TLR4 клетками макроорганизма экспериментальных животных, иммунизированных вакцинным штаммом Yersinia pestis EV НИИЭГ, является актуальным направлением исследований.

Цель работы. *Оценка экспрессии генов TLR2 и TLR4 клетками иммунофагоцитарной системы экспериментальных животных, имунизированных вакцинным штаммом Y. pestis EV на фоне иммуномодуляции селенорганическим соединением 974zh.*

Материалы и методы. *Исследование проводили на 125 сертифицированных беспородных белых мышах. Биологический материал (кровь, селезёнка) обеззараживали, селезёнку гомогенизировали. Выделение РНК и обратную транскрипцию осуществляли с помощью коммерческих комплектов реагентов. Уровень экспрессии генов TLR2 и TLR4 определяли методом полимеразной цепной реакции в реальном времени с использованием специфических праймеров.*

Результаты. *При оценке врождённого иммунитета на примере клеток крови и селезёнки биомоделей выявлены особенности экспрессии генов TLR2 и TLR4 в ответ на введение вакцинного штамма Y. pestis EV на фоне иммуномодуляции препаратом 974zh. Установлено, что данный препарат индуцирует статистически значимое повышение экспрессии генов TLR2 при совместном введении с Y. pestis EV как в дозе 10^4 КОЕ, так и в дозе 10^3 КОЕ.*

Заключение. *Таким образом, Y. pestis EV на фоне иммуномодуляции препаратом 974zh стимулирует экспрессию генов TLR2 и TLR4, что может свидетельствовать о повышении иммуногенных свойств вакцинного штамма Y. pestis EV под влиянием этого препарата.*

Ключевые слова: *экспрессия генов, TLR, селенорганическое соединение, иммунитет*

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INTRODUCTION

The greatest contribution to the prevention and control of infectious diseases has been made by vaccination aimed at developing an immune response that provides immunity to infectious disease pathogens. Great success in the control and prevention of especially dangerous infections has been achieved thanks to the already created vaccines. Most vaccines against especially dangerous infections are attenuated strains of pathogens or inactivated pathogens that have not only immunogenic and protective activity, but also residual virulence and reactogenicity. Chemical, subunit and combination vaccines do not have sufficient immunogenic activity and cannot be compared with live vaccines in terms of effectiveness [1]. Therefore, the search for non-specific factors that can reduce the negative impact degree of live vaccines on the body and increase their immunogenic activity, allowing to reduce the dose of antigen, is relevant. Adjuvants can enhance the immune response to the vaccine administration through various mechanisms, including activation of humoral and cellular factors of innate immunity [1]. Natural immunity forms an early line of macroorganism defense against microbes with subsequent initiation of adaptive immunity. Adjuvants are able to initiate immune reactions of the innate immune system through pattern recognition receptors (PRRs) [2].

One of the PRR families includes Toll-like receptors (TLRs), which recognize the molecular structures of pathogens and are an important element in the mechanism of both innate and adaptive immune responses [3]. To date, at least 10 types of TLRs have been identified in humans and 13 in mice. TLRs are mainly expressed on tissue cells that perform immune functions and directly communicate with pathogens. The receptors differ in adapter proteins and are localized both on the cell membrane and inside the cell, ensuring the intracellular activation signal conduction [4].

Toll-like receptors of types 2 and 4 are believed to be specific for the early encounter of pathogenic bacteria with host cells. Receptors of these two types have a wide range of activating ligands localized on bacteria. *TLR2* and *TLR4* are expressed on monocytes, macrophages, neutrophils and myeloid dendritic cells, on endothelium, intestinal epithelial cells and hepatocytes. When TLR interacts with ligands, primary proinflammatory factors are induced, followed by immediate development of mechanisms of both innate and acquired immunity.

The use of immunomodulatory adjuvants makes it possible to activate innate immunity by stimulating TLR, which can be used in the development of new drugs for the treatment of infectious diseases and the creation of vaccines for their prevention [5]. In recent years, synthetic origin compounds that affect immunogenesis have been actively studied and introduced into practice as adjuvants [6, 7].

Previously conducted animal experiments have shown that the experimental synthetic organoselenium drug 2,6-dipyridinium-9-selenabicyclo[3.3.1]nonane dibromide (974zh) has immunotropic properties. Combined use with the *Y. pestis* EV NIIEG vaccine strain allows maintaining its immunogenicity while reducing the antigen load by an order of magnitude (from 10^4 CFU to 10^3 CFU) and reduces the allergic reaction during vaccination [8, 9].

Considering the positive effect of this compound on the macroorganism, studies of an experimental synthetic organoselenium compound in combination with vaccine strains as an adjuvant, which will induce an increase in the expression of Toll-like receptor genes, are promising.

THE AIM OF THE STUDY

Study of the organoselenium compound 974zh effect on the expression of *TLR2* and *TLR4* genes in peripheral blood cells and spleen of experimental animals when administered *Y. pestis* EV NIIEG.

MATERIALS AND METHODS

In this study, we used the synthetic organoselenium compound 2,6-dipyridinium-9-selenabicyclo[3.3.1] nonane dibromide (974zh) (A.E. Favorsky Irkutsk Institute of Chemistry, Siberian Branch of the Russian Academy of Sciences) and the vaccine strain *Y. pestis* EV NIIEG (Irkutsk Antiplague Research Institute, Rospotrebnadzor).

In the experiment, certified outbred white mice (125 pcs.) of both sexes, standard in weight (18–20 g) and housing conditions, were used as biomodels. Work with animals was carried out in accordance with the requirements of Directive 2010/63/EU of the European Parliament and of the Council of the European Union of September 22, 2010 on the protection of animals used for scientific purposes and the "Rules of Good Laboratory Practice" approved by Order of the Ministry of Health No. 199n dated April 01, 2016. The study was approved by the local Ethics Committee of the institute (protocol No. 3 dated June 01, 2020; protocol No. 7 dated November 15, 2021).

The animals were divided into four experimental groups and one control group (25 individuals each). The test 974zh at a dose of 2.5 mg/kg of live weight was administered to the animals subcutaneously in the left hind paw in a volume of 0.5 ml, the cell culture was administered subcutaneously in the right hind paw in a volume of 0.5 ml. Biomodels of the 1st experimental group were inoculated with the *Y. pestis* EV NIIEG vaccine strain at a dose of 10^3 CFU per individual, those of the 2nd experimental group – at a dose of 10^4 CFU, those of the 3rd experimental group – at a dose of 10^3 CFU together with the drug 974zh, those of the 4th experimental group – at a dose of 10^4 CFU in combination with 974zh. Intact white mice were used in the control (V) group. Observations were carried out for 21 days. White mice were humanely removed from the experiment. Biological material was collected

on the 1st, 3rd, 7th, 14th and 21st days. The spleen was homogenized (grinded). Whole blood was used.

The material was disinfected according to the guidelines MU 3.5.5.1034-01. Samples in a volume of 100 µl were placed in Eppendorf microcentrifuge tubes, mixed with 300 µl of lysis buffer and heated at a temperature of 65 °C for 15 min.

The RNA molecule was isolated using a reagent kit for the isolation of total RNA from whole blood, cell cultures and tissue samples RNA-EKSTRAN (OOO Sintol, Moscow). To cleave residual double-stranded DNA in the samples, the enzyme DNase (OOO Sintol, Moscow) was used according to the attached instructions.

The synthesis of the first DNA strand on the RNA matrix was carried out using a set of reagents for the reverse transcription (RT) reaction (OOO Sintol, Moscow).

The expression of *TLR2* and *TLR4* was studied using a reagent kit for real-time polymerase chain reaction (RT-PCR) in the presence of SYBS Green 1 (OOO Sintol, Moscow). RT-PCR was carried out in a thermocycler detecting DT-prime (OOO DNA Technologies, Moscow). Specific primers and their sequences used in the reaction are presented in Table 1.

Statistical processing of the obtained data was performed using the MS Excel software package (Microsoft Corp., USA). Statistical significance was assessed using the Mann – Whitney U-test. The relative concentration (RC) of TLR gene copies was calculated in the RealTime_PCR v. 7.7 program (DNA Technologies LLC, Moscow) and expressed in conventional units (c.u.). The results were considered statistically significant at $p < 0.05$.

RESULTS AND DISCUSSION

It was established that the organoselenium compound 974zh induces an increase in the expression of *TLR2* genes in the blood on the 1st day with a subsequent increase by the 3rd and 7th days, and in the spleen – on the 3rd and 14th days when this drug is administered together with the vaccine strain *Y. pestis* EV at a dose an order of magnitude lower than the generally accepted one, i.e. 10^3 CFU. Thus, in group III of animals, the relative concentration of TLR2 in the blood was 12.8 c.u. on the 1st day of the study, 37.9 c.u. on the 3rd day, and 25 c.u. on the 7th day. Thus, the median values of TLR2 RC in blood cells were 2.8 times higher than the values of group I on the 1st day of the study, 12.3 times on the 3rd, and 22.7 times ($p < 0.05$) on the 7th day. The median value in animals of group III was 2.1 times higher on the 1st day and 7.1 times ($p < 0.05$) on the 3rd day compared to group II. In addition, the level of *TLR2* gene expression in animals of group III statistically significantly increased compared to that in group IV and was 2.8 times higher on the 1st day, 11.6 times on the 3rd, 13.2 times on the 7th, and 2.8 times ($p < 0.05$) on the 14th day of the study. In the blood cells of animals of group I, the expression of this type of Toll-like receptor did not increase and was lower than in the other groups of experimental animals (fig. 1a).

In the spleen cells of white mice of group III, the RC expression of *TLR2* genes was significantly higher compared to the same indicator in other experimental groups and in the control. On the 3rd day, the RC was 947 c.u., which is 4.7 times ($p < 0.05$) higher than in group I, 1.7 times ($p < 0.05$) higher than in group II, and 155.2 times ($p < 0.05$) higher than in group IV. On the 14th day of observation, the RC of group III was 501.1 c.u. and was statistically significantly higher than the same indicator in all other groups of experimental animals (fig. 16).

The level of *TLR4* gene expression in the blood of experimental animals immunized with *Y. pestis* EV (10^3 CFU) in combination with an organoselenium compound (Group III) was statistically significantly higher by 5.5 times ($p < 0.05$) than the expression of genes of this type of Toll-like receptor in animals that were administered only the vaccine strain *Y. pestis* EV at a dose of 10^4 CFU (Group II), and 2.4 times ($p < 0.05$) higher compared to mice immunized with *Y. pestis* EV at a dose of 10^4 CFU together with the 974zh (Group IV) on the 1st day of observation. A statistically significant increase in the median RC expression of *TLR4* genes was observed on the 7th day in blood samples of animals of Group III relative to animals of Group I and was 3.9 times higher ($p < 0.05$). In other cases, no statistically significant increase in expression occurred. On the 3rd, 14th, and 21st days, no statistically significant increase in the relative concentration of *TLR4* gene expression in blood cells was observed (fig. 2a).

Administration of the experimental 974zh in combination with *Y. pestis* EV at a dose of 10^3 CFU (Group III) to biomodels increased the expression of *TLR4* genes in spleen cells. On the 1st day, an increase in concentration was observed compared to Group V (control) and Group II, where white mice were administered only the vaccine strain *Y. pestis* EV at a dose of 10^4 CFU. Compared to other experimental groups, *TLR4* expression was lower on the 1st day. The organoselenium preparation induced *TLR4* gene expression on the 3rd and 14th days. The relative concentration of gene expression in Group III on the 3rd day was 1500 c.u. i.e., 17.8 times ($p < 0.05$) higher than the concentration in group I, 2.3 times ($p < 0.05$) higher than in group II, and 256.4

TABLE 1

SEQUENCE OF MOUSE TLR PRIMERS FOR REAL-TIME PCR

No.	Gene	Sequence (5′ → 3′)	Size (bp)
1	TLR2	F: 5′-CAGCTGGAGAACTCTGACCC-3′ R: 5′-CAAAGAGCCTGAAGTGGGAG-3′	193
2	TLR4	F: 5′-CAA CAT CAT CCA GGA AGGC-3′ R: 5′-GAA GGC GAT ACA ATT CCA CC-3′	206

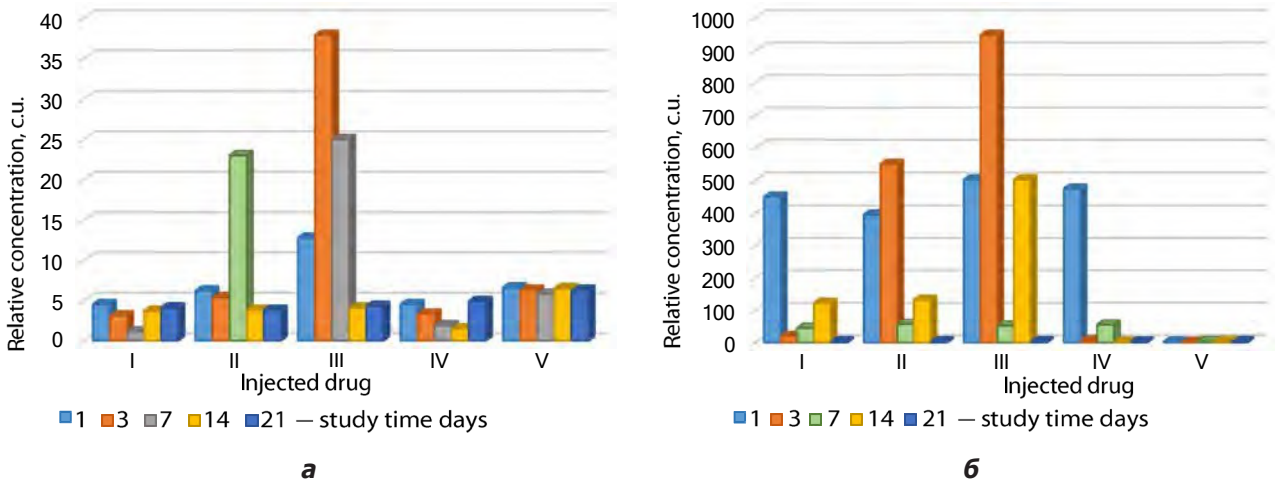

FIG. 1.
*Relative concentration of TLR2 gene expression in blood (**а**) and spleen (**б**) cells of white mice (c. u.): I – Y. pestis EV at a dose of 103 CFU; II – Y. pestis EV at a dose of 104 CFU; III – Y. pestis EV at a dose of 103 CFU + 974zh; IV – Y. pestis EV at a dose of 104 CFU + 974zh; V – control group; * – p < 0.05*

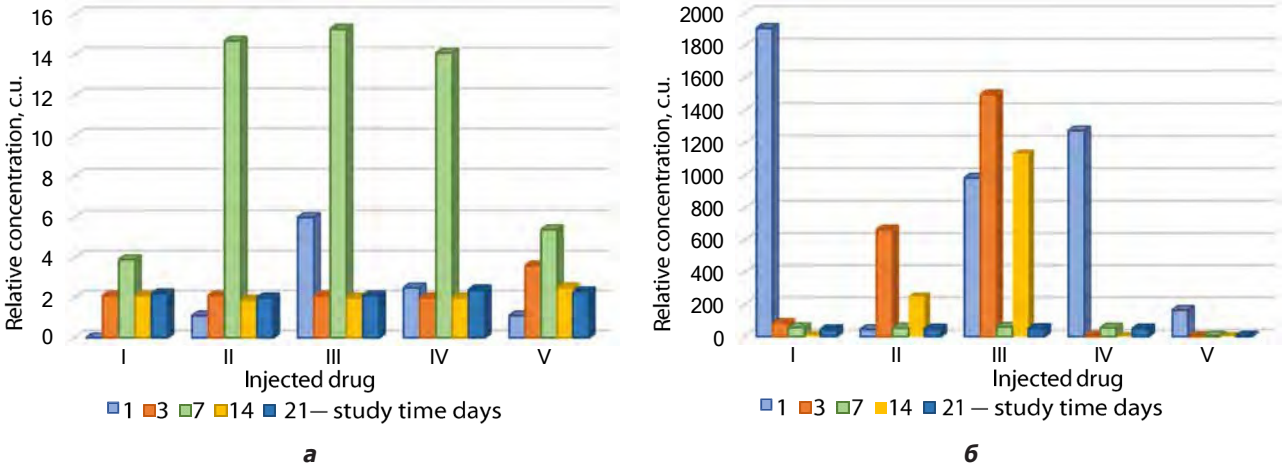

FIG. 2.
*Relative concentration of TLR4 gene expression in blood (**а**) and spleen (**б**) cells of white mice (c.u.): I – Y. pestis EV at a dose of 103 CFU; II – Y. pestis EV at a dose of 104 CFU; III – Y. pestis EV at a dose of 103 CFU + 974zh; IV – Y. pestis EV at a dose of 104 CFU + 974zh; V – control group; * – p < 0.05*

times ($p < 0.05$) higher than in group IV. On the 14th day, the level of *TLR4* gene expression in the spleen cells of animals in group III was also statistically significantly higher than in groups I, II, and IV, by 133.7, 4.5, and 283.8 times, respectively. On the 7th and 21st days, no statistically significant differences were recorded between the median values of *TLR4* gene expression in the group of biomodels immunized with *Y. pestis* EV at a dose of 10^3 CFU in combination with 974zh and other experimental groups (fig. 2б).

CONCLUSION

Thus, the revealed features of *TLR2* and *TLR4* gene expression in the innate immune cells of biomodels in response to the administration of *Y. pestis* EV NIIEG strains in terms of level and kinetics depend on the amount of the administrated vaccine strain antigen (CFU) and the presence or absence of the administrated 974zh. This experimental organoselenium compound induces an increase in the expression of *TLR2* genes when co-administered with *Y. pestis* EV at a dose an order of magnitude lower than the generally accepted one (10^3 CFU) on the 1st, 3rd and 7th days of observation in blood cells and on the 3rd and 14th days in spleen cells.

In response to the administration of the 974zh with the *Y. pestis* EV vaccine strain to experimental biomodels, an increase in *TLR4* expression was recorded in blood cells on the 1st and 7th days, in spleen cells – on the 1st, 3rd and 14th days of the experiment. Studies have shown that when administrating

a synthetic organoselenium compound in combination with the *Y. pestis* EV vaccine strain with a decrease in the immunizing dose to 10^3 CFU, there is an increase in the expression of the *TLR2* and *TLR4* genes in the blood and spleen cells of biomodels at almost all observation periods.

The *Y. pestis* EV administration both at a standard dose (10^4 CFU) and at a dose an order of magnitude lower (10^3 CFU), but without the experimental organoselenium preparation, did not cause significant and statistically significant changes in the expression of genes of the studied types of Toll-like receptors.

All of the above suggests that increased expression of *TLR2* and *TLR4* genes can enhance the immune response to the vaccine and contribute to effective combat against plague infection. Therefore, the experimental selenium-containing compound 2,6-dipyridinium-9-selenabicyclo[3.3.1]nonane dibromide (974zh) can be considered as a promising adjuvant.

Conflicts of interest

No potential conflict of interest relevant to this article reported.

REFERENCES

1. Svitich OA, Lavrov VF, Kukina PI, Iskandaryan AA, Gankovskaya LV, Zverev VV. Agonists of receptors of the innate immunity and defective viral particles as new generation of adjuvants. *Epidemiology and Vaccinal Prevention*. 2018; 17(1): 76-86. (In Russ.). [Свитич О.А., Лавров В.Ф., Кукина П.И., Скандарян А.А., Ганковская Л.В., Зверев В.В. Перспективы использования агонистов рецепторов врожденного иммунитета и дефектных вирусных интерферирующих частиц в качестве адъювантов нового поколения. *Эпидемиология и вакцинопрофилактика*. 2018; 15(1): 76-86]. doi: 10.31631/2073-3046-2018-17-1-76-86

2. Andreev YuYu, Toptygina AP. Adjuvants and immunomodulators in vaccines. *Immunologiya*. 2021; 42(6): 720-729. (In Russ.). [Андреев Ю.Ю., Топтыгина А.П. Адьюванты и иммуномодуляторы в составе вакцин. Иммунология. 2021; 42(6): 720-729]. doi: 10.33029/0206-4952-2021-42-6-720-729

3. Koval'chuk LV, Khoreva MV, Nikonova AS. Recognition receptors of innate immunity (NLR, RLR, and CLR). *Journal of Microbiology, Epidemiology and Immunobiology*. 2011; 88(1): 93-100. (In Russ.). [Ковальчук Л.В., Хорева М.В., Никонова А.С. Распознающие рецепторы врожденного иммунитета (NLR, RLR и CLR). *Журнал микробиологии, эпидемиологии и иммунобиологии*. 2011; 88(1): 93-100].

4. Mamedova LN, Tarasova GN. Clinical and pathogenetic TLR description. *Medical Herald of the South of Russia*. 2012; (1): 12-15. (In Russ.). [Мамедова Л.Н., Тарасова Г.Н. Клинико-патогенетическая характеристика TLR. Медицинский вестник Юга России. 2012; (1): 12-15].

5. Nikonova AA, Khaitov MR, Khaitov RM. Prospects of Toll-like receptor agonists and antagonists for prevention and treatment of viral infections. *Medical Immunology (Russia)*. 2019; 21(3):397-406. (In Russ.). [Никонова А.А., Хаитов М.Р., Хаитов Р.М. Перспективы использования агонистов и антагонистов Toll-подобных рецепторов для профилактики и лечения вирусных инфекций. *Медицинская иммунология*. 2019; 21(3): 397-406]. doi: 10.15789/1563-0625-2019-3-397-406

6. Kostinov MP, Akhmatova NK, Khromova EA, Kostinova AM. Cytokine Profile in human peripheral blood mononuclear leukocytes exposed to immunoadjuvant and adjuvant-free vaccines against influenza. *Front Immunol*. 2020; 11(1351): 1-10. doi: 10.3389/fimmu.2020.01351

7. Talayev V, Zaichenko I, Svetlova M, Matveichev A, Babaykina O, Voronina E, et al. Low-dose influenza vaccine Grippol Quadrivalent with adjuvant Polyoxidonium induces a T helper-2 mediated humoral immune response and increases NK cell activity. *Vaccine*. 2020; 38(42): 6645-6655. doi: 10.1016/j.vaccine.2020.07.053

8. Dubrovina VI, Starovoytova TP, Yurieva OV, Vityazeva SA, Pyatidesyatnikova AB, Ivanova TA, et al. Structural rearrangement of organs of white mice vaccinated with Yersinia pestis EV in combination with organoselenium compound 974zh. Acta biomedica scientifica. 2022; 7(3): 110-120. (In Russ.). [Дубровина В.И., Старовойтова Т.П., Юрьева О.В., Витязева С.А., Пятидесятникова А.Б., Иванова Т.А., и др. Структурная перестройка органов белых мышей, вакцинированных *Yersinia pestis* EV в сочетании с селенорганическим соединением 974zh. *Acta biomedica scientifica*. 2022; 7(3): 110-120]. doi: 10.29413/ABS.2022-7.3.12

9. Dubrovina VI, Starovoitova TP, Yur'eva OV, Pyatidesyatnikova AB, Potapov VA, Musalov MV, et al. Effect of a synthetic organoselenium compound on post-vaccination immunopoiesis in the red bone marrow and cell composition of peripheral blood of white mice vaccinated with *Yersinia pestis* EV. *Bull Exp Biol Med*. 2021; 171: 651-655. doi: 10.1007/s10517-021-05287-0

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