

The dynamics of the synthesis of transfected MMSC urea and alpha fetoprotein

	Day after transfection		
	6	12	21
Urea, pg / cell / hour	5,23±0,12	20,01±0,24*	25,57±0,42*
PCG alpha-fetoprotein / 10 ⁶ cells / hour	13,62±0,51	10,56±0,19	8,14±0,28*

Note: * - significance of differences from 6 days after transfection (p <0.05)

Thus, as a result of the work, cells with biochemical and histological signs of hepatocytes were obtained.

The procedure for obtaining hepatocytes from multipotent mesenchymal stromal cells is simple and allows you to fully control the properties of the resulting cells.

The availability of MMSC and their ability to expand in vitro allows the production of hepatocytes for clinical use in the treatment of liver failure.

Conclusion

In the process of research, optimization of protocols for the isolation of multipotent mesenchymal stromal cells from lipoaspirates and transfection of cells with a plasmid vector including the hepatocyte growth factor gene was performed. This made it possible to obtain cells from multipotent mesenchymal stromal cells from human adipose tissue that exhibit phenotypic signs of hepatocytes.

REFERENCES

1. F. EBöhm, U.A. Köhler, T. Speicher, S.Werner, EMBO Mol Med. 2010 Aug;2(8):294-305. doi: 10.1002/emmm.201000085,
2. P.A. Lysy, D. Campard, F.Smets, M.Najimi, E.M Sokal. Stem cells for liver tissue repair - p. Hoffmann K, Nagel AJ, Tanabe K, Fuchs J, Dehlke K, Ghamarnejad O, Lemekhova A, Mehrabi A. Markers of liver regeneration-the role of growth factors and cytokines: a systematic review. BMC Surg. 2020 Feb 12;20(1):31. doi: 10.1186/s12893-019-0664-8. PMID: 32050952; PMCID: PMC7017496
3. Si. Zizhen, Xue Wang, Changhui Sun, Yuchun Kang, Jiakun Xua, Xidi Wang, Yang Hui.. Biomedicine & Pharmacotherapy, **114**, 108765, (2019)
4. M. Alvarez-Dolado, Pardal R. Garcia-Verdugo, Nature **425**, 968 (2003)
5. Jimenez-Puerta GJ, Marchal JA, López-Ruiz E, Gálvez-Martín P. Role of Mesenchymal Stromal Cells as Therapeutic Agents: Potential Mechanisms of Action and Implications in Their Clinical Use. J Clin Med. 2020 Feb 6; 9(2). Epub 2020 Feb 6. <https://doi.org/10.3390/jcm9020445>

COVID-19: VACCINE AND DIAGNOSTIC TECHNOLOGIES

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Abstract

The fact the SARS-CoV-2 coronavirus causes an unusual infection in the humans it have been described before and will yet be analyzed by many virologists and clinicians in future. Much remains unclear with this infection, for example: 1) why do older people get seriously ill, but children don't; 2) will be effective the vaccine being developed by the traditional method, as it was with smallpox, polio, measles, etc., or not; 3) how the coronavirus biological features influence on the development and the using of monospecific genetic and serological diagnostic kits? This publication makes attempt to clear about the need to develop and acquire not ready vaccines and diagnostic kits, but the introduction of new non traditional technologies, because there are specific features related to biological features of the coronavirus, ecological factors or local biotopes for each region (climate zone, country, continent, etc.).

Keywords: SARS-CoV-2, COVID-19, CRISPR/Cas, AADH, vaccine, PCR, IgM and IgG-cross-reactivity, technologies.

The main genome in the evolutionary and adaptive process of all life on the planet (including humans) is the genome of bacteria (prokaryotes, including archaea), which rapidly reacts to changing environmental factors by genetic modifications and its transmitted to all mammals, amphibians, multi- and one cellular organisms, including plants [1, 2]. Given that: 1) bacteria appeared on earth about 3.5 billion years ago, and humans 2.6 millions; 2) per one human gene accounts for about one million genes of bacteria living in his body, aerosols and on all surfaces; 3) the cycle of reproduction in bacteria is minutes, whereas in a person decades; 4) bacteria are rapidly adapted to external factors and have all mechanisms for transferring modifications to

the biocenotic environment; 5) the mitochondria of human cells contain the genetic code of bacteria; 6) about 300 bacterial genes are found in human chromosomes; 7) bacteria are able to adapt to all habitats on earth and in space [1,3], - as result, man is a product of bacterial evolution and has a close relationship and interdependence with them [1,3,4].

Why do viruses appear? The bacteria adjusted to the external factors form a new biocenotic environment around them. Rapidly formed a bacterial immunity is used by prokaryotes through retrovirus-like mechanisms, including the CRISPR/Cas spacer adaptation system, on the "cut and paste" principle, to edit the im-

immune and hormonal systems of the macroorganism (including human) to new environment factors [5,6]. The mechanism of such environment forming is to exchange small fragments of genetic information (molecular motifs) between bacteria and other micro- and macroorganisms. Naturally, from such molecular motifs are formed a whole complex (set) or adaptogen (unlike the pathogen - the virus). The process of exchange by adaptogens (through aerosol, enterally, through contacts, etc.) occurs unnoticeably for a person. The virus as the causative agent of an infectious disease, appears from the adaptogen only when one of the participants in the evolutionary process violates the natural course of this evolution. In the latter case, either the bacteriophage or the virus will try to remove the weak link, resulting in adaptation manifesting itself as a disease [7,8].

How a new coronavirus could have appeared.

The SARS-CoV-2 coronavirus is one example of formation from adaptogens (non-pathogenic molecular motifs or spacers) a new coronavirus – the virus with new pathogenic properties. An evolutionarily formed and invisible for humans such a system of adaptation is the normal existence of human populations in a certain biocenotic environment. Viruses, as infectious agents, appear only when a person's immune and hormonal systems are changed or violated (ecology, alcohol, smoking, drugs, poor nutrition, etc.). In this case, only those (the population of people) who have similar disorders in the functioning of the immune and hormonal systems get sick. As a rule, these are populations of people living in the same or similar environmental conditions. The 2019 outbreak of the Chinese COVID-19 coronavirus in Wuhan was another confirmation of the universality of this mechanism working. In the region lived a very small group of people, and unique, artificially created, in nature incompatible for cohabitation, group of animals, whose adaptation to cohabitation has given the adaptogen with the viral properties. Human history has already accumulated a lot of experience about the need for conscious behavior in relation to the possibility of overcoming the interspecies barrier by viral pathogens [8]. One such example is the import of muskrats to the Siberian forests of Russia in the post-war years for

hunting purposes. As a result, the pathogen of Omsk hemorrhagic fever was revealed [9].

Antiseptics and the second wave of diseases.

The normal circulation of the conventional respiratory coronaviral-like adaptogen provided by bacteria, in this region has failed to provide cross-protection against a new pathogen for some people, while for the vast majority of persons, adaptation took place either with flu-like symptoms, or completely unnoticed. The main genome (the genome of bacteria) coped with its task, despite the fact that people used antibacterial and antiseptic agents, after which people began to get infected not by tens, but by hundreds and, in some cases, thousands. In addition, conditions (widespread use of antiseptics) had been artificially created to form the second wave of infection and the more serious consequences of somatic diseases and complications. SARS-CoV-2, in this sense, has become a kind of signal to people about the violation of living conditions. The medical approach to solving this problem (antiseptics) has only provoked the situation, and the second wave of coronavirus, from this point of view, is understandable, as adaptation (or immunization) of the human population by bacteria should still take place in any case.

COVID-19 and somatic markers. In the population of people living in Southeast Asia (China, Mongolia, Japan, Korea, Vietnam), the somatic complex produced by hepatocytes and responsible for the utilization of an alcohol in the body (alcohol dehydrogenase - ADH and acetaldehyde dehydrogenase - AADH), differ in activity compared to Europeans and North Americans [10,11]. High activity of ADH (allelic gene variant - ADH1B*47His) and low activity of AADH (allelic gene ALDH2*2) are characteristic for citizens of Southeast Asia countries. Mortality from coronavirus in these countries ranges from 0.3 (China) to 1.3 (Japan) per 100 thousand population (table). In the inhabitants of Europe and North America, containing a highly active gene for ADH and a highly active gene for AADH (for example, the allelic gene ALDH 7), the mortality rate from COVID-19 per 100 thousand residents varies from 49.7 (France) to 73.4 (Spain). Mixed variants of AADH activity give intermediate mortality rates (Canada, Russia, Germany).

Somatic marker of hepatic AADH and mortality from COVID-19 in the countries of Southeast Asia, Europe and America

Country	Population, million (as of 20.10.2020)	Mortality (as of 23.10.2020)		Enzyme activity* (estimated)	
		Total	Per 100 000 inhabitants	ADH/% of the population	AADH/% of the population
USA	329,9	228381	69,2	High/up to 80%	High/up to 80%
Spain	46,9	34521	73,4	High/up to 80%	High/up to 80%
Italy	60,2	36968	61,5	High/up to 80%	High/up to 80%
France	68,9	34210	49,7	High/up to 80%	High/up to 70%
Japan	125,9	1685	1,3	High/up to 80%	Low/up to 80%
China	1 406,1	4694	0,3	High/up to 80%	Low/up to 80%
South Korea	51,8	455	0,9	High/up to 80%	Low/up to 80%
Canada	38,3	9862	25,7	High/up to 70%	High/up to 50% Low/up to 30%
Russia	146,7	25242	17,2	High/up to 70%	High/up to 70% Low/up to 10%
Germany	83,1	10044	12,1	High/up to 60%	High/up to 70% Low/up to 10%

* Allelic gene of highly active ADH - ADH1B*47His; gene for highly active AADH - ALDH 7; low-level activity AADH gene - ALDH2*2

The table shows that there is a positive correlation between the content of the enzyme AADH and the lethality from COVID-19. It can be assumed that the correction of the activity of the enzyme AADH will regulate the mortality rate from coronavirus.

Prospects of adaptation to COVID-19. Prospects of population people adaptation to COVID-19 is on the understanding the meaning of contradictions between biology and medicine to use biological (natural) mechanisms for medical prevention purposes. The main problem in traditional vaccinology is the need to eliminate pathogens (viruses, bacteria) from the environment. Now we can with some certainty assume that vaccines developed by traditional methods on the principle of excluding the pathogen from the environment are a way of forming ecological and epidemiological niches (holes) [12]. The use of traditional vaccines against smallpox, polio, measles, whooping cough, diphtheria, tetanus, etc. from a medical point of view, they have had a huge and undeniable protective effect. From a biological, evolutionary point of view, this effect is temporary. Each new people generation, like the present, will face more complex biological problems resulting from uncontrolled behavior in relation to the environment ("disease X") [13].

Retrovirus-like (CRISPR/Cas) spacer adaptation of the immune (anti-infectious) system of a person occurs on the principle of stimulating the necessary (foreign to the body) antibody clones, i.e. there is a kind of individual vaccination or personalized immunocorrection. At the same time, somatic spacer adaptation is designed to exclude the possibility of autoantibodies formation (rheumatoid arthritis, Alzheimer's disease, systemic lupus erythematosus, etc.), of the allergic reactions, tumors, diabetes, etc. in a macroorganism. But all this occurs when in the evolutionary process there is no adverse human impact on the main genome - the genome of bacteria. Natural disasters, man-made disasters, cosmic matter, etc., are only an addition to the number of undesirable elements in this process, since, they are either local in nature, then there is what is observed at the present stage of evolution, or comprehensive, ending with the disappearance of civilizations.

The evolutionarily created mechanism of adaptation of the plant and animal world to changing environmental conditions (ecology) consists in the need for constant correction of the genetic apparatus of living systems. It can be assumed that the signal of the need for such correction is a reduction of affinity in epitope-paratope (antigen-antibody) interaction at the initial stage of spacer adaptation, acting on the principle of the phage display operation. Based on the fact that: 1) there are tandem short polynucleotide and peptide repeats in the genome and proteins of human (animal) cells responsible for immune and somatic adaptation, 2) bacterial system of spacer CRISPR /Cas adaptation is based on the use of similar tandem repeats, 3) the coincidence of tandem repeats of bacteria adapted to coronavirus, with tandem repeats located in the corresponding human cells, - all this is a condition for mononucleotide (drift), or polynucleotide (shift) correction of human (animal) in immune (infectious) and hormonal (somatic) systems [14-16].

The current system of specific prophylaxis of viral and bacterial infections (vaccination), aimed to neutralize and remove of the pathogen from an environment

circulation, temporarily and partially leads to a certain positive success, which is currently observed with a number of infections, as well as the fact that this method of vaccination does not work with other pathogens (HIV, hepatitis C, etc.). For HIV and SARS-CoV-2 viruses that cause human immunodeficiency in the entire body and respiratory tract, respectively, vaccines cannot be developed in the traditional way aimed at neutralizing and removing viruses from the population, since in these cases, immunodeficiency states will be artificially stimulated. As a result, the situation of infectious and somatic diseases will only get worse.

COVID-19 vaccine. Due to their biological features, coronaviruses, including SARS-CoV-2, suppress non-specific and specific immune defenses in the upper and lower respiratory tract on the early stage of infection. As a result, chronic respiratory bacterial (streptococcus, staphylococcus, leptospire, etc.) and may be viral (flu, parainfluenza, RS-virus, etc.) infections are appeared [17]. This, in turn, leads to a "cytokine storm" and the production of the severe acute respiratory syndrome (SARS) [16]. The use of an injection form of vaccine to COVID-19 prepared by traditional methods (subunit, recombinant, vector, whole-virion, synthetic, etc.), aimed to eliminate SARS-CoV-2 from the body, will not set up the necessary volume of the immune and hormonal systems of a person, because the necessary all mechanisms for full adaptation will not be involved (cellular receptors, mitochondrial resources, cytokine components, chaperone mechanisms, etc.). Moreover, as was described above the possibility of developing an immunodeficiency state of the respiratory tract in such inject-vaccinated patients is not excluded, which in turn will lead to the formation of a collective immunodeficiency.

Because children do not get COVID-19 (they do not have chronic respiratory infections due to their age), they can serve as a source of ready-made bacterial adaptogens (vaccines) for adults. Taking into account the fact that bacterial adaptogens of different geographical zones have their own specific features, besides it's about immune and hormonal (somatic) adaptation of adults and the elderly living in this region, the source of the vaccine must be sexually mature children, infected in a mild or asymptomatic form SARS-CoV-2 (there is a positive reaction in the PCR). These children contain and release into the environment a coronavirus-adapted microflora (prokaryotes), which are the basis for the vaccine production. It is important that for older men and women, adaptogens to coronavirus should be obtained from children living in environmentally close conditions or from grandchildren and granddaughters, respectively. Some time before, to a child with measles the healthy small children were brought to play. It was a practice of natural vaccination.

According to our observations, in families where high school students who had a mild form of COVID-19, contacted with their grandparents, they "vaccinated" older without serious health consequences. Belarus is a unique experiment in this regard, although it cannot serve as a "clean" control for other countries due to the fact that the quarantine was partially applied and antiseptics were widely used. However, the difference in mortality rates from COVID-19 compared to other countries where complete isolation of people and

antiseptics were introduced will allow conclude in favor of one of the approaches to respond to the pandemic. Based on the technology described above for creating a coronavirus vaccine, it can be assumed that the Belarusian variant of the fight against coronavirus has advantages not only from an economic, but also medical and general biological points of view.

In general, as for the COVID-19 vaccine, it should not be about the finished vaccine, but about the technology of its preparation. Regarding SARS-CoV-2, cocktails (aerosol, yogurt, etc.) based on microflora adapted to COVID-19 will serve as the main condition for protecting the adult population from severe consequences. In the future, such aerosol (respiratory, enteral) cocktails, obtained taking into account the individual antigenic characteristics of each person (immunoantigenograms for personalized immunocorrection), will serve as the basis at creating a new method and system (technology) for the protection of humans and animals and it will bring the vaccination procedure closer to the natural adaptation process.

The goal of adaptive vaccination will be to prevent the appearance of viral infection from adaptogens formed by prokaryotes. It is interesting to assume that the classic (traditional) way of immunization against pneumococcal or other respiratory infections can significantly reduce the likelihood of developing SARS from coronaviruses. In this case, the patient will be protected by antibodies against reactivation of bacterial chronic infectious pathogens in the lungs. In principle, induced antibodies by any pathogens of the respiratory group can prevent the development not only of SARS, but also due to the presence of cross-reacting antigenic determinants with coronavirus, the appearance of the virus itself.

It is logical to assume that the failure of the developed vaccines against AIDS (HIV-infected people develop not local, but general immunodeficiency) is that HIV does not have the necessary set of peptides that can stimulate antibodies to prevent the development of opportunistic diseases. In this case, the creation of the bacterial (prokaryotic) cocktail based on individual immunoantigenogram against opportunistic congenital and acquired chronic infections and somatic diseases, will prevent the development of AIDS and subsequent severe somatic complications.

Laboratory diagnosis of the SARS-CoV-2 infection. Current molecular genetic (PCR) and immunobiological (serological) monospecific diagnostic test systems aimed to detect genetic material and specific antibodies in COVID-19 can not be without false-positive and false-negative results at present. Due to its biological characteristics, coronavirus infection leads to suppression of the immune system at the point of entry into the body and causes exacerbation (reactivation) of chronic respiratory infections, which, in turn, leads to the stimulation of antibodies to the chronic bacterial and viral respiratory [18]. In this case, antibodies to, for example, respiratory syntenial virus or pneumococcus may appear. At the same time, amino acid and nucleotide analysis of the structural components of pneumococci, staphylococci and other respiratory (including viral) infections showed that they have similar and/or identical antigenic determinants as in coronaviruses. As a result, it is almost impossible to distinguish coronavirus antibodies from bacterial or other viral ones. In

this case, the increase in the titer of antibodies to a specific respiratory group of infections characteristic of this region, detected in the multiplex diagnostic test system (immunoantigenogram), will confirm serologically positive PCR test for coronavirus. On the other hand, given the existence of the prokaryotic CRISPR/Cas adaptation mechanism, PCR analysis of any material, including bacterial-contaminated water and the washes from different surfaces, can reveal of coronavirus-like spacer fragments in bacteria, which will give a false positive result, and, on the contrary, an attempt to analyze material from a patient with a small amount of genetic material (adaptogen) will give a false negative result. However, to partially avoid needless reactions when detecting a virus by classical monospecific PCR, it is needed to determine the optimal quantity of viral infectious particles that can cause the disease (for each pathogen and in each region, it is different, but on average may be about 1000 viral particles) and configure the PCR with this amount.

To confirm the existence in bacteria of a retrovirus-like mechanism of human adaptation to viral infection, including the prokaryotic spacer CRISPR/Cas system, it is appropriate to cite the data of Chinese scientists. They established the ability of SARS-CoV-2 to be transmitted from person to person through aerosols of approximately less than 4, but slightly larger than 1-2 microns (the size of bacteria, while the size of the coronavirus is 0.05-0.2 microns, - ed.) [19]. Researchers studied the aerodynamics of the virus in different rooms of two hospitals in the city of Wuhan, where the COVID-19 pandemic began. They measured the RNA content of the virus in aerosols in February and March 2020. The concentration of RNA in isolation rooms and ventilated areas was very low, but in toilet areas the content of genetic material was increased. In most public areas, the RNA of the coronavirus was not detected, except in areas where there were high density of people. Researchers found high concentrations of viral genetic material in the rooms for medical personnel, and the most of the pathogen was also contained in the aerosols with a size of about one micron. Strict sanitation procedures have reduced the level of viral RNA to undetectable values. However, Chinese specialists believe that in the future it is necessary to establish the ability of SARS-CoV-2 genetic material in aerosols to infect intact individuals.

Conclusions. The main feature of coronavirus SARS-CoV-2 infection is its ability to suppress local immunity at the point of penetration - in the upper and lower respiratory tract. As a result, chronic respiratory bacterial and viral infections are developed. This, in turn, leads to a "cytokine storm" and the production of the severe acute respiratory syndrome (SARS). In this regard, serological diagnostic tests developed using conventional traditional methods aimed at detecting antibodies to the virus cannot be used as an alternative or to assist PCR. In this case, there are antibodies to chronic infections characteristic of a specific local ecological zone.

Vaccines from this point of view are even more difficult for development. It can be assumed that if there is any protection, this protection will be determined and carried out in line with the natural mechanisms observed in the immune category of people, both children and adults. Moreover, immunity to SARS-

CoV-2 virus in adults is of the greatest interest. They have a variety of symptoms, mainly related to chronic, for the most part respiratory infections. Vaccines, therefore, should be developed not against disease (COVID-19), but for a specific person, taking into account environmental factors present in each biocenotic environment (climate zone, country, continent, etc.) and the dominant kind (species) of bacterial respiratory infection. At first, vaccination or prevention of chronic bacterial respiratory infections should have the greatest effect when protecting against COVID-19. Secondly, vaccines against COVID-19 based on traditional technologies (subunit, synthetic, recombinant, whole virions, etc.) will stimulate the body's immunodeficiency states and reduce its protective functions. In the future, it is necessary to develop and implement not specific vaccines or diagnostics, but technologies, which are outlined in the schematic form in this publication above.

REFERENCES

- Falkowski Paul G. (2016) In: "The engines of life. How bacteria have made our world habitable." "Peter." - Transl. English into Russian – 272p.
- Vladyko, A.S. (2020) The Main Genome. – Mat.Int.Conf. "Process Management and Scientific Developments" (Birmingham, United Kingdom, January 16, 2020) P. 51-55 <https://doi.org/10.34660/INF.2020.4.52920>
- Ryan F. (2014) "Violution". Translation from English into Russian. <https://www.e-reading.club/bookreader.php/1053546/Rayan-Violy-uciya.html>
- Vladyko, A. (2019) Biological Weapon or Biological Threat? – J.Envir.Sci.Eng.Tech., No.7, P.54-59. DOI: <https://doi.org/10.12974/2311-8741.2019.07.07>
- Ishino Y, Shinagawa H, Makino K, Amemura M, Nakata A (1987) Nucleotide sequence of the iap gene, responsible for alkaline phosphatase isozyme conversion in *Escherichia coli*, and identification of the gene product. - J.Bacteriol., No.169 (12), P. 5429–33. DOI: <https://doi.org/10.1128/jb.169.12.5429-5433.1987>. PMID 213968.
- Mojica, F.J., Juez, G. & Rodriguez-Valera, F. (1993) Transcription at different salinities of *Haloferax mediterranei* sequences adjacent to partially modified PstI sites. - Molecular Microbiology, Vol. 9, No. 3, P. 613-621.
- Vladyko A.S.. (2019) Main genome and ecology. – Materials of the Inter-University Scientific Congress (Moscow, December 18, 2019r.). – Moscow: Publishing house "Infiniti", 2019.–140p. P. 94-99. DOI: <https://doi.org/10.34660/INF.2019.9.43956>. In Russian
- Vladyko A.S. (2020) Appearance of infections and somatic diseases: COVID-19. - School of Science – 2020. – No.2(27). – P.10-14. <https://doi.org/10.5281/zenodo.3725689> In Russian.
- Yastrebov V.K., Yakimenko V.V. (2014) Omsk haemorrhagic fever: total investigations (1946–2013). – Vopr.virusol., No.59(6), P.5–11. <https://cyberleninka.ru/article/n/omskaya-gemorragicheskayali-horadka-itogi-issledovaniy-1946-2013/viewer> In Russian.
- Anton Evseev (2019) The mill of myths: who is drunker in the world? <https://www.pravda.ru/science/1102387-alcag-oldegidrogenaza/> in Russian
- Joshi, A.U., Van Wassenhove, L.D., Logas, K.R. *et al.* (2019) Aldehyde dehydrogenase 2 activity and aldehydic load contribute to neuroinflammation and Alzheimer's disease related pathology. *Acta neuropathol commun* **7**, 190. <https://doi.org/10.1186/s40478-019-0839-7>
- Zapata J.C., Salvato M.S. (2013) Arenavirus variations due to hosts specific adaptation. – Viruses, No. 5(1), P. 241-78. DOI: <https://doi.org/10.3390/v5010241>
- World Health Organization. (2018) Scientists put on alert for deadly new pathogen – 'Disease X'. <https://www.telegraph.co.uk/news/2018/03/09/world-health-organization-issues-alert-disease-x/>
- Erik J. Sontheimer, Rodolphe Barrangou. (2015). The Bacterial Origins of the CRISPR Genome-Editing Revolution. - Human Gene Therapy. – No.26. - P.413-424.
- Jennifer L. Gori, Patrick D. Hsu, Morgan L. Maeder, Shen Shen, G. Grant Welstead, David Bumcrot. (2015). Delivery and Specificity of CRISPR/Cas9 Genome Editing Technologies for Human Gene Therapy. - Human Gene Therapy. - No.26. – P.443-451.
- Rongxue Peng, Guigao Lin, Jinming Li. (2016). Potential pitfalls of CRISPR/Cas9-mediated genome editing. - FEBS J. – No.283. - P1218-1231.
- Vladyko A.S., Petkevich A.S. (2003) Severe acute respiratory syndrome pathogen: mechanisms of appearance and consequences. - Science and innovation, No 3-4, P. 99-103. In Russian
- Felsenstein, S., Herbert, J.A., McNamara, P.S. *et al.* (2019) COVID-19: Immunology and treatment options.- Clinical Immunology (2019), <https://doi.org/10.1016/j.clim.2020.108448>
- Chia, P.Y., Coleman, K.K., Tan Y.K. *et al.* (2020) Detection of air and surface contamination by SARS-CoV-2 in hospital rooms of infected patients. – Nat.Commun. **11**, 2800 <https://doi.org/10.1038/s41467-020-16670-2>.