The Main Genome is a Source of Adaptogens and the Basis for the Development of a New Vaccination Technology

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Abstract: The appearance of viruses in mammals and plants is provoked by environmental factors - xenobiotics, formed mainly due to unreasonable human activity and resulting from the formation of an ecological (epidemiological) niche filled with molecular motifs of the microbiota - the intestines of mammals and the root system of plants. To do this, bacteria and archaea use retrovirus-like “cut and paste” mechanisms, including, for example, the CRISPR/Cas system, when the molecular motifs of the microbiota try to adapt the immune and hormonal systems. It all depends on how much xenobiotics damage the immune and hormonal systems. Therefore, viruses are not the cause, but the consequence of the disease. The fight against viruses with the help of vaccines prepared on their basis has been violating and restraining the natural mechanisms of regulation of biological processes in plants and mammals. Thus, molecular motifs arising from microbiota bacteria become either apaptogens (viruses) or adaptogens. In the first and second cases, genetic information is released into the environment. In the latter case, there is an adaptation or a kind of vaccination of others by a natural mechanism. This mechanism is also applicable to somatic diseases, such as cardiovascular, autoimmune, oncological, etc. As for the original properties of coronaviruses, it is their ability to suppress innate and acquired nonspecific viral immunity in the respiratory tract. This leads to the reactivation of chronic, mainly bacterial, respiratory infections - pneumococci, staphylococci, hemophiluses, however, fungal infections can also be observed – mucormycosis, aspergillosis, etc. This feature of the virus prompted doctors at the beginning of the epidemic (2020) to use a pneumococcal vaccine, which, as it turned out, similarly to the coronavirus vaccine reduces the severity of the disease and mortality. As for the diagnosis of coronavirus infection and its treatment, as practice has shown, everything depends on the stage of the disease, starting with a viral and ending with a bacterial infection. Similar and identical antigenic determinants in coronavirus and respiratory group bacteria often caused confusion when analyzing the results of serological and molecular biological diagnostic tests in patients with COVID-19. Moreover, the justified use of antibiotics in the post-viral, that is, in bacterial periods, made it possible to successfully treat patients with a positive PCR test for coronavirus on an outpatient basis.

Keywords: Main genome, Molecular motifs, CRISPR/Cas system, Prokaryotes, Microbiota, Adaptogens, Apoptogens, Personal vaccination technology, Diagnostics, Therapy.

INTRODUCTION

Since all viruses live inside the cell, using all cellular mechanisms and resources for this, and leave the cell changed, it is almost impossible to imagine the origin of viruses without the origin of the cell, and, consequently, bacteria and life on the planet. Biological life on earth originated 3.5-3.6 billion years ago with the appearance of oceanic bacteria (prokaryotes) [1, 2]. There are many assumptions about how bacteria appeared, but the main one is the statement that our earth, like other planets of the universe, participated in this unique process. The further evolution of living organisms (plants and animals) depended on the appearance of land and, of course, depended on bacteria. Man appeared in this evolutionary process of bacteria 2.6-2.8 million years ago [3, 4]. This "legacy" as a factor of breeding has remained and exists at the present time. Thus, bacteria are the genetic basis of the evolution of the biological world – the "holder" of the main genome [5].

According to a number of researchers, bacteria occupy a special place in the evolutionary process of biological life. For example, in 2016, the work of the American biologist Pavel Falkovsky was published [2], where the author considers bacteria as *"... engines of life. How they made our world habitable."* As a specialist in the field of biological oceanography, he made a huge contribution to understanding the role of oceans in the coevolution of life and biogeochemical cycles. According to other researchers [6,7], the human intestine contains 100 trillion microbes. The authors claim that the microbiome plays an important role in maintaining normal homeostatic processes and that changes in the gut microbiome are associated with numerous medical disorders, including obesity, diabetes, liver disease, inflammatory bowel disease and even disorders of the central nervous system. As for viral infections, according to the English biologist Frank Ryan [8], presented in the book "Virolution", "*Viruses, their derivatives and closely related structures make up at least 43% of the human genome, which leads to the conclusion that natural selection in humans and their ancestors occurred in partnership with hundreds of viruses.*"

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From these publications follows: 1) for 1 human gene (a person has 29-31 thousand genes, according to other data 20-25 thousand genes), there are approximately 1 million molecular motifs (spacers, units of evolution) located in the genes of bacteria living in the intestine, on the skin, mucous membranes, etc.; 2) the mitochondrial apparatus of mammalian eukaryotic cells, including humans, has the genetic code of bacteria; 3) approximately 300 bacterial genes are contained in the chromosomes of human somatic cells; 4) the reproduction cycle of bacteria is minutes, and they instantly genetically change under the influence of the external environment (ecology), while surviving in extreme habitats, including space.

At the same time, as follows from our analysis [9], it is not viruses and their structures make up 43% of the human genome, but *a human is a small genetic derivative of viruses or, more precisely, adaptogens, which are contained mainly in bacteria and are the source genetic material or the main genome that regulates the processes of existence and appearance of biological diversity (animals and plants).* Bacteria, mentally and morphologically patronizing a person, constantly and every second transmit acquired changes to the human genetic apparatus, using a retrovirus-like mechanism formed over millions of years of evolution - "cut and paste". In addition to retroviruses, bacteria and archaea have such a mechanism - this is a CRISPR/Cas system for editing the genomes of macroorganisms based on tandem repeats available in all viruses, as well as one cellular and multicellular organisms [10-14]. Publications on this part give reason to hope for this mechanism in human and animal gene therapy [15-17]. For example, genome editing using the CRISPR/Cas9 platform precisely modifies endogenous gene targets in many human cell lines and animal models, which can serve as an effective clinical treatment method for patients with hematological diseases [16]. It is assumed that *the identity of tandem repeats in bacteria and humans is necessary for the exact entry of the spacers (molecular motifs) of bacteria into the human genome at the right time and in the right place to correct its immune and hormonal systems, thus, a person adapts to a changed environment.*

COMMON MOLECULAR MOTIFS

According to Cox F.*E.G.*, the Schistosoma mansoni helminth contains an antigenic determinant - B-epitope identical to the HIV-1 vif protein [18]. In 1992, working with the high dangerous tropical viruses Lassa, Marburg and Ebola, cross-reactions between blood serum antibodies from patients with tropical malaria and antigens of these viruses were detected [19]. In the work of M. Tilson and co-authors was shown the blood serum of a patient with an aortic aneurysm contains antibodies specific to the 40 kDa protein of the high dangerous Ebola virus [20]. The author concludes that hemorrhagic manifestations associated with Ebola infection have common mechanisms associated with the appearance of similar proteins in the wall of blood vessels, contributing to their "softening". Comparative analysis of eukaryotic genes showed that out of 289

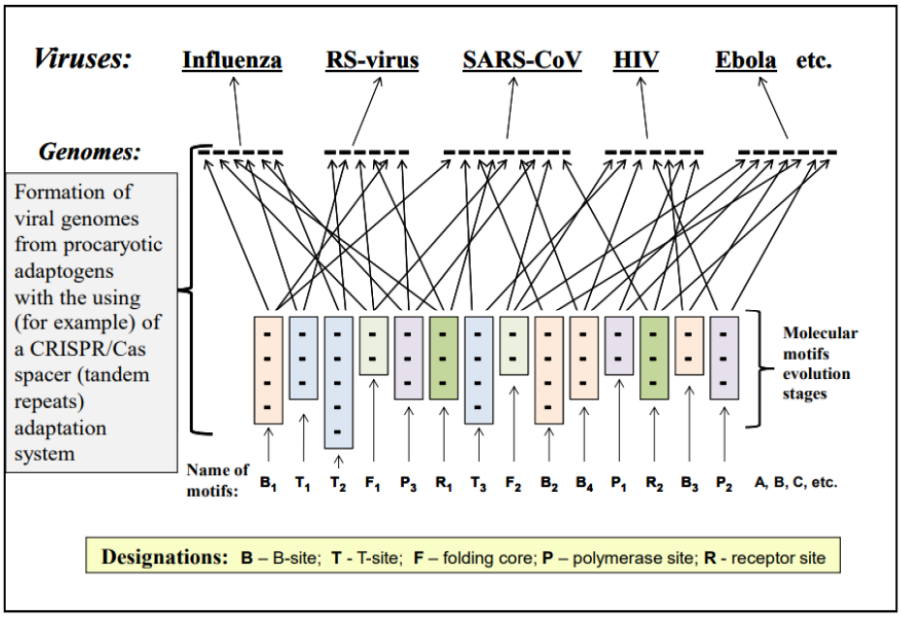


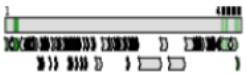
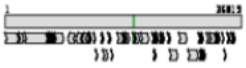
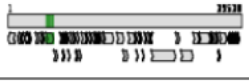
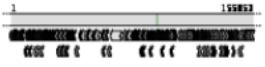
Figure 1: Schematic diagram of the new virus formation from molecular motifs.

genes of infectious disease pathogens in humans, 177 orthologous genes are present in the common fly [21]. In our studies, it has been shown a bovine serum albumin contained amino acid sequences capable to bind antibodies from a patient with hemorrhagic fever with renal syndrome [22]. The data published in 2019 at an international conference held in the USA on the detection of 827,000 new viruses in animals [23] are, in our opinion, nothing more than molecular motifs or spacers, the number of which in nature is estimated in millions and depends on the work of the main genome - the genome of bacteria. From this it can also be concluded that *the proteins of infectious pathogens and somatic proteins have common antigenic structures and, moreover, a common origin associated with the main genome – the genome of prokaryotes*. Thus, the scheme of formation of various viruses from homogeneous molecular motifs can be represented in the form of a diagram [24, 25] shown in Figure **1**.

It can be seen that from a relatively small number of molecular motifs (spacers), whose nucleotide triplets encode 20 amino acids, a huge number of different pathogens are formed. Here, the variety of viruses is similar to music, in which there are only twelve notes and an unlimited number of melodies.

The result of a metagenomic PCR analysis of a coronavirus-positive patient (SARS-CoV-2) confirms this conclusion. The data is presented in Table **1**.

Table 1: Data of Metagenomic Sequencing of the Material in a PCR Positive for Coronavirus of a Belarusian Patient

Coronavirus genome for comparison:							
Assignment	**# Contigs**	**# Reads**	**Coverage (%)**	**Depth of Coverage**	**Identity (%)**		**Genome Coverage**
					NT	**AA**	
SARS-related coronavirus	1	12237	99.8	91.6	99.9	99.9	
Similar or identical genome regions found in other viruses (spacers):							
Streptococcus phage 20617	5	176	7.9	10.2	87.9	90	
Streptococcus phage SMP	1	74	0.9	52.1	80.8	92.5	
Beihai narna-like virus 26	1	53	39.7	12.3	47.4	44.7	
Streptococcus phage 315.1	2	43	3.2	7.4	63.3	64.3	
Hubei narna-like virus 22	1	37	29.4	11.3	43.3	34.6	
Enterococcus virus EFP01	1	3	0.1	3.5	80.4	84.1	
Hum.endogen. retrovir.	1	3	2.5	2.8	94	0	
Mason-Pfizer monkey virus	1	1	3.6	0.8	55	51.1	
Baboon endogen. virus strain M7	1	1	3.2	0.8	59.1	58.4	

The table shows that individual molecular motifs (spacers) in the SARS-CoV-2 coronavirus were found in other viruses representing various groups and families – from pneumococcal phages to mammalian viruses, for example, with 3.6% of the genome of the monkey immunodeficiency retrovirus (Mason-Pfizer monkey virus). The proposed structure of the monkey immunodeficiency virus genome is shown in Figure **2**.

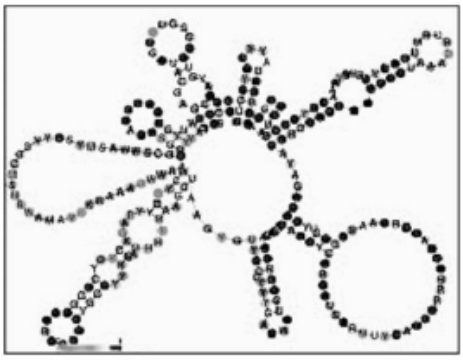


Figure 2: Calculated genome structure of the monkey immunodeficiency virus (Mason-Pfizer monkey virus).

It can be seen this virus contains a large number of tandem repeats that contribute to the formation of loops and spirals and, apparently, these repeats participate in the adaptation of mammals using the CRISPR/Cas mechanism.

PATHOGENETIC FEATURES OF SARS-COV-2

It is known, more noticeable feature of coronaviruses is its ability to suppress innate and acquired nonspecific viral immunity in the respiratory tract [26-29]. As a result, pathogens of chronic, mainly pathogenic bacterial (sometimes mycotic and even parasitic) infections are able to multiply. Pathogenic bacteria are one of the causes of the severe course of the disease, the "cytokine storm" and deaths. It also follows from this, *an antibacterial therapy prescribed at the stage of bacterial post-viral infection is crucial in the favorable outcome of COVID-19*. The using antibiotics at the initial viral stage of infection or prophylactically creates conditions (by the mechanism of xenobiotics) for the subsequent formation of resistant or even drug-dependent forms of pathogenic bacteria. In the latter case, antibiotics become a favorable medium for the reproduction of such bacteria, and the higher of the antibiotic dose, the more they will reproduce and worsen the patient's condition.

To confirm the presence of bacterial infection in coronavirus patients, PCR-positive for SARS-CoV-2 patients at the stage of acute infection development were examined (at the time of examination, patients were in an infectious hospital - in the period before vaccination, April 2020). For this, an enzyme immunoassay for IgM and IgG antibodies to leptospirosis was used. The Leptospira IgG and Leptospira IgM test systems produced by DRG instruments GmbH, Germany, Marburg was used for the analysis. The data are presented in Table **2**.

Table 2: Screening of Sera for Leptospirosis in ELISA-Test in Patients with PCR+ SARS-CoV-2

Patient	IgM	IgG	Gender, age
M.	Equivocal	Negative	Female, 50 y.o
G.	Equivocal	Negative	Male, 20 y.o
L.	Negative	Negative	Male, 28 y.o
Z.	Positive	Negative	Female, 20 y.o

It can be seen that out of 4 patients with a PCR-positive test for coronavirus, only one blood serum (patient L.) gave a negative result for both classes of antibodies, whereas IgM tests in patients M. and G. were equivocal, and in the patient Z. - positive. It is impossible to find out which viral or bacterial antigens stimulated the antibodies in this case, as well as how to treat Z. patient: from coronavirus or antibiotics for leptospirosis?

THE EMERGENCE OF ADAPTOGENS AND VIRUSES

A person with a normal intestinal microbiota and, consequently, a healthy immune and hormonal system lives most of his life without serious infections and somatic diseases. In this case, a person exchanges "healthy" viruses with the external environment (natural vaccine or adaptogens). Conversely, when these systems are damaged by xenobiotics, and the microbiota is unable to restore the normal functioning of the immune and hormonal systems, the microbiome forms apoptogens (pathogenic viruses) that can cause diseases in weakened organisms and do not cause in strong ones. Figure **3** shows the scheme of the molecular motifs circulation (units of evolution) formed by the microbiota (bacteria) for the adaptation of multicellular organisms (plants and animals, including humans) to changing environmental conditions.

It can be seen the development of the infectious process can be divided into 5 stages. From 1 to 4 stages, depending on the immune and hormonal state of the organism, either adaptation (upper part) or

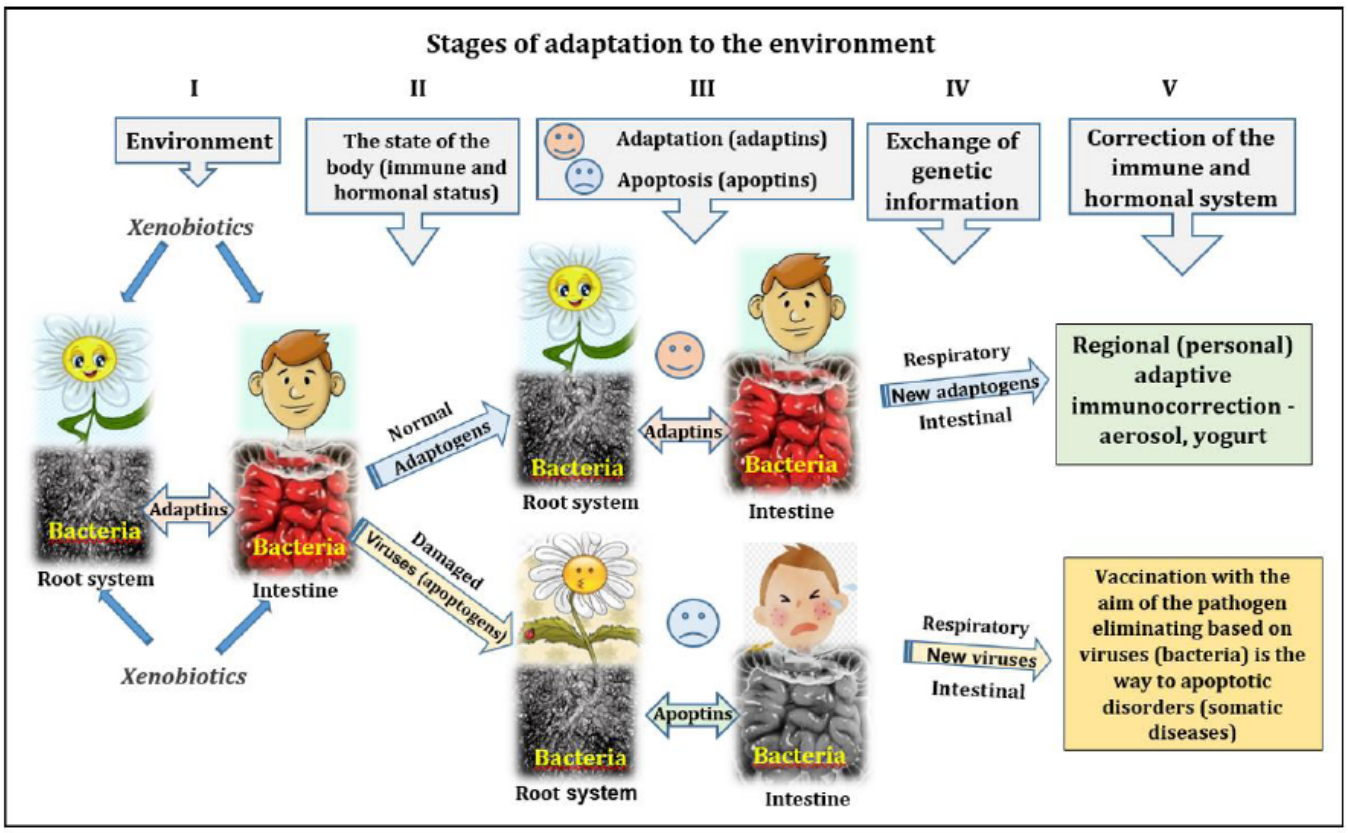


Figure 3: Scheme of distribution of adaptive or apoptotic (viral) molecular motifs in plants and mammals depending on the state of the immune and hormonal systems (stages I-IV) as a basis for choosing the technology (method) of prevention and treatment (stage V)*

Xenobiotics (here) - substances of material and mental origin, foreign to the organism; ***adaptogens*** (here) - genetic structures (molecular motifs) microbiota, initiating the synthesis of adaptin's proteins in the organism; ***adaptins*** (here) - a group of proteins synthesized by the organism in response to xenobiotics in order to adapt one to a changing environment; ***apoptogens*** – (here) genetic structures (molecular motifs) microbiota, initiating the synthesis of apoptin's proteins in the organism; ***apoptins*** (here) - proteins synthesized in the organism by molecular motifs of the microbiota in conditions of damaged immune and hormonal systems**;** ***apoptosis*** (here) - a multi-stage program of the organism's death, regulated by a group of special molecular motifs of microbiota.

* The authors do not pretend to consolidate a new interpretation of the given terms (to avoid overload during decryption and the appearance of new terms).

disease (lower) is formed. In the first case, adaptogens (or non-pathogenic viruses) and their proteins are involved in the process, and in the second - apoptogens or pathogenic viruses and apoptins. At the 5th stage, options for correcting the immune and hormonal systems are being considered. If the correction is carried out with the help of adaptogens, there will be an improvement of the organism, if on the basis of a virus - distant somatic diseases.

DEVELOPING AND ANALYZING ANTIBODY DIAGRAMS (ABD) OF PATIENTS DURING THE CORONAVIRUS PANDEMIC

An example of obtaining and analyzing diagrams of individual antibodies can be data from enzyme immunoassay of individual antibody clones in patients with positive and negative PCR tests for SARS-CoV-2, as well as asymptomatic or severe clinical manifestations (pneumonia). Synthetic B-epitopes and recombinant (to several antigenic determinants) peptides (leptospirosis) were used as the solid phase. The data are presented in Figure **4**.

As follows from the figure, patients aged 30+ (A) and 40+ (B) with negative and positive PCR test for coronavirus, as well as pneumonia, respectively, reacted weakly by IgM and IgG clones to the SARS-CoV-2 phosphoprotein. In the 30-year-old patient without pneumonia, early (IgM) antibodies have just begun to appear, while in a 40-year-old with severe pneumonia gave a weakly positive test for a clone of G-class immunoglobulins to SARS-CoV-2. In addition, antisomatic antibody clones in these patients reacted similarly to an external stimulus, but in higher titers,

which indicates the process of adaptation to any external factors observed during any infection. This conclusion is confirmed by the absence of a reaction from the intestinal microbiota - the absence of antibodies to bifidobacteria. It can be assumed that in this case, the microbiome calmly (without antibody clone titers) reacted "normally" to external irritants. A kind of specific response to the presence of a reaction from the somatic system in these patients can be considered the presence in the external environment of a group of respiratory (vir/bact) pathogens, which is not surprising, since both viral and bacterial infections in the region of residence are constantly circulating and may be involved in the epidemic process. Time will tell – what somatic changes 30 and 40-year-old patients will face in the future. However, in order to predetermine these changes, systematic annual observations and, apparently, additional markers (molecular motifs) are needed. A clone of antibacterial (respiratory-intestinal) antibodies and polyclonal antibodies against leptospirosis is of particular interest. Where did the antibodies to leptospirosis come from in a patient with PCR+ COVID-19 test? Firstly, it is possible that the patient had indeed previously suffered an infection of leptospirosis, and secondly, it was previously shown that the virus and the bacterium have common antigenic structures. For example, it was found that one of the immunodominant antigenic determinants of the SARS-CoV-2 phosphoprotein at the position of amino acids 369-375 (KKDKKKKK) coincides with a large number of similar amino acid sequences located in the proteins of pneumococci, enterococci, staphylococci, klebsiella, etc. [30]. Moreover, seven antigenic sites of the spike protein showed molecular similarity with 54 antigenic determinants found in twelve species of pathogenic bacteria (*Mycobacterium tuberculosis, Mycobacterium leprae, Bacillus anthracis, Borrelia burgdorferi, Clostridium perfringens, Clostridium tetani, Helicobacter Pylori, Listeria monocytogenes, Staphylococcus aureus, Streptococcus pyogenes, Vibrio cholera and Yersinia pestis*), two malaria parasites (*Plasmodium falciparum and Plasmodium knowlesi*) and influenza A virus [31]. In this case, it is difficult to differentiate which B-epitope: coronavirus or bacterial stimulated antibodies. The next group of patients - age 60+ (Figure **4 C** and **D**) significantly reacted with almost all antibody clones to both individual peptides and polyvalent leptospirosis antigen. Both patients are under the supervision of oncologists and are undergoing chemotherapy. At the same time, the PCR test and pneumonia were negative on SARS-CoV-2 in C. patient. It turned out (from the anamnesis) that this patient is a congenital arterial hypotonic. In this regard, it can be assumed that his ACE-2 cell receptors, responsible for attaching the virus to the cell wall, were genetically modified from birth, and he cannot respond clinically to this virus [32]. Pneumonia of moderate severity in D. patient was detected. He had a positive PCR test for coronavirus. In this case, the average severity of pneumonia in a D. cancer patient can be explained by the course of chemotherapy took place several months before the coronavirus pandemic and he gradually adapted to the conditions of reduced immunity, when chronic pathogens are reactivated and the organism was able to adapt to similar conditions created by the coronavirus. And finally, patients E. and F. (Figure **4**) - age 80+ and 70+ with positive and negative PCR tests, respectively. In this case, E. patient completely lacked an immune response to the studied peptides and died of pneumonia in an infectious clinic at the age of 85. As for F. patient, he had from the anamnesis moderate pneumonia with loss of smell and taste. He had a weak reaction with an anti-bifidobacterial IgM clone. Slightly higher titers (IgG) of antibodies were determined in a leptospirosis test system. The patient refused hospitalization and underwent an outpatient course of azithromycin therapy [33], after which he fully recovered. A negative PCR test is apparently associated with a late visit to the diagnostic laboratory.

In general, it is not possible to draw any systemic conclusions from the antibody data of 6 patients presented in Figure **4**. The number of antibody clones analyzed and the modest sample of patients does not even allow speculatively to assume any dynamics. This requires systematic long-term observations carried out everywhere during outpatient monitoring of residents both in the interepidemic period and during epidemics. In this case it will be possible to predict future epidemics with a probable pathogen. In future studies related to obtaining antibody clone diagrams (AbD) should be carried out, as they relate to the development of laboratory diagnostics, revision of vaccination strategies, therapy and, in general, biosafety. Some optimism is caused by data on the possibility of using microbiota adaptogens for the purposes of diagnosis and vaccination of specific infections [34].

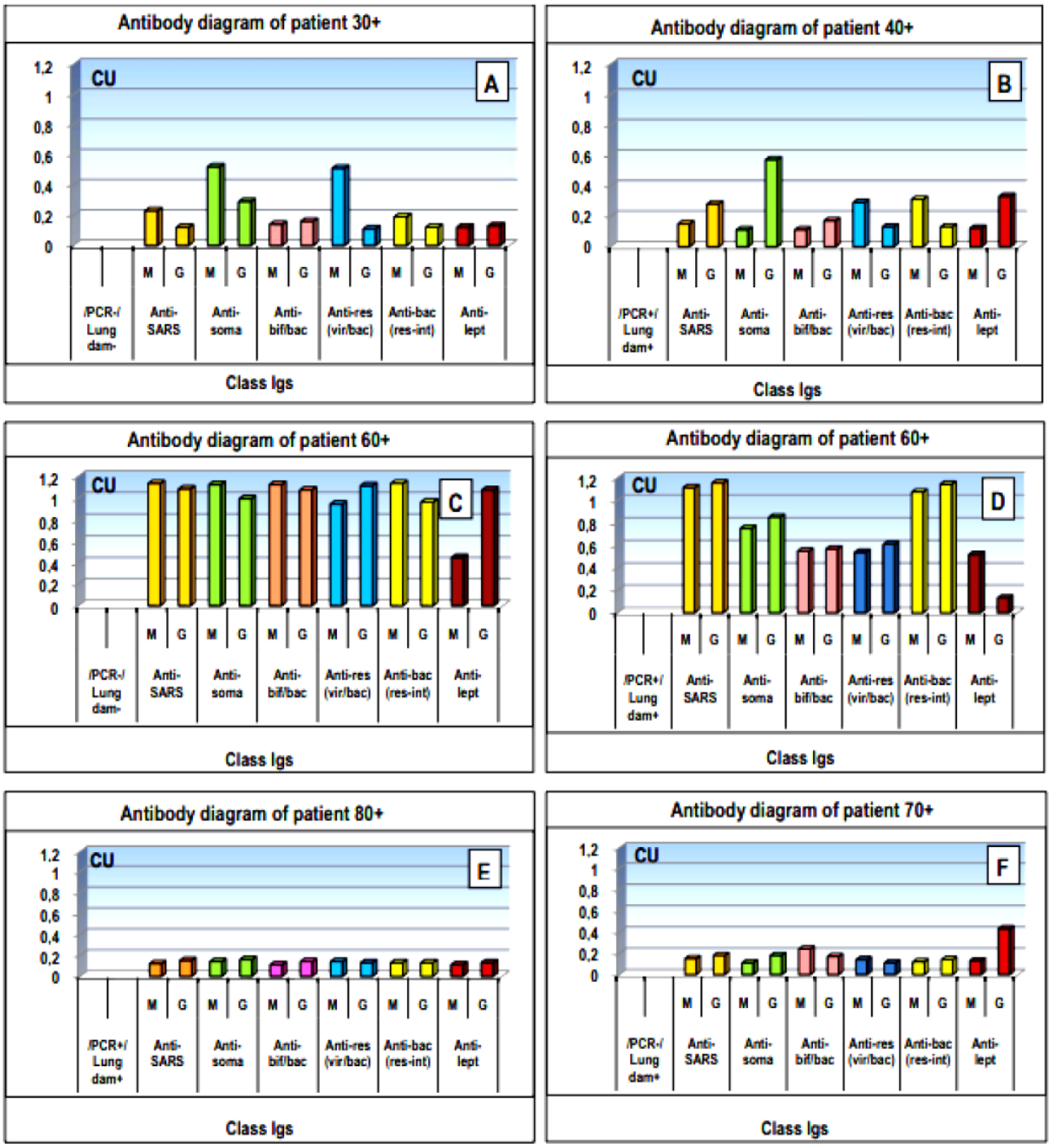


Figure 4: Antibody diagrams (AbD) of different age patients with a positive and negative PCR test for SARS-CoV-2 and the presence or absence of pneumonia in the pre-vaccination period.

CU - antibody ***clone*** activity ***units***: < 0.2 – negative, 0.2-0.4 – weakly positive, 0.4-0.8 – positive, > 0.8 – strongly positive; PCR+ and PCR- - positive and negative test in a polymerase chain reaction, respectively; Lung dam+ and Lung dam- - the presence or absence of pneumonia, respectively; Anti-SARS – CU to the SARS-CoV-2 phosphoprotein; Anti-somatic – CU to the collagen; Anti-bif/bac – CU to intestinal bifidobacteria proteins; Anti-res (vir/bac) – CU to respiratory viral and bacterial proteins; Anti-bac (res–int) – CU to bacterial respiratory and intestinal proteins; Anti-lept - units of polyclonal antibody activity to leptospirosis antigens (Leptospira IgG and Leptospira IgM test system manufactured by DRG instrument GmbH, Germany, Marburg).

CONCLUSION

The technology of creating vaccines, developed more than 200 years ago, based on the stimulation of virus neutralizing antibodies and pursuing the goal of removing the pathogen from circulation in the human population, is unattainable. First, the same type of vaccine stimulates the production of the same type of antibodies to ensure herd immunity, and it is easier for the pathogen to mutate in this monotony; secondly, why remove something that should not be removed, but should adapt according to the natural mechanism.

There is still no vaccine against HIV, hepatitis C and a number of other dangerous infections. There are many questions about the existence of problems related to the somatic consequences of the use of vaccines against smallpox, polio, measles and a number of bacterial infections. We propose a technology of individual vaccination based on personal diagrams of human antibody clones specific to new circulating molecular motifs. Analysis of the profile of antibodies, namely their individual clones to the antigenic structures of the virus in humans before vaccination, will serve as a basis for excluding or including individual immunogens in a personal vaccine. In the future, the data from the antibody diagrams of each person can be transferred to a digital chip or USB flash drive and used in the cocktail device to obtain an aerosol or a nutritional cocktail formed from bifidobacteria adapted to infectious agents by a natural mechanism: xenobiotic (a new structure of the antigen) - a bacterium. Thus, we do not offer a vaccine preparation, but an easily accessible technology that takes into account the peculiarities of both a particular country and the individual biological characteristics of each person.

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