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Research Article

Let`s Pay Attention to Covid and Move Forward

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Abstract:

Introduction: Zoonoses are diseases transmitted from animals to humans and pose a major threat to human health and life. Animals are often asymptomatic carriers of pathogens and spread them in the environment with their excreta. Their course varies from the common cold to more severe and often fatal diseases in humans. Before the COVID-19 infection caused the global pandemic in 2020, coronavirus diseases were primarily of veterinary interest.

The COVID-19 pandemic has changed the way we live and strained healthcare systems around the world. This pandemic has necessitated the development of protective and therapeutic measures against the spread of SARS-CoV-2. The lack of optimal vaccine against SARS-CoV-2 offering long-lasting protection against the different viral variants, as well as a drug, allowing the treatment of all variants of COVID-19 directed us to the use of dietary components and agents that are applicable in the context of competitive inhibition by blocking part of the receptors to protect against coronavirus-related diseases.

Discussion: Lactobacillus and carrageenans may have a protective effect against SARS-CoV-2 infection alone or in combination in healthy subjects. Reducing the viral load in the nasopharynx may drastically reduce the risk of transmission of COVID-19.

Infectious diseases are among the strongest types of selective pressure driving human evolution. Genetics in the coming decades will likely allow us to understand the dynamics of human immune system formation. By learning from our mistakes and successes, we will be able to more successfully deal with the challenges posed by zoonoses in the future.

Keywords: Zoonoses, Lactobacillus, emerging coronavirus, SARS-COV-2, human genom, carrageenan, prevention.

Introduction

In recent decades, we have observed the emergence of several new diseases, were caused by Ebola virus, Zika virus, Nipah virus and coronaviruses (CoV). Before the COVID-19 infection caused a global pandemic in 2020, coronavirus diseases were primarily of veterinary interest. The coronavirus is a single-stranded RNA virus first isolated in 1937. The coronaviruses of the family Coronaviridae (subfamily Coronavirinae, order Nidovirales) were described in detail in the mid-1960s and divided into four genera: Alphacoronavirus, Betacoronavirus (lines A–D), Gammacoronavirus and Deltacoronavirus. Bats are the natural hosts of human coronaviruses from the Alphacoronavirus (HCoV-NL63, HCoV-229E) and Betacoronavirus (SARS-CoV, MERS-CoV, SARS-CoV-2) genera, while rodents are the host for the Betacoronavirus HCoV-OC43 and HCoV-HKU1. (1) By 2020, six types of coronaviruses—HCoV-229E, HCoV-NL63, HCoV-OC43, HCoV-HKU1, severe acute respiratory syndrome (SARS-CoV), and Middle East respiratory syndrome (MERS-CoV) were known to infect humans, and all of them have a zoonotic origin, as confirmed by their genomic sequences. SARS-CoV-2 is the seventh identified representative. (2) All have high mutagenicity and an ability to create new strains, allowing them to adapt to a wide range of hosts. Their course varies from a common cold to more severe and often fatal diseases in humans. (3, 4, 5) During the pandemic, we encountered an interesting approach in some countries. When intermediate virus-carrying was discovered in some farms for industrial breeding of animals, it was decided to kill them. It is good that in this case we did not proceed mechanically to eliminate other animal species such as deer, lions and others, for which there were similar reports. Provided that there was an unprecedented quarantine around the world, it was much easier to introduce her retrograde form. It's just that the workers on these farms didn't have to leave them for about three months. This is enough time not to allow a viral mutation to stabilize and thus cease to be dangerous to humans. If it has already stabilized, there is no significant benefit from the quarantine. Another interesting phenomenon we observed was allowing pets to be walked while other people were quarantined. In this case, another unknown was introduced into the equation, as there was no tracking of how many of the pets became sick and even died from the infection - they could easily become intermediate hosts and pass the infection on to each other and to other owners during walks.

Main

Zoonoses or diseases of animal origin are transmitted from animals to humans and pose a major threat to human health and life. Animals are often asymptomatic carriers of pathogens and spread them in the environment with their excretas. Zoonoses are diseases transmitted between animals and humans as a result of direct contact, indirect contact with the environment or through food. (6) Among the recognized pathogens causing human disease, almost 60% are of animal origin. They cause diseases such as toxoplasmosis, anthrax, rabies, Ebola hemorrhagic fever, MERS-CoV, SARS-CoV, SARS-CoV-2, HIV, etc. (7, 8) Nowadays, of the 1,400 pathogens that cause human disease, 800 have of animal origin. (9)

There are many mechanisms for the transmission of zoonoses and sometimes the same disease can be transmitted in several

ways. Ticks, fleas, mosquitoes and rodents can be mentioned as vectors for their transmission. Modes of transmission include direct contact, skin abrasions and injuries, bites, through food, soil and water. Farmers, slaughterhouse workers and veterinarians are most commonly affected.(10) Patterns in studies of wild and domestic animals only partially overlap with those in humans. But research in animals is much more numerous, in a much more advanced phase, and the experience gained in veterinary medicine can be invaluable to us in understanding the mechanism of action of human pathogens and in treatment. So far, there have been no serious observations on the spread of respiratory and other viruses among the human population and their possible interaction. One of the few studies done in recent years is on Goldman et al. It was made in Kansas city, Missouri among pre-school, primary and secondary school students, and staff members during the 2022/2023 school year. The number of participants is only 894. Self-collected anterior nasal swabs were obtained montly and tested using multiplex viral polymerase chain reaction. They establish that, overall rhinovirus/enterovirus (RV/EV) was detected most frequently 12.1%, followed by all sesonal coronaviruses - HCoV-NL63, HCoV-229E HCoV-NL63, HCoV-OC43 – 5,6%. Among speciments from pre-school and elementary school students, RV/EV - 14.4% / 5.6% respectively, adenovirus -12.2% / 3.3% respectively, sesonal coronaviruses 6.7% / 8.1% and human metapneumovirus 4.4% / 3.7% were detected. Among staff speciments, RV/EV - 4.8%, sesonal coronaviruses 3.8% and SARS-CoV-2 – 3.3% were detected. Influenza and respiratory syncytial virus (RSV) were infrequently detected. (11) The survey highlited the gap in knowledle related to prevalence and symptoms of respiratory viruses among children and in schools, not limited to SARS-CoV-2. Despite the small number of participants in the extract, the high percentage of seasonal corona viruses raises the question of whether some of the SARS-CoV-2 tests conducted during the pandemic were not false positive due to this sesonal circulation.

The studies of wild and domestic animals can be invaluable to us in understanding the mechanism of action of human pathogens and in treatment. I will briefly touch on some of them. Five coronaviruses representing three of the four genera have been identified in pigs. PEDV - porcine epidemic diarrhea virus, TGEV - transmissible gastroenteritis virus and naturally mutated porcine respiratory virus - PRCoV belong to the genus Alphacoronavirus. PEDV replicates almost exclusively in the epithelial cells of the small intestine, causing villous atrophy, malabsorption and severe diarrhea. Cellular entry of this enveloped virus is mediated by the spike (S) glycoprotein, trimers of which mediate attachment of the virus to the target cell and subsequent fusion with the membrane. The S protein has a complex structure and is thought to bind to carbohydrate (sialic acid) and protein (aminopeptidase N) molecules on the cell surface. TGEV also mainly infects the epithelial cells of the small intestine and causes enteritis and fatal diarrhea in piglets. It is clinically indistinguishable from PEDV. Unlike the previous ones, PRCoV infects mostly airway epithelial cells and alveolar macrophages, causing mild or often subacute respiratory disease. Porcine hemagglutinating encephalomyelitis virus (PHEV) belongs to the genus Betacoronavirus. It attacks respiratory and nervous tissues and causes vomiting and neurological disorders in seronegative piglets. The recently identified porcine diarrhea coronavirus PDCoV is of the genus Deltacoronavirus and has an enteric tropism causing mild to moderate disease in young piglets. (12) Another coronavirus representative is the murine hepatitis virus (MHV), mainly attacking the brain and liver. Different disease patterns associated with different MHV strains have been observed. Infectious bronchitis virus (IBV) is a common avian pathogen that replicates in the respiratory tract but also in the epithelial cells of the kidney, oviduct and intestine.

Feline coronaviruses (FCoV) belong to the genus alphacoronaviruses. Feline enteritis virus (FECoV) frequently infects cats. It causes asymptomatic to mild infections of the intestinal tract and can become permanently established in the host (chronic viral infection). Feline infectious peritonitis virus (FIPV) is an example of a coronavirus that allows the targeting of immune cells (monocytes and macrophages) to achieve systemic spread.(13) A similar pattern of immune response was observed in a study conducted on Yersinia infected mice.(14) The ability of a pathogen to replicate efficiently or not in monocytes and macrophages likely depends on the genetic variant carried by the individual. Depending on that, the immune locus of the individual for which allele he is a carrier (protective or "harmful"), probably depends on the variety of antigens that are presented by major histocompatibility complex (MHC) class I molecules of CD8+ T cells, which in turn has an important role in defense against infection. (15) This switch in cell tropism from the intestinal epithelium to the motile cells (monocytes/macrophages) has been suggested to be a turning point in the development of the pathogenesis of FIP, and possibly in other diseases as well. FIPV causes an invariably fatal immune-mediated disease called feline infectious peritonitis (FIP). Infection in non-resolving cell types was achieved by exogenous expression of DC-SIGN, demonstrating that both FIPV type 1 and type 2 use DC-SIGN as a co-receptor. (16, 17) In chronic viral carriage, mutations can lead to a change in the virulence of FIPV. In our follow-up patients during the pandemic, we have observed a similar course of SARS-CoV-2 as in the models discussed above. And at the same time, the question remains open, why both in humans and in animals some individuals do not get sick or get sick mildly, while in others the course is more severe or ends fatally.

Because of the paucity of human research on the impact of pathogens on the type of immune response, i will look into on the study by Jennifer Klunk et al. in "Evolution of immune genes is associated with the black death". They consider, the impact of Yersinia pestis during the second plague pandemic played an important role in the dynamic, that shaped the human immune system. It is the deadliest pandemic in recorded history, killing 30-50% of the Afro-Eurasian population. Before exposure to plague, European survivors of the Black Death likely represented an immunologically naïve population with little or no adaptation to Yersinia pestis. This study may allow

us to shed light on how such pandemics, in this case the coronavirus, have and will contribute to disease susceptibility.

Yersinia pestis is a gram negative bacterium. In the study mentioned above, the authors examined DNA extracts from two European populations before, during and after the second plague pandemic. Their goal is to identify genetic variations in immune-related genes. Immune target genes have been selected based on their role in immune-related processes and include innate immune receptors, immune transcription factors, cytokines, chemokines, and other effector molecules. To detect alleles conferring protection or increased susceptibility to Yersinia pestis, the authors searched target regions for variants showing unexpectedly large changes in allele frequency in samples before and after the plague pandemic. Their impact on gene expression levels in immune cell types that are involved in the host's response to Yersinia pestis infection is monitored. In particular, macrophages are recruited to sites of infection where they interact with bacteria. They phagocytose Yersinia pestis, but some of the pathogens survive and spreading in the lymph nodes, replicate uncontrollably. For the purpose of the study, the authors incubated monocyte-derived macrophages. In the study of changes in the gene expression of macrophages, the data from their cross-infection with live Listeria monocytogenes (gram positive bacteria) and Salmonella typhimurium (gram negative bacteria) were tracked, as well as monocytes activated to Toll-like receptor pathways (TLR, TLR1/ 2, TLR4 and TLR7/8). In vivo, TLR4 detects Yersinia pestis by recognizing lipopolysaccharide (LPS) on the bacterial membrane. Y. pestis attempts to circumvent its detection by deacylating the surface LPS. The authors identified a protective allele (C) conferring protection against Y. pestis by increasing sensitivity to LPS and promoting an effective immune response in contrast to the putatively deleterious T allele. They experimentally demonstrated that carriers of the protective C allele locus presented a greater variety of antigens via major histocompatibility complex molecules to CD8+ T cells, stimulating a protective immune response against Y. pestis. All mice depleted of CD8+ T cells died within one week of challenge with milder forms of Yersinia. (14) In addition to its role in antigen presentation and activation of CD8+ T cells, the locus is involved in viral clearance and cytokine responses. Specifically, levels of interleukin (IL)-1β, which stimulates granulocyte colony stimulation, are significantly reduced in the presence of the protective C alleles, while levels of CCL3 (involved in neutrophil recruitment during infection) are increased. Individuals possessing the locus with more copies of the selectively preferred protective allele are better able to limit the intracellular replication of Yersinia pestis. Macrophages of individuals possessing the protective allele engage in a unique cytokine response to the pathogen and are capable of limiting bacterial replication in vitro. Individuals with more copies of the selectively advantageous haplotype also showed a weaker cytokine response (the levels of IL-1β responsible for pyroptotic cell death were threefold lower) and the authors observed a better ability to limit bacterial growth. Unfortunately, the authors come across a confirmation of the principle – always when you win something, you lose something. Consistent with their hypothesis, the selectively favorable variant is also a risk factor for Crohn's disease and other candidate loci are associated with increased risk of rheumatoid arthritis and systemic lupus erythematosus. (18, 19, 20, 21) To date, the evidence for balanced selection, i.e. the relationship between autoimmune risk alleles and adaptation to past infectious diseases remains tenuous because the agents driving selection remain as yet hidden. (15)

Viruses cause different pathological manifestations, which we observed with the different variants of the virus in our patients. They are directly dependent on the size of the viral inoculum, the presence of co-morbidities and possibly the patient's genome. During the pandemic, algorithms and protocols were developed to treat patients. One thing worried me all time - given that even with clothing and shoes the percentage of "standard" individuals is below 80, how will these algorithms and protocols be adequate for 100% of patients. Infectious diseases exert one of the strongest types of selective pressure on human evolution, especially on medicine. (22, 23) To this we will owe progress in the coming decades. Studying targeted regions of the genome to discover alleles that would protect us from or confer increased susceptibility upon exposure to new and/or recurrent pathogens will be of utmost importance. Using DNA extracts before, during and after the covid pandemic will help to differentiate mutagenic haplotypes. Localization of target immune gene loci will likely help unravel immune-related gene expression processes in immune cell types, innate immune receptors, key immune transcription factors, cytokines, chemokines, and effector molecules. Sequencing the genes in the profiled immune cell types – B cells, CD4+ T cells, CD8+ T cells, natural killer (NK) cells and monocytes that change their gene expression upon stimulation by coronavirus (CoV) will shed light on the type of immune response. Based on this, these algorithms and protocols will be adequate in treatment, and until this happens, personalization in treatment should play a major role. Genetics will likely allow us to identify loci characterizing genetic variation in immune-related genes and shaping today's disease susceptibility. Adaptive immunity to associated viruses or microbes may reduce susceptibility or increase disease severity. Mutations in the SARS-S gene play a role, but a key role is probably played by the genetic variant carried by the individual for the transition of tropism from intestinal epithelium to macrophages. (24, 25)

The coronavirus infection is a receptor disease. The coronavirus is capable of attacking many tissues and organs. The viral life cycle consists of viral attachment, entry, and replication. Coronaviruses are able to exploit various cell surface molecules - proteins and carbohydrates - to gain access to enter target cells. Viral entry results from the interaction between the virion and the host cell. Enveloped viruses can enter directly through the cell surface after binding to the receptor or reach endosomes by endocytosis. Angiotensin-converting enzyme 2 (ACE2) is regarded as the receptor providing SARS-COV-2 viral entry and its expression has been found on type II pneumocytes and enterocytes - major viral target cells. (26, 27, 28) As an alternative receptor for SARS-CoV and HCoV-229E, the specific lectin intercellular adhesion molecule-3 binding non-integrin (L-SIGN), which is expressed on the endothelial cells of the liver and lung, was assumed. Some coronaviruses possess hemagglutinin esterase (HE) and use sialic acid binding activity. The ability of betacoronaviruses to bind carbohydrates has been mapped. A lineage betacoronaviruses (A-βCoVs) are

a group of clinical importance in humans and animals. At these, binding to O-acetylated Sias (O-Ac-Sias) is mediated by hemagglutinin esterase (HE), a homodimeric type I envelope glycoprotein. (29, 30, 31) After initial binding to the receptor, the virus must fuse its envelope with the host cell membrane to deliver his own nucleocapsid to the host cytosol. Spike glycoprotein (SARS-S) plays a dual role in entry: mediating receptor binding and membrane fusion. SARS-S is classified as a large type I transmembrane protein. Large changes of SARS-S occur during the fusion process. These changes can be initiated by receptor binding, but may need additional triggers such as pH acidification or proteolytic activation. This allows the entry of proteins and genomic information of SARS-COV-2 into the cytoplasm of host cells - the site of replication of SARS-COV-2. Unlike other coronaviruses, SARS-CoV-2 does not use aminopeptidase N (APN) and dipeptidyl peptidase 4 (DPP4) as a receptor (32). Like SARS-CoV, SARS-CoV-2 uses metallocarboxyl peptidase angiotensin receptor (ACE2) to enter human cells. (33, 34, 35) Proteases (Cathepsins L and G) of host cells play an important role in the activation of SARS-S and are responsible for the infectivity of SARS-COV-2. (36) In order to switch to an active state, viral glycoproteins - class I binding protein often depend on host cell proteases for cleavage. (37, 38) The peptidase activity of ACE2 is critical for the virion to gain access to the host cytosol. Binding of SARS-COV-2 to ACE2 is thought to trigger receptor-mediated endocytosis and transport of virions into host cell endosomes. ACE2 is highly expressed in capillary-rich organs such as the lung and kidney, but also in the gut and brain . It is not impossible that in certain patients ACE plays the role of an alternative receptor.

It is believed that agents that protect the mucosa from initial infection may prevent the spread of the virus between individuals. The use of dietary components and agents to block the intestinal and nasopharyngeal epithelial cell receptors used by SARS-COV-2 will allow a reduction of the viral load in the nasopharynx. Most of the secretions produced in the nasopharynx are swallowed and enter the gastrointestinal tract. The hypothesis is based on the possibility to protect patients against the COVID-19 infection by inhibiting the viral life cycle using the S surface protein layer of lactobacilli and local application of carrageenans in the nasopharynx.

The genus Lactobacillus is a common inhabitant of the gastrointestinal tract of humans and animals. The ability of Lactobacillus to adhere to epithelial surfaces is extremely important for maintaining persistent colonization in the mammalian gut as well as other tissues. The peptidoglycan layer of the Lactobacillus cell wall is covered by a variety of substances - lipoteichoic acids, neutral and acidic polysaccharides and surface proteins. Many species of the genus Lactobacillus possess a surface protein layer (SLAP), which is made up of arrays of single protein, non-covalently linked, forming the outermost envelope of the cell. The protein of the cell surface layer (S-layer) is composed of crystalline arrays of protein subunits. SLAPs have been identified as being involved in adhesion access. Virus-induced apoptosis is critical for SARS-CoV-2 pathogenesis and replication. Xiaoyan Zhang et al. investigated the ability of the S surface protein layer of Lactobacillus acidophilus to inhibit PEDV-induced apoptosis in vero cells as a possible protective mechanism in humans. (39) The antiviral efficacy of the S-layer was evaluated by analyzing the viral load as well as the activity of the apoptotic factors (caspase-3 and caspase-8), which are activated by extrinsic and intrinsic pathways and are responsible for the morphological features of apoptosis. (40) An increase in the levels of caspase-3 and caspase-8 is observed during PEDV infection, especially in the later stages. (41) PEDV, mediating cell apoptosis, induces the activation of caspase-3 and caspase-8. The virus can also induce caspase-independent apoptosis by activating mitochondrial apoptosis-inducing factor (42), possibly in long covid syndrome. When studying the inhibitory effect of the S surface protein layer, the different mechanism of inhibition in bacteria and viruses is striking. For example, Lactobacillus acidophilus S-layer has significant antagonistic activity against Salmonella enterica serovar Typhimirium (another zoonosis) on Caco-2 cells. (43, 44, 45) The antimicrobial mechanism of the S-layer of Lactobacillus acidophilus is manifested in competition for binding sites on the surface of host epithelial cells and direct interaction between it and the cell surface of Salmonella Typhimirium. (46) In contrast to bacteria, Lactobacillus acidophilus S surface layer antagonizes entry and replication, but not PEDV attachment in vero cells and only when pretreated with S surface layer. Antiviral activity of the S-layer protein is not based on competition with PEDV for host cell surface binding sites. The S-layer protein was previously shown to bind to the C-type lectin DC-specific intercellular adhesion molecule 3-engaging non-integrin (DC-SIGN, CD209). (47) DC-SIGN is a cell surface adhesive factor that facilitates the entry of viruses belonging to several different families into host cells. Lactobacillus-derived S-layer protein may play an important role in the antimicrobial and antiviral activity of probiotic strains. Probiotics are live microorganisms, usually contained in food, that when ingested in sufficient numbers play an important role in the control of the host's gut microbiota and in the modulation of the host's immune response. S-layers are thought to function as protective coatings, maintain cell shape and ion exchange, and participate in adhesion to biotic and abiotic surfaces. In the gastrointestinal tract (GIT), L. acidophilus regularly encounters many antigen-presenting cells, dendritic cells (DC). (48) These cells express DC-specific ICAM-3 capture protein (DC-SIGN), which is a cell surface receptor and which is mainly presented on DC. It recognizes the mannose and fructose glycans that are present on the surfaces of microbes and viruses. DC play a very important role in the innate and adaptive immune response.(49) It has been shown that DC-SIGN can potentiate the cellular entry of various viruses such as HIV type 1, hepatitis C, Ebola, Dengue, and SARS. (50) DC have also been shown to interact with L. acidophilus. This contact involves DC-SIGN and the S surface protein layer presented on the bacterial cell envelope and regulates the induction of a number of cytokines involved in cellular immune regulation. (51, 52) In practice, the Lactobacillus S-layer protein is used to inhibit JUNV (Argentine Hemorrhagic Fever Virus) infection by directly

interacting with the DC-SIGN receptor. (53) Cells expressing DC-SIGN can be infected by JUNV, but almost complete inhibition of JUNV infection was found when they were treated with purified S-layer protein from L. acidophilus ATCC 4365 before infection. Inhibition was observed only when S-layer protein was used in the early stages of viral infection.

Another easy-to-use option for the prevention of coronavirus infection are sprays containing sulfated polysaccharides - carrageenans, silver ions and eucalyptus oil, helping to reduce the attachment and entry of the virus into the target cells of the nasopharynx. The proposed preparations do not have cytotoxic effects. They reduce the viral load in the nasopharynx, protect the mucosa from initial infection, reduce the risk of infection and help reduce the spread of the virus between individuals. Iota-carrageenan has been shown to interfere with the attachment and entry of papillomavirus or rhinovirus due to its sulfated polysaccharide characteristics that mimic cellular heparan sulfates or virus particle aggregates. (54, 55) Inhibition of viral entry by i-carrageenan has also been demonstrated for influenza A and human coronavirus OC43. Thus, i- and k-carrageenans, which differ only in the number and location of sulfate residues on the hexose backbone, potentially inhibit SARS-CoV-2 through a similar mechanism. This is supported by a recent study that confirmed the inhibition and suggested aggregation of SARS-CoV-2 by i-carrageenan. (56, 57, 58) Sprays containing eucalyptus oil fight respiratory infections by killing viruses, bacteria and fungi. They also speed up the movement of the cilia of the covering epithelium and help to clean our airways faster.

Discussion:

Many drugs alone or in combination have been developed for the treatment of COVID-19, but none allow the treatment of all variants of COVID-19. The optimal vaccine against SARS-CoV-2 implies a potent immune response offering long-lasting protection against the different viral variants. Infectious diseases exert one of the strongest types of selective pressure on human evolution, especially on medicine. Genetics in the coming decades will likely allow us to identify loci characterizing the genetic variation of immune-related genes and to understand the dynamics of human immune system formation. The beginning has probably already been made. First, many of cell and gene therapies utilize viral vectors genetically modify or replace a faulty genes. Viral vectors designed with specific payload gene need to be transduced and expressed in the target primary cells such as T-cells and hemapoietic stem cells. Before being exposed to COVID-19, most of humanity was probably an immunologically naïve population with little or no adaptation to it. Discovering what combination of factors prevented COVID-19 in the majority of the human population from achieving modification or replacement of immune-related genes will likely help us improve the effectiveness of the above-mentioned therapies in the future. Second, research by Dr. Wei Luo (Indiana University School of Medicine) on the mechanisms regulating B-cell signaling in the germinal center response may provide an answer to the reasons limiting long-term humoral memory. His innovative solution is to include a Toll-like receptor (TLR7) activating polymeric nanoparticle adjuvant to improve targeting to lymph nodes and sustain immune cell activation. This adjuvant is likely to support immune activation, achieve enhancement of the germinal center response, and thus elicit a broad antibody response capable of targeting multiple viral variants.

Due to the early stage of such research, protection and prevention are paramount. The use of foods containing Lactobacillus is indicated because the S surface layer of Lactobacillus exhibits antagonism towards viral entry and replication. This is due to its binding to DC-SIGN, which is an adhesive factor on the cell surface facilitating the entry of viruses. The antiviral effect of i- and k-carrageenans is most likely based on reduced attachment and entry of the virus into target cells. Their actions are applicable to the majority of the human population. In the presence of genetically determined alterations of innate and acquired immunity or even primary immunodeficiency disease, the susceptibility of this part of the human population to COVID-19 is likely to be different. In persistently infected hosts (chronic viral infection) with the presence of genetically determined changes in innate and acquired immunity, mutations can lead to the transformation of the virus into a virulent strain or cause variations in its virulence. I guess, that Lactobacillus and carrageenans may have a protective effect against SARS-CoV-2 infection alone or in combination in healthy subjects. Reducing the viral load in the nasopharynx will drastically reduce the risk of transmission of COVID-19.

Mutations in the SARS-S gene play a role, but genetic variation is likely to play a key role. Adaptive immunity to associated viruses or microbes may reduce the susceptibility or increase the severity of the disease carried by the individual for the transition of tropism from the intestinal epithelium to macrophages. Little is known about the presence of preexisting T cells in humans with the potential to recognize the SARS-CoV-2 virus. Le Bert et al. have examined T-cell responses to structural (nucleocapsid protein, NP) and non-structural (NSP-7 and NSP-13) ORF1 regions of SARS-CoV-2 in convalescent COVID 19 patients. The study observed the presence of CD4+ and CD8+ T cells recognizing multiple NP regions as well as SARS-CoV-2-specific T cells in individuals without a history of SARS and SARS-CoV-2 or contact with SARS and SARS-CoV-2 in the control group. Le Bert et al. concluded that infection with betacoronaviruses induces multispecific and long-lasting T-cell immunity to structural NP. They observed that epitope characterization of NSP 7 specific T cells of human coronaviruses circulating among animal betacoronaviruses showed recognition of protein fragments with low homology to the “common cold”(59).

Can in practice block all the receptors allowing the entry of the virus? Probably not, especially when the individual's genome has left receptors “unlocked”. The human genome includes 20000 to 25000 genes. But do they alone determine the type of immune response or is it determined by the interaction with the 8 million genes of bacteria, viruses, protozoa and fungi on or in us. We will probably get an answer to this question in the coming decades. By learning from our mistakes and successes, we will be able to more successfully deal with the challenges posed by zoonoses in the future.

Conflict of interests

The author declares that there is no conflict of interest.

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None.

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