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THE MOLECULAR MECHANISM BY WHICH VITAMIN D PROTECTS AGAINST COVID-19

Ljubiša Mihajlović (1), Milica Mihajlović (2), Vladan Mihajlović (3)

(1) ACADEMY OF TECHNICAL AND EDUCATIONAL STUDIES OF NIS, CEO GENEINFO NIS; (2) CENTER FOR FORENSIC AND APPLIED MOLECULAR GENETICS, FACULTY OF BIOLOGY, UNIVERSITY OF BELGRADE; (3) FACULTY OF MEDICINE, UNIVERSITY OF NIS

Abstrakt: The SARS-CoV2 virus, which causes COVID-19, exerts its pathophysiological effect by intensively binding to the angiotensin-converting enzyme 2 receptor (ACE2) on the host cells. By blocking the ACE2 receptor, the physiological functions of the cell are inhibited, which are important for the normal function of various organs, and especially for the protection of the lungs. Therefore, the number of functionally active ACE2 receptors is extremely important for the body's resistance to COVID19. More receptors equal greater resistance of the host. An increased number of ACE2 receptors gives the body more time to mobilize an adequate immune response. Experience to date from the immediate fight against COVID19 has confirmed this rule: (A) women are generally more resistant (the ACE2 receptor gene is on the X chromosome, and women have two X chromosomes), (B) younger people are more resistant to the virus (ACE2 expression decreases with age), (C) patients with chronic diseases are more sensitive (have a reduced number of ACE2). Therefore, an increase in the number of ACE2 receptors is extremely important for the body's protective power in the fight against the SARS-CoV2 virus. Vitamin D increases the expression of the ACE2 gene, which increases the number of ACE2 receptors, which can be of significant aid in the fight against COVID-19.
Keywords: COVID-19, ACE2, Vitamin D

Molecular mechanism of the pathophysiological action of the SARS-CoV2 virus

Man has long lived alongside corona viruses and there has never been a pandemic of this magnitude. However, the new corona called SARS-CoV2 which first appeared in Wuhan (China), rapidly spread across the planet and evolved into a serious pandemic.

The question is why did SARS-CoV2, unlike other previous coronaviruses, become so pathogenic? What caused this virus to become so deadly and infectious?

There is already an answer to this question. The key point is that the new corona virus SARS-CoV2 has acquired a new mutation in its S protein that allows it to bind almost 1000 times more intensively to the ACE2 receptor [1]. The new mutation is in a part of the S protein called the furin cleavage site, which results in easier opening of the S protein and more intense binding to the ACE2 receptor, which is the gateway for the virus to infect cells.

So, the pathological effect of SARS-CoV2 virus is caused by the intensive binding to the ACE2 receptor, also by inactivation of the ACE2 receptor. That is, by knocking the ACE2 receptor out of function2. This coincides perfectly with patients who have ACE2 receptor dysfunction. Consequences of ACE2 receptor dysfunction are: Severe Acute Respiratory Syndrome, Heart Disease, Hypertension, Essential, Kidney Disease, Myocardial Infarction, Intracranial Aneurysm, Malaria, Vascular Disease, and Cardiovascular System Disease… [2]

The number of ACE2 receptors is crucial when it comes to the host's response to the SARS-CoV2 virus

The body's ability to fight the virus increases with an increase in the number of functioning ACE2 receptors. Taking this into consideration, we can conclude that people who have fewer ACE2 receptors are more likely to develop serious symptoms. The current

experience from the fight with COVID19 only confirms this rule.

(A) Women are more resilient due to the fact that they have more ACE2 receptors [3]. The gene that codes the ACE2 receptors is located on the X chromosome. Some experts will argue that one X chromosome is inactivated in women (Barr body). However, 15-25% of the genes located on the inactivated X chromosome escape the process of inactivation and remain active [4], also during embryonal development both X chromosomes are active.

(B) Children and the young are usually asymptomatic or have mild symptoms, while a more serious cases of COVID19 are usually present in the elderly.

This is due to the fact that the production of ACE2 receptors drops with age.

Scientists who have analyzed the ACE2 receptor in 30 different tissues (over 1000 patients) have concluded that the expression of the ACE2 receptor is significantly reduced in those over the age of 60 [3]. This is in line with the results from the field, where younger patients usually have mild symptoms, while on the other hand the elderly have far worse symptoms and more often than not succumb to the disease.

(C) People with chronic illnesses, especially type 2 diabetes are far more sensitive to the SARS-CoV2 virus and have worse symptoms.

The same group of scientists that have found a decrease in the number of ACE2 receptors with age have also found that patient with type 2 diabetes have a significant reduction in the number of ACE2 receptors [3]. Examples from the field show that patients with type 2 diabetes often develop worse symptoms.

How Vitamin D works as a preventative and protective measure?

Vitamin D works as a preventative measure in the fight against COVID 19 by increasing the expression of the ACE2 receptor. Vitamin D is a liposoluble vitamin (with a steroid structure) that has to bind to its VDR (Vitamin D Receptor) receptor within the cell nucleus in order for it to have an effect. The VDR belongs to a superfamily of ligand-inducible transcription factors. Vitamin D regulates the expression of a large number of genes including the gene that codes the ACE 2 receptor. Vitamin D increases the expression of the ACE2 gene [5,6]. Due to this increased expression the amount of ACE2 receptors also increases.

Conclusion:

From the information mentioned above we come to the conclusion that Vitamin D has a protective effect in the case of infection with the novel coronavirus. This protective effect is especially apparent in the elderly and in people with chronic disease.

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