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Press release
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Scientists in Graz conduct research on the COVID-19 pandemic Not vitamin D, but underestimated vitamin K as a central player?

Graz, 17 November 2022: Since early 2020 we have been under the spell of the COVID-19 pandemic. Measures have been dropped or weakened and case numbers are on the rise again. Scientists have been trying to work out why some people develop life-threatening SARS-CoV-2 infections, some suffer from long COVID and others have hardly any symptoms. Not only genetic constellations but also the immune system, lifestyle and nutritional habits have been discussed as potential causes. Med Uni Graz scientists are on the trail of indicator biomarkers that can help answer these questions. They have now published their most recent findings on the role of vitamin K in COVID-19 in the renowned journal "Antioxidants."

COVID-19: Disease progression as the great unknown

In Austria alone, over 20,000 people have died of or with COVID-19. After a SARS-CoV-2 infection starts harmlessly, some people develop life-threatening pneumonia five to fourteen days later. This severe disease progression can affect anyone, primarily people with pre-existing conditions but also healthy young athletes. Harald Mangge of the Med Uni Graz Clinical Institute of Medical and Chemical Laboratory Diagnostics conducts research on the relationship between metabolism and the immune system in order to understand how SARS-CoV-2 takes a particularly severe course in certain people. He and his colleagues want to find biomarkers that are linked to a severe course of the disease and at best enable measures that prevent such courses. A current publication in the renowned journal "Antioxidants" presents new findings on vitamin K—a vitamin that has rarely been the subject of COVID-19 research to date.

Vitamin K: the forgotten and underestimated vitamin

Like vitamins A, D and E, vitamin K is a fat-soluble vitamin. It occurs naturally as vitamin K1 (phylloquinone) and vitamin K2 (menaquinone). While phylloquinone is predominantly found in green plants, menaquinone is produced by bacteria present in the human gut such as *E. coli*. K2 is the more active form of the vitamin.

Vitamin K1 or K2: Which form is better?

Most probably, it is vitamin K2 because it is involved in bones, protection of the blood vessels and connective tissue and the immune system. Vitamin K1 is mainly active in the liver and breaks down quickly in the blood. Vitamin K2, however, reaches the other organs via the blood

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and remains active there for a long time. There are three different subtypes of vitamin K2: MK-4, MK-7 and MK-9. The most valuable is MK-7, which is best absorbed by the body and remains in the blood the longest, performing its protective function.

Why are scientists in Graz focusing on vitamin K?

In patient blood samples from the first and second COVID-19 waves, the Graz researchers "hunted" for potential indicators that exhibit marked changes at an early stage of the disease. The focus was on known laboratory parameters, for example inflammatory markers, as well as metabolic products and initially vitamin D, yet no effect on COVID-19 disease progression was found.

Not least because impaired coagulation has been associated with severe COVID-19 disease progression, the scientists then turned their attention to vitamin K. Another factor was that Graz lab specialists led by Andreas Meinitzer had developed a special method for reliable measurement of all vitamin K subtypes, in which Vitamin K1 as well as the K2 "building blocks" menaquinone-4 (MK-4) and menaquinone-7 (MK-7) play an important role.

Vitamin K2 subtype menaquinone-7 (MK-7) at the center of COVID-19 disease

The main observation was a dramatic and specific reduction in menaquinone-7 in patients with severe COVID-19 pneumonia as compared to those with non-COVID-19 pneumonia and healthy controls.

What does this mean? With reference to the complex functions of vitamin K2, this is an interesting question that fascinates the researchers in Graz. Vitamin K2 is made up of two homologues, menaquinone-4 and menaquinone-7. "While the effect of vitamin K1 is limited to the liver, where it is central to the formation of coagulation factors, vitamin K2 is involved in bone metabolism, the health of the blood vessels and cardiovascular system, chronic kidney disease, disease of the nervous system, cancer and immune system defenses. Furthermore, it is not known how important the vitamin K2 components MK-4 and MK-7 are in these processes. The fact is that a constant dietary supply of MK-7 is required and thus most likely the determining factor," says Harald Mangge on the role of vitamin K.

Why is the menaquinone-7 (MK-7) level in the blood so low in COVID-19 pneumonia?

In connection with COVID-19, MK-7 plays an important role in coagulation factors and the protection of elastic fibers, which are important for healthy tissue function in the lungs and other parts of the body. COVID-19 pneumonia goes hand in hand with an inflammatory storm and consumes a great amount of MK-7. The consequences are a coagulation system that has gone awry and stressed fibrous proteins.

"The massive release of inflammatory factors in the cytokine storm (a derailment of the immune system) in the lungs also releases enzymes that are the final straw for the elastic fibers. The destruction of lung tissue is hardly reversible. In COVID-19 pneumonia, the combined effect of MK-7 deficiency, a tendency for thrombosis, vascular damage and hyperinflammation is so strong that it delivers a knockout punch to the lung tissue," says Harald Mangge.

"To sum up, MK-7 deficiency seems to be the element connecting COVID-19 pneumonia, tissue destruction and thrombotic vascular disease. In any case, providing the body with a good supply of vitamin K2 is positive and should motivate people to increase consumption of fermented foods containing MK-7 such as fermented soybeans (natto)," concludes Harald Mangge, reporting the observations of his team.

Profile: Harald Mangge

Harald Mangge is a specialist in laboratory medicine at Med Uni Graz who conducts research on the immune system, lifestyle, inflammation and metabolism. His work focuses on biomarkers of serious systemic disease, overweight and obesity. In a large number of scientific papers, he has demonstrated the significance of disturbed communication between chemical messengers of the fatty tissue and those of the immune system in adiposity-related complications.

Further information and contact

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To the publication:

Dramatic Decrease of Vitamin K2 Subtype Menaquinone-7 in COVID-19 Patients

by Harald Mangge, Florian Prüller, Christine Dawczynski, Pero Curcic, Zdenka Sloup, Magdalena Holter, Markus Herrmann and Andreas Meinitzer. *Antioxidants* 2022.

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