

Vitamin D improves immune response to tuberculosis, study finds

В Cell lysate Cell lysate Cathelicidin mRNA (fold change) 10.000- VDR^{wt} 3 ● VDR^{wT} Cathelicidin protein (fold change) VDRR80W VDRR80W 1.000 2. 100 10 1 0.1 Cathelicidin GAPDH 0.01 1,25(OH)₂D₃: 1,25(OH)₂D₃ Mtb : Mtb : С D n.s. ■VDR^{R80W} • VDR^{WT} 15 15 5 5 Mean of differences Mean of differences 10 10 CFU × 105 CFU x 105 5 5 0 0 Mtb : Mtb : + 1,25(OH)₂D₃: 1,25(OH),D3:

Reduced vitamin D-induced cathelicidin expression and M. tuberculosis elimination in macrophages from the HVDRR patient (A) mRNA and (B) protein levels of cathelicidin in macrophages from control subjects (VDR^{WT}) and the HVDRR patient (VDR^{R80W}). The macrophages were treated with $1,25(OH)_2D_3$ and M. tuberculosis as indicated below the graphs. The cathelicidin levels were normalized to the cathelicidin levels in (A) untreated and (B)

January 9 2023



1,25(OH)₂D₃-treated control cells. (C, D) Estimation plots of the CFU levels in macrophages infected with M. tuberculosis in the absence and presence of vitamin D from control subjects (VDR^{WT}) and the HVDRR patient (VDR^{R80W}). (A–D) Data from three independent experiments each with macrophages from three control subjects and the HVDRR patient. ns: not significant, *p Frontiers in Immunology (2022). DOI: 10.3389/fimmu.2022.1038960

A rare patient has made it possible for researchers to prove that vitamin D—the "sun vitamin"—helps the body fight tuberculosis.

Most people probably associate <u>tuberculosis</u> with a leaky loft in 19thcentury Paris. But as a matter of fact, tuberculosis is not ancient history.

It is estimated that 2 billion people globally suffer from the disease today. And each year, more than 1.5 million people die from it—mainly on the <u>southern hemisphere</u> in countries like South Africa, Namibia and Mozambique.

But vitamin D can help the immune system fight tuberculosis, a new study recently published in *Frontiers in Immunology* concludes.

"For the first time, we have shown that vitamin D improves the immune system's ability to fight the <u>tuberculosis bacterium</u>, Mycobacterium tuberculosis," says Associate Professor Martin Kongsbak-Wismann from the LEO Foundation Skin Immunology Research Center at the University of Copenhagen.

A special patient made it possible for the researchers to prove the connection. She was born with a mutation that makes her body incapable of responding to vitamin D. The mutation is seen in very few people, and only around 200 occurrences of the mutation have been reported



globally.

"We have compared <u>cells</u> from the female patient with cells from patients who are able to absorb vitamin D, and this revealed a difference between the two. It is easier for the <u>immune cells</u> of patients capable of absorbing vitamin D to fight tuberculosis. In the female patient, vitamin D does not do anything; her body simply does not respond to it," says Martin Kongsbak-Wismann.

Today, tuberculosis is treated with antibiotics, but in the past, many tuberculosis patients were admitted to sanatoriums and made to lie out in the sun. This caused their vitamin D levels to rise. Therefore, researchers have long suspected that vitamin D can help fight tuberculosis, but they did not have direct proof, until now.

Beneficial to give vitamin D to people exposed to infection

Martin Kongsbak-Wismann hopes the study can generate attention to the fact that vitamin D treatment is a useful tool for preventing and treating tuberculosis.

"It might be a good idea to give vitamin D to people highly exposed to infection with tuberculosis, e.g., the populations of specific African countries. Even though we still do not know how different levels of vitamin D affect the risk of infection and the severity of the disease, at least it would not cause any <u>negative side effects</u>," he says.

However, you can still develop tuberculosis even though you take vitamin D supplements.

"You need to look at it this way: If you are exposed to infection, your



immune system will try to fight the Mtb. And vitamin D will strengthen parts of the immune system. But if you have inhaled a lot of Mtb particles or other parts of your immune system do not function properly, you may still develop tuberculosis, even though your vitamin D level is normal. So it is not a 'wonder drug,' but it is bound to help," Martin Kongsbak-Wismann concludes.

How does vitamin D strengthen the immune system?

More specifically, the study showed that the female patient produced very few cathelicidins, which is a natural toxin found in the immune cells of the lungs needed to fight tuberculosis. In most people infected by tuberculosis, tuberculosis bacteria attack the immune cells of the lungs.

The immune cells fight the bacteria by eating them. But the tuberculosis bacterium has developed various evasive mechanisms that reduce the immune cells' ability to digest and thus to kill the Mtb.

"You could say that the tuberculosis bacterium has developed a way to lull the immune cells to sleep. This enables the disease the hide inside the immune cells, making it invisible to other parts of the immune system," Martin Kongsbak-Wismann explains.

This is where vitamin D enters the picture. Because vitamin D is able to counteract the soporific effect of the tuberculosis bacteria by making the immune cells produce more of the cathelicidin toxin.

"Cathelicidin is like a microscopic needle that is able to pierce the tuberculosis bacteria. And when it does, it weakens the bacteria's soporific effect on the immune cells. This restores the immune cells' ability to kill tuberculosis bacteria," says Martin Kongsbak-Wismann.

"We were amazed by the effect of vitamin D. In immune cells from



healthy control subjects, vitamin D improved the cells' ability to fight Mtb, whereas in the female patient's immune cells we saw no response to vitamin D. This shows that vitamin D is key to the <u>immune system</u>'s ability to fight Mtb and prevent tuberculosis."

More information: Fatima A. H. Al-Jaberi et al, Reduced vitamin Dinduced cathelicidin production and killing of Mycobacterium tuberculosis in macrophages from a patient with a non-functional vitamin D receptor: A case report, *Frontiers in Immunology* (2022). DOI: 10.3389/fimmu.2022.1038960

Provided by University of Copenhagen

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