Researchers Discover How Vitamin D Inhibits Inflammation

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DENVER — Researchers at National Jewish Health have discovered specific molecular and signaling events by which vitamin D inhibits inflammation. In their experiments, they showed that low levels of Vitamin D, comparable to levels found in millions of people, failed to inhibit the inflammatory cascade, while levels considered adequate did inhibit inflammatory signaling. They reported their results in the March 1, 2011, issue of The Journal of Immunology.

“This study goes beyond previous associations of vitamin D with various health outcomes. It outlines a clear chain of cellular events, from the binding of DNA, through a specific signaling pathway, to the reduction of proteins known to trigger inflammation,” said lead author Elena Goleva, assistant professor of pediatrics at National Jewish Health. “Patients with chronic inflammatory diseases, such as asthma, arthritis and prostate cancer, who are vitamin D deficient, may benefit from vitamin D supplementation to get their serum vitamin D levels above 30 nanograms/milliliter.”

Current national guidelines suggest that people should maintain a minimum blood serum level of 20 ng/ml, although there is much scientific debate about optimum levels. Vitamin D has long been known to contribute to bone health by promoting the absorption of calcium. In recent years, much attention has been paid to its possible immune and inflammatory benefits. Low vitamin D levels have been associated with several diseases including asthma, cancer, diabetes, and arthritis.

In the current study researchers examined the specific mechanisms by which vitamin D might act on immune and inflammatory pathways. They incubated human white blood cells with varying levels of vitamin D, then exposed them to lipopolysaccharide (LPS), a molecule associated with bacterial cell walls that is known to promote intense inflammatory responses.

Cells incubated with no vitamin D and in solution containing 15 ng/ml of vitamin D produced high levels of cytokines IL-6 and TNF-alpha, major actors in the inflammatory response. Cells incubated in 30 ng/ml vitamin D and above showed significantly reduced response to the LPS. The highest levels of inflammatory inhibition occurred at 50 ng/ml.

Through a complex series of experiments, the researchers identified a new location where the vitamin-D receptor appears to bind directly to DNA and activate a gene known as MKP-1. MKP-1 interferes with the inflammatory cascade triggered by LPS, which includes a molecule known as p38, and results in higher levels of IL-6 and TNF-alpha.

“This newly identified DNA-binding site for the vitamin-D receptor, and the specific pathways inhibited by higher levels of vitamin D provide a plausible mechanism for many of the benefits that have been associated with vitamin D,” said Dr. Goleva. ‘The fact that we showed a dose-dependent and varying response to levels commonly found in humans also adds weight to the argument for vitamin D’s role in immune and inflammatory conditions.”

National Jewish Health is the leading respiratory hospital in the nation. Founded 121 years ago as a nonprofit hospital, National Jewish Health today is the only facility in the world dedicated exclusively to groundbreaking medical research and treatment of patients with respiratory, cardiac, immune and related disorders. Patients and families come to National Jewish Health from around the world to receive cutting-edge, comprehensive, coordinated care. To learn more, visit the media resources page.

Media Contacts

Our team is available to arrange interviews, discuss events and story ideas.
William Allstetter
303.398.1002
allstetterw@njhealth.org

Adam Dormuth
303.398.1082
dormutha@njhealth.org