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Lung airway cells activate vitamin D and increase immune response

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Vitamin D is essential to good health but needs to be activated to function properly in the human body. Until recently, this activation was thought to happen primarily in the kidneys, but a new University of Iowa study finds that the activation step can also occur in lung airway cells.

The study also links the vitamin D locally produced in the lung airway cells to activation of two genes that help fight infection. The study results appear in the Nov. 15 issue of the *Journal of Immunology*, now online.

In addition to contributing to calcium absorption and bone health, vitamin D is increasingly recognized for its beneficial effects on the immune system. Vitamin D deficiency has been recently linked to increased risk of some infections, autoimmune diseases such as multiple sclerosis and type 1 diabetes, and some cancers.

"The more scientists have been studying vitamin D, the more we learn about new roles it plays in the human body," said the study's lead author Sif Hansdottir, M.D., fellow in internal medicine in the University of Iowa Carver College of Medicine. "The active form of vitamin D is known to affect the expression of more than 200 genes, so we were interested both in the possible lung-specific production of active vitamin D and in vitamin D-dependent production of proteins that fight infections."

The first step in vitamin D activation takes place in the liver, where an

enzyme called 25-hydroxylase converts vitamin D into a "storage" form. The next step takes place typically in the kidneys, but in recent years, tissue and organs such as skin, intestines, breast and prostate have been found also to express the enzyme that completes vitamin D conversion.

The University of Iowa team, based in the laboratory of Gary Hunninghake, M.D., professor of internal medicine and the study's senior author, used cells from deceased human donors to demonstrate that the presence of the enzyme 1 alpha-hydroxylase in the airway cells helps convert the storage form of vitamin D into its active form.

"When we put the storage form of vitamin D on the lung airway cells, we saw them convert it to the active form," Hansdottir said. "The next step was to investigate whether this active form could affect the expression of genes."

The team then showed that vitamin D activated by airway cells affects two genes involved in immune defense. One gene expresses a protein called cathelicidin that can kill bacteria. The second gene, called CD14, produces a protein that helps cells recognize different kinds of pathogens that could be a threat.

"Vitamin D converted by the kidneys circulates in the bloodstream, but vitamin D converted by other organs appears to stay within those organs and protect them from infection," Hansdottir said. "We were able to see this happen in cells lining the trachea and main bronchi."

The team also found that when lung airway cells are infected by a virus, they express more of the enzyme that activates vitamin D. Hansdottir said the team is very interested in pursuing studies on the role of viral infections in vitamin D production and subsequent effects on lung infections.

"Vitamin D not only increases proteins involved in bacterial killing but also can dampen inflammation," Hansdottir said. "Controlling inflammation through vitamin D is good because too much inflammation can cause problems such as sepsis and seems to contribute to autoimmune disease."

Hansdottir noted that vitamin D insufficiencies and deficiencies (which are more severe) are fairly common, particularly for people living in northern latitudes. While vitamin D can be generated through sun exposure, such exposure is generally not recommended as a remedy because of skin cancer risks. Instead, supplements can be used.

The American Academy of Pediatrics recently recommended that the vitamin D dosage for children be increased to 400 IU (international units) per day. Optimal daily intake for adults is still being studied but may be as high as 800 to 1,000 IU.

Source: University of Iowa