

## Versatile vitamin A plays multiple roles in the immune system

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Although it has been known for some time that vitamin A deficiency is linked with an impaired ability to resist infections, exactly how vitamin A and its metabolites contribute to the immune response is not well understood. Somewhat paradoxically, research has indicated that vitamin A can also act as an immunosuppressive agent. Now, a study published by Cell Press in the March issue of the journal *Immunity* sheds light on how this critical vitamin integrates into both pro-inflammatory and antiinflammatory immune responses in the gastrointestinal tract.

The vitamin A metabolite retinoic acid (RA), along with one of its receptors RAR has been shown to have anti-inflammatory properties. Specifically, RA has been shown to induce production of regulatory T cells that help dampen the immune response to self and foreign antigen, including the bacteria that are normally present in the gastrointestinal tract. However, vitamin A insufficiency is associated with increased mortality to common gastrointestinal and lung infections and poor responses to vaccines, and there is evidence that in addition to its regulatory role, RA may help to stimulate the pro-inflammatory immune response to overcome infection. It is not clear how RA accomplishes these seemingly disparate roles.

"Gaining an understanding of the metabolites that control vitamin A dependent immunity and the relevant signaling pathways invoked is critical to resolving the paradox of why retinoids are immunosuppressive in some contexts, yet vital for host protective immunity," explains senior study author, Dr. Yasmine Belkaid from the National Institute of Allergy



and Infectious Diseases. In their study, Dr Jason Hall, primary author of the study, and colleagues demonstrated that immune responses to infection and vaccination were compromised upon loss of vitamin A, and that RA served to activate the T cells driving these responses. Based on their findings, the researchers propose that RA influences the immune response during the initial stages of activation and can amplify, in a context dependent manner, the capacity of the host t develop regulatory or inflammatory responses.

"The gastrointestinal tract must be able to tolerate constant exposure to food and the beneficial microbes that colonize this site, while maintaining the capacity to rapidly respond to encounters with pathogens," says Dr. Belkaid. "These conflicting pressures confront the immune system responsible for defending the gastrointestinal tract with a unique challenge. In our study, we identified RA/RAR? signaling pathway as a fitting system to accomplish these tasks, promoting generation of regulatory T cells and likely tolerance during normal conditions and adaptive T cell responses when faced with pathogen." Taken together, these findings reveal a fundamental role for Vitamin A in the development of both regulatory and inflammatory arms of immune responses and establish nutritional status as a broad regulator of the immune system.

## Provided by Cell Press

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