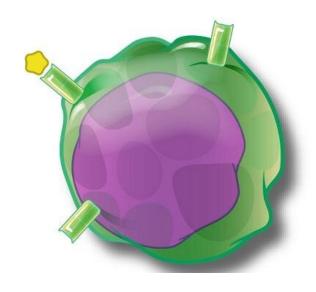


## Researchers investigate molecule, VISTA, which keeps immune system quiet against cancer

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An artist's depiction of a T cell. Credit: NIAID

Researchers led by Dartmouth's and Dartmouth-Hitchcock's Norris Cotton Cancer Center are studying a valuable target in regulating the immune response in cancer and autoimmunity. VISTA is a tempering molecule that hinders T cells in the immune system from activating against self-antigens such as cancer cells. Their new publication describes how VISTA controls T-cell responses.

While strong immune responses are needed to help protect the host from infections, the immune system also must curb the magnitude of those responses to limit the damage it can potentially cause. Over the past 8-10 years, a team of researchers at Dartmouth's and Dartmouth Hitchcock's Norris Cotton Cancer Center, led by Randolph Noelle, Ph.D., have identified some of the molecules that the immune system uses to temper immunity. While these molecules are

usually good, they also limit the magnitude of the <a href="immune response">immune response</a> to cancer. The team has learned that turning off these "brakes" on immunity allows therapeutic response to cancer. VISTA (V-domain Ig suppressor of T-cell activation) is one of these tempering molecules that negatively regulates immunity.

The team describes how VISTA controls immune T-cell responses in their study, "VISTA, a checkpoint regulator of naïve T-cell quiescence and tolerance in the periphery," newly published in *Science*.

"We have learned that keeping your immune system quiet is a challenging and very active process," says Noelle. "VISTA mediates immune system function and its loss can result in the development of unwanted immune responses. But VISTA may also be a valuable target in regulating the immune response in cancer and autoimmunity."

VISTA keeps the immune system's T-cell compartment passive and prevents activation of the <a href="mmune system">immune system</a> to self-antigens such as developing <a href="cancer cells">cancer cells</a>. "Like other negative checkpoint regulators, blocking VISTA in cancer may enhance the host's ability to make protective tumor-specific immune responses," says Noelle.

Currently, there is an antibody specific to VISTA that is going to be used in Phase I clinical trials in cancer to see if it is safe and if it can amplify the immune response to cancer in patients. If so, this antibody may be valuable in the development of drugs and vaccines to provide therapeutic response to cancer and cancer cures.

**More information:** M.A. ElTanbouly el al., "VISTA is a checkpoint regulator for naïve T cell quiescence and peripheral tolerance," *Science* (2019). science.sciencemag.org/cgi/doi...



## 1126/science.aav0524

C. Brown el al., "Enforcing T cell innocence," *Science* (2019). <u>science.sciencemag.org/cgi/doi ...</u> 1126/science.aaz7741

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