

Researchers develop novel immunotherapy to target colorectal cancer

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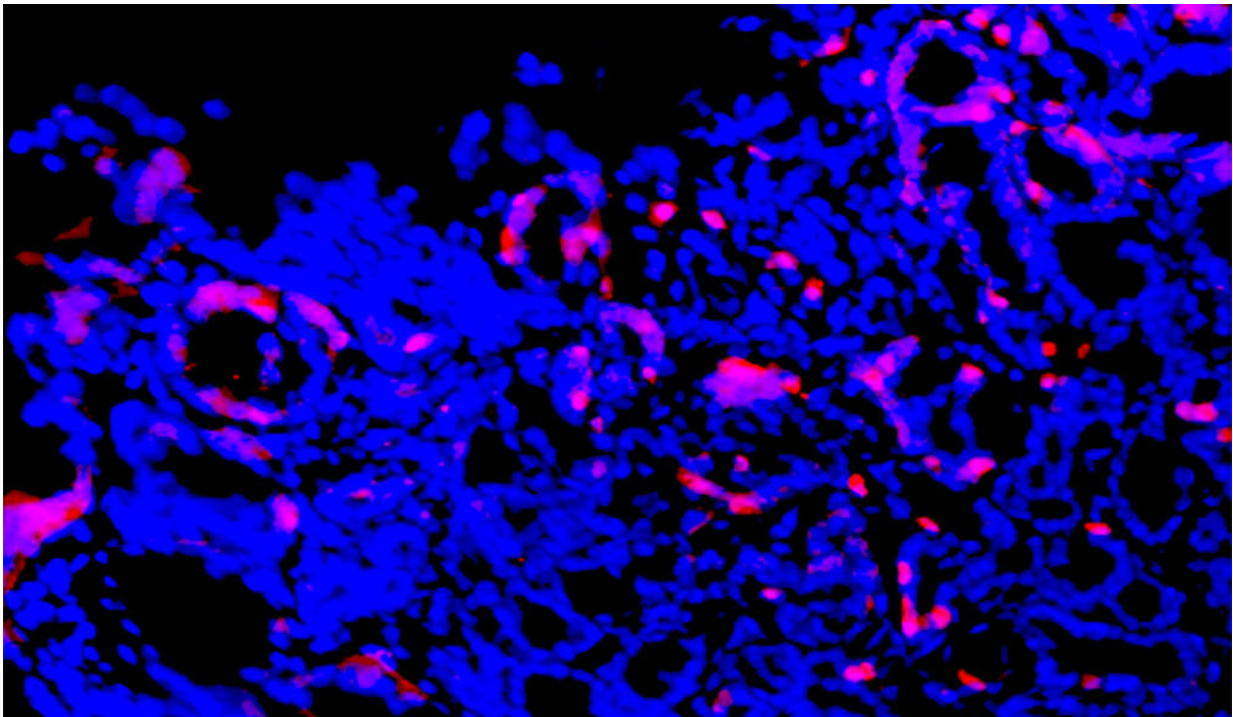


Image depicts intestinal tumor cell death (red stain) after anti-DKK2 antibody treatment. Cell nuclei are stained blue. Credit: Yale University

A Yale-led research team has developed an antibody that blocks tumors in animal models of colorectal cancer. If the finding is confirmed in clinical trials, the antibody-based treatment could become an effective weapon against colorectal cancer, and possibly other cancers, that resist

current immunotherapies, the researchers said.

The study was published in *Nature Medicine*.

Certain cancers fail to respond to existing immunotherapy drugs that are designed to unleash the body's immune system against tumors. To investigate alternative approaches to these cancers, the Yale-led team focused on a protein molecule, DKK2, an inhibitor of Wnt proteins. Wnt proteins had been previously implicated in the promotion of tumors.

To explore the molecule's role in [cancer](#), the researchers crossbred a mouse model of [colorectal cancer](#) with mice lacking DKK2. They discovered that the offspring had fewer and smaller tumors, according to senior study author and professor of pharmacology Dan Wu.

"We found that this Wnt inhibitor, DKK2, which was thought to inhibit tumor formation, promoted tumors through suppression of [tumor immunity](#)," Wu said. Additionally, they learned "if you inactivate, or neutralize, or blockade this inhibitor, it causes reduction of [tumor formation](#) through activation of the host's immune system."

Based on this finding, the researchers developed an antibody to "inhibit the inhibitor" and target colorectal cancers. They also observed that the antibody was effective in blocking a subset of melanomas when used with other immunotherapy drugs.

Wu, who is a member of Yale Cancer Center, believes that the antibody has potential as a new immunotherapy inhibitor to treat these and other cancers.

More information: Qian Xiao et al. DKK2 imparts tumor immunity evasion through β -catenin-independent suppression of cytotoxic immune-cell activation, *Nature Medicine* (2018). [DOI: 10.1038/nm.4496](https://doi.org/10.1038/nm.4496)

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