Improving natural killer cancer therapy

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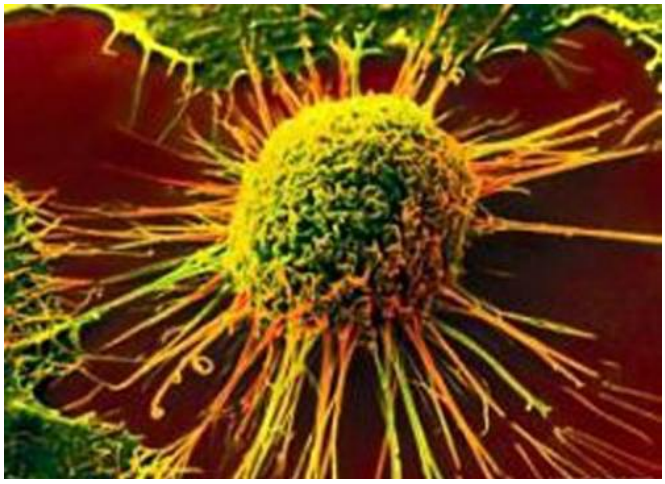

Researchers at Vanderbilt University Medical Center have discovered a potential way to "tune up" the immune system's ability to kill cancer cells.

In a paper published recently, Eric Sebzda, Ph.D., assistant professor of Pathology, Microbiology and Immunology, graduate student and first author Whitney Rabacal and colleagues describe their discovery in mice of a tolerance mechanism that restrains the activity of natural killer (NK) cells, and a potential way to overcome it.

NK cells are a type of white blood cell that specifically recognize and destroy tumor cells. NK cell-mediated tumor therapy—essentially, injections of NK cells—is a cutting-edge technique currently used clinically. It can sweep the blood clean of cancer cells in leukemia patients; however, the remission is often short-lived.

In the paper, published in the May 10, 2016 issue of the *Proceedings of the National Academy of Sciences*, they report that a transcription factor, Kruppel-like factor 2 (KFL2) is critical for NK cell expansion and survival.

KLF2 both limits immature NK cell proliferation and instructs mature NK cells to home to niches rich in interleukin 15 (IL-15), which is necessary for their continued survival.

"This is the same process likely used by cancer cells to avoid destruction by NK cells," Sebzda said. In particular, tumors may avoid immune clearance by promoting KLF2 destruction within the NK cell population, thereby starving these cells of IL-15.

Increased expression of IL-15 can improve immune responses against tumors. Unfortunately, it's not easy to introduce the cytokine only within a tumor microenvironment, and high, systemic levels of IL-15 can be toxic.

Recruitment of cells to the tumor microenvironment that "transpresent" IL-15 may overcome this barrier and thus may improve NK cell-mediated cancer therapy, although the methodology hasn't been worked out yet. "Our paper should encourage this line of inquiry," Sebzda said.

More information: Whitney Rabacal et al, Transcription factor KLF2 regulates homeostatic NK cell proliferation and survival, *Proceedings of the National Academy of Sciences* (2016). DOI: 10.1073/pnas.1521491113

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