New immunotherapy inhibits tumor growth and protects against metastases

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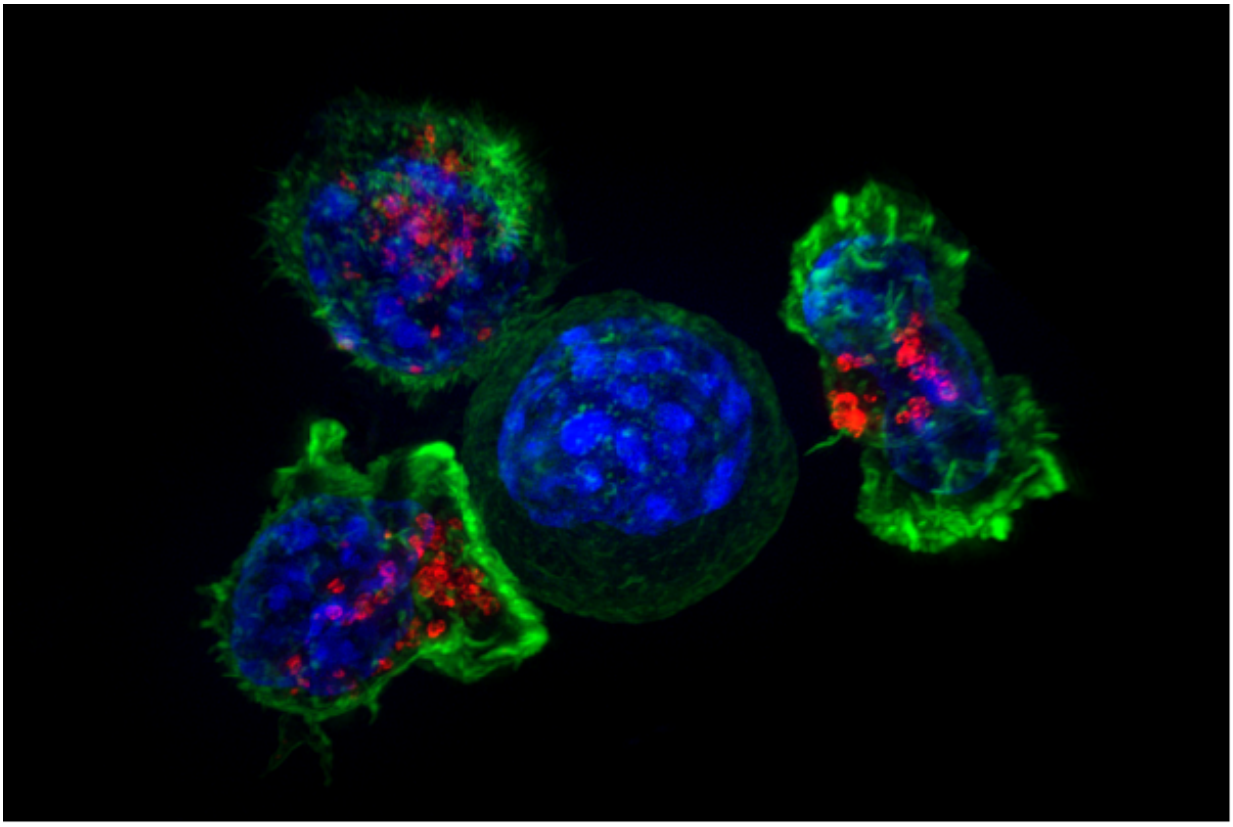

Killer T cells surround a cancer cell. Credit: NIH

Scientists at the VIB-UGent Center for Medical Biotechnology have taken important steps toward the development of cancer-targeting immunotherapy. The research team developed a treatment in mice that

destroys part of the tumor and stimulates the immune system to attack persistent surviving cancer cells. In addition, the researchers demonstrated that the treatment provides protection against tumor formation in other areas of the body. Their findings have been published in *Nature Communications*.

Chemo- and radiotherapy are effective in reducing tumor size, but they unfortunately also affect healthy cells. The human immune system, a more accurate weapon, has evolved to recognize and eliminate disease-causing cells. However, cancer cells employ a range of strategies to confuse and thwart the immune system. Immunotherapies, which help stimulate the immune system to better identify specific cancer cells, show promising results, but are still in need of a great deal of improvement.

The team of Prof. Xavier Saelens (VIB-UGent Center for Medical Biotechnology) seeks to enhance immunotherapy approaches by provoking a certain type of cell death called necroptosis in cancer cells. Previous VIB research has demonstrated that when cells die from necroptosis, the immune system activates.

Ph.D. student Lien Van Hoecke (VIB-UGent Center for Medical Biotechnology): "This phenomenon is also called immunogenic cell death, as the dying cells become examples for the immune system, which then learns and remembers which cells to search for and attack." Building on that knowledge, the team sought a way to provoke necroptosis in cancer cells and thus 'teach' the immune system how to attack tumors. The researchers explored MLKL, a protein that plays a crucial role in necroptosis.

Lien Van Hoecke (VIB-UGent Center for Medical Biotechnology) said, "We developed an immune therapy that causes part of the cancer cells to produce MLKL. As a result, these cancer cells die. The dead cells then

activate the immune system, which attacks tumor cells that survived the initial treatment."

Prof. Xavier Saelens (VIB-UGent Center for Medical Biotechnology) said, "Our treatment not only inhibits primary tumor growth in mice, but also provides protection against untreated tumors and disseminated tumors. This is because the immune system is able to recognize cancer cells located in other areas of the body after confronting destroyed cells in the treated tumor. The outcomes of our study open up a number of avenues for the application of this therapy in humans."

More information: Lien Van Hoecke et al. Treatment with mRNA coding for the necroptosis mediator MLKL induces antitumor immunity directed against neo-epitopes, *Nature Communications* (2018). DOI: 10.1038/s41467-018-05979-8

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