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Scientists give tumor-fighting cells a boost in battling bone marrow cancer

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Researchers from Belgium led by Prof. Dirk Elewaut of the VIB-UGent Center for Inflammation Research and the team of Prof. Vanderkerken and Prof. Menu at the Hematology and Immunology lab of the VUB uncovered a new way to enhance the function of a specific type of immune cell that destroys tumors in multiple myeloma, a form of bone marrow cancer considered incurable. In their study, the scientists blocked a hormone-related mechanism that suppresses these immune cells, restoring their ability to battle tumor growth. The results are groundbreaking in the fight against cancer, as they reveal a new form of cancer immunotherapy. The research team's findings are published in leading scientific journal *Leukemia*.

As we get older, more fat accumulates in our bone marrow. This increase in bone marrow fat coincides with an elevated risk of developing multiple myeloma. This phenomenon was the starting point of a study led by Dirk Elewaut (VIB-Ghent University, University Hospital Ghent), which sheds light on the role of leptin, a hormone produced by fat cells, in reducing the effectiveness of cancer-fighting immune cells called natural killer T cells (NKT cells) and increasing the risk of cancer. The scientists were able to successfully block the leptin receptor to augment protection against cancer. This was a collaborative project with the Hematology and Immunology group of Prof. Karin Vanderkerken and Prof Eline Menu at VUB.

Keeping immune cells responsive

NKT cell-stimulating immune therapies used today to fight cancer are limited due to the fact that after the initial stimulation, the cells go into a state called 'anergy', which makes them dormant and unresponsive for a period of time. This undermines their normal function to protect against harmful pathogens and mutated cells. As a result, if additional treatments are needed, NKT cells no longer respond as they normally do.

Prof. Dirk Elewaut (VIB-Ghent University, University Hospital Ghent): "What makes our findings so important to the development of new cancer treatments is that we were able to restore the function of NKT cells under conditions when they would normally be in a state of anergy."

New tech leads to new observations

To learn more about what happens when NKT cells go into anergy, the scientists used a form of microscopy for the first time in this application that gives them an in-depth look at processes in vivo. As a result, they were able to make valuable observations leading to new insights into immune response mechanisms.

Prof. Dirk Elewaut (VIB-Ghent University, University Hospital Ghent): "NKT cells normally move around in our tissues, patrolling constantly for danger signals. We saw that when they are stimulated, they rapidly stop migrating and start to produce very potent mediators that protect against many diseases, such as cancer. By contrast, NKT cells in anergy were unable to stop and continued to move around. By blocking leptin receptors, we observed that we could modulate this movement."

Translating results to other tumors

Cancer immunotherapy is a rapidly evolving area of medicine that has important and hopeful prospects for cancer patients. Following up on the

study, future research could investigate whether the same mechanisms are at work in other types of tumors, especially in more aggressive cancers with currently limited treatment options.

Prof. Dirk Elewaut (VIB-Ghent University, University Hospital Ghent): "Our goal is to further evaluate this principle in both hematological – or blood-related – tumors and non-hematological tumors, potentially shining a light on future therapeutic avenues for other types of cancer as well."

More information: M Favreau et al. Leptin receptor antagonism of iNKT cell function: a novel strategy to combat multiple myeloma, *Leukemia* (2017). DOI: 10.1038/leu.2017.146

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