

New insights in cancer therapy from cell death research

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Researchers in the group of Prof. Dr. Peter Vandenabeele (VIB/UGent) show that killed tumour cells can serve as a potent vaccine that stimulates the immune system to prevent the outgrowth of cancer cells. This finding opens novel perspectives for the use of necroptosis as a part of immunotherapy and for the screening for novel or existing cancer drugs that induce this type of immunogenic cell death.

Prof. Peter Vandenabeele (VIB/UGent): "In our research group we investigate the molecular mechanisms of different types of <u>cell death</u>. This is very fundamental research. Recently, more and more evidence is emerging that cell death plays an essential role in cancer and other diseases. This research perfectly illustrates this. It gives a good feeling that a better understanding of mechanisms of cell death on the long run may lead to more efficient cancer immunotherapy".

Immunogenic cell death - a novel approach to kill cancer cells

Every second, one million cells die by programmed cell death in a healthy human body. Immune cells efficiently clear the body from these dying cells without eliciting an inflammatory response. Elimination of cancer cells by induction of cell death is also one of the main goals in anti-cancer therapy, resulting in the reduction of tumour mass. In the past decade, a number of anti-cancer drugs have been described to not only kill the cancer cells, but also to elicit an immune response in the patient - a phenomenon referred to as immunogenic cell death.

Dr. Dmitri V. Krysko (VIB/UGent): "The great power of immunogenic cell death is that the body's immune system becomes activated to specifically eliminate the cancer cells. Antigen-presenting cells phagocytize the necroptotic cancer cells and instruct the immune system to trace, recognize and kill any living tumour cells."

Necroptosis as a new target in cancer therapy

To date, this type of immunogenic cell death has been described only for programmed cell death elicited by a number of cancer drugs. Tania Løve Aaes and Dmitri V. Krysko under the guidance of Peter Vandenabeele, show that another type of regulated cell death program termed necroptosis is also highly immunogenic.

PhD student Tania Løve Aaes (VIB/UGent): "In our research, we developed a system that can elicit necroptosis in cancer cells. We administered these killed cancer cells in mice and found that they have a clear protective effect against tumour growth. We are now studying the findings in other relevant tumour models."

Prof. Peter Vandenabeele (VIB/UGent): "Many cancer cells develop resistance to the induction of cell death by apoptotic pathways. With this research we hope to provide an alternative way to kill cancer cells by inducing another type of immunogenic cell death, that is necroptosis, to kill cancer cells and to elicit a specific anti-cancer immune response. These results could pave the way for necroptosis as a novel target in cancer immunotherapy.

These findings are published in *Cell Reports* on March 31, 2016. The work was performed at the Inflammation Research Center (VIB/UGent) and the Cancer Research Institute Ghent (CRIG/UGent).

More information: Vaccination with Necroptotic Cancer Cells Induces Efficient Anti-Tumor Immunity, Love Aaes et al., *Cell Reports* 2016

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