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Cancer can be combated with reprogrammed macrophage cells

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Researchers at Karolinska Institutet have generated antibodies that reprogramme a type of macrophage cell in the tumour, making the immune system better able to recognise and kill tumour cells. The study, which is published in the journal *Cell Reports*, could lead to a new therapy and provide a potentially important diagnostic tool for breast cancer and malignant melanoma.

Immunotherapy, in which the immune system is enhanced in order to kill tumour cells, especially the kind designed to activate the immune system, is changing the way we treat cancer. Unlike other forms of cancer therapy, immunotherapy targets not the tumour itself but specific cells in the immune system to unleash the ability of the immune system to kill the tumour.

"We've found a new way of using antibodies for immunotherapy that activates immune cells, called macrophages, in the tumour," says research team member Mikael Karlsson at the Department of Microbiology, Tumor and Cell Biology. "This makes it easier for the immune system to recognise the tumour and animal studies of three different cancers have given promising results."

In 2013, the leading scientific journal *Science* called cancer immunotherapy the year's most groundbreaking advancement. Antibodies that increase the ability of T-cells to kill tumour cells have proved particularly effective and created new opportunities for treating previously untreatable cancer.

Not sufficiently effective

However, for some patients, T-cell modified immunotherapy has not been sufficiently effective, as some tumours still manage to conceal themselves from the immune system by emitting signals that prevent the immune cells from recognising them. Another reason for the occasional failure of the therapy is that tumours do not trigger as strong an immune reaction as, for example, infections do.

For the present study, the researchers focused on macrophages, immune cells whose normal function is to combat infection. Some macrophages, however, affect their environment in the tumour in a way that makes it easier for cancer cells to survive and spread. Commonly dominant in tumours is a type of macrophage that prevents T-cells and other immune cells from recognising and killing cancer cells.

Stopped the tumours

The researchers managed to reprogramme and activate these macrophages by using an antibody targeted at a protein on their cell surface, which stopped the tumours from growing and spreading in mice. The antibody therapy also
boosted a type of T-cell-modifying immunotherapy in clinical use. The researchers also show that this type of macrophage can be found in human breast cancer and malignant melanoma, and therefore hope to be able to develop an antibody that can one day be used for treating these patients.

"We now hope that this new therapy, which has so far been tested preclinically, will one day be used in combination with another immunotherapy to make it even more efficacious," says Professor Karlsson. "We are also looking into whether the presence of this type of

macrophage in human tumours can be used clinically for the diagnosis of cancer diseases."

More information: Reprogramming tumor associated macrophages by antibody targeting inhibits cancer progression and metastasis. *Cell Reports*, published online 19th of May 2016, doi 10.1016/j.celrep.2016.04.084

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