

New antibody breakthrough to lead the fight against cancer

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Killer T cells surround a cancer cell. Credit: NIH

Scientists at the University of Southampton have developed a new antibody that could hold the key to unlocking cancer's defence against the body's immune system.

In a new study published in *Immunity*, the team, which is based at the Centre for Cancer Immunology, engineered [antibodies](#) to target a particularly significant immune receptor called 4-1BB, which can activate killer T-[cells](#) to find and destroy [cancer](#) cells.

The team discovered that 4-1BB, which is a target for immunotherapy, is present mainly on a population of T cells within the tumour called regulatory T cells, which switch off the killer T cells. Killer T cells also expressed 4-1BB, but to a lesser extent, the team found.

In a pre-clinical tumour setting an anti-4-1BB antibody that deleted regulatory T cells caused regression of the tumour. However, because the type of antibody that is good at deleting regulatory T-cells is not as good at stimulating killer T-cells and vice versa, it is not possible to use a regular type of antibody to harness both therapeutic approaches.

The Southampton team, funded by Cancer Research UK and in collaboration with BioInvent International, were able to design and engineer an antibody that can both delete regulatory T cells within the tumour and therefore remove the suppression they exert and activate the killer T cells at the same time. In laboratory studies, this dual-purpose antibody was highly effective in eradicating tumours.

The study is the culmination of more than 10 years of research from Southampton scientists and their collaborators. They believe that this finding could lead to a new wave of cancer-fighting antibodies

"Antibody immunotherapy has transformed patient outcomes in a number of cancers, but responses are frequently restricted to a minority of patients," said Professor Stephen Beers, who jointly led the study with Professor Aymen Al-Shamkhani and Dr. Juliet Gray.

"This is really very exciting breakthrough. Immune activating antibodies

targeting immune receptors like 4-1BB have failed to translate successfully to the clinic but hold great potential if we can understand how to target them successfully in cancer patients. We have identified some of the reasons that stop them treating cancer and for the first time, demonstrated that you can combine the two approaches of deleting regulatory T cells and activating killer T cells. This could potentially improve the way we treat patients in the clinic."

The research findings can be applied to both ovarian cancer and a common form of non-melanoma skin cancer called Squamous Cell Carcinoma. However, the Southampton team believe that they could be applicable to more cancers, following further research.

Dr. Sean Lim, Cancer Research UK's expert in immunotherapy, said: "This study is an important step towards improving immunotherapy. It helps us to understand why this type of treatment isn't as successful in patients as hoped. But critically, it also presents a potential solution as to how we can overcome these challenges to develop effective [immunotherapy](#) that works for more [patients](#).

More information: Sarah L. Buchan et al. Antibodies to Costimulatory Receptor 4-1BB Enhance Anti-tumor Immunity via T Regulatory Cell Depletion and Promotion of CD8 T Cell Effector Function, *Immunity* (2018). [DOI: 10.1016/j.immuni.2018.09.014](https://doi.org/10.1016/j.immuni.2018.09.014)

Provided by University of Southampton

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