Getting antibodies into shape to fight cancer

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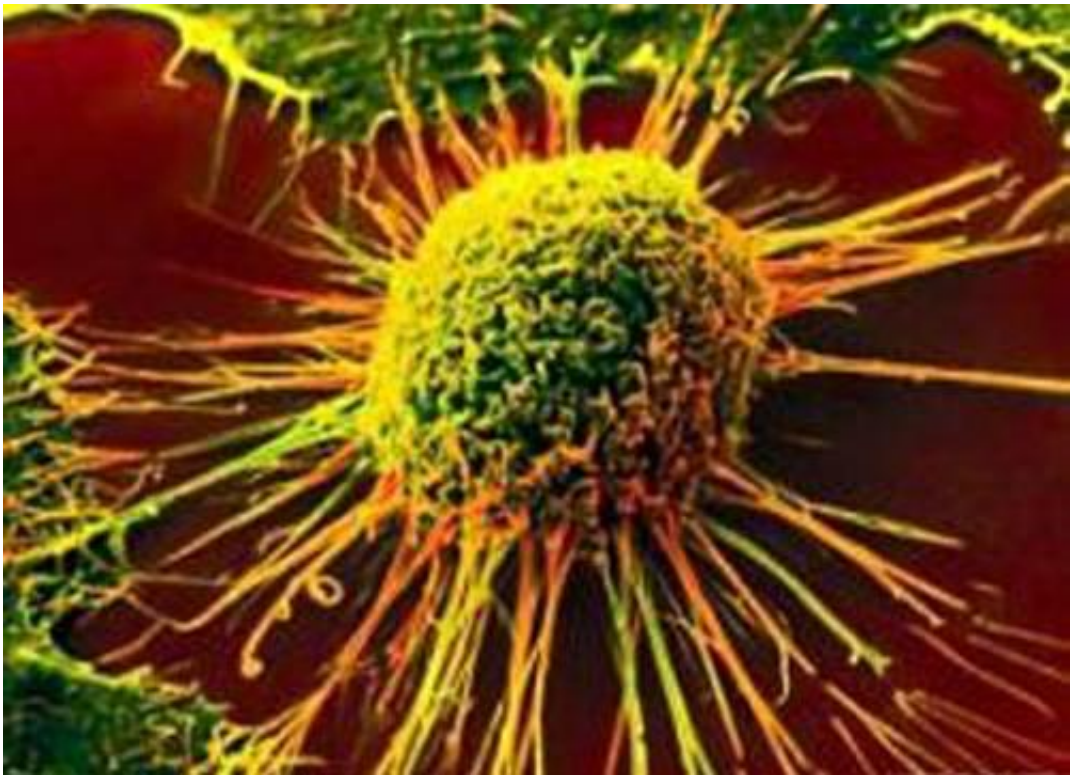

Scientists at the University of Southampton have found that the precise shape of an antibody makes a big difference to how it can stimulate the body's immune system to fight cancer, paving the way for much more effective treatments.

The latest types of treatment for cancer are designed to switch on the immune system, allowing the patient's own immune cells to attack and

kill cancerous cells, when normally the immune cells would lie dormant.

In a study, funded by Cancer Research UK and published in the journal *Cancer Cell*, the Southampton team have found that a particular form of antibody, called IgG2B, is much more effective at stimulating cancer immunity than other types. Unlike other forms of antibody, IgG2B can work independently without needing help from other immune cells, making it more active and able to work in all tissues of the body. The team have also been able to engineer antibodies that will be locked into the particular shape (called a locked B structure) that is most active, making them much stronger immune stimulators than previous drugs.

Dr Ann White, who led the study, comments: "We know that the immune system provides a natural protection against cancer, which can only grow by finding a way around our defences. Antibody treatments are now able to correct this problem for many types of cancer, but we still need them to work better.

"It is early days, but this important discovery could enable us to treat more cancers effectively. Our next task is to bring these novel IgG2B antibodies into trials for cancer patients and we are engineering ways to make them effective in the clinic."

The team is now working to discover why the IgG2 molecule works better in a locked B structure. To do this the molecule has been crystallised and an x-ray shone through it so the structure can be assessed. It is the first time that the IgG2 has been crystallised.

Professor Nic Jones, Cancer Research UK's chief scientist, said: "This research has zeroed in on how we can make immunotherapy treatments more effective against cancer. Energising the immune cells in our body and getting them to treat cancer cells as a threat gives us a better shot at beating cancer. Immunotherapy is part of the future of cancer treatment

and it's important that we use our best immunotherapy weapons to fight the disease."

More information: Conformation of the human immunoglobulin G2 hinge imparts superagonistic properties to immunostimulatory anti-cancer antibodies, *Cancer Cell*, 2014.

Provided by University of Southampton

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