

Hope for pioneering immunotherapy treatment for childhood cancer

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Cancer Research UK scientists at the University of Southampton have developed a potential new antibody treatment which, in the laboratory, shows significantly increased survival from neuroblastoma - a form of childhood cancer which grows from undeveloped tissue of the nervous system. It is hoped that it could one day be used to treat children with the disease. Their findings will be presented at the NCRI Cancer Conference in Birmingham on Monday.

The researchers have developed two monoclonal antibodies (mAbs) called anti-4-1BB, anti-CD40, and investigated a third called anti-CTLA-4, which bind to molecules in the immune system. It is hoped that these antibodies can be used to boost or 'super charge' the body's immune system to help it fight cancer.

The body's immune response is generally much weaker to cancer than it is to infections, and in most cases it does not stop tumours from growing. These antibodies are designed to recognise the response that the immune system produces and stimulate it, so that it is more effective in attacking and killing cancer cells.

They found that 40 to 60 per cent of the tumours treated with the stimulatory antibodies were destroyed in laboratory models. With more aggressive tumours, the antibodies alone did not significantly slow tumour growth, however, when the researchers paired one of the monoclonal antibodies with a peptide called Survivin a similar survival benefit was seen.

Survivin is a good immunotherapy target because it is present in 80 to 100 per cent of neuroblastoma tumours, but rarely seen in normal tissue. Peptides work by training the immune system to recognise the cancer cells.

The three monoclonal antibodies were tested independently and will be developed by the scientists to see if they can improve them further.

Neuroblastoma is a solid form of tumour that normally develops in the abdomen. It affects around 100 children in the UK each year - most cases are diagnosed under the age of five.

Dr Juliet Gray, clinical lecturer in oncology at the University of Southampton, and a paediatric oncologist at Southampton General Hospital, who will present the findings at the NCRI Cancer Conference, said: "Although this work is still at a pre-clinical stage, we hope it has enabled us to identify a way that we can provide effective immunotherapy treatment against neuroblastoma. More research is needed to understand how these antibodies work and how they should be used to treat neuroblastoma. We then hope to take the approach into a phase 1 clinical trial in children with this disease.

"Six out of ten children with neuroblastoma can be successfully treated with conventional chemotherapy. But for those children who don't respond well to this treatment, immunotherapy could become a vital new treatment option."

Although immunotherapy is a relatively new form of treatment, a number of monoclonal antibodies are licensed to treat adult cancers or are in clinical trials. Similar approaches which use mAbs to trigger the immune system to attack and kill cancer cells include Rituximab for non Hodgkin's lymphoma (NHL)

and some types of leukaemia and Alemtuzumab for chronic lymphocytic leukaemia (CLL). Another potential antibody treatment called anti-GD2 - which uses a slightly different method of tackling the disease - has also shown promising results for neuroblastoma in clinical trials.

Cancer Research UK's Professor Martin Glennie, director of the Cancer Sciences Division at the University of Southampton School of Medicine, who also worked on the study, said: "We very much hope these results will enable us to develop a pioneering immunotherapy treatment for a childhood cancer. In theory this approach enables us to kill cancer cells without damaging healthy cells, resulting in fewer toxic side effects such as hair loss, nausea and tiredness.

"The next stage of our work will be to see if the treatment is a safe and effective treatment for children and also seek to understand how these antibodies can be used in combination with other treatments to maximise their effect."

Dr Lesley Walker, Cancer Research UK's director of cancer information, said : "This is exciting work but it's very early days. If the promise of immunotherapy holds true in clinical trials in children it will give us another option to use in the fight against neuroblastoma."

Source: National Cancer Research Institute
