

Stem cell approach primes immune system to fight cancer

Stem cell techniques have been used in the lab as a new way of priming the body's own immune cells to attack cancer, in a proof-of-principle study by Oxford University scientists.

The technical advance opens up the possibility of using stem cells derived from a patient's skin as a source of key immune cells, called dendritic cells, which can orchestrate an immune response against a tumour. But much further work would be needed to turn this into a therapy ready to be used with cancer patients.

"The patient would in effect be treated with their own immune cells to prime an attack on their tumour, but those cells would have been derived from a biopsy of their skin," explains Dr Paul Fairchild of the Sir William Dunn School of Pathology at Oxford University, who led the work.

The Oxford researchers used recently established techniques to turn skin cells from a healthy adult back into a stem cell state. These 'induced pluripotent stem (iPS) cells' are capable of renewing themselves indefinitely and can be coaxed to form any cell type - muscle, nerve, heart tissue, and so on.

Dr Paul Fairchild and Dr Kate Silk prompted the human iPS cells to form dendritic cells using an approach that would be suitable for clinical use (no animal-based material or supplements to aid growth were used).

After providing the dendritic cells with components of a melanoma, the team showed the cells could initiate a full immune response to melanoma markers in cell cultures in the lab.

The study was funded by the UK Medical Research Council and the Oxford Martin School, and is published in the journal *Gene Therapy*.

"We've worked out how to generate the particular dendritic cells that are necessary to get a good immune response against tumours," says Dr Fairchild, who is also co-director of the Oxford Stem Cell Institute at the Oxford Martin School, University of Oxford.

"We think it is a significant step forward to produce these cells and show they can generate an immune response under culture conditions in the lab. But it's important not to underestimate the difficulty in getting to a point where we could consider using the cells as a therapy against cancer in patients."

Dendritic cells are important parts of the immune system. They orchestrate and control the body's immune response to foreign bacteria and pathogens. Dendritic cells do this by taking up components of the pathogen, or 'antigens', and presenting them to other parts of the immune system to teach them what to seek out and destroy - like a policeman giving a

bloodhound a scent to track down.

Dendritic cells can also set off potent immune responses against cancer, by taking up antigens associated with the tumour.

Clinical trials have been conducted previously in which dendritic cells have been taken from a cancer patient's blood. The dendritic cells are then presented with antigens to prime them for an attack on the patient's tumour, before introducing the immune cells back into the patient.

Results using this type of cancer immunotherapy have been mixed, though occasionally startlingly good, says Dr Fairchild. He suggests that this variability could be because blood cells are taken from patients who have often had several rounds of chemotherapy, affecting the bone marrow where blood cells are made. There also appears to be large variation between patients in their dendritic cells, and so in the effectiveness of this therapy.

But most importantly, the dendritic cells isolated from patients' blood are not able to fire up both arms of the immune system to fight the tumour - they only produce antibodies rather than activating T cells. It is the T cells seeking out and destroying the cancer cells that is crucial for a potent anti-tumour response.

Only a subset of dendritic cells, present in trace amounts in the blood, can stimulate both an antibody and a T cell immune response.

Dr Fairchild and his team believe that the stem cell techniques they have developed could overcome all these problems.

By working from the patient's skin cells, it is possible to by-pass many of the effects of chemotherapy. There would be less patient-to-patient variation in the effectiveness of the dendritic cells. The lab-grown cells would provide an ongoing source of immune cells for multiple rounds of the cell therapy.

And the Oxford researchers have shown their stem cell approach produces a population of dendritic cells capable of stimulating both an antibody and a T cell immune response.

"For the first time, we now have a good experimental model for investigating these important dendritic cells that are normally only present in trace amounts," says Dr Fairchild. "While we've developed protocols to make dendritic cells in a way that's suitable for medical use, any clinical trials would be a long way off."

He adds: "We would envisage that any future immune cell therapy based on this approach would be used with patients where other treatments have failed, where there is no other way to go."

Source: Oxford University

For more, visit: <https://www.bizcommunity.com>