

CCLG: The Children & Young People's Cancer Association research: Creating a new immunotherapy approach to fight aggressive medulloblastoma

Project title: Overcoming tumour heterogeneity with next generation CAR T-cells for the effective treatment of paediatric medulloblastoma

Project stage: Ongoing (started May 2023, planned end April 2027)

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Led by: Dr Laura Donovan, UCL Great Ormond Street Institute of Child Health



About the project

Medulloblastoma is one of the most common types of childhood brain tumour, and has four subtypes. Group 3 is one of the highest-risk subtypes, and only one patient out of twenty will survive this type of medulloblastoma. They are also much more likely to have their cancer return after treatment, at which point it cannot be cured. Whilst there have been great improvements for many medulloblastoma patients, the physical and mental cost to survivors is high and high-risk tumours are still very difficult to treat. This shows that children with medulloblastoma desperately need new targeted treatments that cause less damage to their growing brains.

CAR-T therapy has shown lots of promise for some types of cancer, like leukaemia. This treatment trains a patient's own immune cells to hunt down and kill cancer cells, based on proteins on the cancer cell surfaces, called antigens. However, medulloblastoma cells can have very varied antigens, meaning that the CAR-T cells cannot find the cancer, and these trained cells do not always survive for long inside the body.

To address this, Dr Laura Donovan from the Institute of Child Health has developed a 'dual' CAR-T cell that can recognise two different antigens. By targeting two antigens rather than just the one, her team's treatment will overcome the issues of medulloblastoma cells showing different antigens and also improve the chance of the CAR-T cells locking on to the cancer cells.

In this project, Dr Laura Donovan's team will be working out the best way to use their new treatment. They will be testing different versions of dual CAR-T cells and investigating their effect on medulloblastoma cells. By finding out exactly how the CAR-T cells work, and which are the most effective versions, the researchers hope to generate enough evidence to get their treatment into clinical trials.

Progress

The team have created and tested several versions of their dual CAR T cells in the laboratory, with two designs working especially well. They were better at killing cancer cells and remained more active over

time than current CAR T cell therapies.

Over the past year, the researchers have been extensively testing the two leading dual CAR T cells in animal models. They explored how well the treatment worked against different forms of the disease, including newly formed tumours, tumours that had spread, and tumours that had returned after treatment. These studies showed that the dual CAR T cells improved survival, reduced tumour growth, and showed strong activity compared to CAR T cell treatments already being tested in patients. This shows that targeting two tumour markers at the same time could be a good way to fight medulloblastoma.

What's next?

The researchers are now analysing their results and data to understand why the dual CAR T cells are more effective. This will include looking at how well the cells survive and remain active over time.

They will also test their most effective dual CAR T cells in models with a working immune system. This will help them see how the treatment performs in a more realistic tumour environment, where cancers can suppress the immune response.

Based on the results so far, the researchers still hope to begin early clinical trials within the next five years.



#Pearl Power



The Children &
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