

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

Lead researcher: Dr Laura Donovan, UCL Great Ormond Street Institute of Child Health

Project Stage: Ongoing (started May 2023, planned end April 2026)

Funded by: Christopher's Fund, Tyler's Superhuman Fund, Faith's Future, Bailey's Little Star Fund, Team Rory, and #PearlPower

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 successfully created seven new types of CAR T-cells and tested them in different types of medulloblastoma in the lab. Compared to the currently used CAR T-cells, two of Dr Donovan's new cells were better at fighting tumours and survival. The researchers have tested these further and confirmed their ability to fight cancer cells for longer. Their evidence shows that the new CAR T-cells are good at fighting the entire medulloblastoma tumour, including the cells that contribute to relapse and spread.

WHAT'S NEXT?

In the next 12 months, the researchers will test the new CAR T-cells in animal models to see how effective they are at different stages of medulloblastoma, like at diagnosis, relapse, and spread. They will assess survival rates with the treatment, side effects, tumour size, tissue composition, and whether it prevents the cancer from spreading around the body or growing back. If successful, they hope to move their CAR T-cells into early clinical trials within five years.



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