Exploiting and enhancing brain-resident immune cells for the treatment of paediatric brain stem glioma (DIPG)

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DIPG is a fatal brain cancer that affects children, with no effective treatments. This research project is proposing a new combination of treatments targeting the immune system in the brain to treat DIPG. First, the cancer cells will be labelled with a "flag" so the immune system can see them. The investigator will then use another treatment to block the "don't eat me" signals on the cancer cells, so the immune system can attack the cancer. This new treatment could help save the lives of children with DIPG, who currently have a 0% chance of survival.

Project Synopsis and Aims

Diffuse intrinsic pontine glioma (DIPG, or diffuse midline glioma) is a fatal, highly aggressive brain tumour affecting children. Less than 10% of children diagnosed with DIPG are still alive 2 years later, highlighting an urgent need for improved treatments.

The problem: Due to the location of the tumour in a vital part of the brain, surgery is not an option in the treatment of DIPG. Currently, the only treatment shown to prolong survival is radiotherapy, however this only offers palliative relief of symptoms. No chemotherapy treatments for DIPG currently exist, and previous chemotherapy clinical trials using a single drug have also been unsuccessful. Novel combination treatments are desperately needed.

Major finding: Therapies targeting the immune system have shown remarkable clinical outcomes in other cancers, but not in brain tumours. This is in part because the brain has a specialised immune system less reliant on T cells, which are the target of most immunotherapy approaches. Instead, cells called microglia are the most common immune cell of the brain, comprising up to 50% of some brain tumours. Brain tumour cells, including DIPG cells, avoid microglial attack by expressing a "don't eat me" signal called CD47. Blocking CD47 with a therapeutic antibody (a-CD47) results in remarkable disease control by increasing the ability of microglia to recognise and kill brain cancer cells.