Brain Tumour Research Centre of Excellence at the Institute of Cancer Research (ICR)
Impact Report for Dr. Michael Josephson MBE

Brain tumours are indiscriminate and are the biggest cancer killer of children and adults under 40. Almost 700 children and young people are diagnosed with a primary brain tumour in the UK each year. Of these 420 are aged 0-14 years old.

Paediatric brain tumours present a unique challenge in that treatment is complex and tailored to each child requiring a multidisciplinary team of specialists. The Brain Tumour Research Centre of Excellence at the Institute of Cancer Research is focused on improving outcomes for a particularly aggressive group of paediatric brain tumours known as paediatric-type diffuse high-grade gliomas (PDHGG).

PDHGG have no effective treatments, and prognosis is just nine to 12 months. These tumours include diffuse midline glioma, a tumour that is typically found in the midline structures of the brain and represents the deadliest form of childhood cancer. Tumours of the midline structures cannot be removed surgically as the risk to vital areas that control breathing, heart-rate and sleep is too high. Even a small operation in this region could damage parts of the brain that are essential for life. Diffuse Intrinsic Pontine Gliomas (DIPG), a subset of DPHGG, are most common in children aged 5-10 and have an average survival of just under 12 months.

Current treatments options include chemotherapy and radiotherapy. However, unlike adults, children's brains are still developing, making treatments like radiotherapy particularly damaging.

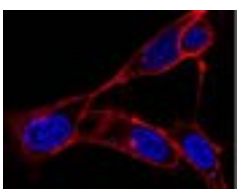
Jasmine Freeman, known as the warrior princess, was diagnosed in February 2023 after experiencing ongoing headaches and double vision. An MRI scan revealed an inoperable midline glioma and the only treatment option was radiotherpay to slow the disease. Sadly Jasmine passed away in January 2024, less than a year from her diagnosis.

Director of the our paediatric Brain Tumour Research Centre of Excellence at ICR, Professor Chris Jones and his dedicated research team, are robustly testing novel combinations of drugs to target these childhood tumours and to generate the laboratory data needed to support the application and launch of new clinical trials. The research being undertaken spans the gap between basic biology and clinical benefit, an area that is particularly difficult to find investment. In addition to testing and fast-tracking promising treatment options to clinical trial, they are also exploring a number of innovative ways to treat PDHGG through three collaborative PhD studentships with other world-leading labs within the ICR. These include:

- **Destroying tumour causing proteins** - Dr Gary Newton, based at the Centre for Cancer Drug Discovery at ICR, is working with a Brain Tumour Research-funded PhD student to develop new drugs which break down cancer-specific proteins found in distinct groups of PDHGG tumours, and is working to ensure they cross the blood brain barrier.

- **Using viruses to kill tumours and activate the immune system** - Dr Julia Cockle, from the Royal Marsden Hospital, is working with another Brain Tumour Research-funded PhD student, to investigate using oncolytic (anti-cancer) viruses as a novel treatment approach for paediatric high-grade glioma.

- **Light-activated therapy that targets tumour cells** - Dr Gabriella Kramer-Marek, located at the ICR Centre of Cancer Imaging, is working with Jacob Reeves, also a Brain Tumour Research-funded PhD student, to investigate the use of light with immunotherapy strategies (photoimmunotherapy) to target PDHGG cancer cells.



By investing in innovative translational research, Brain Tumour Research hopes to increase the number of clinical trials for children with brain tumours providing hope for new, kinder and more effective treatments.

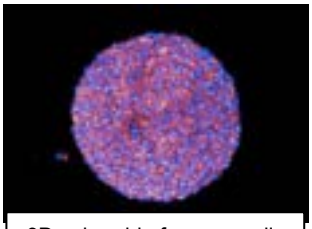
The Impact of your £50,000 donation from the 2024 ball

Your donation of £50,000 from the 2024 ball has enabled us to fund the first year of PhD student Jacob Reeves who is working with Dr Gabriella Kramer-Marek on light-activated therapy that targets paediatric high grade glioma cells.

Jacob said: *"Thanks to Brain Tumour Research funding, we are exploring cutting-edge treatments for rare and devastating childhood brain cancers, which could improve the lives and outcomes of patients. I'm honoured to be a part of the valuable research happening at the Brain Tumour Research Centre of Excellence at the ICR."*

As part of a four-year PhD program, Jacob is focused on photoimmunotherapy, an innovative treatment approach that combines targeted therapy with light to destroy cancer cells and alert the immune system to the tumour.

The approach works by delivering a light-sensitive drug to cancer cells. These cells are then exposed to near-infrared light (essentially a bright red light), which activates the drug, disrupting the cell membrane (outer lining) and killing the cell. Crucially, this also alerts the immune system to the tumour, triggering an immune response. In lab models, it has already been shown to be effective in glioblastoma, a highly aggressive glioma in adults.



3D spheroid of cancer cells

So far, Jacob has shown this drug successfully targets the PDHGG cancer cells and reaches the tumour in experimental models. Now entering the second year of his Brain Tumour Research-funded PhD, Jacob is aiming to prove the innovative approach can improve survival and activate the immune system in paediatric tumours.

Jacob explains his work in this short video clip: https://youtu.be/RpjHscO5Bzw

Dr Gabriela Kramer-Marek, Jacob's PhD supervisor led the team that successfully applied this treatment to glioblastoma models in the laboratory. She says:

"Your financial support provides the opportunity to apply my expertise and this promising treatment to the study of childhood brain tumours for the first time. By enhancing our understanding and application of this technology, we can better tailor treatment to the unique challenges of PDHGG, minimise harm to surrounding healthy tissues, and ultimately improve survival rates reducing treatment-related morbidities"

Jacob's PhD will span a total of four years, and the progress he has made to date is impressive. The costs for the first year were met by your very generous donation of £50,000 which covered his PhD expenses of tuition fees, stipend fees and laboratory consumables such as pipettes, solutions and dishes, as well as the additional costs of MRI scans needed for this invaluable research.

On behalf of all at Brain Tumour Research, thank you for your support, enabling the progress that Jacob is making possible.