Research Grants 2025

Brain tumour | Investigating Glioblastoma Therapy Using a Novel Small Molecule Agent

Associate Professor Chris French

Glioblastoma (GBM) is a highly aggressive brain tumour with poorly effective treatments. [1] The current standard treatment is the Stupp protocol consisting of maximal safe resection of tumour followed by the drug temozolomide combined with radiotherapy.[2] However the prognosis remains very poor with disease recurrence typically within 12 months. Additionally, there is evidence that tumours treated with this conventional treatment become more resistant and aggressive [3].

There is an enormous therapeutic gap to find more effective treatments. One potentially effective strategy is to use combinations of drugs that are known to have strong anti-tumour effects. There is similarly a great need and opportunity to understand how drugs inhibit tumour cells using state of the art analysis of cellular pathways.

We have recently discovered that a drug, "NS1643", that inhibits "hERG" "ion channels" [4] in the membranes of aggressive brain tumour cells has remarkable suppressive effects, much greater than the currently primary drug treatment, temazolamide, at realistic clinical dosages. The inhibitory effect of this ion channel target is quite unexpected and opens up a wide range of experimental and therapeutic opportunities.

This grant proposal is to follow up our exciting discovery of the anti-tumour effect of NS1643 to discover how it works and to test its effectiveness across a wide range of glioblastoma subtypes. In particular we will use recently developed state of the art techniques to "drill down" on the mechanisms that make this drug so potent. This information is likely to allow us to identify other effective drugs already available, and potentially to design novel antitumour molecules. Additionally, this research will allow us to explore whether our drug enhances the effect of the currently used agent temozolomide.

Grant $20,000

THE ROYAL MELBOURNE HOSPITAL NEUROSCIENCE FOUNDATION

Brain tumour | Investigating Glioblastoma Therapy Using a Novel Small Molecule Agent

Progress Report

Our prior work has demonstrated the remarkable suppression of the aggressive brain tumour cell line SMA-560 with NS1643 and the generous grant from Royal Melbourne Hospital Neuroscience Foundation has enabled us to expand this work further to the most common, and most deadly, brain cancer - glioblastoma. Over the last year we have focused on understanding the mechanism of action of NS1643.

We have found that, while NS1643 potently suppresses almost all patient-derived glioblastoma cell lines tested, there exists a small subset which appear relatively resistant to NS1643. Crucially, each cell line represents an individual patient's tumour, with unique biology. This variability in response provides a valuable opportunity to identify which patients are most likely to benefit from NS1643, while also offering insight into the role of potassium channels in glioblastoma physiology.

To best understand the biological determinants underlying this variability, we have collaborated with bioinformatician Associate Professor Michael Menden to combine our results with publicly available cancer datasets. Preliminary results suggest there does, in fact, exist a vulnerability that can be specifically targeted with NS1643, affording a glimpse into the molecular pathways that drive sensitivity and resistance.

Beyond limiting the growth of glioblastoma, we have also demonstrated that NS1643 is effective in limiting the invasivity of this highly aggressive cancer. This is achieved by limiting both the individual cell motility and the secretion of enzymes used to degrade surrounding tissue. However, one of the major challenges for the development of drugs to treat brain cancer is ensuring that the treatment can effectively reach the brain, and this can only be achieved if the drug is able to cross the blood-brain barrier. Excitingly, we have demonstrated, using a mouse model, that NS1643 readily crosses the blood-brain barrier, supporting NS1643 as a promising drug candidate for further development.

Preliminary findings from this study were presented at the Australian Brain Cancer Research Alliance (ABCARA) Scientific Research Symposium in 2025. This resulted in the establishment of a new collaboration with Associate Professor Guillermo Gomez based on shared interests in potassium ion channels as therapeutic targets in brain cancer.

Brain tumour | Investigating Glioblastoma Therapy Using a Novel Small Molecule Agent

Progress Report

Over the next phase of the project, we will extend mechanistic studies to better define how NS1643 so potently inhibits the growth of glioblastoma and better establish its interaction with temozolomide, the current standard of care chemotherapy for glioblastoma. We are currently finalising experiments to support these already promising findings and expect publication in the coming year!