## **Research Grants 2025**

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

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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

