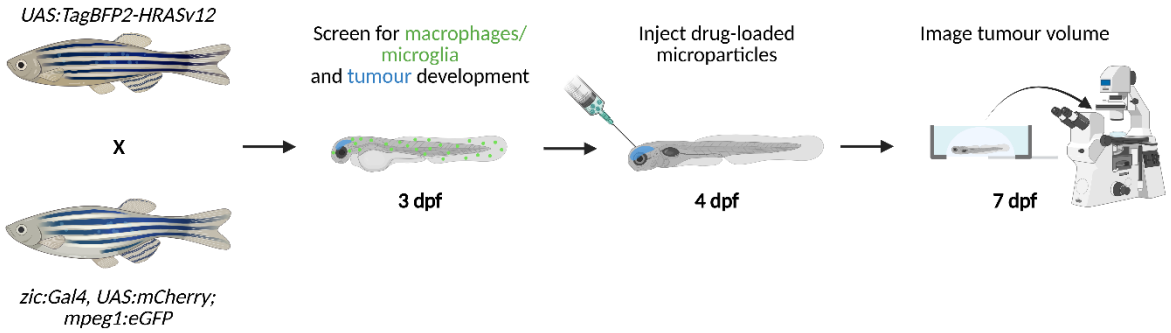
UNTANGLING THE ROLE OF MICROGLIA IN TUMOUR COLONISATION THROUGH TARGETED DRUG DELIVERY

Background: Glioblastoma is the most common form of primary brain tumour in adults, with an average survival of only 12-18 months from diagnosis. In other cancers, immunotherapies that drive immune cells to attack the tumour have been very effective, but it has been difficult to achieve the same results in glioblastoma. Treating glioblastoma is difficult for several reasons; a natural protective barrier surrounds the brain (the blood brain barrier) that often prevents anti-cancer drugs from reaching the tumour, and the tumour exploits large numbers of immune cells to help support its growth, making it difficult for immunotherapies to turn the immune system against the tumour. The majority of immune cells that support glioblastoma growth are macrophages and microglia, which can make up to 50 % of the tumour bulk in glioblastoma. Under healthy conditions, macrophages and microglia are specialised to eat debris and dead or dying cells, meaning they have a lot of potential to eat cancer cells if they can be turned against the tumour.

This project: A promising approach to treat glioblastoma is to use microscopic particles, where drugs are held within a protective shell that can enter the brain and make sure that drugs are only delivered to specific target cells. As macrophages and microglia are specialised to eat debris, they are very good at taking up microscopic particles where other cells would struggle. In this project, a microscopic, biodegradable particle was designed to improve delivery of immune-stimulatory, anti-cancer drugs to macrophages and microglia in GBM. The drugs selected for delivery were all already approved for the treatment of other diseases, but had not been used to treat glioblastoma because they could not easily reach the brain alone. By repurposing these drugs and loading them into particles, it was possible to stimulate macrophages and microglia into action against the tumour and reduce its size in a zebrafish model of glioblastoma. Further investigations are required to understand exactly how each of the drug used is reducing tumour size. But future work may be able to build on these findings to improve patient treatment.



The future: This work has been submitted as part of a PhD thesis, and we also expect to publish it as a short communication in the scientific literature. More work is required to improve these particles before they can be considered as a potential route to treating GBM patients, but this project has already highlighted the potential for repurposing existing drugs for treating glioblastoma. As yet, follow-on funding to further investigate these drugs and develop the particles has not been secured.

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