Glioblastoma is a highly aggressive, invasive brain cancer that is difficult to cure by conventional therapies such as chemotherapy or radiation. This resistance to therapy is largely due to glioblastoma cells failing to undergo apoptosis (premature cell death). Last year, I was fortunate to be awarded the Tempe Mann Travelling Scholarship to investigate a new experimental treatment for glioblastoma developed by the Yun Laboratory in Seoul, South Korea. Their strategy was to engineer a virus that could attack the tumour without affecting the healthy brain cells (such as astrocytes). Through their experiments they discovered that a molecule known as TRAIL (tumour necrosis factor related apoptosis-inducing ligand) could induce apoptosis in glioblastoma cancer cells, leaving healthy brain cells unaffected. They engineered a virus to express the genetic code to produce TRAIL molecules and showed how injections of this virus were able to significantly reduce the tumour growth. While effective, the modified virus treatment was unable to completely eradicate the tumour. With the Tempe Mann Travelling Scholarship, I was able to develop a mathematical model that captured the formation of glioblastoma and determined ways of improving the therapeutic efficacy of this virotherapy.

For the first stage of the research project, I visited Prof. Chae-Ok Yun and co-workers in her laboratory. Together, we defined the experimental basis on which the mathematical model could be formulated and discussed their hypothesis for treatment failure. I then travelled to Indiana University in Bloomington, to work with Prof. Paul Macklin, in the Department of Intelligent Systems Engineering. Under his guidance I developed a computational and mathematical platform that simulates the growth and formation of glioblastoma. With this platform, I then investigated the experimental TRAIL-based virus treatment.

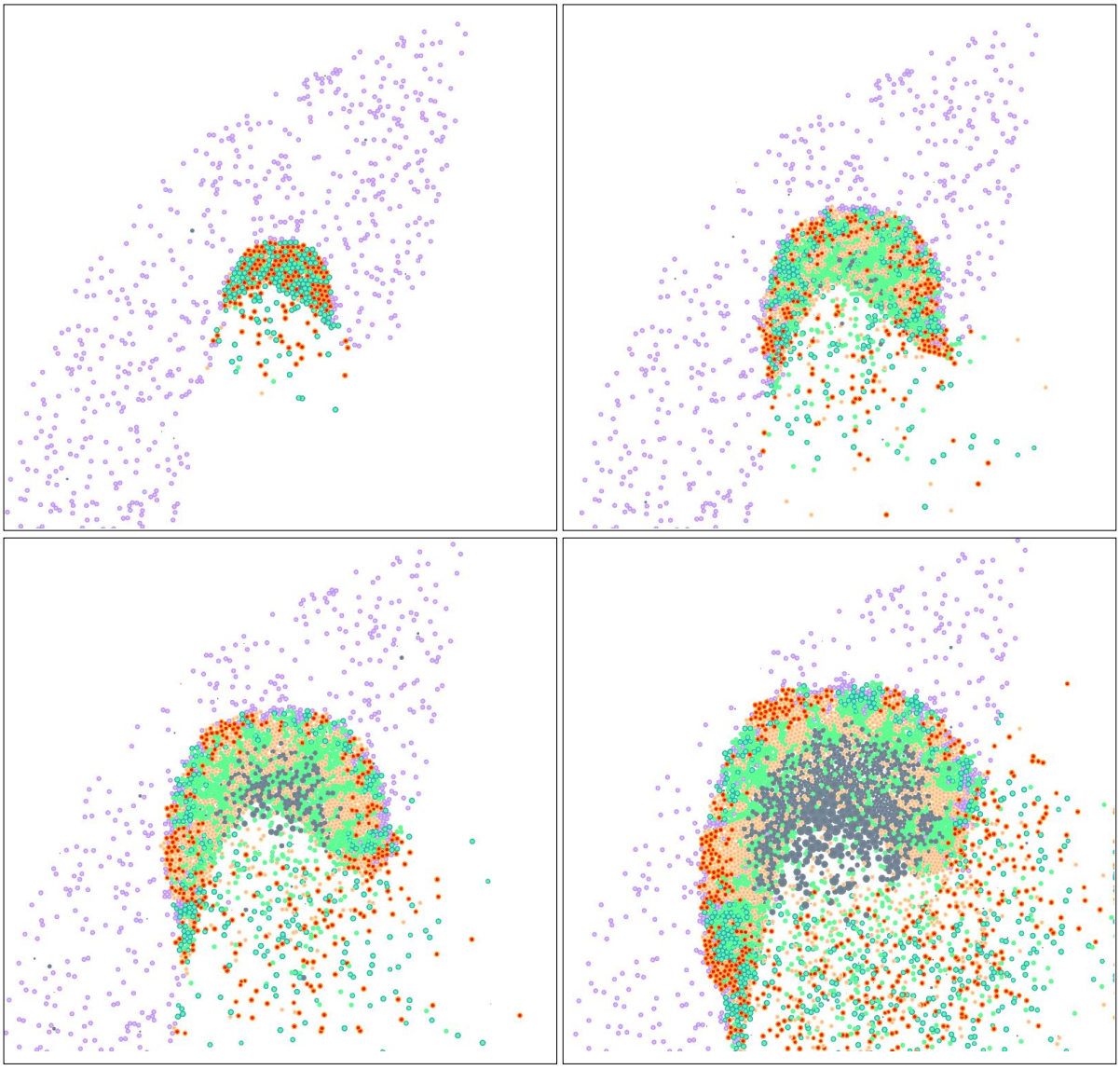
The mathematical and computational framework developed with Prof. Macklin was able to realistically capture the growth and treatment of glioblastoma (see figures on the following page). From our investigations, we determined that the secretion rate of TRAIL (the rate at which TRAIL molecules leave the virus-infected cell) is a significant factor in treatment success. If TRAIL is secreted too quickly from the virus-infected cell, we were able to show that this would reduce the overall treatment efficacy and was the reason that treatment was failing. We therefore proposed to the experimentalists that this characteristic should be manipulated to improve treatment efficacy. Additionally, using the platform we were also able to determine that if the virus was able to replicate twice as quickly, the treatment could completely eradicate the glioblastoma. This manipulation in the replication rate could be achieved by modifying the base virus.

The platform I developed through this scholarship is malleable to other glioblastoma therapies. Currently, I am working on publishing the platform, so that it may be used by other experimentalists to help inform the treatment of glioblastoma. Overall, there were three main outcomes of my research:

1. The mathematical framework developed captured the formation and treatment of glioblastoma using a genetically engineered TRAIL-expressing virus and could easily be used by experimentalists
2. Success of treatment with the TRAIL-expressing virus depends significantly on the secretion of TRAIL from the virus-infected cell
3. Tumour eradication is possible if the replication rate of the virus can be increased

I'd like to sincerely thank the AFGW for the Tempe Mann Travel Scholarship. From this award I was able to improve the understanding behind glioblastoma treatment using TRAIL-based virotherapy. Additionally, new mathematical techniques were pioneered that can be useful in a range of applications and form a cornerstone of future cancer treatment modelling. This award enabled me to foster interdisciplinary cross-continental collaborations between Australia, South Korea and the United States, strengthening international bonds for the University of Sydney and developing academic connections that encourage future interdisciplinary research. Overall, this award has been significant in developing my future career as a mathematician and towards developing a more effective treatment for glioblastoma.

Adrianne Jenner (PhD Candidate and Tempe Mann Travelling Scholarship recipient)



The above figures are snapshots of the simplified glioblastoma formation. The purple cells are healthy astrocytes (brain cells) and the green and orange shaded cells are cancerous glioblastoma cells. The dark grey cells represent the necrotic core of the tissue. Notice the cells that leave the tumour bulk and migrate away are common characteristics of glioblastomas