

TCS/21/05 - Developing representative models of the blood-tumour barrier to enhance drug development for glioblastoma

Glioblastoma (GBM) is an incurable, aggressive brain tumour that affects all age groups. No new treatments have been approved since 2005, and numerous new drugs that showed promise in the laboratory have failed to improve outcomes for patients. The brain is protected from circulating chemicals by the 'blood brain barrier' (BBB), which plays an important role in the healthy brain but unfortunately prevents many drugs from getting into brain tumour cells at sufficiently high levels to kill them. However, previous research has shown that GBM cells cause changes to the BBB that increases its leakiness and could be used to improve drug delivery. Now we need more information about these changes in order to design drugs that will cross the 'leaky' BBB and penetrate brain tumour cells more effectively. To obtain this information we will (1) establish how GBM cells affect the BBB, using existing patient samples and laboratory models of GBM; and (2) measure drug levels in GBM and the surrounding brain to understand how changes in the structure of the BBB affect drug delivery to the tumour cells and the normal brain. In the longer term we will use this information to develop new laboratory models of the 'leaky' BBB that exists in GBM, and use them to develop drugs that are much more likely to get into brain tumour cells at high enough levels to kill them.