Identifying new potential brain tumour drugs through computational analysis and literature mining

Kadjane Nithianandasivam\(^1,\alpha\), Aisha Ghani\(^1,\beta\), Ryan K. Mathew\(^1,2\), Heiko Wurdak\(^1\)

\(^1\)Medical School, University of Leeds, United Kingdom
\(^2\)Department of Neurosurgery, Leeds General Infirmary, United Kingdom

\(\alpha\)Corresponding author: um15kn@leeds.ac.uk
\(\beta\)Corresponding author: um15ag@leeds.ac.uk

Abstract

**Introduction:** Glioblastoma Multiforme (GBM) is the most common primary malignant brain tumour, with a median survival 15-18 months with maximal treatment. Little progress has been made to alter this prognosis significantly over the past few decades. Thus, there is an urgent need to identify novel therapeutics to improve the outcomes for GBM patients.

**Methods:** A small molecule compound (KHS101) has been shown to specifically perturb GBM tumour cell metabolism. However, as with any new pro-drug, progression onto clinical trials is hampered by the significant financial and developmental burden. Therefore, we aimed to utilise a publicly available database, The Connectivity Map (CMap): L1000 Platform combined with literature mining to identify potential compounds with a similar gene expression profile linked to their mechanism of action to that of KHS101, that could then be repositioned for the treatment of GBM. The gene expression signatures of KHS101 were uploaded into CMap: L1000 to find similar effects in the embryonic kidney cell line, HA1E.

**Results:** The top twenty results closely resembling the gene expression signatures of KHS101 were selected, and through literature mining it was found that the majority of compounds had already been linked to GBM. Five compounds; Tyrphostin A9, Bithionol, BNTX, MG-132 and Brazilin, have similar characteristics to KHS101.

**Conclusions:** The five identified compounds should therefore be investigated further in patient-derived GBM cell lines and glioma stem cells (GSCs). Computational analysis has therefore shown to be promising in accelerating the progress in finding novel GBM treatments.