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Translated from Japanese

## Existing anti-cancer drug repurposed for glioblastoma treatment confirmed at Nanyang Technological University in Singapore

On May 8, Nanyang Technological University (NTU) in Singapore announced that researchers from NTU Lee Kong Chian School of Medicine (LKCMedicine) and the National Neuroscience Institute (NNI) have confirmed that an existing anti-cancer drug can be repurposed to treat advanced brain tumours. The results of the research were published in the academic journal *Neuro-Oncology*.



Glioblastoma is one of the deadliest brain tumours, with only 5% of patients surviving for more than five years. The cancer is difficult to treat and often resistant to treatment. As a result, recurrence of glioblastoma is virtually inevitable.

Currently, a chemotherapy drug called temozolomide (TMZ) is used to treat glioblastoma. TMZ damages the DNA of cancer cells and prevents them from dividing. However, many glioblastoma cancer cells acquire resistance to TMZ and grow again.

This resistance occurs because glioblastomas are composed of cell populations with different properties, and some cells adapt and resist TMZ.

To understand the cellular mechanisms behind this drug resistance and to find potential drug targets for resistant glioblastoma, the researchers compared the activity of protein kinases (enzymes involved in cell signaling pathways linked to cancer growth and metastasis) in patient-derived mesenchymal glioblastoma (ME) and proneural glioblastoma (PN) cells. They found that a class of protein kinases called mitogenactivated protein kinases (MAPKs) was activated in ME, particularly p38MAPK and MEK/ERK MAPKs.

The researchers performed an experiment in which ME cells from the patient were transplanted into mice, and found that mice treated with a combination of the p38 MAPK inhibitor ralimetinib, the MEK inhibitor binimetinib, and TMZ survived for 72.5 days, longer than mice treated with TMZ alone (63 days).

"Our study shows that glioblastoma acquires drug resistance through multiple pathways, suggesting the need for more precise treatment of this disease," said Andrew Tan, Associate Professor at LKCMedicine, co-lead of the study. The researchers plan to conduct clinical trials of this treatment. They also plan to use cutting-edge molecular profiling techniques and artificial intelligence techniques such as machine learning to improve strategic combinations and drug delivery of drugs for glioblastoma.

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