Department of Neurosurgery
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Chairman: Prof. Dr. med. Ch. Nimsky

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Gamma-Aminobutyric Acid (GABA) and Lung Cancer Metastasis

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Background

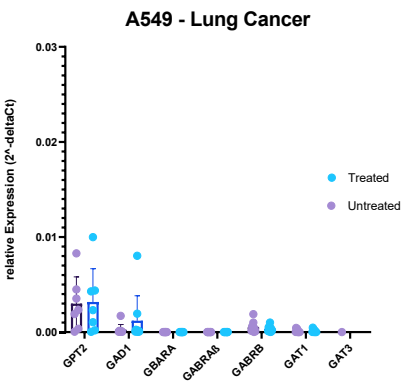
GABA is the main inhibitory neurotransmitter in the brain and can be exploited by cancer cells to support growth and survival. Brain metastases, especially from lung cancer, adapt to the neuronal environment and may use GABA as an alternative energy source via the TCA cycle, promoting tumor progression and therapy resistance..

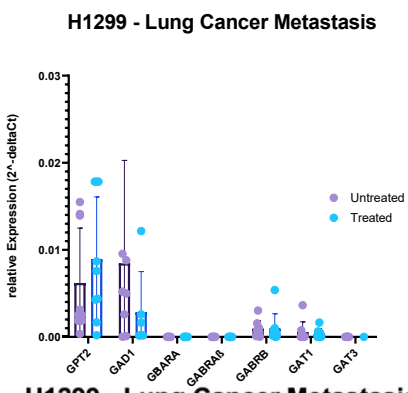
Methods

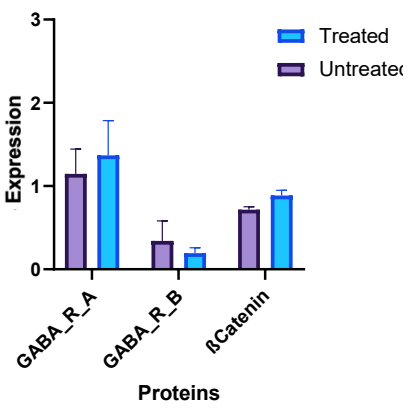
Lung cancer brain metastasis cells were cultured with 1.5 mM GABA or under respective control conditions. After 24 hours of pre-culture in standard medium, GABA was added. Gene and protein expression were analyzed using qPCR and Western Blot. In addition, proliferation (CellTiter-Glo®) and scratch migration assays were performed with and without GABA. All experiments were conducted in triplicates to ensure reproducibility.

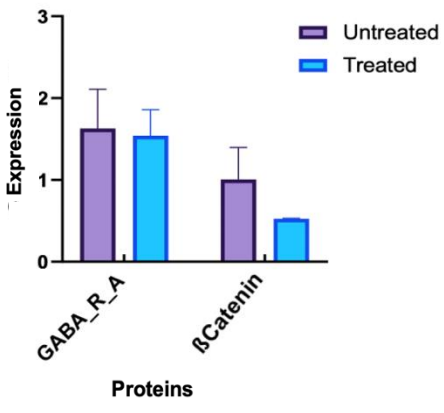
Results

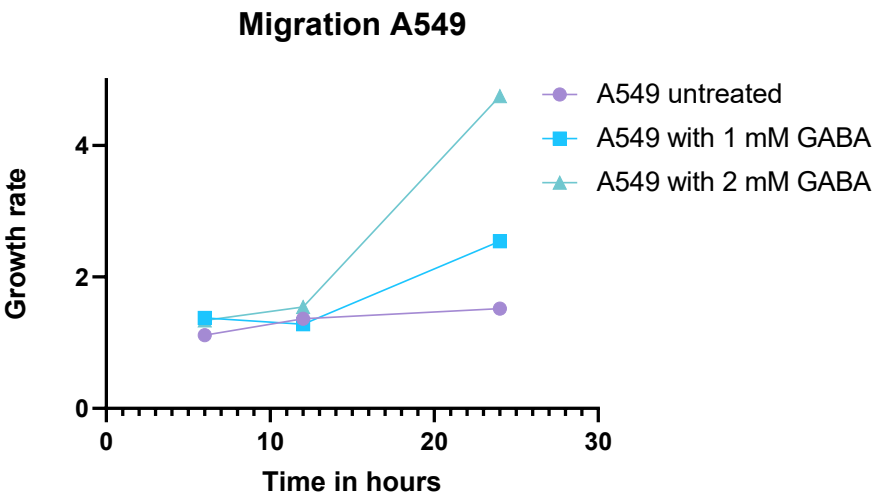
GABA treatment led to cell line-specific responses: GPT2 and GAD1 were upregulated in H1299 and A549 cells, respectively. β-Catenin and GABA A receptor increased in A549 but decreased in H1299 cells. GABA B receptor expression declined in both. Functionally, A549 cells showed increased proliferation and migration, whereas both were reduced in H1299 cells.

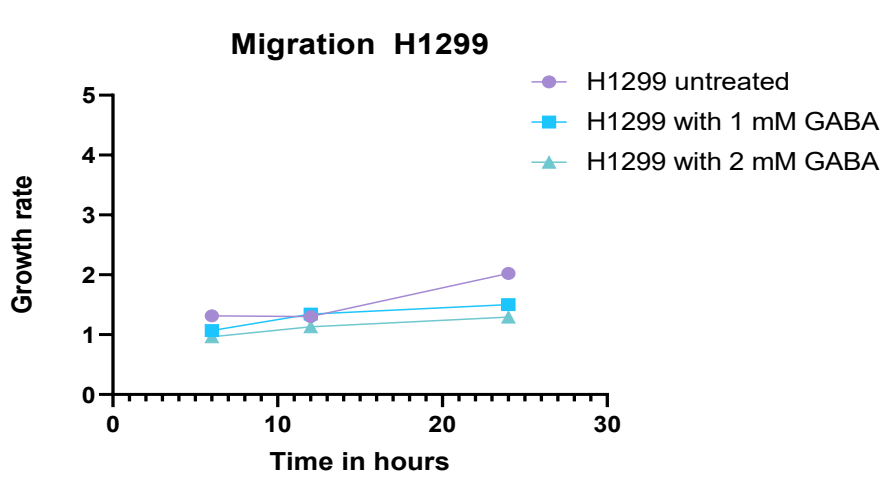


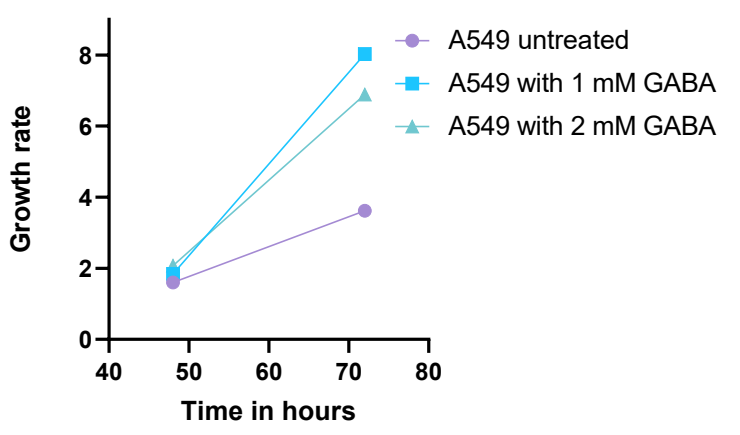


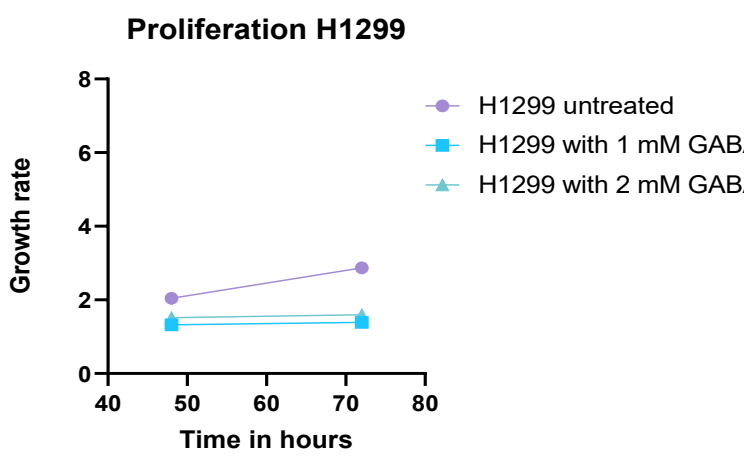












Conclusions

GABA modulates proliferation, migration, and the expression of metabolic and receptor-related genes in a cell line-specific manner. The divergent responses of A549 and H1299 cells suggest that the GABAergic system may contribute to differential adaptation mechanisms in lung cancer brain metastases, potentially offering targets for subtype-specific therapeutic intervention.

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