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Investigation Of The Effects Of Supplementary Therapy Candidate Molecules In Breaking Chemotherapy Resistance In Glioblastoma Cells And Retrospectively Supporting The Findings With Primary Tumors

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KEY WORDS (at least 5 words)

- ✓ Glioblastoma (GBM)
- ✓ Temozolomide (TMZ)
- ✓ Fisetin
- ✓ Berberine
- ✓ Drug resistance

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THESIS ABSTRACT

In the current thesis, the effects of natural compounds fisetin and berberine, which are predicted to have complementary therapy potential, alone or in combination with TMZ, to suppress anticancer properties, increase the efficacy of TMZ and increase TMZ resistance-breaking potential in TMZ-sensitive, -intrinsic and -acquired resistant cells, in normoxic and hypoxic environments was aimed to determine. In the study, acquired resistant cell line was created from the TMZ-sensitive cell line. The supportive effects of the selected molecule on the ZEB1 and MSH2 genes in overcoming drug resistance have been validated in both cell lines and primary GBM patients. All findings were investigated for the first time as a flavonoid-TMZ combination, aiming to obtain preliminary data on innovative treatment approaches and TMZ resistance in GBM.

APPLICATION AREAS OF THE THESIS RESULTS

The current project can contribute to highlight variable biomarkers in resistance mechanisms to improve both survival rates and quality of life in GBM patients with very short lifespans, and is particularly important for personalized medicine. Combination therapy used to break treatment resistance has been found to be preferable to suppress the harmful effects of a chemotherapy drug and increase its effectiveness at lower doses with natural compounds. In conclusion, our findings showed that dietary natural bioflavonoids, especially fisetin, may be a potential drug candidate as anti-cancer agent, which can both support TMZ and be effective in breaking resistance, even in different mechanisms in GBM.

ACADEMIC ACTIVITIES

Thesis Projects: THIZ-2021-747 & TYL-2023-1365

Ferah, Sena et al. "Investigation of the effects of fisetin with the combination of chemotherapy drug temozolomide to the biological behaviour of glioblastoma cells," 5th International Eurasian Virtual Conference on Biological and Chemical Sciences (EurasianBioChem) , 23-25 November 2022.

Ferah, Sena et al. "Fisetin additively affects the Temozolomide response of Glioblastoma cells under normoxia and hypoxia" Molecular oncology, 17 Suppl 1(Suppl 1), 1-597, EACR 2023: Innovative Cancer Science, 12-15 June 2023, Torino, Italy.

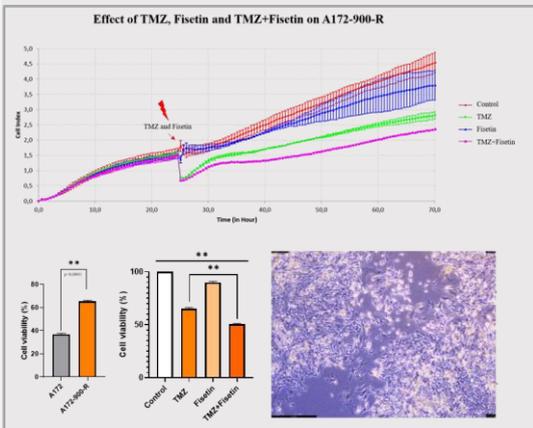


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