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Can adjuvant therapy with anti-depressant drugs influence on *Glioblastoma multiforme* stem cell population? *In vitro* studies

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Despite the substantial progress in neuro-oncological diagnostics and radiotherapy, the median survival time of patients suffering from *Glioblastoma multiforme* of the brain rarely exceeds 13 months. Aggressive character of Glioblastoma causing invasion of tumor cells deep into brain parenchyma makes a radical surgical intervention impossible which compromises the chance for cure. Thus, a limited efficacy of the presently used therapy prompts researchers to search for new solutions. The mechanisms decisive for Glioblastoma chemo resistance remain an essential and still largely unresolved problem. We perform our studies on Glioblastoma stem cells which, according to the tumor stem cell hypothesis, can be responsible for induction of tumor resistance to conventional therapies. Since a majority of Glioblastoma patients require adjuvant therapy with anxiolytic, analgesic, hypnotic and pro-cognitive drugs, the main aim of the presented experiments was to evaluate the interaction between drugs used in clinical practice (temozolomide and antidepressant drugs) on cell populations of T98G glioblastoma stem cell line. Since stereotaxic and fluorescence methods demonstrated a layered structure of Glioblastoma, characterized by areas differing in the oxygenation level, in our studies we used a comprehensive experimental *in vitro* model representing different possible histo-pathological diagnoses encountered in clinic. The studies were conducted under six experimental conditions: acute hypoxia, chronic hypoxia, moderate hypoxia, hypoxia/re-oxygenation, "physiological" conditions and standard laboratory conditions which were tested only for comparison. In each of these models, the effect of temozolomide alone or temozolomide with an antidepressant drug (imipramine, fluoxetine, amitriptyline, escitalopram, agomelatine) on cell populations of T98G glioblastoma multi-forme stem cell line was investigated using a flow cytometer (Aria, BD).

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