# Temozolomide-Resistant Human T2 and T98G Glioblastoma Cells

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The generation of tumor cells resistant to chemo- and radiation therapy is one of the unresolved problems of oncology. The study of the conditions and mechanisms of temozolomide (first-line drug in glioblastoma therapy) resistance formation is carried out on cultured cell lines. Considering the heterogeneity of glioblastomas, it is important to study the responses of different cell lines to temozolomide. The aim of this work was to obtain and characterize temozolomide-resistant T2 and T98G cell lines. The source of temozolomide was the drug Temodal® in lyophilized form for preparation of an infusion solution. T98G cells are known to be highly resistant to temozolomide; the response of T2 cells to the drug has not been studied yet. A single exposure to 1 mM temozolomide resulted in changes in T2 cell populations composition – an increase of the proportion of giant mononuclear cells and cells with fragmented nuclei. As a result, the number of cells in $G_0/G_1$ cell cycle phases decreased, while the number of polyploid cells increased by four times. The cells that reactivated proliferation and were exposed to 2 mM temozolomide for the second and third times differed morphologically and in proliferation activity from the cells that underwent a single treatment, and approximated to the intact cells in many respects. After a single incubation with 2 mM temozolomide T2 cells recovered 90% monolayer in 48 days, after the second treatment – in 13 days, and after the third exposure – in 2 days only. Temozolomide resistance formation by T2 cells was not accompanied by changes in the initially high levels of multiple drug resistance genes *ABCC1*, *ABCG2*, and *ABCB1* activities, as well as *MGMT* gene activity. The formation of temozolomide resistance in T2 glioblastoma cell culture is most likely due to the action of other mechanisms. Consequently, T2 cell line can provide a source of temozolomide-resistant cells and be used as a model of recurrent glioblastoma. T98G cells, as expected, showed an extremely high level of resistance to temozolomide. The drug at doses lower than 5 mM had no prominent effect on these cells.

*Keywords:* glioblastoma, T2, T98G, resistant cells, temozolomide, Temodal®, *MGMT*, *ABCC1*, *ABCG2*, *ABCB1*