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Effect of tiazofurin on cell cycle and apoptosis induction on C6 rat glioma cells

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Purpose: The objective of the present study was to investigate the effect of tiazofurin (TZF), an inhibitor of IMP dehydrogenase activity, on cell cycle of C6 rat glioma cells. In addition, the ability of TZF to induce apoptosis in these cells, alone or in the presence of cycloheximide, an inhibitor of de novo protein synthesis, was also studied.

Methods: Cell cycle changes, were investigated by flow-cytometric analysis of PI stained C6 cells upon 24–72 h treatment with TZF (15–60 uM) and/or cycloheximide (1 mg/ml). Apoptosis, detected by flow-cytometry as a subdiploid pick, was confirmed using TUNEL (TdT mediated dUTP nick-end labeling) technique.

Results: TZF induced accumulation of cells in Go/G1 phase with simultaneous decrease in S phase of the cell cycle in a dose dependent manner. Flow-cytometric detection of apoptosis showed 52% of apoptotic cells after 72 h incubation in the presence of 60 uM TZF. Simultaneous incubation with TZF and cycloheximide decreased percentage of apoptotic C6 cells to 17.8%. TUNEL labelling confirmed time and dose dependence of apoptosis induction.

Conclusion: TZF retarded the cell cycle progression and induced apoptosis in C6 rat glioma cells. Induction of apoptosis was in part dependent on de novo protein synthesis.