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Temozolomide-mediated radiosensitization of human glioma cells in a zebrafish embryonic system.

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Abstract

The zebrafish (Danio rerio) is a popular vertebrate model for biomedical research. The rapid development, transparency, and experimental accessibility of the embryo offer opportunities for assessing the developmental effects of anticancer treatment strategies. We therefore systematically investigated parameters for growing U251 human glioma cells expressing red fluorescent protein (U251-RFP) in zebrafish embryos. Factors optimized include injection volume, number of cells injected, anatomic site of injection, age of the embryo at the time of injection, and postinjection incubation temperature. After injection into the embryos, the U251-RFP cells proliferated and the resultant tumors, and even individual cells, could be visualized in real-time via fluorescence microscopy without the need for sacrifice. These tumors recruited host zebrafish vasculature, suggesting cancer cell-host tissue interactions. Having optimized parameters for introducing and growing these human cells in the zebrafish embryos, we exposed both embryos and transplanted cancer cells to ionizing radiation and temozolomide, either alone or in combination. The human tumors in each embryo were substantially diminished following exposure to ionizing radiation and the decrease was further enhanced by pretreatment with temozolomide. In contrast, temozolomide had no discernible effects on embryonic development. These results together support the relative safety of temozolomide during embryonic development, as well as its anticancer efficacy when combined with radiation. These results suggest the value of the zebrafish model for in vivo testing of the efficacy and safety of anticancer strategies, especially on the very young.

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