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Characterization of Fenretinide on Meningioma Cells

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Meningiomas are the most common primary brain tumors. Although the majority are benign, up to 30% are malignant and are associated with detrimental effects on both morbidity and mortality. The standard treatment for these tumors is surgery and/or radiation, but for recurring or aggressive tumors, no effective therapies are available for their treatment. Retinoids have been used with efficacy in a variety of tumor types. Their roles as differentiating agents are particularly appealing for childhood and brain tumors, and have been proposed, but not well studied in meningiomas. Fenretinide is a novel retinoid, in that unlike other agents, it has been demonstrated to induce apoptosis in cancer cells (e.g. leukemia, neuroblastoma and lung cancer). In addition, this retinoid has a favorable side effect profile. We propose to characterize the effects of fenretinide on the viability and radiosensitivity of meningiomas. We utilized three immortalized cell lines in our experiments, including IOMM-Lee, HeLa and SF3061 cells. We performed in vitro cellular assays to study the effects of varying concentrations of fenretinide in several key aspects of meningioma tumor biology. Our studies demonstrated that fenretinide has the ability to halt cell proliferation in a dose-dependent manner at physiologically relevant drug levels. Fenretinide in combination with radiotherapy had no effect on the capacity of meningioma cells to grow into colonies and in some cases, increasing doses of fenretinide resulted in radioprotection. Finally fenretinide did not seem to have much of an effect on the cell cycle of the meningioma cells. These results, suggest that fenretinide might be useful in treating meningiomas, but that care may be required to determine the best timing in association with radiation. Future studies will involve studies of the impact of fenretinide on cellular invasion, within an in vivo model of meningioma, and a phase I/II trial in meningioma patients.