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Differentiation therapy exerts antitumor effects on stem-like glioma cells.

Campos B, Wan F, Farhadi M, Ernst A, Zeppernick F, Tagscherer KE, Ahmadi R, Lohr J, Dictus C, Gdynia G, Combs SE, Goidts V, Helmke BM, Eckstein V, Roth W, Beckhove P, Lichter P, Unterberg A, Radlwimmer B, Herold-Mende C.

Division of Neurosurgical Research, Department of Neurosurgery, University of Heidelberg, Heidelberg, Germany.

Abstract

PURPOSE: Stem-like tumor cells comprise a highly tumorigenic and therapy-resistant tumor subpopulation, which is believed to substantially influence tumor initiation and therapy resistance in glioma. Currently, therapeutic, drug-induced differentiation is considered as a promising approach to eradicate this tumor-driving cell population; retinoic acid is well known as a potent modulator of differentiation and proliferation in normal stem cells. In glioma, knowledge about the efficacy of retinoic acid-induced differentiation to target the stem-like tumor cell pool could have therapeutic implications. **EXPERIMENTAL DESIGN:** Stem-like glioma cells (SLGC) were differentiated with all-trans retinoic acid-containing medium to study the effect of differentiation on angiogenesis, invasive growth, as well as radioresistance and chemoresistance of SLGCs. In vivo effects were studied using live microscopy in a cranial window model. **RESULTS:** Our data suggest that in vitro differentiation of SLGCs induces therapy-sensitizing effects, impairs the secretion of angiogenic cytokines, and disrupts SLGCs motility. Further, ex vivo differentiation reduces tumorigenicity of SLGCs. Finally, we show that all-trans retinoic acid treatment alone can induce antitumor effects in vivo. **CONCLUSIONS:** Altogether, these results highlight the potential of differentiation treatment to target the stem-like cell population in glioblastoma. Copyright (c) 2010 AACR.

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