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Spheres Isolated from 9L Gliosarcoma Rat Cell Line Possess Chemoresistant and Aggressive Cancer Stem-Like Cells

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The rat 9L gliosarcoma is a widely used syngeneic rat brain tumor model that closely simulates glioblastoma multiforme when implanted in vivo. In this study, we sought to isolate and characterize a subgroup of cancer stem-like cells (CSLCs) from the 9L gliosarcoma cell line, which may represent the tumor-initiating subpopulation of cells. We demonstrate that these CSLCs form clonal-derived spheres in media devoid of serum supplemented with the mitogens epidermal growth factor and basic fibroblast growth factor, express the NSC markers Nestin and Sox2, self-renew, and differentiate into neuron-like and glial cells in vitro. More importantly, these cells can propagate and recapitulate tumors when implanted into the brain of syngeneic Fisher rats, and they display a more aggressive course compared with 9L gliosarcoma cells grown in monolayer cultures devoid of mitogens. Furthermore, we compare the chemosensitivity and proliferation rate of 9L gliosarcoma cells grown as a monolayer to those of cells grown as floating spheres and show that the sphere-generated cells have a lower proliferation rate, are more chemoresistant, and express several antiapoptosis and drug-related genes, which may prove to have important clinical implications.

Disclosure of potential conflicts of interest is found at the end of this article.