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The role of cancer stem cells in radiation response of glioblastoma multiforme

Glioblastoma multiforme (GBM) is one of the most aggressive human malignancies with a dismal prognosis. Ionizing radiation (IR) is a standard therapy for GBM but remains only palliative because of radioresistance and tumor recurrence. The mechanisms underlying tumor radioresistance are manifold and, in part, accredited to a special subpopulation of tumorigenic cells. The so-called glioma stem cells (GSCs) are bestowed with the exclusive ability to self-renew and repopulate the tumor. GSCs are reported less sensitive to radiation-induced damage through preferential activation of DNA damage checkpoint responses and increase in DNA damage repair. During every boost of radiation GSCs become enriched and increase in number as the competing non-stem counterparts die, which leads to accelerated repopulation. We present a cellular Potts model that simulates glioma growth and radiation response. We parameterize and calibrate this model through in vitro experiments of U87-MG human glioblastoma cell line. Simulations reveal the kinetics underlying tumor radiation response and accelerated repopulation that yields aggressive recurrence. Potential GSC-associated mechanisms are analyzed in contributing the radiation-induced repulse of GBM including higher radioresistant and asymmetric division loss.