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Radioresistance of glioma stem cells: Intrinsic characteristic or property of the 'microenvironment-stem cell unit'?

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Abstract

There is increasing evidence that glioblastoma possess 'stem-like' cells, low concentrations of which can initiate a tumour. It has been proposed that these cells are radioresistant, and that this property contributes to the poor treatment outcomes of these tumours. In this paper we propose that radioresistance is not simply an intrinsic characteristic of glioma stem cells but a result of interactions between these cells and microenvironmental factors, i.e. the 'microenvironment - stem cell unit'. The critical role of the microenvironment, along with glioma stem cells, is supported directly or indirectly by the following observations: glioma stem cells have been shown to reside preferentially in specific niches, the characteristics of which are known to influence cellular responses to radiation; radiation modifies environmental factors; and, contrarily to the consistency of clinical data, in vitro experiments have reported a wide variety in the radiation response of these cells. The paper, therefore, focuses on the interaction between tumour stem cells and the microenvironment, analyzing how its various elements (endothelial cells, extracellular matrix, cytokines, nitric oxide, oxygen levels) are affected by radiation and how these might influence the response of tumour stem cells to radiation. Finally, we summarize the ongoing debate on the optimal culture conditions for glioma stem cells and the difficulties in designing assays that reliably characterize their radiation response.

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