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Stem Cell-Based Therapies and Glioblastoma: A Seminal Matter

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LETTER TO EDITOR

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To the Editor,

Glioblastoma is the most frequent malignant primary brain tumour and is also among the most aggressive and recalcitrant of cancers. Despite aggressive surgical and adjuvant oncological treatments including chemoradiotherapy, prognosis is poor and newer treatments are being explored. An excellent recent article reviews the role of stem cell-based therapies in glioblastoma [1]. The purpose of this letter is to share some observations which may add to the scope of this topical and highly relevant paper.

Tropism of certain stem cells to glioblastoma allows for their modification as vectors to carry a payload of anti-tumour therapeutics. These may include pro-drugs, pro-apoptotic and anti-proliferative factors, anti-angiogenics, immunomodulators, extracellular vesicles, oncolytic viruses, or nanoparticles as payload [1]. Furthermore, combinatorial approaches with conventional therapies have been suggested here. Among the most potent mediators of neural stem cell migration to experimental brain tumours is vascular endothelial growth factor (VEGF), whose upregulation is perpetuated by the hypoxic tumour microenvironment [2]. Anti-VEGF strategies are established therapies in glioblastoma, including bevacizumab [3]. Potentially antagonistic interactions may need to be anticipated here, including those pertaining with anti-angiogenic factors.

Another factor that warrants further scrutiny is the association between neural stem cells and tumour stem cells in glioblastoma which are implicated in tumourigenesis and recurrence [4,5]. Clinical and experimental evidence would suggest that endogenous neural stem cells are the cell of origin in glioblastoma [6]. Surgically derived tissue from normal subventricular zone (uninvolved by tumour), where neural stem cell niches are located, was shown to contain driver mutations that evolve into glioblastoma [7]. Understanding better the interactions between endogenous neural stem cells and glioblastoma cells is indicated. There may be a role in stabilising the endogenous neural stem niche to prevent propagation of glioblastoma. Better still, this subpopulation of stem cells could be engineered to deliver an above-mentioned anti-tumour therapeutic agent. In other words, there may be promise in modifying the existing neural stem cells in endogenous neurogenic niches to act as vectors (e.g., through selective transfection), as opposed to *ex vivo* modification of stem cells.

Theoretical risk of further tumourigenesis with multipotent neural stem cells is low (compared with pluripotent stem cells) [8]. In similar inference, inadvertent trophic support to tumour, as a result of stem-like behaviour, is expected to be lesser in neural stem cells. However, ultimately it will be for clinical studies to deem the role of stem cell-based therapies for glioblastoma in the future. To this end, it is satisfying to see that Phase 1 studies are underway.

Taken together, there is optimism in neural stem cells in the treatment of glioblastoma. Abadi and colleagues [1] are again congratulated on an interesting and thought-provoking review.

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Declaration of Competing Interest

The author declares that he has no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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