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The tumour ecology of quiescence: niches across scales of complexity

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Abstract

Quiescence is a state of cell cycle arrest, allowing cancer cells to evade anti-proliferative cancer therapies. Quiescent cancer stem cells are thought to be responsible for treatment resistance in glioblastoma, an aggressive brain cancer with poor patient outcomes. However, the regulation of quiescence in glioblastoma cells involves a myriad of intrinsic and extrinsic mechanisms that are not fully understood. In this review, we synthesise the literature on quiescence regulatory mechanisms in the context of glioblastoma and propose an ecological perspective to stemness-like phenotypes anchored to the contemporary concepts of niche theory. From this perspective, the cell cycle regulation is multiscale and multidimensional, where the niche dimensions extend to extrinsic variables in the tumour microenvironment that shape cell fate. Within this conceptual framework and powered by ecological niche modelling, the discovery of microenvironmental variables related to hypoxia and mechanosignalling that modulate proliferative plasticity and intratumor immune activity may open new avenues for therapeutic targeting of emerging biological vulnerabilities in glioblastoma that cannot be anticipated from genomics alone.

Keywords: Glioblastoma; cell cycle; intratumor heterogeneity; niche; quiescence; tumour ecology.

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