Evidence for label-retaining tumour-initiating cells in human glioblastoma.


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Abstract

Individual tumour cells display diverse functional behaviours in terms of proliferation rate, cell-cell interactions, metastatic potential and sensitivity to therapy. Moreover, sequencing studies have demonstrated surprising levels of genetic diversity between individual patient tumours of the same type. Tumour heterogeneity presents a significant therapeutic challenge as diverse cell types within a tumour can respond differently to therapies, and inter-patient heterogeneity may prevent the development of general treatments for cancer. One strategy that may help overcome tumour heterogeneity is the identification of tumour sub-populations that drive specific disease pathologies for the development of therapies targeting these clinically relevant sub-populations. Here, we have identified a dye-retaining brain tumour population that displays all the hallmarks of a tumour-initiating sub-population. Using a limiting dilution transplantation assay in immunocompromised mice, label-retaining brain tumour cells display elevated tumour-initiation properties relative to the bulk population. Importantly, tumours generated from these label-retaining cells exhibit all the pathological features of the primary disease. Together, these findings confirm dye-retaining brain tumour cells exhibit tumour-initiation ability and are therefore viable targets for the development of therapeutics targeting this sub-population.

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