

Glioblastoma tumors harbor a subset of viable, replication competent tetraploid tumor cells that may increase the adaptive capacity of patient tumors in response to therapy

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The presence of a high degree of heritable cellular phenotypic variation, known more simply as tumor heterogeneity, is a hallmark of aggressive solid tumors. Diverse cell types within a tumor responds differently to therapies, increasing the evolutionary capacity of tumors and allowing tumors to more rapidly adapt to therapy and other stresses. The presence of intratumor heterogeneity is a fundamental obstacle preventing the development of general treatments for cancer. Designing novel therapies that address intratumor heterogeneity is thus crucial for the long-term survival of cancer patients. Here we report the identification of proliferative and viable tetraploid tumor cell subpopulation present with Glioblastoma (GBM) tumors with chromosomal instability (CIN). Using xenograft tumor models, we demonstrate that a tetraploid cell population is maintained in xenograft tumors and that clonally expanded tetraploid cells support tumor formation and progression *in vivo*. Most importantly, we show that the tetraploid cells can be resistant to conventional therapy and are enriched within the tumor-initiating cell subpopulation. Intriguingly, cancer tetraploid cells appear to have a unique drug sensitivity profile, opening the possibility of designing therapy regimes to specifically target this tumor subpopulation in GBM patients with a CIN signature. Together these data identify GBM tetraploid tumor cells as a potentially important therapeutic target in the challenge to overcome heterogeneity in adult brain cancer.

Biography

Angus Harding received his Ph.D. from the University of Queensland in 2004, and conducted his post-doctoral research at Washington University School of Medicine in St Louis. His research focus investigating cellular signal transduction has been recognized with 20 publications, including manuscripts in Nature Cell Biology, Current Biology and Brain. He has recently begun investigating tumor biological systems, with the aim of developing a systems-level understanding of brain tumor evolution and adaptation. He has an independent research group at The University of Queensland.

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