

Polyploid tumor cells increase phenotypic heterogeneity within glioblastoma tumors

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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. A particularly dangerous cellular phenotype present within heterogeneous tumors is therapy resistance. Despite the fact that therapy resistant cells are typically rare in untreated tumors, they have repeatedly been demonstrated to be the causal agent driving disease relapse and patient death in many different cancers. Designing novel therapies that eliminate therapy resistant tumor cells from patient tumors is thus crucial for the long-term survival of cancer patients. Here, we report the identification of a proliferative, viable, and polyploid tumor cell subpopulation present within glioblastoma (GB) patient tumors. Using xenograft tumor models, we demonstrate that polyploid cell populations are maintained in xenograft tumors and that clonally expanded polyploid cells support tumor formation and progression *in vivo*. We show that the polyploid cells are resistant to conventional therapy, in part due to infrequent cell division due to a delay in the G_0/G_1 phase of the cell cycle. Polyploid tumor cells are significantly larger and more metabolically active than euploid cancer cells, and this correlates to an increased sensitivity to the effects of glycolysis inhibition. Together these data identify GB polyploid tumor cells as a potentially important subpopulation of cells that are well positioned to contribute to disease recurrence in adult brain cancer patients, and suggest tumor metabolism as a promising point of therapeutic intervention against this subpopulation.

Biography

Angus Harding completed his Ph.D. at the University of Queensland in 2004. His research interests are signal transduction, systems biology and cancer cell biology. His primary research aim is to establish a systems biology approach to adult brain cancer. Adult brain cancers are a complex, rapidly evolving disease state in which multiple cellular systems have been hijacked to drive the unregulated proliferation and invasion of tumour cells. There is a pressing need to incorporate systems biology approaches into cancer research programs to decipher the complexities of cancer biology. His hope is that this approach will contribute to delivering better drug regimes to patients.

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