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De-differentiation: A critical malignant phenotype in glioblastoma

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Glioblastoma is an aggressive tumor of the brain incorporating various malignant processes including angiogenesis, hypoxia, metastasis, elevated expression of cancer stem cell markers and de-differentiation. Our study focuses on CCF-STTGI (Grade IV Human Astrocytoma) cells, which have undergone de-differentiation, showed more cancer stem cell-like characteristics and thus resembled high grade glioma. The astrocytic origin of the de-differentiated cells was confirmed by analyzing GFAP and S100 β , which are key markers of glial cells. The levels of some cancer stem cell markers, including CD133, CD44, ABCG2, Sox-2, integrin- α 6, and Ep-CAM were significantly up-regulated in de-differentiated CCF-STTGI cells. Three dimensional tumour spheroid forming capacity was markedly higher in de-differentiated cells. Significantly, high tubule forming capability was observed in de-differentiated cells using an *in vitro* tubule formation assay. Furthermore, hypoxic studies were carried out by inducing both nutritional and physical stress, which revealed high angiogenic potential of de-differentiated cells. We have also analyzed the phosphorylation profiles of kinases and their protein substrates, which are critical for understanding the cellular response to changes in their environment. De-differentiated cells have shown significant change in the expression levels of mitogen activated protein kinases (MAPKs), like p38 α , CREB, and p70S6 kinase, along with ERK1/2. In conclusion, our data demonstrates key insights into the malignant transformation following de-differentiation of cells. Our findings hold promising potential for the development of therapeutics to target de-differentiation of tumors, which can lead to an aggressive form of drug resistant glioblastoma.

Biography

Narinderbir Singh has completed his Bachelor of Science (Biotechnology) from Guru Nanak Dev University, Amritsar, India, and Master of Science (Biotechnology) from Swinburne University of Technology. He is currently pursuing his PhD at Deakin University, School of Medicine, Australia. He was awarded Deakin University School of Medicine Post Graduate Research Scholarship for a PhD in 2012. He had previously presented his work at International Nanomedicine Conference, Sydney 2014, and in Brain Research Symposium, Melbourne 2014.

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