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Identification of a progenitor cell of origin capable of generating diverse meningioma histological subtypes.

Kalamarides M, Stemmer-Rachamimov AO, Niwa-Kawakita M, Chareyre F, Taranchon E, Han ZY, Martinelli C, Lusic EA, Hegedus B, Gutmann DH, Giovannini M.

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Abstract

Meningiomas are among the most common primary central nervous system tumours in adults. Studies focused on the molecular basis for meningioma development are hampered by a lack of information with regard to the cell of origin for these brain tumours. Herein, we identify a prostaglandin D synthase-positive meningeal precursor as the cell of origin for murine meningioma, and show that neurofibromatosis type 2 (Nf2) inactivation in prostaglandin D2 synthase (PGDS) (+) primordial meningeal cells, before the formation of the three meningeal layers, accounts for the heterogeneity of meningioma histological subtypes. Using a unique PGDSCre strain, we define a critical embryonic and early postnatal developmental window in which biallelic Nf2 inactivation in PGDS (+) progenitor cells results in meningioma formation. Moreover, we identify differentially expressed markers that characterize the two major histological meningioma subtypes both in human and mouse tumours. Collectively, these findings establish the cell of origin for these common brain tumours as well as a susceptible developmental period in which signature genetic mutations culminate in meningioma formation. *Oncogene* advance online publication, 17 January 2011; doi:10.1038/onc.2010.609.

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