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Detection of microsatellite instability and loss of heterozygosity of DVL1, DVL2 and DVL3 gene in astrocytic brain tumors

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Astrocytomas are the most common and deadliest form of primary brain tumours. According to the WHO classification, there are four grades of astrocytoma, considering their histology, molecular characteristics and prognosis. Despite recent advances in understanding the molecular basis of development and progression of astrocytomas, additional research is required to develop more effective therapies. Although aberrant functioning of Wnt signalling pathway has been detected in variety of human cancers, little is known about its role in astrocytoma. We aim to investigate the incompletely understood role of Dishevelled (DVL) gene family, which is considered to be the central hub of Wnt signalling. In the present study, DNA isolated from 80 human astrocytoma with different clinical grades and their matched blood samples were analysed for PCR/loss of heterozygosity (LOH)/microsatellite instability (MSI), by using polymorphic microsatellite markers D1S468 and D1S243 for DVL1, D1S17960 for DVL2 and D3S1262 for DVL3 gene. Constant presence of microsatellite instability was observed in all loci investigated and in each astrocytoma grade, while allelic loss of polymorphic repeats was present mainly in high grade astrocytoma. The highest frequency of MSI was identified at locus D1S468 (27%), while D1S243, D17S960 and D3S1262 markers showed 14.3%, 16% and 18% of MSI of all informative cases, respectively. Marker D1S468 showed statistically significant difference of MSI between grades (p=0.016). LOH was found in 4.5%, 6.6%, 20% and 16% of analysed heterozygous samples for markers D1S468, D1S243, D17S960 and D3S1262, respectively. These data show that astrocytoma harbor defective cellular DNA MMR mechanisms and suggest that MSI is an early event in brain tumorigenesis while LOH may occur at a later stage.

Taken together, these data indicate that most cancers commonly have several predefined and ordered event trajectories, which might be crucial in understanding specific tumour biology, and in providing new opportunities for early detection and cancer prevention.