Spetses Summer School

an EACR - FEBS advanced lecture course

Molecular Mechanisms in Signal Transduction and Cancer

August 16 - 24, 2017
Anargyrios and Korgialenios School
Spetses, Greece

Invited speakers

René Bernards Hans Bos Boudewijn Burgering
Ivan Dikic Caroline Dive Clare Isacke
Richard Marais Madelon Maurice René Medema
George Mosialos Joan Seoane Peter Sicinski
Matthew Vander Heiden (IUBMB) Mike Yaffe

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deadline: April 1, 2017

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Changes in gene structure and protein expression of DVL1, DVL2, DVL3 and transcription factors TCF1 and LEF1 in astrocytic brain tumors

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Astrocytic brain tumors are the most common primary CNS neoplasm and are classified into 4 malignancy grades according to the WHO. In the present study key players of Wnt signaling DVL1, DVL2, DVL3, TCF1 and LEF1 were investigated in the set of 80 human astrocytoma. Genetic changes were analysed by PCR/LOH/MSI method by using polymorphic microsatellite markers D1S468 and D1S243 for DVL1, D1S17960 for DVL2 and D3S1262 for DVL3 gene. Protein expression and localization were examined by immunohistochemistry. Constant presence of microsatellite instability was observed in all loci investigated in almost every astrocytoma grade, while allelic loss 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 21,4%, 18% 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%, 8,6%, 20% and 18% 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. The results on protein expressions of DVL1, DVL2 and DVL3 showed moderate or strong expression in glioblastoma tissues in 32.4%, 71,7% and 82.4% of samples respectively. Our findings demonstrated that transcription factors of the Wnt pathway were upregulated. Strong TCF1 and LEF1 expression was observed in 52.5% and 70% of glioblastomas while astrocytoma grade I showed almost opposite expression levels with weak or no expression in the 61.1% for both proteins. Expressions of DVL3, TCF1 and LEF1 were mutually correlated and significantly associated with the histological malignancy grade.

Our findings suggest that molecular changes of wnt signaling play important roles in astrocytic tumor etiology. The novel molecular features may provide resource for future investigative efforts to understand the pathogenesis mechanisms, tumor biology and ultimately develop effective therapies against this deadly cancer.