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Expression of notch signaling pathway genes in human astrocytic gliomas of different WHO grades

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A strocytic gliomas are the most common type of brain malignancies accounting for more than half of all brain tumors. Though these tumors have been classified into four grades based on their malignancy, it is more appropriate to differentiate by discovering dysregulated pathways which can be used as biomarkers for diagnosis. Notch signaling is one such pathway which plays an important role in determining cell fates and is involved in cell proliferation, differentiation, and apoptosis. Since it is found to play a critical role in oncogenesis, we investigated the role of Notch signaling in astrocytic gliomas, with an aim to identify biomarkers. Using Real time PCR, we assessed the expression of Notch pathway genes including receptors (Notch-1, Notch-2, Notch-3 and Notch-4), ligands (Delta-Like ligand 3, Jagged-1 and Jagged-2), downstream targets (HEY2 and HES1) as well as activators and inhibitors (Deltex-1 and NUMB) along with other genes involved in the pathway in 18 formalin fixed paraffin embedded (FFPE) patient samples of different WHO grades and compared it with normal FFPE brain samples. We show that Notch-1 is overexpressed in 14 out of 18 tumor samples and Notch-3 is overexpressed in 7 out of 18 tumor samples. However the ligands showed low expression compared to non-neoplastic tissue. mRNA of Hes1 but not Hey2, both of which are major downstream molecules of the Notch pathway, was also down regulated. Our results clearly show that Notch pathway genes particularly Notch-1 is dysregulated and can be used as a biomarker for a more precise diagnosis of astrocytic gliomas. Further, studies are required to understand specific molecular events to discover more functional markers characteristic of each stage.

Biography

Narayanappa Rajeswari is an associate professor and member of Indian Association for Cancer Research (IACR). She has 18 International and 7 National publications. In 1994, she got Young Scientist Award by Indian Society of Human Genetics. Presently, she is engaged (i) to identify and characterize genes involved in the development and progression of human cancers; (ii) to understand mechanisms of the alterations in carcinogenesis; (iii) to translate the basic research outcomes into clinical research that will eventually improve detection, diagnosis, prognosis, prevention and treatment of human cancers.

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