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August 2006, 65:8 > Exploring the Distinctive Biological...

< Previous | Next >

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Exploring the Distinctive Biological Characteristics of Pilocytic and Low-Grade Diffuse Astrocytomas Using Microarray Gene Expression Profiles.

Original Articles

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Abstract:


Although World Health Organization (WHO) grade I pilocytic astrocytomas and grade II diffuse astrocytomas have been classified for decades as different clinicopathologic entities, few, if any, data are available on the biologic features explaining these differences. Although more than 50 microarray-related studies have been carried out to characterize the molecular profiles of astrocytic tumors, we have identified only 11 that provide sound data on low-grade astrocytomas. We have incorporated these data into a comparative analysis for the purpose of identifying the most relevant molecular markers characterizing grade I pilocytic and grade II diffuse astrocytomas. Our analysis has identified various interesting genes that are differentially expressed in either grade I or grade II astrocytomas when compared with normal tissue and/or high-grade (WHO grade III and IV) astrocytomas. A large majority of these genes encode adhesion, extracellular matrix, and invasion-related proteins. Interestingly, a group of 6 genes (TIMP4, C1NH, CHAD, THBS4, IGFBP2, and TLE2) constitute an expression profile characteristic of grade I astrocytomas as compared with all other categories of tissue (normal brain, grade II, and high-grade astrocytomas). The end products (proteins) of these genes act as antimigratory compounds, a fact that could explain why pilocytic astrocytomas behave as compact (well-circumscribed) tumors as opposed to all the other astrocytic tumor types that diffusely invade the brain parenchyma. Having validated these molecular markers by means of real-time reverse transcriptase-polymerase chain reaction, an integrated model was proposed illustrating how and why

pilocytic astrocytomas constitute a distinct biologic and pathologic entity when compared with diffuse astrocytomas.

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