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Possible interactions between HDACs and TGF-beta/ Smads pathway in Glioblastoma

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Glioblastoma (GBM) is the most common and aggressive tumor of the Central Nervous System (CNS). Unfortunately, patients afflicted with this disease have a very poor prognosis, due to high level of invasiveness and resistance to standard therapies (1). Although the molecular profile of GBM has been extensively investigated, the events responsible for its pathogenesis and progression remain largely unknown. Reports have indicated that HDAC (Histone deacetylases) dependent epigenetic modifications (2) and the Tgfβ/Smad pathway (3) play roles in GBM tumorigenesis. The aim of this study was to evaluate the involvement and the possible interaction between these two molecular cascades in the pathogenesis, therapeutic responsiveness and prognosis of GBM. Immunohistochemestry (IHC) was performed on microdissected GBM samples, collected from 14 patients (n.8 men and n.6 women) ranging in age from 43 to 74 years. The patients were previously divided, on the basis of their overall survival (OS), into three groups: low, intermediate and high OS. Patients with poor prognosis showed hyperexpression of HDAC4 and HDAC6, an activation of the Tgfβ/Smad pathway, with high levels of IL-13, Smad2, PDGF and MMP3 expression, compared to the intermediate and high OS groups, whereas the expression of Smad7 was reduced. The high OS group also exhibits an increase in p21 immunostaining, which represents a common target of the two cascades. The IHC data was confirmed by Immunoblotting. Our results suggest that both HDAC4 and HDAC6 together with the Tgfβ/Smad pathway are involved in progression of GBM and could be a useful prognostic markers and may predict responsive to therapy.

References

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Keywords

GBM; HDAC; Tgfβ; Smad.