High TGFβ-Smad Activity Confers Poor Prognosis in Glioma Patients and Promotes Cell Proliferation Depending on the Methylation of the PDGF-B Gene

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Summary

TGFβ acts as a tumor suppressor in normal epithelial cells and early stage tumors, and becomes an oncogenic factor in advanced tumors. The molecular mechanisms involved in the malignant function of TGFβ are not fully elucidated. We demonstrate that high TGFβ-Smad activity is present in aggressive, highly proliferative gliomas and confers poor prognosis in patients with glioma. We discern the mechanisms and molecular determinants of the TGFβ oncogenic response using a transcriptomic approach and analyzing primary cultured patient-derived gliomas and human glioma biopsies. The TGFβ-Smad pathway promotes proliferation through the induction of PDGF-B in gliomas with an unmethylated PDGF-B gene. The epigenetic regulation of the PDGF-B gene dictates whether TGFβ acts as an oncogenic factor inducing PDGF-B and proliferation in human glioma.