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Celecoxib can induce vascular endothelial growth factor expression and tumor angiogenesis.

Xu K, Gao H, Shu HK.

Corresponding Author: Hui-Kuo G. Shu, Department of Radiation Oncology, Emory University School of Medicine and Emory Winship Cancer Institute, 1365 Clifton Road, NE, Room C-3082, Atlanta, GA 30322. hgshu@emory.edu.

Abstract

Increased COX-2 expression has been linked to increased angiogenesis and a worse prognosis in patients with malignant gliomas and other tumor types. This led to our interest in assessing the response of glioma cell lines to treatment with celecoxib, a selective COX-2 inhibitor. However, contrary to its reported antiangiogenic effects, treatment with celecoxib actually induced the expression of VEGF in multiple glioma as well as other cancer cell lines. This induction of VEGF was comparable to, if not greater than, that found after exposure of cells to hypoxia. Pharmacologic inhibition and siRNA silencing of p38-mitogen-activated protein kinase and the Sp1 transcription factor revealed their involvement in this celecoxib-induced VEGF expression. Consistent with the documented role of Sp1 in this effect, VEGF induction was found to involve transcriptional activation and not to change the stability of VEGF mRNA. The biological significance of this effect was confirmed in vivo by showing both induction of VEGF expression and microvessel density in tumor xenografts and increased angiogenesis in a matrigel plug assay in nude mice that were administered celecoxib. We speculate that treatment with celecoxib may, in some instances, enhance tumor cell expression of VEGF as well as angiogenesis and, consequently, may have detrimental effects on the response of tumors to this drug. *Mol Cancer Ther*; 10(1); 138-47. ©2011 AACR.

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