

Promoter region methylation and reduced expression of thrombospondin-1 after oxygen-glucose deprivation in murine cerebral endothelial cells.

許重義

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Abstract

Angiogenesis is induced in response to ischemia. Thrombospondin-1 (TSP-1) is a potent angiostatic factor. Silencing of TSP-1 expression may contribute to the postischemic angiogenesis. Upregulation of TSP-1, in contrast, may terminate the postischemic angiogenesis. A possible mechanism that silences TSP-1 expression is the DNA methylation of its promoter region. DNA methylation has been reported following cerebral ischemia. The present study aimed to explore whether methylation of the promoter region of TSP-1 regulates its expression after oxygen-glucose deprivation (OGD) in murine cerebral endothelial cells (CECs) in vitro. Sublethal OGD increased the extent of methylation of the promoter region of TSP-1 with a concurrent decrease in TSP-1 mRNA and protein expression in CECs. After reoxygenation, demethylation of the TSP-1 promoter region led to the restoration of TSP-1 mRNA and protein expression. The extent of methylation of the promoter region of TSP-1 was inversely correlated with the extent of TSP-1 gene expression at mRNA and protein levels after OGD. Oxygen-glucose deprivation-induced reduction in the TSP-1 mRNA level was not accompanied by a change in mRNA stability. These findings raise the possibility that OGD downregulation of TSP-1 expression is at least in part due to methylation of its promoter region.