Hypoxia induces discoidin domain receptor-2 expression via the p38 pathway in vascular smooth muscle cells to increase their migration

徐國基

Chen SC;Wang BW;Wang DL;Shyu KG

摘要

Abstract

Discoidin domain receptor- 2 (DDR2) is a receptor tyrosine kinase that binds to the extracellular matrix. We investigated the role of hypoxia in DDR2 expression in vascular smooth muscle cells (VSMCs) and the underlying mechanism. Subjecting VSMCs to hypoxia (2.5% O2) induced DDR2 expression; treatments with a specific inhibitor (SB203580) of p38 mitogen-activated protein kinase (MAPK) or p38-specific small interference RNA (siRNA) abolished this hypoxia-induced DDR2 expression. Gel shifting assays showed that hypoxia increased the Myc-Max-DNA Myc–Max–DNA binding activity in the promoter region of DDR2; inhibition of p38 MAPK activation by SB203580 and p38-specific siRNA blocked hypoxia-induced DDR2 promoter activity. Hypoxia also induced matrix metalloproteinase- 2 (MMP-2) activity in VSMCs and increased their migration. These VSMC responses to hypoxia were inhibited by DDR2- and p38-specific siRNAs. Our results suggested that hypoxia induces DDR2 expression in VSMCs at the transcriptional level, which is mediated by the p38 MAPK pathway and contributes to VSMC migration.