

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

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摘要: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.