CX-4945, a small molecule inhibitor of CK2, inhibits angiogenesis by affecting the vascular endothelium and suppressing hypoxia-activated Hif-1α transcription


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Abstract

CK2 is a catalytically serine/threonine kinase that is implicated in multiple pathways involved in cancer progression including angiogenesis. Silenced CK2 activity has been associated with malignant transformation and suppression tumor growth. CX-4945 activity results in inhibition of proliferation and migration through disruption of CK2 signal transduction. CX-4945 inhibition results in suppression of angiogenesis in a variety of xenograft models.

Keywords: CK2, angiogenesis, tumor growth, CX-4945

Introduction

CK2 is an evolutionarily conserved serine/threonine kinase that plays a key role in the regulation of cellular proliferation and survival. It is an important modulator of pro-angiogenic signaling pathways and is overexpressed in a variety of human cancers. CX-4945, a small molecule inhibitor of CK2, has been shown to inhibit proliferation and migration of endothelial cells in vitro and in vivo.

Materials and Methods

2D and 3D models of human cancer cell lines were used to determine the effects of CX-4945 on cell proliferation and migration. In vivo studies were performed in nude mice bearing xenografts of human cancer cell lines. Tumor volume was measured and analyzed using calcein AM assay and migration was assessed using CellTiter-Glo. The effects of CX-4945 on hypoxia-induced Hif-1α transcription were determined using luciferase reporter assay.

Results

CX-4945 inhibited proliferation and migration of endothelial cells in vitro. CX-4945 also inhibited proliferation and migration in vivo. The effects of CX-4945 on tumor growth were determined using Southern blot analysis and migration was assessed using CellTiter-Glo. The effects of CX-4945 on hypoxia-induced Hif-1α transcription were determined using luciferase reporter assay.

Conclusion

CX-4945 is a potent inhibitor of CK2 that suppresses angiogenesis and inhibits tumor growth. The results of this study provide evidence for the potential of CX-4945 as a therapeutic agent for the treatment of cancer.

References


CX-4945 Inhibits Migration of Pancreatic Adenocarcinoma BxPC-3 Cells

Effect of CX-4945 on Akt signaling and inhibition of HUVEC Proliferation

CX-4945 Reduces Expression/Secretion of IL-6 in BxPC-3 Cells

CX-4945 Inhibits Migration of Pancreatic Adenocarcinoma BxPC-3 Cells

CX-4945 Reduces Microvessel Density in Prostate Cancer PC3 Xenograft Model

References


Key references shown in brackets

Abbreviations:

HIF-1α: hypoxia-inducible factor-1 alpha
HIF: hypoxia inducible factor
Akt: protein kinase B
P53: tumor suppressor gene
pVHL: von Hippel-Lindau tumor suppressor gene
CK2: casein kinase 2
HUVEC: human umbilical vein endothelial cell
PCR: polymerase chain reaction
ELISA: enzyme-linked immunosorbent assay
HDAC: histone deacetylase
OH: hydroxylation
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Highlights

• CX-4945 is a potent inhibitor of CK2 that suppresses angiogenesis and inhibits tumor growth.
• The effects of CX-4945 on hypoxia-induced Hif-1α transcription were determined using luciferase reporter assay.
• CX-4945 inhibited proliferation and migration in vivo.

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