CDK7 inhibitor BS-181 Small Molecule (Tool Compound)

Catalogue number: 151712
Sub-type: Inhibitor
Images:

Contributor

Inventor: R Charles Coombes
Institute: Imperial College
Images:

Tool details

***FOR RESEARCH USE ONLY**

Name: CDK7 inhibitor BS-181 Small Molecule (Tool Compound)

Alternate name:

Class:
Conjugate:
Description: BS-181 is a highly selective CDK inhibitor for CDK7 (and with lower selectivity to other kinases) with antitumoral activity in vitro and no apparent toxicity. Cyclin-dependent protein kinases (CDKs) have a central function in the regulation of cell proliferation, apoptosis and gene expression. CDK7 regulates the activation of CDK1, CDK2, CDK4, CDK5 and CDK6 and is involved in the regulation of transcription as part of the transcription factor TFIIHcomplex. A common feature of cancer is the over-expression of CDK7, making it an attractive target for anti-cancer drug development. The pyrazolo[1,5-a] pyrimidine compound BS-181 is a highly selective CDK7 inhibitor (IC50: 21 nM) with 42-fold selectivity over CDK2 (IC50: 880 nM), which is the only other CDK that is inhibited in concentrations lower than 1 M. In MCF-7 cells, BS-181 inhibited the phosphorylation of CDK7 substrates, promoted cell cycle arrest and apoptosis to inhibit the growth of cancer cell lines, and showed antitumor effects in vivo. The compound was stable in vivo with a plasma elimination half-life in mice of 405 minutes after i.p. administration of 10 mg/kg. The same dose of compound inhibited the growth of MCF-7 human xenografts in nude mice.
Purpose: Inhibitor
Parental cell:
Organism:
Tissue:
Model:
Gender:
Isotype:
Reactivity:
Selectivity: More than 40-fold selective for CDK7 than CDK1, 2, 4, 5, 6, or 9.
Host:
Immunogen:
Immunogen UNIPROT ID:
Sequence:
Growth properties:
Production details:
Formulation:
Recommended controls:
Bacterial resistance:
Selectable markers:
Additional notes:

Target details

Target:

Target alternate names:

Target background:

Molecular weight: 416.99

Ic50: 21 nM

Applications

Application: BS-181 is stable in vivo with a plasma elimination half-life in mice of 405 minutes after i.p. administration of 10 mg/kg. BS-181 inhibits the growth of MCF-7 xenografts in the nude mice model in a dose-dependent manner, with 25% and 50% reduction in tumor growth after 2 weeks of treatment at 10 mg/kg/day and 20 mg/kg/day, respectively without apparent toxicity. BS-181 is a small molecule inhibitor of CDK7 in a cell-free environment, which displays more potential activity than roscovitine with IC 50 of 510 nM. Among the CDKs and other 69 kinases from many different classes, BS-181 shows high inhibitory selectivity for CDK7, inhibits CDK2 at concentrations lower than 1 Î?M which being inhibited 35-fold less potently (IC50 with 880 nM) than CDK7, shows slight inhibition for CDK1, CDK4, CDK5, CDK6 and CDK9 with IC50 values higher than 3.0 Î?M, and only shows inhibition for several kinases from other classes at high concentrations (>10 Î?M). BS-181 promotes cell cycle arrest and inhibits the cancer cell growth of a range of tumor types, including breast, lung, prostate and colorectal cancer with IC50 in the range of 11.5-37 Î?M. In MCF-7 cells, BS-181 inhibits the phosphorylation of the CDK7 substrate RNA polymerase II COOH-terminal domain (CTD), and promotes cell cycle arrest and apoptosis to inhibit the growth of cancer cell lines.
Application notes:

Handling

Format:
Concentration:
Passage number:
Growth medium:
Temperature:
Atmosphere:
Volume:
Storage medium:
Storage buffer:
Storage conditions: Ambient
Shipping conditions: Dry Ice

Related tools

Related tools: CDK inhibitor BS-194 Small Molecule (Tool Compound)

References

References: Barvaux et al. 2004. Mol Cancer Ther. 3: 1215-20 (PMID: 15426188)