Inhibitors, Agonists, Screening Libraries
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Data Sheet

Product Name: PKC412
Cat. No.: HY-10230
CAS No.: 120685-11-2
Molecular Formula: C35H30N4O4
Molecular Weight: 570.64
Target: PKC
Pathway: Epigenetics; TGF-beta/Smad
Solubility: DMSO: ≥ 21 mg/mL

BIOLGICAL ACTIVITY:

PKC412 is an inhibitor of protein kinase C (PKC) and can inhibit other kinases including PKC isoforms (α, β, γ), PDK1, PDGFRβ, VEGFR2, Syk, PKCη, Flk-1, Flt3, Cdk1/B, PKA, c-Kit, c-Fgr, c-Src, VEGFR1 and EGFR.

In Vitro: PKC412 shows a broad antiproliferative activity against various tumor and normal cell lines in vitro, and is able to reverse the Pgp-mediated multidrug resistance of tumor cells in vitro. Exposure of cells to PKC412 results in a dose-dependent increase in the G2/M phase of the cell cycle concomitant with increased polyploidy, apoptosis and enhanced sensitivity to ionizing radiation[1]. Midostaurin with ponatinib induced substantial inhibition of KIT-, Lyn-, and STAT5 activity, but did not suppress Btk in HMC-1 cells and primary neoplastic mast cells[2]. PKC412 inhibits EN fusion tyrosine kinase in hematopoietic Ba/F3 cells. PKC412 significantly inhibits EN phosphorylation in M0-91 and IMS-M2 cells in a dose-dependent manner[3].

In Vivo: PKC412 strongly inhibits retinal neovascularization as well as laser-induced choroidal neovascularization in murine models[1]. PKC412 (25 mg/kg, i.p.) protects mouse livers of the K18 Arg90Cys-overexpressing transgenic mice from Fas-induced apoptosis[4].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: PKC412 is dissolved in DMSO[3]. Proliferation is determined by trypan blue dye exclusion test. Cells in suspension are seeded in six-well plates at a density of 1×10^5 cells/mL in the presence of different concentrations of PKC412 for 3 days. In control wells, DMSO instead of PKC412 is added. After the treatment, 10 μL of the cell suspension is mixed with 10 μL of 0.4% trypan blue, and alive cells are counted manually using a hemacytometer. Results are calculated as the percentage of the values measured when cells are grown in the absence of the reagent. All experiments are performed in triplicate.

Animal Administration: PKC412 is dissolved in DMSO[4]. K8-deficient, K18-deficient, and human K18 R90C-overexpressing mice with age of 6-8 weeks are used in the assay. Age and sex matched mice are treated with PKC412 (25 mg/kg), daily for 4 d or with an equal volume of DMSO as vehicle (both administered intraperitoneally). On day 5 post-treatment, apoptosis is induced by intraperitoneal injection of Fas ligand (Fas-L) (0.15 μg/g body weight). Mice are fasted overnight before Fas Ab injection, and 18 mice are used per DMSO or PKC412 group for the Fas-treated mice while 6 mice are used per DMSO or PKC412 group for the control non-Fas-treated mice. Mice are sacrificed by CO₂ inhalation 6 h after Fas Ab injection. Blood is collected by intracardiac puncture, and livers are harvested for hematoxylin and eosin (HE) staining (after fixation in 10% formalin) or frozen in optimum cutting temperature compound for immunofluorescence staining.

References:

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