Inhibitors, Agonists, Screening Libraries

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Data Sheet

Product Name: PKC412
Cat. No.: HY-10230
CAS No.: 120685-11-2
Molecular Formula: C_{35}H_{30}N_{4}O_{4}
Molecular Weight: 570.64
Target: PKC
Pathway: Epigenetics; TGF–beta/Smad
Solubility: DMSO: ≥ 21 mg/mL

BIOLOGICAL ACTIVITY:
PKC412 is an inhibitor of protein kinase C (PKC) and can inhibit other kinases including PKC isoforms (α, β, γ), PDFRβ, VEGFR2, Syk, PKCθ, 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:
[2]. Gleixner KV, et al. Synergistic growth–inhibitory effects of ponatinib and midostaurin (PKC412) on neoplastic mast cells carrying KIT D816V.

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