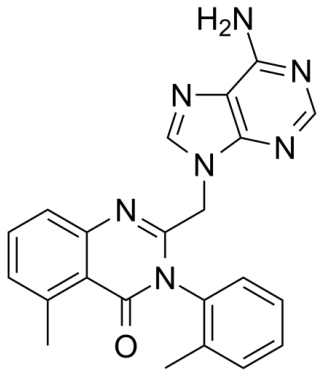
Data Sheet

Product Name:	IC-87114
Cat. No.:	CS-0184
CAS No.:	371242-69-2
Molecular Formula:	C22H19N7O
Molecular Weight:	397.43
Target:	PI3K
Pathway:	PI3K/Akt/mTOR
Solubility:	DMSO : 10 mg/mL (25.16 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

IC-87114 is a potent and selective **PI3Kδ** inhibitor with **IC_{50}** of 0.5 μM. IC50 & Target: IC50: 0.5 μM (PI3Kδ)[1] **In Vitro:** IC-87114 (IC87114), an analog of the original inhibitor, is synthesized and tested for PI3Kδ selectivity relative to the other class I PI3Ks. The IC_{50} of IC87114 for PI3Kδ inhibition is 0.5 μM whereas the IC_{50} values for PI3Kα, PI3Kβ, and PI3Kγ are >100, 75, and 29 μM, respectively. Thus IC87114 is 58-fold more selective for PI3Kδ relative to PI3Kγ, and over 100-fold selective relative to PI3Kα and PI3Kβ. IC87114 selectively antagonizes PI3Kδ over at least a concentration range of 0.3-10 μM[1]. IC-87114 (10 μM) is also used to selectively inhibit PI3Kδ catalytic activity to address this question. IC87114 (10 μM) effectively inactivates Akt in macrophages after treatment for 1 hour (n=6; P<0.001 versus control). The effect of IC-87114 (IC87114) is next detected ton AP-1 DNA-binding activity. The electrophoretic mobility shift assay assay demonstrates that DNA-binding activity of AP-1 is significantly increased after the treatment with TNF-α (10 ng/mL; P<0.001) and TNF-α (20 ng/mL; P<0.001). IC87114 alone induces AP-1 DNA-binding activity after treatment for 1 hour. Furthermore, there is stronger AP-1 DNA-binding activity after costimulation of IC87114 (10 μM) and TNF-α (0-20 ng/mL) than only treatment with TNF-α (0-20 ng/mL; n=5; P<0.01). IC87114 (10 μM) also effectively inhibits p110δ catalytic activities (Akt phosphorylation) in macrophages with or without TNF-α treatment for 24 hours (n=6; P<0.001)[2]. **In Vivo:** Treatment with PD 89059 (10 mg/kg), IC-87114 (0.3 mg/kg) and BAY 11-7085 (10 mg/kg), significantly (P<0.05) reduces the OVA- induced inflammatory cell influx into the airways and the histopathological airway remodeling. However, these treatments does not significantly improve OVA induced-AHR (P>0.05). Of note, the observed reduction in the histopathological airway remodeling induced by PD 89059, IC-87114 and BAY 11-7085 are less effective as compared to the reduction seen with AG 1478 and SU6656[3].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: [2]The murine macrophage cell line RAW264.7 and peritoneal macrophages from both types of mice are maintained in Dulbecco's modified Eagle's medium (DMEM) with 10% fetal calf serum (FCS). Cultures are maintained at 37°C in a humidified incubator in a 95% O_2 plus 5% CO_2 atmosphere. Cells are treated with varied concentrations of TNF-α and used IC-87114 (IC87114) to inhibit PtdIns(3,4,5)P3-dependent phosphorylation of Akt before TNF-α stimulation at early time points (30 min)[2].

Animal Administration: [3]Mice[3]

BALB/c mice are immunized once by i.p. injection of 10 μg ovalbumin (OVA) in 0.2 ml of alu-Gel-S on day 0. Ten days later, mice are intranasally (i.n.) challenged with OVA (30 μg in 50 μL PBS) or PBS, once daily, over four consecutive days. To investigate if ERK1/2, PI3Kδ and NF-κB are signaling effectors downstream of EGFR transactivation, six treatment groups (A-F, 10-30 animals per group) are established. Mice in groups A and B are pretreated intranasally with 0.2 mL of the vehicle for the drugs. Groups C, D and E are pretreated with the same volume of three different drugs (PD 98059, IC-87114 and BAY 11-7085, respectively) at 10 mg/kg, 10 mg/kg and 0.3 mg/kg respectively, and group F with Dexamethasone (1 mg/kg), 1 h before each i.n. challenge with OVA. These doses are chosen from previous studies where they are shown to be effective.

References:

[1]. Sadhu C, et al. Essential role of phosphoinositide 3-kinase delta in neutrophil directional movement. J Immunol. 2003 Mar 1;170(5):2647-54.

[2]. Zheng L, et al. Inactivation of PI3Kδ induces vascular injury and promotes aneurysm development by upregulating the AP-1/MMP-12 pathway in macrophages. Arterioscler Thromb Vasc Biol. 2015 Feb;35(2):368-77.

[3]. El-Hashim AZ, et al. Src-dependent EGFR transactivation regulates lung inflammation via downstream signaling involving ERK1/2, PI3Kδ/Akt and NFκB induction in a murine asthma model. Sci Rep. 2017 Aug 30;7(1):9919.

CAIndexNames:

4(3H)-Quinazolinone, 2-[(6-amino-9H-purin-9-yl)methyl]-5-methyl-3-(2-methylphenyl)-

SMILES:

O=C1N(C(CN2C3=C(C(N)=NC=N3)N=C2)=NC4=CC=CC(C)=C14)C5=C(C)C=CC=C5

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