

Product Data Sheet

Product Name: RBC8
Cat. No.: GC10906

Chemical Properties

Cas. No. 361185-42-4

Chemical Name 6-amino-4-(2,5-dimethoxyphenyl)-3-(naphthalen-2-yl)-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile

SMILES COC1=CC(C2C(C#N)=C(N)OC3=C2C(C4=CC=C5C(C=CC=C5)=C4)=NN3)=C(OC)C=C1

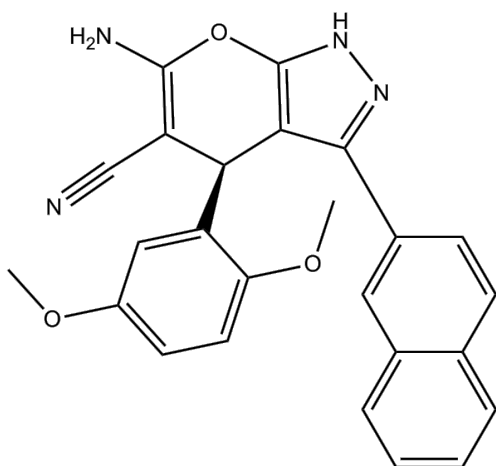
Formula $C_{25}H_{20}N_4O_3$ M.Wt 424.45

Solubility DMF: 30 mg/mL, DMSO: 30 mg/mL, DMSO:PBS(pH 7.2) (1:2): 0.33 mg/mL, Ethanol: 0.25 mg/mL Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Caution: Product has not been fully validated for medical applications. For research use only.

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Cell lines J82 cells

Preparation method The solubility of this compound in DMSO is > 10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Reacting condition 0–15 µM, 1h

Applications In J82 cells overexpressing FLAG-RalA, treatment with RBC8 for 1h reduced the activation of RalA. RBC8 dose-dependently inhibited cell spreading in WT MEF cells. RBC8 treatment inhibited colony formation in H2122 and H358 cell lines with the IC₅₀ of 3.5 µM and 3.4 µM, respectively.

Animal experiment [1]:

Animal models H2122 and H358 human lung cancer xenograft mice models

Dosage form Intraperitoneal injection, 50 mg/kg/d for 21 days

Application In mice bearing H358 and H2122 xenografts, RBC8 (50 mg/kg i.p.) inhibited tumor growth via specific inhibition of RalA and RalB.

Other notes Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

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References:

[1]. Yan C, Liu D, Li L, et al. Discovery and characterization of small molecules that target the Ral GTPase. Nature, 2014, 515(7527): 443-447.

Background

RBC8 inhibit Ral GTPase with IC₅₀ values of 3.5 μ M and 3.4 μ M in Ral-dependent lines H2122 and H358 [1].

RalA and B are Ras-like GTPases. They are important drivers of metastasis and tumor growth [1].

RBC8 reduced the activation of RalA in living cells. Ral is required for spreading murine embryonic fibroblasts (MEFs) and lipid raft exocytosis on fibronectin-coated cover slips. In these cells, the spreading of WT MEFs was inhibited by the depletion of RalA via siRNA, whereas caveolin deficient (Cav1^{-/-}) MEFs were resistant to RalA depletion. Treatment with RBC8 inhibited only the cell spreading in the WT MEFs, it did not inhibited the cell spreading in Cav1^{-/-} MEFs. A Ral pull-down assay showed that RBC8 inhibited the activation of both RalA and RalB in both the H2122 and H358 cell lines. In H2122 and H358 cells with Ral knockdown by siRNA, treatment with RBC8 did not show further inhibition of colony formation [1].

In nude mice inoculated with H2122 human lung cancer cells subcutaneously, treatment with RBC8 at 50 mg/kg/d for 21 days (except weekends) intraperitoneally showed an inhibitory effect on tumor growth to a similar extent as dual knockdown of RalA and B. H358 is a lung cancer line. In this cell line, similar results were yielded [1].

Reference:

[1]. Yan C, Liu D, Li L, et al. Discovery and characterization of small molecules that target the Ral GTPase. Nature, 2014, 515(7527): 443-447.

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