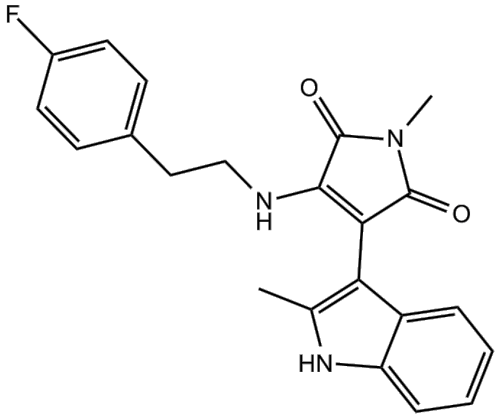
Product Data Sheet

Product Name: IM-12
Cat. No.: GC16617

Chemical Properties

Cas. No.	1129669-05-1		
SMILES	FC1=CC=C(C=C1)CCNC2=C(C(N(C)C2=O)=O)C3=C(C)NC4=CC=CC=C34		
Formula	$C_{22}H_{20}FN_3O_2$	M.Wt	377.41
Solubility	≥ 18.85mg/mL in DMSO	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

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Kinase experiment: Cells are lysed in RIPA buffer, supplemented with protease and phosphatase inhibitors and centrifuged for 5 min at 15,000 rpm. Immunoprecipitation of GSK-3β is performed with a specific mouse monoclonal anti GSK-3β [G8] antibody with 5 μg/sample for 2 h at 4°C. The bound protein is precipitated with Protein A/G-Plus agarose-beads (10 μL beads per sample). GSK-3β kinase activity is measured in a reaction mixture containing final concentrations of: 4 mM MOPS pH 7.2; 0.4 mM EDTA; 1 mM EGTA; 2.5 mM β-glycerophosphate; 4 mM MgCl2; 40 μM BSA; 0.05 mM DTT. 10 μg/sample pGS-2 peptide substrate is used[1].

Cell experiment: To measure viable cells, 50-100 μL of cell suspension is analyzed using CASY technology with the appropriate program. ReNcell VM cells are seeded at a defined cell number and proliferated for 24 h. Then the medium is changed to proliferation medium with added substances at indicated concentrations. The cell number is determined every 24 h. Cells are exposed to the added drugs during the whole experiment, whereas the media is changed every 24 h[1].

References:

[1]. Schmole AC, et al. Novel indolylmaleimide acts as GSK-3beta inhibitor in human neural progenitor cells. Bioorg Med Chem. 2010 Sep 15;18(18):6785-95.

Background

IM-12 is a potent inhibitor of GSK-3β with IC50 value of 53 nM [1].

Glycogen synthase kinase-3β (GSK-3β) is a proline-directed serine-threonine kinase and is involved in neuronal cell development, energy metabolism and body pattern formation. Inhibition of GSK-3β can cause β-catenin accumulation.

IM-12 is a potent GSK-3β inhibitor. In ReNcell VM cells, IM-12 significantly increased total β-catenin by 27% and at a concentration of 3 μM increased the β-catenin amount most. In ReNcell VM cells, IM-12 (3 μM) inhibited GSK-3β to a remaining activity of 27 ± 5%. Also, IM-12 significantly increased

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the cell doubling time to 26.5 ± 0.9 h and significantly inhibited cell proliferation. In ST14A cells, IM-12 caused an accumulation of β-catenin around the nucleus. In ReNcell VM cells transfected with TOPFlash, IM-12 increased TCF-activity. In cells transfected with TOP and pCAGGS-S33Y (a vector containing β-catenin), IM-12 significantly increased TCF-activity by 270%. In ReNcell VM cells, IM-12 significantly increased the level of βIIItub+ cells to 3.7 ± 0.7%, which suggested that IM-12 increased neuronal differentiation [1].

Reference:

[1]. Schmöle AC, Brennführer A, Karapetyan G, et al. Novel indolylmaleimide acts as GSK-3beta inhibitor in human neural progenitor cells. Bioorg Med Chem, 2010, 18(18): 6785-6795.

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