FR 180204

Cat. No.: HY-12275
CAS No.: 865362-74-9
Molecular Formula: C₁₈H₁₃N₇
Molecular Weight: 327.34
Target: ERK
Pathway: MAPK/ERK Pathway; Stem Cell/Wnt
Storage: Powder  -20°C  3 years
         4°C    2 years
         In solvent  -80°C  6 months
                   -20°C  1 month

SOLVENT & SOLUBILITY

In Vitro  DMSO : ≥ 50 mg/mL (152.75 mM)
* “≥” means soluble, but saturation unknown.

Preparing Stock Solutions

<table>
<thead>
<tr>
<th>Solvent Mass</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>3.0549 mL</td>
<td>15.2746 mL</td>
<td>30.5493 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.6110 mL</td>
<td>3.0549 mL</td>
<td>6.1099 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.3055 mL</td>
<td>1.5275 mL</td>
<td>3.0549 mL</td>
</tr>
</tbody>
</table>

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description  FR 180204 is an ATP-competitive, selective ERK inhibitor with $K_i$ of 0.31 μM and 0.14 μM for ERK1 and ERK2, respectively.

IC₅₀ & Target  

<table>
<thead>
<tr>
<th>ERK2</th>
<th>ERK1</th>
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</thead>
<tbody>
<tr>
<td>0.14 μM (Ki)</td>
<td>0.31 μM (Ki)</td>
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</table>

In Vitro  In AP-1-transfected cells, FR180204 dose-dependently inhibits AP-1 transactivation with IC₅₀ of 3.1 μM[1]. FR 180204 inhibits spontaneous mesothelioma cell growth[2].

In Vivo  FR180204 (100 mg/kg, i.p., b.i.d.) significantly decreases the severity of symptoms and body weight loss in collagen-induced arthritis mice[2]. In a mouse model of dengue virus (DENV) infection, FR180204 limits hepatocyte apoptosis, reduces DENV-induced liver injury, and improves clinical parameters[4].
PROTOCOL

Kinase Assay [1]

Nunc-Immuno MaxiSorp plates are coated with 20 μg/mL MBP solution in phosphate-buffered saline (PBS). After washing with PBS containing 0.05% Tween 20 (T-PBS), blocking buffer (T-PBS containing 3% BSA) is added to each well and the plates are incubated for 10 min at room temperature. After washing with T-PBS, chemical compounds, ATP and recombinant ERK2 diluted in assay dilution buffer (20 mM Mops, pH 7.2, 25 mM β-glycerol phosphate, 5 mM EGTA, 1 mM sodium orthovanadate, 1 mM dithiothreitol, and 50 μg/mL BSA) and are added to each well. Vehicle groups (containing 0.1% DMSO) and kinase-withdrawal groups are used for the control and basal determinations. After incubation for 1 h at room temperature, plates are washed twice with T-PBS. Anti-phospho MBP antibody (0.2 μg/mL) is added to each well, and the plates are incubated for 1 h at room temperature. After washing, anti-mouse HRP-conjugated polyclonal antibodies are added and the plates are incubated for 30 min.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Administration [2]

In brief, mice are randomized and grouped by body weight immediately before treatment. Bovine CII is dissolved in 0.1mol/Lacetic acid at the concentration of 10 mg/mL and then emulsified in an equal volume of Freund’s complete adjuvant H37Rv. Apart from a naive group, each mouse is immunized with 25 μL of the CII emulsion into the tail base, followed by a boost injection 3 weeks after primary injection (day 0). FR180204 and methylprednisolone are ground and suspended in 0.1% methylcellulose solution to a volume of 5 mL/kg. Drugs are given by twice daily intraperitoneal injection from days 0 to 12 in accordance with pharmacokinetic studies with superior area under the curve and Cmax values of i.p. versus s.c. or p.o. administration. The initial administration is 30 min before the boost CII injection. The clinical score of arthritis is obtained by summing the visual severity grade of each limb, scored as follows: 0, no arthritis; 1, one swollen digit; 2, two or more swollen digits or swelling of the entire paw without ankylosis; 3, gross swelling with ankylosis of the paw. Body weight is measured on day 12.

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REFERENCES


