**PP121**

Cat. No.: HY-10372  
CAS No.: 1092788-83-4  
Molecular Formula: C₁₇H₁₇N₇  
Molecular Weight: 319.36  
Target: mTOR; PDGFR; VEGFR; Src  
Pathway: PI3K/Akt/mTOR; Protein Tyrosine Kinase/RTK  
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: 20 mg/mL (62.63 mM; Need ultrasonic)

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Solvent Concentration</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 mM</td>
<td>3.1313 mL</td>
<td>15.6563 mL</td>
<td>31.3126 mL</td>
</tr>
<tr>
<td></td>
<td>5 mM</td>
<td>0.6263 mL</td>
<td>3.1313 mL</td>
<td>6.2625 mL</td>
</tr>
<tr>
<td></td>
<td>10 mM</td>
<td>0.3131 mL</td>
<td>1.5656 mL</td>
<td>3.1313 mL</td>
</tr>
</tbody>
</table>

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

### In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline  
   Solubility: ≥ 2 mg/mL (6.26 mM); Clear solution

2. Add each solvent one by one: 10% DMSO >> 90% corn oil  
   Solubility: ≥ 2 mg/mL (6.26 mM); Clear solution

3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)  
   Solubility: ≥ 2 mg/mL (6.26 mM); Clear solution

**BIOLOGICAL ACTIVITY**

**Description**  
PP121 is a multi-targeted kinase inhibitor with IC₅₀s of 10, 60, 12, 14, 2 nM for mTOR, DNK-PK, VEGFR2, Src, PDGFR, respectively.

<table>
<thead>
<tr>
<th>IC₅₀ &amp; Target</th>
<th>mTOR</th>
<th>PDGFR</th>
<th>VEGFR2</th>
<th>Src</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10 nM (IC₅₀)</td>
<td>2 nM (IC₅₀)</td>
<td>12 nM (IC₅₀)</td>
<td>14 nM (IC₅₀)</td>
</tr>
</tbody>
</table>
**In Vitro**

PP121 blocks the PI3K pathway by direct inhibition of PI3K/mTOR in two glioblastoma cell lines, U87 and LN229. PP121 potently inhibits the proliferation of a diverse panel of tumor cell lines containing mutations in the PI3-K pathway components PIK3CA, PTEN, or RAS. PP121 induces a G0/G1 arrest in most tumor cells. PP121 directly inhibits Src in cells and reverses its biochemical and morphological effects. PP121 potently inhibits the Ret kinase domain in vitro (IC50<1 nM). PP121 potently blocks VEGF stimulated activation of the PI3-K and MAPK pathways. PP121 inhibits VEGFR2 autophosphorylation at low nanomolar concentrations, confirming that this molecule directly targets VEGFR2 in cells. PP121 inhibits Bcr-Abl induced tyrosine phosphorylation in K562 cells as well as BaF3 cells that express Bcr-Abl[1].

**In Vivo**

Oral administration of PP121 remarkably inhibits Eca-109 xenograft growth. Mice body weights are not significantly affected by PP121 or the vehicle treatment. PP121 oral administration dramatically inhibits activations of Akt-mTOR and NFkB in xenograft tumors. p-Akt Ser 473 and p-IKKa/b are both inhibited by PP121 administration[2].

### PROTOCOL

#### Kinase Assay [1]

Purified kinase domains are incubated with inhibitors (PP121) at 2- or 4-fold dilutions over a concentration range of 50-0.001 µM or with vehicle (0.1% DMSO) in the presence of 10 µM ATP, 2.5 µCi of γ-32P-ATP and substrate. Reactions are terminated by spotting onto nitrocellulose or phosphocellulose membranes, depending on the substrate; this membrane is then washed 5-6 times to remove unbound radioactivity and dried. Transferred radioactivity is quantitated by phosphorimaging and IC50 values are calculated by fitting the data to a sigmoidal doseresponse using Prism software[1].

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

#### Cell Assay

Cells grown in 96-well plates are treated with PP121 at 4-fold dilutions (10 µM - 0.040 µM) or vehicle (0.1% DMSO). After 72 h cells are exposed to Resazurin sodium salt (22 µM) and fluorescence is quantified. IC50 values are calculated. For proliferation assays involving single cell counting, non-adherent cells are plated at low density (3–5% confluence) and treated with drug (2.5 µM) or vehicle (0.1% DMSO). Cells are diluted into trypan blue daily and viable cells counted using a hemocytometer[1].

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

#### Animal Administration [2]

Mice: Eca-109 cells are injected into the axillary regions of nude mice (5×10^6 cells/mouse). When the tumor volumes reach around 200 mm^3, the mice are randomly separated to three groups: Untreated control, PP121 (30 mg/kg) and vehicle (10% 1-methyl-2-pyrrolidinone and 90% PEG 300) group. Tumor volumes and the mice body weights are measured every 10 d[2].

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

### REFERENCES


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

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