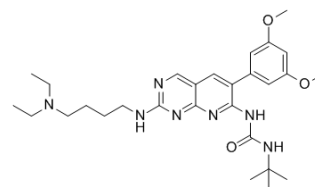


## Data Sheet

Product Name:	PD173074
Cat. No.:	HY-10321
CAS No.:	219580-11-7
Molecular Formula:	C <sub>28</sub> H <sub>41</sub> N <sub>7</sub> O <sub>3</sub>
Molecular Weight:	523.67
Target:	FGFR; VEGFR
Pathway:	Protein Tyrosine Kinase/RTK
Solubility:	DMSO: ≥ 52 mg/mL



### BIOLOGICAL ACTIVITY:

PD173074 is a potent **FGFR1** inhibitor with **IC<sub>50</sub>** of 25 nM and also inhibits **VEGFR2** with **IC<sub>50</sub>** of 100-200 nM, 1000-fold selective for FGFR1 than PDGFR and c-Src.

IC<sub>50</sub> & Target: IC<sub>50</sub>: 25 nM (FGFR1), 100-200 nM (VEGFR2)

**In Vitro:** PD 173074 inhibits autophosphorylation of FGFR1 in a dose-dependent manner with an IC<sub>50</sub> in the range 1-5 nM. PD 173074 is an ATP-competitive inhibitor of FGFR1 with an inhibitory constant (K<sub>i</sub>) of 40 nM<sup>[1]</sup>. PD 173074 and SU 5402 produce concentration-dependent reductions in FGF-2 enhancement of granule neuron survival, with IC<sub>50</sub> values of 8 nM and 9 μM, respectively. PD 173074 does not inhibit neurotrophic and neuritogenic actions of FGF-2 signalling molecules in cerebellar granule neurons. PD 173074 and SU 5402 concentration-dependently inhibits the neurite growth response, when tested on FGF-2-treated granule neurons growing on polylysine/laminin, with IC<sub>50</sub>s of 22 nM and 25 μM, respectively<sup>[2]</sup>. PD173074 effectively antagonizes the effect of FGF-2 on proliferation and differentiation of OL progenitors in culture. Mitogen-activated protein kinase (MAPK) activation, a downstream event after activation of either FGFR or PDGFR, is also blocked by PD173074 in OL progenitors stimulated with FGF-2 but not PDGF<sup>[3]</sup>.

**In Vivo:** PD 173074 (1 mg/kg, i.p.) exhibits dose-dependent inhibition of FGF-induced neovascularization and angiogenesis in mice<sup>[1]</sup>. D173074 (25 mg/kg, p.o.) significantly inhibits tumor growth in mice<sup>[4]</sup>.

### PROTOCOL (Extracted from published papers and Only for reference)

**Cell Assay:** <sup>[1]</sup>An NIH 3T3 cell line overexpressing VEGFR2 (Flk-1) has been described previously. This cell line also expresses FGFR1 endogenously. Cells (1×10<sup>6</sup>) in DMEM supplemented with 10% calf serum are seeded in 10 cm<sup>2</sup> dishes and allowed to grow for 48 h. The medium is then removed and the cells are made quiescent in starvation medium (DMEM with 0.1% calf serum). After 18 h, the cells are incubated for 5 min with various concentrations of PD 173074 prepared in starvation medium. The cells are then stimulated with growth factor [VEGF (100 ng/mL) or aFGF (100 ng/mL) and heparin (10 μg/mL)] for 5 min at 37°C. The cells are washed with ice-cold PBS and lysed in 1 mL of lysis buffer (25 mM HEPES pH 7.5, 150 mM NaCl, 1% Triton X-100, 10% glycerol, 1 mM EGTA, 1.5 mM MgCl<sub>2</sub>, 1 mM PMSF, 10 μg/mL aprotinin, 10 μg/mL leupeptin) containing phosphatase inhibitor (0.2 mM Na<sub>3</sub>VO<sub>4</sub>). For inhibition studies of FGFR1, cell lysates are immunoprecipitated with antibodies to FGFR1, and then analyzed by SDS-PAGE and immunoblotting with antibodies to phosphotyrosine. For inhibition studies of VEGFR2, cell lysates (20 μL) are analyzed directly by SDS-PAGE and immunoblotted with antibodies to phosphotyrosine. **Animal Administration:** PD173074 is dissolved in 0.05 mol/L lactic acid buffer.<sup>[4]</sup> Six-week-old athymic nude mice are inoculated subcutaneously with 3×10<sup>5</sup> NIH 3T3 cells expressing Y373C FGFR3 and Ras V12. Intraperitoneal injections of either 20 mg/kg PD173074 or 0.05 mol/L lactic acid buffer are initiated on the day of tumor injection and continued for 9 days. Ten mice for each experiment are included.

### References:

- [1]. Mohammadi M, et al. Crystal structure of an angiogenesis inhibitor bound to the FGF receptor tyrosine kinase domain. *EMBO J.* 1998 Oct 15; 17(20):5896-904.
- [2]. Skaper SD, et al. The FGFR1 inhibitor PD 173074 selectively and potently antagonizes FGF-2 neurotrophic and neurotropic effects. *J Neurochem.* 2000 Oct;75(4):1520-7.
- [3]. Bansal R, et al. Specific inhibitor of FGF receptor signaling: FGF-2-mediated effects on proliferation, differentiation, and MAPK activation are inhibited by PD173074 in oligodendrocyte-lineage cells. *J Neurosci Res.* 2003 Nov 15;74(4):486-93.
- [4]. Trudel S, et al. Inhibition of fibroblast growth factor receptor 3 induces differentiation and apoptosis in t(4;14) myeloma. *Blood.* 2004 May 1; 103(9):3521-8.
- [5]. Mahe M, et al. An FGFR3/MYC positive feedback loop provides new opportunities for targeted therapies in bladder cancers. *EMBO Mol Med.* 2018 Feb 20. pii: e8163.

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

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