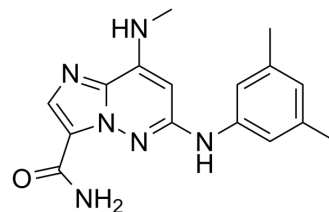


TyK2-IN-2

Cat. No.:	HY-101762												
CAS No.:	2098466-94-3												
Molecular Formula:	C ₁₆ H ₁₈ N ₆ O												
Molecular Weight:	310.35												
Target:	JAK; Phosphodiesterase (PDE)												
Pathway:	Epigenetics; JAK/STAT Signaling; Protein Tyrosine Kinase/RTK; Stem Cell/Wnt; Metabolic Enzyme/Protease												
Storage:	<table border="0"> <tr> <td>Powder</td> <td>-20°C</td> <td>3 years</td> </tr> <tr> <td></td> <td>4°C</td> <td>2 years</td> </tr> <tr> <td>In solvent</td> <td>-80°C</td> <td>6 months</td> </tr> <tr> <td></td> <td>-20°C</td> <td>1 month</td> </tr> </table>	Powder	-20°C	3 years		4°C	2 years	In solvent	-80°C	6 months		-20°C	1 month
Powder	-20°C	3 years											
	4°C	2 years											
In solvent	-80°C	6 months											
	-20°C	1 month											



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 25 mg/mL (80.55 mM)
 * "≥" means soluble, but saturation unknown.

Concentration	Mass		
	1 mg	5 mg	10 mg
1 mM	3.2222 mL	16.1108 mL	32.2217 mL
5 mM	0.6444 mL	3.2222 mL	6.4443 mL
10 mM	0.3222 mL	1.6111 mL	3.2222 mL

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

BIOLOGICAL ACTIVITY

Description

TyK2-IN-2 (Compound 18) is a potent and selective TYK2 inhibitor with IC₅₀s of 7 nM, 0.1 μM and 0.05 μM for TYK2 JH2, IL-23 and IFNα, respectively. TyK2-IN-2 also inhibits phosphodiesterase 4 (PDE4) with an IC₅₀ of 62 nM. TyK2-IN-2 can be used for the research of inflammatory and autoimmune diseases^[1].

IC₅₀ & Target

Tyk2 JH2 7 nM (IC ₅₀)	PDE4 62 nM (IC ₅₀)
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In Vitro

A co-crystal structure of TyK2-IN-2 (Compound 18) bound to the TYK2 JH2 is solved. First, limited room between C8 and the hinge is seen, consistent with the loss in affinity seen with groups larger than methylamino at this position. There are also hydrogen bonds revealed between the NH of the C8 methylamine and from N1 of the IZP core to the 'hinge' (Val690). Additional hydrogen bonds are observed from the oxygen of the C3 amide to Lys642 and to the hinge carbonyl of Glu688 through a bridging water molecule. The pocket proximal to the C3 amide of the TYK2 JH2 domain contains a combination of residues which are largely unique relative to the kinome such as a small residue (Ala671) under the "gatekeeper" (Thr687)

and the replacement of the highly kinase-conserved DFG motif by DPG which alters the positioning of the conserved catalytic Lys642 and Asp759. The ability of the C3 amide to fit and bind to this pocket is believed to be a key source of kinome selectivity for TyK2-IN-2 (Compound 18)^[1].

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

REFERENCES

[1]. Moslin R, et al. Identification of imidazo[1,2-b]pyridazine TYK2 pseudokinase ligands as potent and selective allosteric inhibitors of TYK2 signalling. Medchemcomm. 2016 Dec 15;8(4):700-712.

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

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