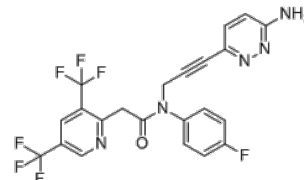


**Product Name** : RP-6685  
**Cat. No.** : PC-49348  
**CAS No.** : 2832047-80-8  
**Molecular Formula** : C<sub>22</sub>H<sub>14</sub>F<sub>7</sub>N<sub>5</sub>O  
**Molecular Weight** : 497.377  
**Target** : DNA/RNA Synthesis  
**Solubility** : 10 mM in DMSO



1. Bubenik M, et al. *J Med Chem.* 2022 Oct 13;65(19):13198-13215.

## Biological Activity

RP-6685 (RP6685) is a potent, selective and orally bioavailable inhibitor of **DNA polymerase theta (Polθ)** with IC<sub>50</sub> of 5.8 nM in PicoGreen assay (0.3 nM Polθ enzyme).

RP-6685 displays no inhibition against Pols α, ε, γ, ν (IC<sub>50</sub> values >100 uM).

RP-6685 is extremely potent with an IC<sub>50</sub> of 550 pM against the pol activity of full-length Polθ and inactive on the ATPase activity.

RP-6685 treated cells isolated from tumors showed a modest trend toward increased micronuclei and γH2AX, which are hallmarks of DNA damage.

RP-6685 treatment caused a dosedependent decrease in MMEJ-mediated DNA repair in treated HEK293 cells, RP-6685 exhibited a potency of 0.5 uM in DSB repair of AAVS1 loci.

RP-6685 (80 mg/kg) showed tumor regression in an HCT116 BRCA2-/- mouse tumor xenograft model.

## References

