

Reference model: <i>R.i.</i> RT				
	Prp8	HCV NS5B	TERT	HIV RT
Dali <i>de novo</i> search Z-score	15.4	14.9	8.9	7.4
TM-score	0.698	0.682	0.534	0.505
Dali pairwise alignment Z-score	15.4	14.6	11.2	10.5
Reference model: <i>R.i.</i> RT- Δ RT0				
TM-score	0.700	0.671	0.646	0.586
Dali pairwise alignment Z-score	12.3	12.0	12.2	10.5

Supplementary Table 1: TM-align scores and Dali pairwise alignment Z-scores for the alignment between *R.i.* RT domain and various RT or RT-like domains. The *de novo* Dali search was only performed using complete *R.i.* RT monomer (*R.i.* RT, top row) as the query structure because *R.i.* RT monomer without the RT0 motif (*R.i.* RT- Δ RT0) failed to identify additional significant hits besides Prp8 and HCV NS5B. In structural alignments, either the complete *R.i.* RT monomer (*R.i.* RT, top rows) or the *R.i.* RT monomer without the RT0 motif (*R.i.* RT- Δ RT0, bottom rows) were used as references as indicated in the table heading. The target structures for comparison are the finger and palm subdomains from Prp8 (PDBID: 4I43, residues 882–1303)³², HCV RNA polymerase (PDBID: 1C2P, residues 1–385)⁴², TERT (PDBID: 3DU6, residues 151–406)⁴⁰ and HIV RT p66 subunit (PDBID: 2HMI, residues 1–246)⁴¹. The TM-scores were produced by TM-align⁴⁴ with a value between 0–1. Higher TM-score indicates higher structural similarity. The Dali pairwise alignment Z-scores were produced by the Dali pairwise alignment server⁴³ and similarly higher Z-score suggests higher structural similarity.