

**Supplementary information, Table S1A.** RNA-binding affinities of wild-type and mutant YTH<sup>YTHDF2</sup>

YTH <sup>YTHDF2</sup>	m6A RNA			A-RNA One-step binding mode Kd (μM)
	One-step binding mode Kd (μM)	Two-step binding mode Kd (μM)		
		First step	Second step	
wild-type	6.90	2.54	79.13	21.39
R411A	17.26	7.81	1063	51.58
R441A	19.20	7.35	302	44.32
K416A	62.75	-		112.7
R527A	62.94	-		222.0
W432A	16.46	-		15.16
W486A	17.61	-		17.81

FP assays were performed using wild-type and mutant YTH<sup>YTHDF2</sup> toward unmodified RNA (A-RNA) and m6A-RNA. The binding affinities were calculated according to one- and two-step binding modes as indicated in Figure S1A.