



Supplementary information, Figure S1 (A) Structural superimposition of free (palecyan) and m^6A bound YTH-YTHDF2 (blue). The key residues involved in m^6A recognition are shown in sticks and the mononucleotide m^6A is shown in yellow stick.

(B) Trp432, Trp486 and Trp491 form an aromatic cage for m^6A reading. The distances between the N6-methyl moiety of m^6A mononucleotide and the aromatic cage residues are indicated by the dashed lines in orange.

(C) Structural superimposition of the YTH domain of human YTHDF2 (YTH-YTHDF2, shown in blue ribbon representation) with human YTHDC1 (YTH-YTHDC1, shown in yellow ribbon representation) and *Zygosaccharomyces rouxii* ZrMRB1 (YTH-ZrMRB1, shown in gray ribbon representation).

(D) Structural superimposition of aromatic cages of the YTH domains. The residues forming the aromatic cage in YTH-YTHDF2 (Trp432, Trp486, and Trp491) and the corresponding residues of YTH-YTHDC1 (Trp377, Trp428, and Leu439) and YTH-ZrMRB1 (Trp200, Trp254, and Tyr260) are shown as blue, yellow, and gray sticks, respectively. The m^6A s anchored in YTH-YTHDF2, YTH-YTHDC1, and YTH-ZrMRB1 are depicted as yellow, cyan, and purple lines, respectively.