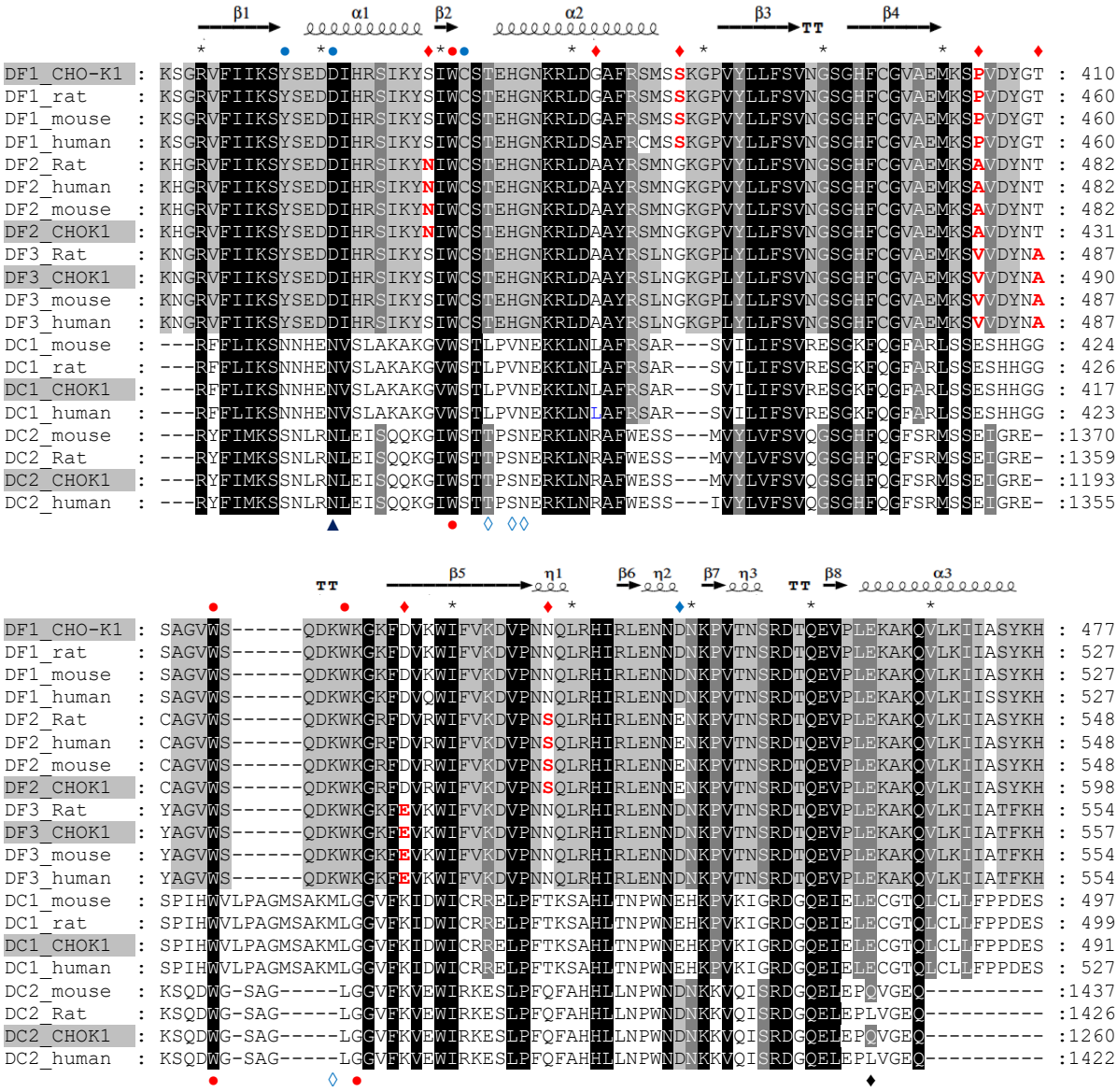
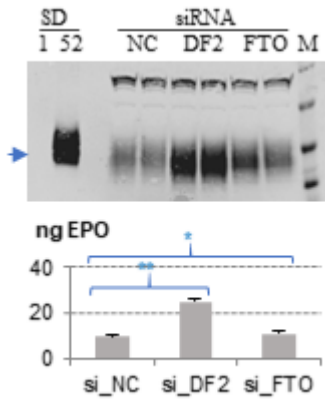


Figure S1. Multiple alignment of YTH domains

YTH domain amino acid sequences of YTH containing proteins from mouse, rat, human and CHO cells were aligned using CLUSTALX software with default settings. Identical or similar residues shared by different number of sequences were displayed using GenDocs program with shading from white to black. Secondary elements in the YTH domain shown above the alignment were from the on-line service at http://espript.ibcp.fr/ESPript/ESPript/ using the protein structure of the YTH domain of human DF1 (PDB: 4RCJ). Amino acid positions are shown at the end of each line on the right side. TT, strict β-turns; arrows, β-strands; coils, α-helices; η, 3_{10}-helix. M6A pockets of DF and DC1 are shown above and below the alignment, respectively. Red, full circles, aromatic residues critical for m6A recognition (WWW in DF proteins and WWL in DC proteins); blue shuttle shape, residues that are DC1 unique for the preference of G-1 (the position preceding the m6A nucleotide); dark blue triangle, residues has been

experimentally shown to involve in the stronger m6A binding activity of the YTH domain of DC1; dark blue shuttle shape under the alignment, residues unique for CHO-K1 and mouse in the YTH domain of DC2; red filled shuttle above the alignment, residues unique for either DF1, DF2 or DF3; sky-blue filled shuttle, residues unique for DF2 and DC1.

Figure S2. Impact of knockdown DF2 and FTO on EPO expression.



Western blot analysis of EPO expression in CHO-K1 cells co-transfected with siRNA (top) and quantification (bottom). SiRNA for negative control (NC). Molecular weight (M), Standard EPO in ng (1, 52). Samples taken for analysis: 30uL supernatant at Day 2 post transfection. Blue arrow on the left is the expected molecular weight (38kD) of glycosylated EPO.

Table S1

A. Primers sequences (5'-3') used in the construction of overexpression vector CMV-DF2

Primers	Sequence **(5'-3')**
DF2for	ATGTCGGCCAGCAGCCTCTTGGA
DF2rev	TTATTTCCCACGGCCTTGACGCTCCTTTTTAACA
FLAG2YN	ACAAGGATCATGATATTGATTACAAGGACGACGATGACAAGATGTC GGCCAGCA
3FLAGBamfor	GGGGATCCATGGACTATAAGGACCACGACGGAGACTACAAGGATCA TGAT
Y2endXho	GATCTCGAGTTATTTCCCACGGCCTTGACGCT

B. SiRNA sequences (5'-3')

Gene	Si_RNASequence (5'-3')
DF1	CAAATGTAAACATGCCAGTTTCA
DF2	ACCTAAACTGAAGACCAAGAATGGC
DF3	CTACCATTGGTGCAAAGCCAACTGC
METTL3	AAATTGATGCTTGCATGGATTCTGAG
METTL14	ACAAAGATTCCAGTACCTTTCTTAA
WTAP	GCAGTCAGGATGAACTGAATGAC
ALKBH3	CCCCATCATTGCGTCACTTAGTTTT
FTO	CACTTGGCATGTTGGTTTCAAGATA

C. Primers for qPCR

Genes	**Forward primers (5' -3')**	**Reverse primers (5' -3')**
DF1	CAGTTAAGACGGTGGGTTCAG	CATCTTGGGCTGTGGTTTTG
DF2	CAGTTTGCCTCCAGCTACTATT	GCAAGGCCATTCTTGGTCTTC

DF3	AGCAGTGGTATGACTAGCATTG	CAATTCCCACATTGCCCTTG
METTL3	TTGCATGGATTCTGAGGGTC	CCAGGTAGCGGATATCACAAC
METTL14	CGGAAGTGCCTGGATGAAG	AAGCTCTGCGTTCCCTTAAG
WTAP	AGCAGAGTTGGCTTTACAGAAG	CTGTCGTGTCTCCTTCAATTG
ALKBH3-human	TGTATCCTGGCTTTGTTGAC	TCTCCATACCATGCTGTAAGTC
ALKBH3-CHO	TGTCTATATCCTGGCTTTGTGG	GCTCTCCATACCATGCTGTAAG
BH3_320	CATGGCTTGAATTGGGAATGA	TTCCTAGCAGCAGTACCTGGCT
BH3_470	TAGGAACCATCTTTCCCAGACA	TGTCAATCACTCTGGGTTCTG
HPRT1	TTTACCTCACCGCTTTCTCG	TCATCACTAATCACGACGCTG
SON	CTGTAACAGTAGGAGTGGATC	GGAGTCCATAGTGCTAGAGGC
RPL30	GTCCATCAACTCGAGGCTC	TTTCAGATTTCCTCAGGGCC
FTO	TGCACCATCAATTACACAGAGG	CACAAAGGCACAGCATCTTC
28S	GTTCTCTCCGGTCACGC	TGACTCGCGCACGCGTTAGAC
28S_304	CAAAGCGGGTGGTAAACTCC	TTCACGCCCTCTTGAACTCT
28S_1322	GCGTTAGGACCCGAAAGATG	GTCTTTCGCCCCTATACCCA
M6A_RNA	CGACATTCCTGAGATTCCTGG	TTGAGCAGGTCAGAACACTG
Unmodified RNA	CTGAAGGAGCCTGTGATCTG	GTGGCACACGTTACATTTCTG
EPO	TGTGGATAAAGCCGTCAGTG	GGAAGAGTTTGCGGAAAGTG
GFP1	GAGAGAACCCACTGCTTACT	GAACTTGTGGCCGTTTACGT
GFP181	GACGTAAACGGCCACAAGTT	GTAGGTCAGGGTGGTCACGA
GFP299	TCGTGACCACCCTGACCTAC	GTCTTGTAGTTGCCGTCGTC
GFP424	GACGACGGCAACTACAAGAC	GGCGGATCTTGAAGTTCACC
GFP564	ACAACGTCTATATCATGGCCG	GTGCTCAGGTAGTGGTTGTC
GFP659	ACCACTACCAGCAGAACACC	CTTGTACAGCTCGTCCATGC
GFP806	ATCACTCTCGGCATGGACGA	TGGCAACTAGAAGGCACAGT
GFP1017	CGACTGTGCCTTCTAGTTGC	AGGAAAGGACAGTGGGAGTG

Table S1. Primers used in the construction of the vector CMV-DF2 (A), siRNA sequences (B) and in qPCR (C).

Regular used primers for qRTPCR of GFP and ALKBH3 (BH3) are bold.