

Supplementary Figures

Figure S1

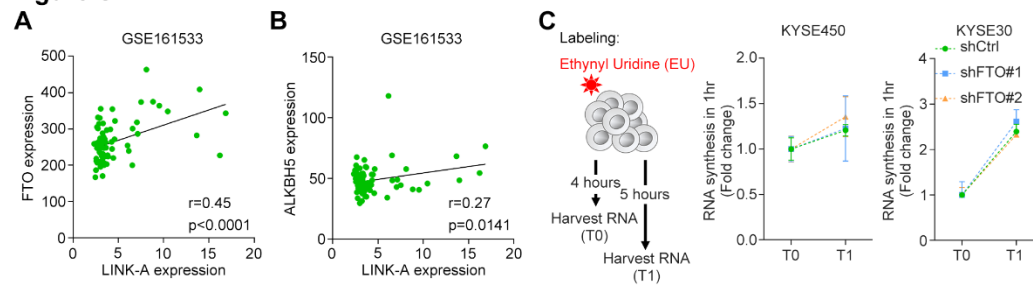


Fig. S1. FTO stabilizes LINK-A by m6A demethylation. A, B Correlations between LINK-A expression and FTO or ALKBH5 expression were determined using Pearson correlation analysis in the GEO database. **C** Dynamics of RNA synthesis calculated for the indicated cells. Cartoon of the experimental scheme is shown on the left. The data are presented as the mean $\pm$ s.d. values; $n = 3$.

Figure S2

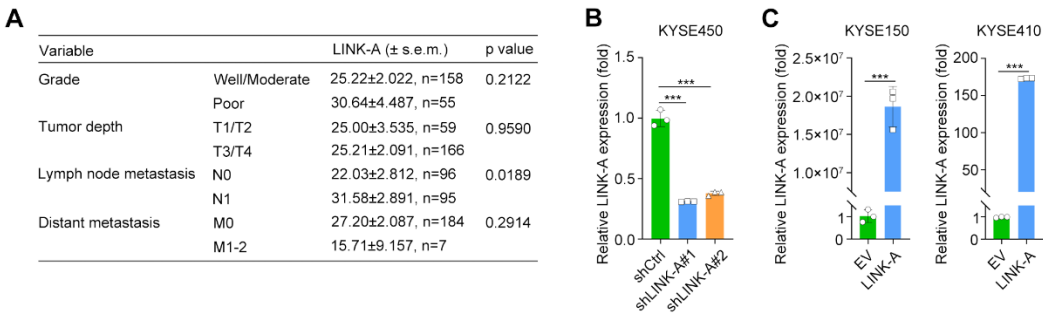


Fig. S2. LINK-A promotes ESCC malignancy. **A** Correlation analyses of LINK-A expression with other clinicopathological features in patients with ESCC. Unpaired Student's *t* test. **B**, **C** RT-qPCR analysis of LINK-A expression in indicated cells. The data are presented as the mean $\pm$ s.d. values; unpaired Student's *t* test, ****p* < 0.001; *n* = 3.

Figure S3

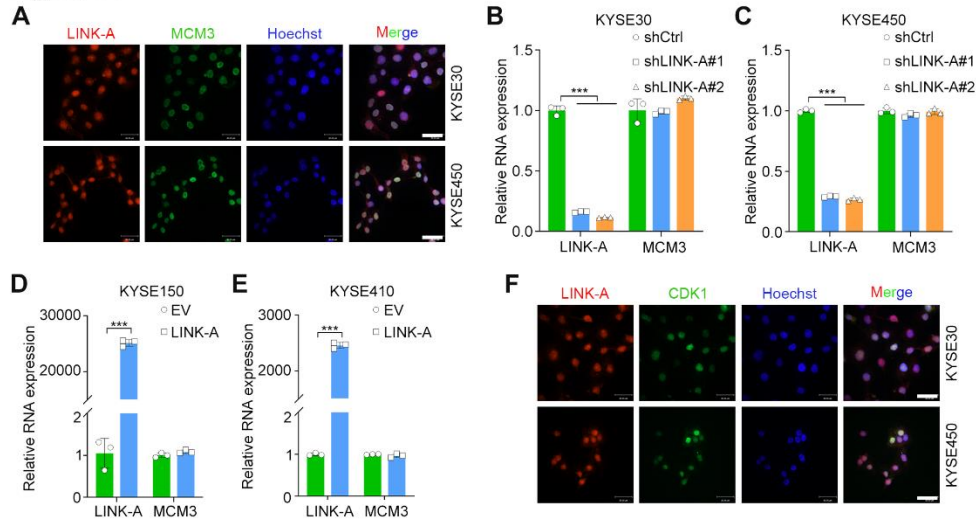


Fig. S3. LINK-A promotes MCM3 phosphorylation by mediating the interaction between MCM3 and CDK1. **A** FISH and IF analysis of LINK-A (red) and MCM3 (green) in the indicated cells. Nuclei (blue) were labeled with Hoechst. The scale bar represents 30 μ m. **B-E** RT-qPCR analysis of LINK-A and MCM3 expression in the indicated cells. The data are presented as the mean $\pm$ s.d. values; unpaired Student's *t* test, ****p* < 0.001; *n* = 3. **F** IF analysis of LINK-A (red) and CDK1 (green) in the indicated cells. Nuclei (blue) were labeled with Hoechst. The scale bar represents 30 μ m.

Figure S4

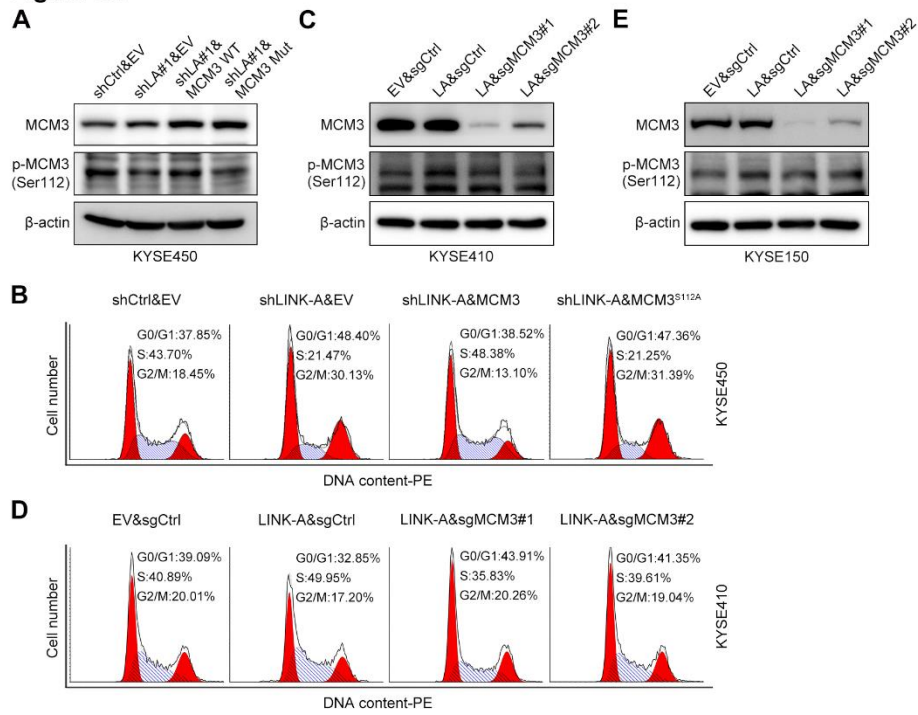


Fig. S4. MCM3 mediates LINK-A to facilitate cell cycle progression. A, C, E Western blot analysis of MCM3 and phosphorylated MCM3 in the indicated cells. **B,** **D** Representative images of cell cycle analyses in the indicated cells.

Figure S5

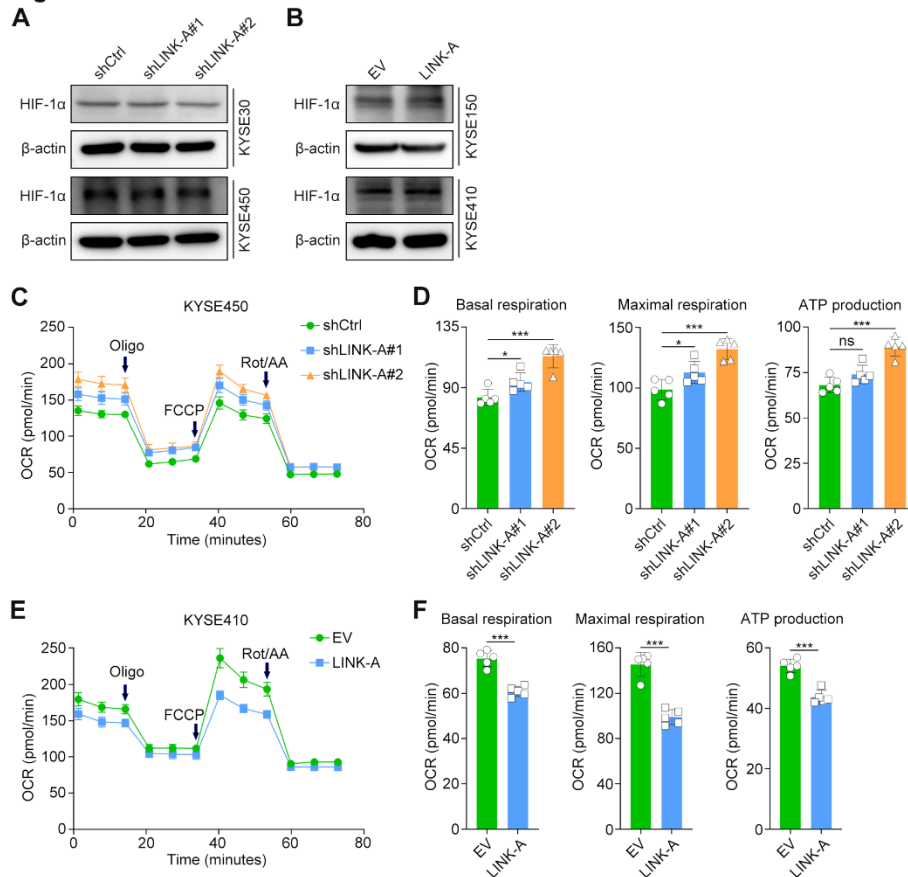


Fig. S5. LINK-A induces HIF-1α transcriptional activity by sequestering HIF-1α from MCM3. A, B Western blot analysis of HIF-1α expression in the indicated cells. **C-F** Measurement of the OCR and mitochondrial respiration level using a Seahorse assay in LINK-A-silenced KYSE450 cells (**C** and **D**) and LINK-A-overexpressing KYSE410 cells (**E** and **F**). The data are presented as the mean ± s.d. values; unpaired Student's *t* test, * $p < 0.05$, *** $p < 0.001$, ns: no significance; $n = 5$.

Supplementary Tables

Table S1. shRNA and sgRNA sequences

Sequence (5' to 3')	Name
AGATGTAGTTCTAGTTCAT	shLINK-A#1
GGTCTTCATTCTTACGCTT	shLINK-A#2
CCCATTAGGTGCCCATATTTA	shFTO#1
CGGTTCACAACCTCGGTTTAG	shFTO#2
GCTGGACGATGTGGAGCTGC	sgMCM3#1
GCACCGTTACAGAGCACCTG	sgMCM3#2

Table S2. RT-qPCR primers

Sequence (5' to 3')	Name
CCGGGAAACTGTGGCGTGATGG	GAPDH-F
AGGTGGAGGAGTGGGTGTCGCTGTT	GAPDH-R
TCCCAGGGCGAGGCTTATCCATTG	U1-F
GCGAACGCAGTCCCCCACTACCAC	U1-R
CCTCTGACTGATGCTTCC	LINK-A-F
CACCTGGCTGTCTTATTCC	LINK-A-R
TCTTCTCACAACCTGCGACG	HLA-H-F
TGCGTGGGGACTTTAGAACC	HLA-H-R
AGTTGATCAAGGCCGTGGAA	HCP5-F
TTCCTGGGACACAGAGGACT	HCP5-R
AGCGCCTAAGAAATGCCTGT	DLGAP1-AS2-F
AGCTGTTCATTCAGCCACGA	DLGAP1-AS2-R
ACCTCGGGATCCCATTCTT	CCDC18-AS1-F
TGTAAAACGGCCACACCCTT	CCDC18-AS1-R
TTTCATGGCCTGGTAGCGTT	LINC01207-F
GTCCCTGAGAGTGGCTAGGA	LINC01207-R
CCTGCCCCGATCCTACTTGTC	SLC44A3-AS1-F
CAGGCTACATGGTCACCGAA	SLC44A3-AS1-R
GGCTCTCTCAGTTAGCTGGC	LINC03004-F
CACGACTTGTATGCCCCTGA	LINC03004-R

AGAGAGCCCCTTTGTAACGC	MIR34AHG-F
GAGAGGCATCTGAGTGCTGG	MIR34AHG-R
CCGAGCTCAGTTATGGCACA	MIR205HG-F
ACGCACACTCCAGATGTCTC	MIR205HG-R
AGTTCGTCCCAAAGTCGTCC	MCM3-F
GGGGATTGTTCTCCTCATCCT	MCM3-R
AGAATGTCTGTGACGATGTGG	FTO-F
GCACTTTCTGTATCGATTGCC	FTO-R
CGGCGAAGGCTACACTTACG	ALKBH5-F
CCACCAGCTTTTGGATCACCA	ALKBH5-R
TGCTTGCCAAAAGAGGTGGA	HIF-1 α -F
TTCTGTGTCGTTGCTGCCAA	HIF-1 α -R
ACCAGGACAGCCAATACAAG	PDK1-F
CCTCGGTCACTCATCTTCAC	PDK1-R
ATCTTGACCTACGTGGCTTGGA	LDHA-F
CCATACAGGCACACTGGAATCTC	LDHA-R
CGCAAGAAATCCCGGTATAA	VEGF-F
TCTCCGCTCTGAGCAAGG	VEGF-R
GGTGGGGTCATGTGTGTGG	BCL2-F
CGGTTCAAGGTACTCAGTCATCC	BCL2-R
TGAGCATCGTGGCCATCTTT	SLC2A1-F
CCGGAAGCGATCTCATCGAA	SLC2A1-R

TGCCACCAGACTAAACTAGACG	HK2-F
CCCGTGCCCACAATGAGAC	HK2-R
CCAGGGATTTCAGTCGATGT	Firefly-Luc-F
AATCTCACGCAGGCAGTTCT	Firefly-Luc-R
GTGGTGGGCCAGATGTAAAC	Renilla-Luc-F
ACCAGATTTGCCTGATTGTC	Renilla-Luc-R
