**Supplementary Material**

**FTO-mediated autophagy promotes progression of clear cell renal cell carcinoma via regulating SIK2 mRNA stability**

**Table S1.** Sequences of primers.

**Table S2.** Primary antibodies.

**Figure S1.** Immunofluorescence staining with mRFP-GFP-LC3 in ccRCC cell lines.

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**Figure S7.** Representative images of metastatic lung tumors and hematoxylin and eosin staining, and quantification of lung tumors.

**Figure S8.** Representative IHC staining images of N-cadherin and E-cadherin and quantification of IHC score.
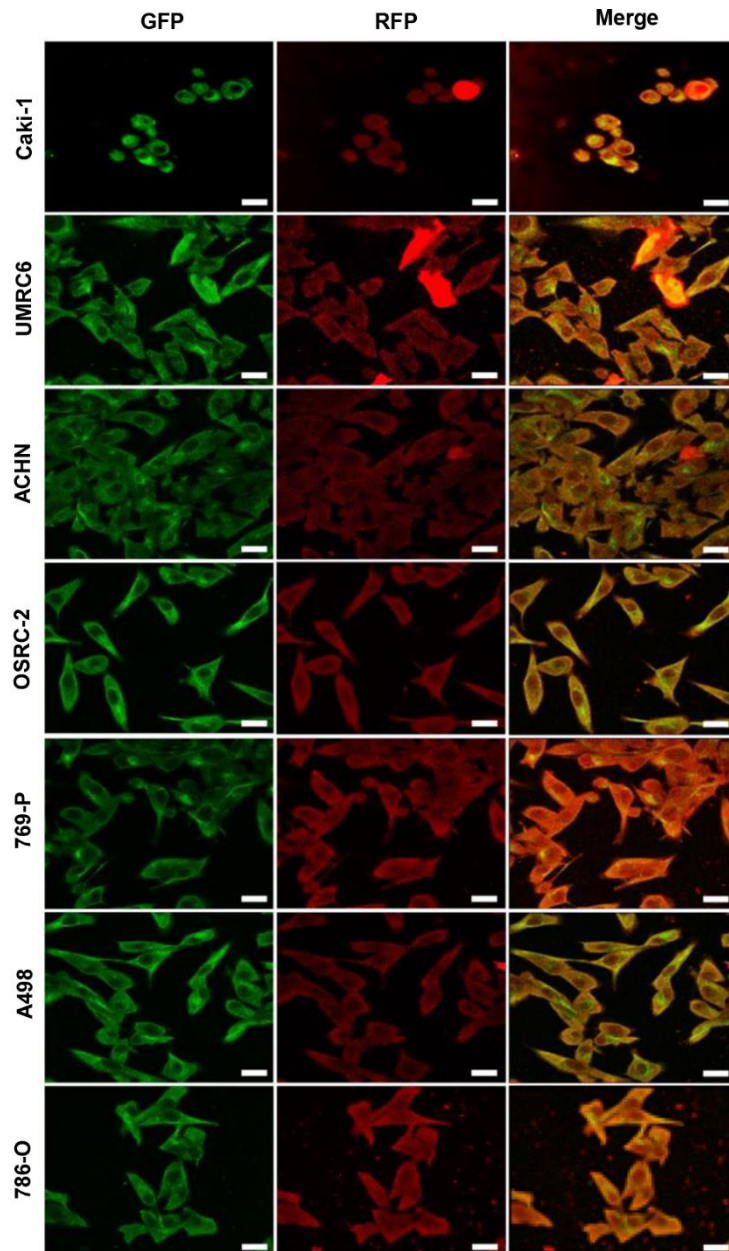
**Table S1.** Sequences of primers

| Gene Symbol | Sequences |
|---|---|
| FTO | Forward 5′- ATTCTATCAGCAGTGGCAGC -3′ |
| | Reverse 5′- GGATGCGAGATACCGGAGTG -3′ |
| ULK1 | Forward 5′- CCTCGGTCAGGAAATCCCCA -3′ |
| | Reverse 5′- GAGCTGTGCAGGAAGCCA -3′ |
| ATG3 | Forward 5′- CCCCAGGATGCAGAATGTGA -3′ |
| | Reverse 5′- TCCAGCTGCCACAAACTCTT -3′ |
| ATG4B | Forward 5′- TCCATCGCTGTGGGGTTTTT -3′ |
| | Reverse 5′- TCCAGTCGCTCTACATCAGA -3′ |
| ATG4D | Forward 5′- ACACATCCTCAGGAAAGCCG -3′ |
| | Reverse 5′- TGACCACAGACTTCCACTCG-3′ |
| ATG5 | Forward 5′- GCAACTCTGGATGGGATTGC -3′ |
| | Reverse 5′- AGGTCTTTCAGTCGTTGTCTGAT -3′ |
| ATG7 | Forward 5′- AGCATCCAGAAGGGGGCTA -3′ |
| | Reverse 5′- TGCAGCAATGTAAGACCAGTCA -3′ |
| ATG10 | Forward 5′- ACATTCCAACGTTATTGTGCAG -3′ |
| | Reverse 5′- GCTCGAAAGCCTCCTCCAT -3′ |
| ATG12 | Forward 5′- TGCTGGAGGGGAAGGACTTA -3′ |
| | Reverse 5′- CCATCACTGCCAAAACACTCA -3′ |
| ATG13 | Forward 5′- AGCCCGGAACCACTCTT -3′ |
| | Reverse 5′- TCACTTGGACAGTCTTGAGGG -3′ |
| ATG14 | Forward 5′- TACGTGGCTGTGGAGCG -3′ |
| | Reverse 5′- CCTTCCATAGCTTTTAACACTTCTT -3′ |
| ATG16L1 | Forward 5′- TTGGCCCAGAAACTACAGGC -3′ |
| | Reverse 5′- CCAGTTGAGCTAACTCCCCA -3′ |
| SIK2 | Forward 5′- CTGAAGCCAGGCGAAAATTCT -3′ |
| | Reverse 5′- TTGCCAGCAGTTCACCACTTT -3′ |
| PIK3C2A | Forward 5′- GGTTCCGATCCTCTGCGTT -3′ |
| | Reverse 5′- GGTTCCGATCCTCTGCGTT -3′ |
| RNF34 | Forward 5′- GGAGAGCTTATGGATGGAGACC -3′ |
| | Reverse 5′- GGTTCCGATCCTCTGCGTT -3′ |
| IGF2BP1 | Forward 5′- TTGGGACGCCATCAGTACCTA -3′ |
| | Reverse 5′- TTGGCTAAACTCTCTACGACTCT -3′ |
| IGF2BP2 | Forward 5′- TGCACATCCCCAACTGTGAC -3′ |
| | Reverse 5′- TGTAGAAGAGATGACACTCGGG -3′ |
| IGF2BP3 | Forward 5′- AGACACACTGAATCACCTGAAGT -3′ |
| | Reverse 5′- AGGGCGACACTGCTTTTTCTT -3′ |
| YTHDF1 | Forward 5′- GGGGACAAGTGGGTCTCAAG -3′ |
| | Reverse 5′- AGGGTGTCGCTGTGAAAGC -3′ |
| YTHDF2 | Forward 5′- GTTGGTAGCGGGTCCATTACT -3′ |
| | Reverse 5′- GGTCTTCAGTTTAGGTTGCTGT -3′ |
| YTHDF3 | Forward 5′- GGTGTATTTAGTCAACCTGGGG -3′ |

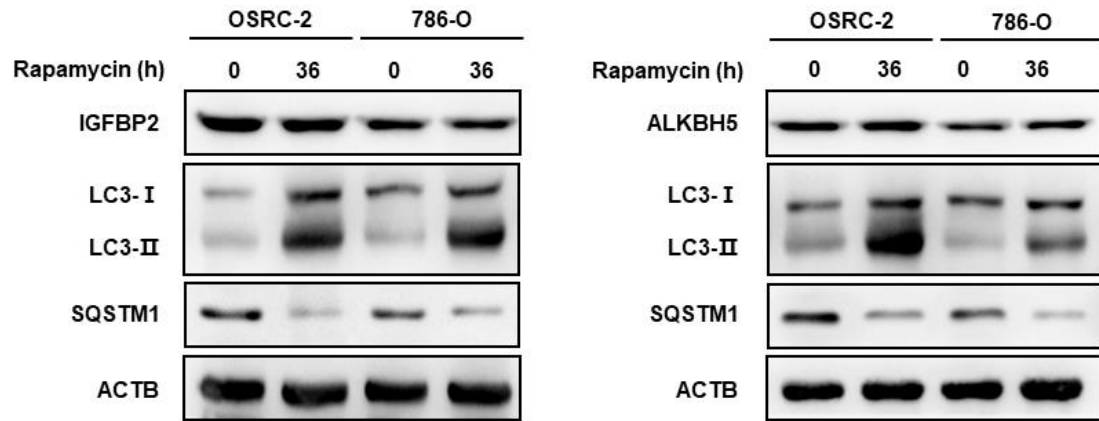| | |
|---|---|
| | Reverse 5′- AAGAGAACTAGGTGGATAGCCAT -3′ |
| METTL3 | Forward 5′- TTGTCTCCAACCTTCCGTAGT -3′ |
| | Reverse 5′- CCAGATCAGAGAGGTGGTGTAG-3′ |
| METTL16 | Forward 5′- CTCTGACGTGTACTCTCCTAAGG -3′ |
| | Reverse 5′- TACCAGCCATTCAAGGTTGCT -3′ |
| WTAP | Forward 5′- CTTCCCAAGAAGGTTCGATTGA -3′ |
| | Reverse 5′- TCAGACTCTCTTAGGCCAGTTAC -3′ |
| VIRMA | Forward 5′- CCTTCCTGGGCTAGTGCAAA -3′ |
| | Reverse 5′- TTTTGTTTCTTTTGGTACAGCCAT -3′ |
| ZC3H13 | Forward 5′- TCTGATAGCACATCCCGAAGA -3′ |
| | Reverse 5′- CAGCCAGTTACGGCACTGT -3′ |
| RBM15 | Forward 5′- ACGACCCGCAACAATGAAG -3′ |
| | Reverse 5′- GGAAGTCGAGTCCTCACCAC -3′ |
| RBM15B | Forward 5′- ACCTGGACCACAGCGTATCT -3′ |
| | Reverse 5′- GGGTTGCGACCAATCACTC -3′ |
| RBMX | Forward 5′- CTTCAGGACCAGTTCGCAGTA -3′ |
| | Reverse 5′- TCACGACCACTTGAGTAGAGAT -3′ |
| YTHDC1 | Forward 5′- CTTCTGATGAGCAAGGGAACAA -3′ |
| | Reverse 5′- GGCCTCACTTCGAGTGTCATAA -3′ |
| YTHDC2 | Forward 5′- CAAAACATGCTGTTAGGAGCCT -3′ |
| | Reverse 5′- CCACTTGTCTTGCTCATTTCCC -3′ |
| HNRNPC | Forward 5′- TCCTCCTCCTATTGCTCGGG -3′ |
| | Reverse 5′-AGCCACTTTTGCCCCTTCG -3′ |
| FMR1 | Forward 5′- ACTTACGGCAAATGTGTGCCA -3′ |
| | Reverse 5′- GCAGACTCCGAAAGTGCATGT -3′ |
| LRPPRC | Forward 5′- CGGAGGACTACTGAGCCCA -3′ |
| | Reverse 5′-AGCGGCAGGTATCATTAAAAACT -3′ |
| HNRNPA2B1 | Forward 5′- TGGAGGTAGCCCCGGTTATG -3′ |
| | Reverse 5′- GGACCGTAGTTAGAAGGTTGCT -3′ |
| ALKBH5 | Forward 5′- ATGCACCCCGGTTGGAAAC -3′ |
| | Reverse 5′- GACTTGCGCCAGTAGTTCTCA -3′ |

**Table S2.** Primary antibodies

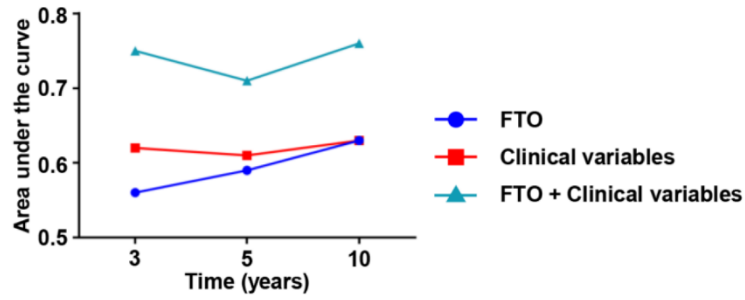| Primary antibodies | Manufacturer, Catalogue number |
|---|---|
| Rabbit anti-m$^6$A | Synaptic Systems, 202003 |
| Rabbit anti-LC3- I/II | Abcam, ab192890 |
| Mouse anti-GFP | Abcam, ab1218 |
| Rabbit anti-RFP | Abcam, ab185921 |
| Rabbit anti-SQSTM1 | Abcam, ab109012 |
| Rabbit anti-ACTB | Abcam, ab8227 |
| Rabbit anti-FTO | Abcam, ab126605 |
| Rabbit anti-GAPDH | Abcam, ab9485 |
| Rabbit anti-Ki67 | Abcam, ab15580 |
| Rabbit anti-SIK2 | Abcam, ab245211 |
| Rabbit anti- IGF2BP2 | Abcam, ab128175 |
| Rabbit anti-ATG5 | Cell Signaling Technology, 9980S |
| Rabbit anti-ATG7 | Cell Signaling Technology, 8558S |
| Rabbit anti-IGFBP2 | Proteintech, 11065-3-AP |
| Rabbit anti-ALKBH5 | Proteintech, 16837-1-AP |
| Rabbit anti-PIK3C2A | Proteintech, 22028-1-AP |
| Rabbit anti-N-cadherin | Proteintech, 66219-1-Ig |
| Rabbit anti-E-cadherin | Proteintech, 20874-1-AP |
| Rabbit anti-RNF34 | ABclonal, A8517 |

**Figure S1.** Immunofluorescence staining with mRFP-GFP-LC3 in ccRCC cell lines.

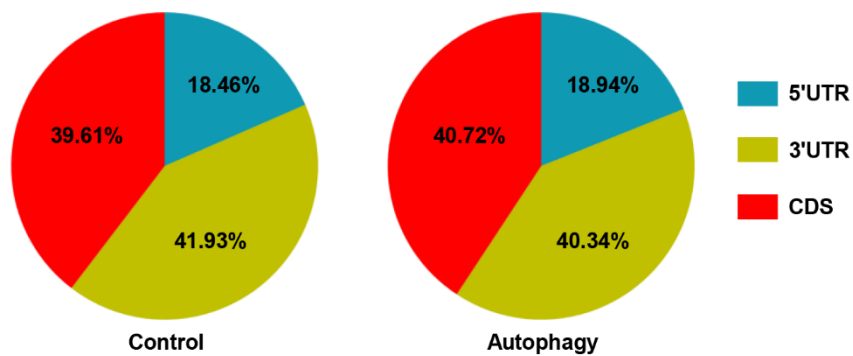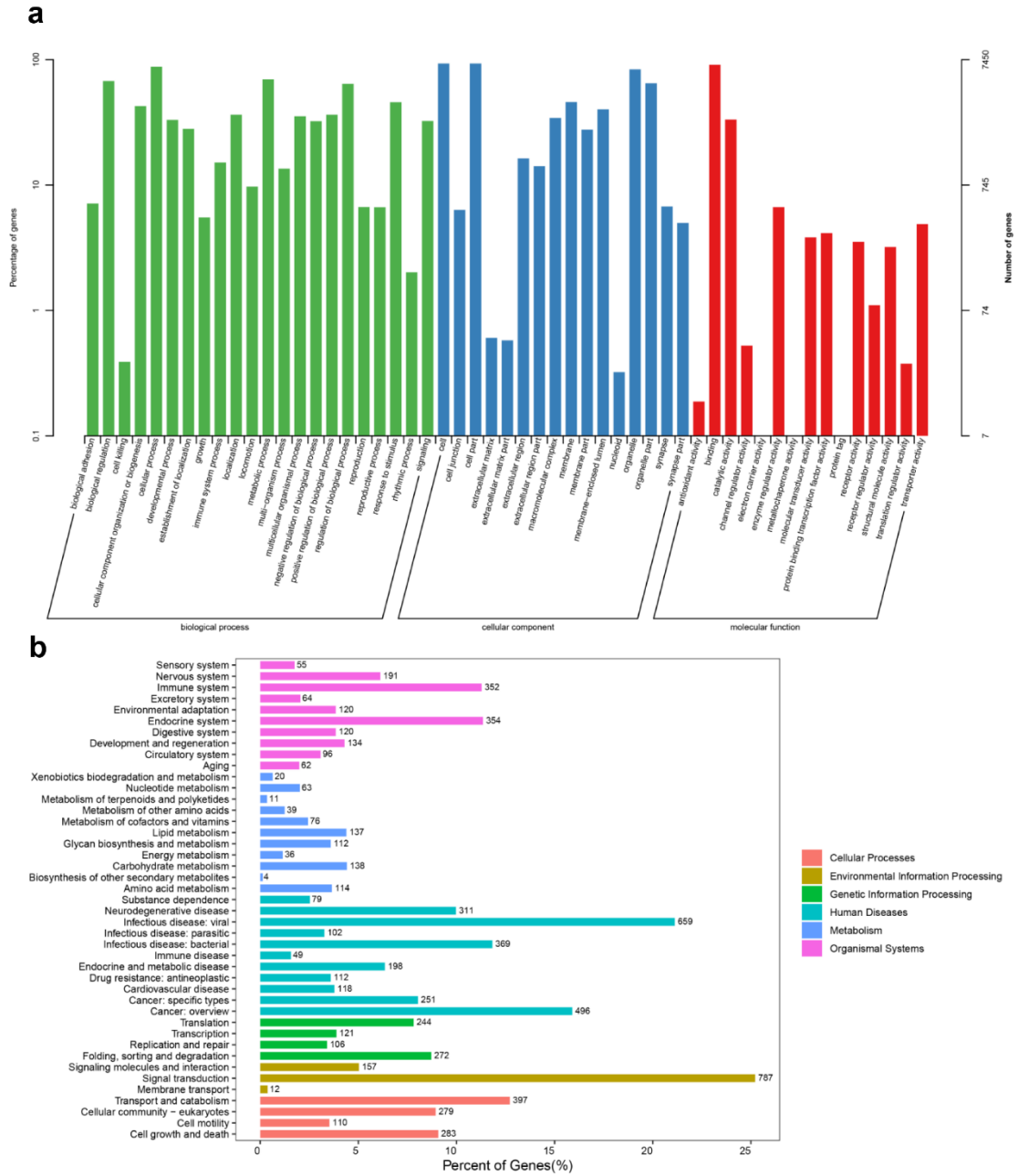Red puncta signify autolysosomes and yellow puncta signify autophagosomes. Scale

bar, 10 μm.

**Figure S2.** IGFBP2 and ALKBH5 expression in OSRC-2 and 786-O cells treated with
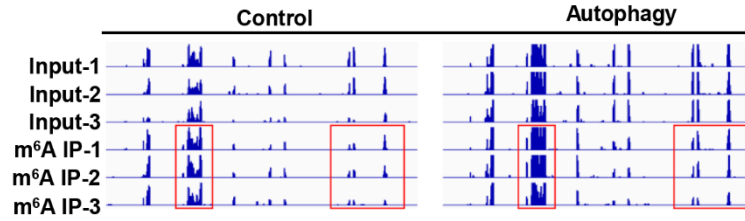
rapamycin.

**Figure S3.** The time-dependent receiver operating characteristic (ROC) analysis for the FTO risk score, the clinical variables risk score, and the combined FTO and clinical variables risk scores in the ccRCC cohort.
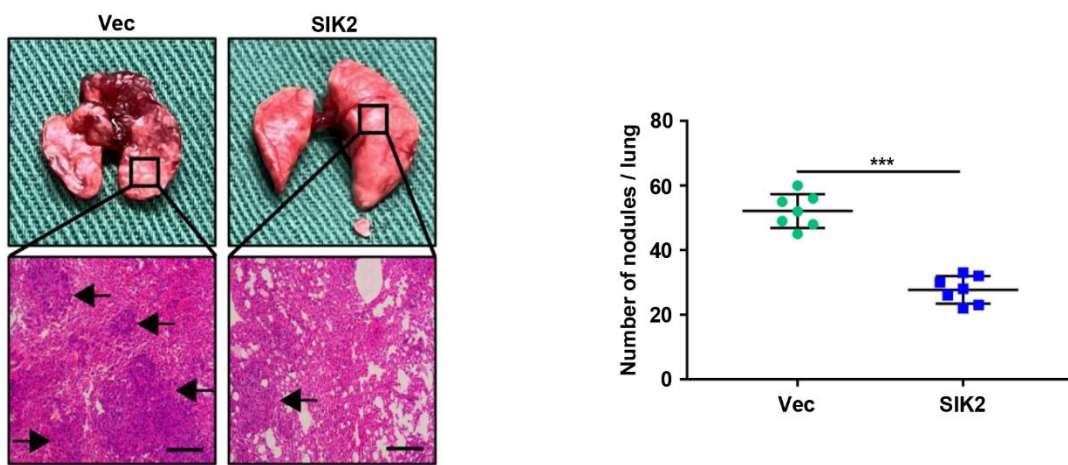


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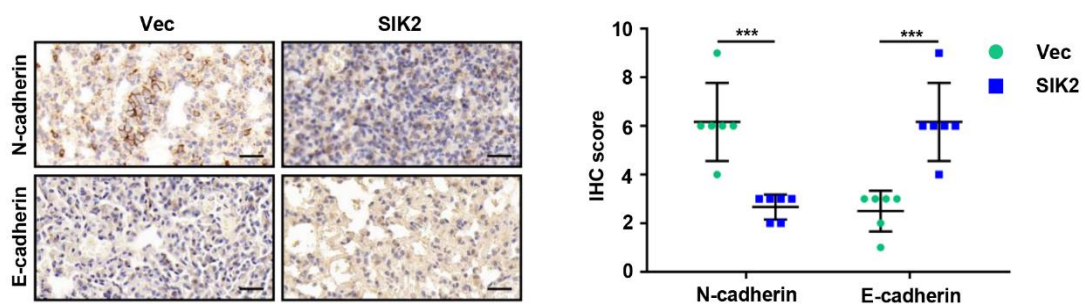
**Figure S6.** MeRIP-seq data revealed that m$^6$A abundance in the SIK2 mRNA was markedly increased during autophagy flux.



**Figure S7.** Representative images of metastatic lung tumors and hematoxylin and eosin (H&E) staining (left panel), and quantification of lung tumors (right panel).



**Figure S8.** Representative IHC staining images of N-cadherin and E-cadherin (scale bar, 100μm, left panel) and quantification of IHC score (right panel). Error bars, SEM; ***, P < 0.001.