Supplementary Table 1. Effects of m6A on RNA metabolism.

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| m6A methylation modification-related proteins | Modified RNAs | Diseases | Findings  | Refs  |
| writers | METTL3 | PKC-η mRNA | diabetes | PKC-η, FAT4, and PDGFRA mRNAs expression rose as a result of the reduction of m6A methylation brought on by METTL3 silencing, which prevented diabetes-related peripapillary cell dysfunction and reduced retinal vascular complications. The protective effect of METTL3 was, however, abrogated by overexpression of YTHDF2 | [43] |
| FAT4 mRNA |
| PDGFRA mRNA |
| SLC7A11 m6A | hepatoblastoma | IGF2BP1 recognizes METTL3-mediated m6A modification of SLC7A11 mRNA and prevents the recruitment of the BTG2/CCR4-NOT complex to PABPC1 by competitive binding to PABPC1 and inhibits the deacetylation of SLC7A11 mRNA, ultimately leading to tumorigenesis in hepatoblastoma. | [44] |
| LncRNA D63785 | neuronal cell injury | Through enhancing METTL3-dependent Lnc-D63785 m6A methylation, oxygen glucose deprivation/re-oxygenation (OGD/R) decreases Lnc-D63785 expression, causing an accumulation of miR-422a and the apoptosis of neuronal cells. | [45] |
| FBXW7 mRNA | lung adenocarcinoma (LUAD) | By embedding m6A modification in the CDS of FBWX7 mRNA, METTL3 regulates FBXW7's potential to act as a tumor suppressor, which eventually promotes apoptosis and inhibits cell proliferation via FBXW7 to decrease growth in LUAD. | [46] |
| ZMYM1 mRNA | gastric cancer | The HuR (known as m6A binding protein) binding site on ZMYM1 was targeted by METTL3-mediated m6A methylation modification to increase ZMYM1 expression in the genesis of gastric cancer. | [47] |
| miR-143 | myocardial infarction | METTL3 enhanced the m6A modification of pri-miR-143, which resulted in the transition of pri-miR-143 into mature miR-143-3p; miR-143-3p significantly reduce the expression of Yap and Ctnnd1; miR-143-3p blocked cardiomyocytes proliferation via its interaction with Yap and Ctnnd1. | [48] |
| lncRNA H19 | Protective effect of hypoxic preconditioning (HPC) was dependent on METTL3/METTL14-mediated abundant m6A methylation and overexpression of lncRNA H19. | [49] |
| METTL14 |
| miR-149-3p | intestinalinflammation and Colorectal carcinoma (CRC) | MiR-149-3p was down-regulated by enterotoxigenic bacteroides fragilis, leading to the development of CRC and intestinal inflammation. This process was controlled by METTL14-dependent m6A methylation, which regulated the processing of pri-miR149 by DGCR8. | [50] |
| SOX4 mRNA | CRC | METTL14 mediates m6A methylation of SOX4 mRNA, reduces SOX4 mRNA expression and inhibits the deterioration of CRC | [51] |
| lncRNA XIST | Knockdown of METTL14 induces the low m6A methylation level of lncRNA XIST, augments lncRNA XIST expression and promotes tumorigenicity and metastasis of CRC | [52] |
| CYP1B1 | cervical carcinoma | METTL14 is influenced by its upstream signal (piRNA-14633) to induce the m6A methylation of CYP1B1 and promote the malignancy of cervical carcinoma. | [53] |
| lncRNA TINCR | diabetes | The expression of the lncRNA TINCR was inhibited by METTL14-mediated m6A methylation modification, which lowered the stability of the NLRP3 mRNA and caused its downregulation. Finally, downregulation of NLRP3 prevented the progression of diabetes cardiomyopathy. | [54] |
| METTL16 | lncRNA RAB11B-AS1 | hepatocellular carcinoma | lncRNA RAB11B-AS1 was directly bound to by METLL16, which also caused lncRNA RAB11B-AS1 to undergo m6A modification, lowered lncRNA RAB11B-AS1 transcript stability, and thus downregulated lncRNA RAB11B-AS1 transcript level. Eventually, the tumor-suppressive roles of RAB11B-AS1 in hepatocellular carcinoma reversed. | [55] |
| cyclin D1 mRNA | gastric cancer | METTL16 enhances the stability and expression of cyclin D1 mRNA in gastric cancer cells through m6A modification. Subsequently, this accelerates gastric cancer cells cycle. | [56] |
| WTAP | MXD2 mRNA | mTORC1-driven cancers | mTORC1 increases m6A methylation on MXD2 mRNA promotes its degradation by increasing the expression of methyltransferase complex regulatory subunit, WTAP, through eIF4A/4B-dependent translation. | [57] |
| ETS1 mRNA | hepatocellular carcinoma | The WTAP-regulated modification of m6A led to post-transcriptional repression of ETS1, which resulted in the down-regulation of ETS1 mRNA expression that would have prevented the development of hepatocellular carcinoma, eventually enhancing the proliferative potential and tumor growth of hepatocellular carcinoma cells. | [58] |
| KIAA1429(VIRMA) | GATA3 mRNA | KIAA1429 promoted m6A methylation on the 3' UTR of GATA3 pre-mRNA, subsequently causing the dissociation of the RNA-binding protein HuR and the degradation of GATA3 pre-mRNA | [59] |
| SIRT1 mRNA | CRC | KIAA1429 promotes colorectal tumor growth via regulating the expression and stability of SIRT1 mRNA in an m6A-dependent manner. | [60] |
| BTG2 mRNA | lung adenocarcinoma | The m6A levels of BTG2 mRNA was reduced by the knockdown of KIAA1429, which also contributed to the carcinogenesis of lung adenocarcinoma by stimulating the expression of BTG2 and increasing the YTHDF2-dependent stability of BTG2 mRNA. | [61] |
| lncRNA CCAT1 | prostate cancer | By generally lowering m6A levels and lowering the stability and abundance of carcinogenic lncRNAs CCAT1 and CCAT2, VIRMA downregulation reduces the aggressive phenotype of prostate cancer. | [62] |
| lncRNA CCAT2 |
| RBM15 | TMBIM6 mRNA | Laryngeal squamous cell cancer (LSCC) | RBM15 enhances the m6A modification of TMBIM6 mRNA; subsequently, IGF2BP3 bound to the m6A site in the 3’UTR region of TMBIM6 and strengthen the stability of TMBIM6. Ultimately, this progress promotes the proliferation of LSCC. | [63] |
| HK2 mRNA | osteosarcoma | The interaction between circ-CTNNB1 and RBM15 led to the promotion of HK2, GPI, and PGK1 expression through m6A modification, which in turn facilitated in the glycolysis process and triggered osteosarcoma development. | [64] |
| GPI mRNA |
| PGK1 mRNA |
| CLDN4 mRNA | Gestational diabetes Mellitus | RBM15 emerges as insulin resistance by directing the m6A modification of CLDN4 and decreasing CLDN4 expression. | [65] |
| erasers | ALKBH5 | Drp1 mRNA | liver fibrosis | Loss of ALKBH5 enhances the m6A modification of Drp1 mRNA; YTHDF1 discerns the above m6A site and increases Drp1 mRNA stability, which promotes mitochondrial fission, eventually leading to hepatic stellate cell proliferation and migration and liver fibrosis. | [66] |
| SOCS3 mRNA | osteosarcoma | ALKBH5 reduces the m6A modification of SOCS3 mRNA, which prevents YTHDF2-mediated SOCS3 degradation and increases SOCS3 expression. This inactivates the STAT3 pathway, which blocks osteosarcoma proliferation and growth. | [67] |
| WIF-1 mRNA | pancreatic cancer | ALKBH5 reduces the m6A modification of WIF-1 mRNA and upregulates the expression of WIF-1 protein, which inactivates the Wnt pathway and inhibits pancreatic tumorigenesis. | [68] |
| CCL28 mRNA | acute kidney injury (AKI) | By boosting CCL28 m6A methylation to upregulate CCL28 levels, ALKBH5 deletion enhances CCL28 mRNA stability. Increased CCL28 levels attract Treg cells, which shield the kidney from being inhibited by the invasion of inflammatory cells. | [69] |
| FTO |  | heart failure; myocardial ischemia | In failing hearts, FTO expression reduces, which causes an abnormal rise in transcriptome-wide m6A methylation and a decline in the contractile activity of the cardiomyocytes. | [36, 70] |
| FOS mRNA | ovarian aging | The m6A methylation of abundant FOS mRNA in the 3′UTR is brought about by FTO downregulation, and IGF2BP2 recognizes the m6A locus on FOS and supports the stability and translation of mRNA, ultimately causing ovarian aging. | [71] |
| readers | YTHDF1 | CNOT7 mRNA | osteosarcoma | Osteosarcoma cells have increased YTHDF1 expression, which stimulates recognition of CONT7 translation initiation by recognizing the m6A region of CONT7 to encourage cell proliferation, migration, and invasion. | [72] |
| YTHDF2 | LHPP mRNA | prostate cancer | By identifying the m6A methylation sites on cancer suppressor genes (LHPP and NKX3–1), YTHDF2 triggers mRNA degradation, which drives prostate cancer proliferation and migration. | [73] |
| NKX3–1 mRNA |
| UBXN1 mRNA | glioma | By identifying the m6A methylation sites on UBXN1 mRNA, YTHDF2 triggers mRNA degradation, which actives NF-κB pathway and drives glioma proliferation and migration. | [74] |
| Myh7 mRNA | cardiac hypertrophy | YTHDF2 suppresses cardiac hypertrophy via recognizing the m6A site on Myh7 mRNA to promote its degradation | [75] |
| PKC-η mRNA | diabetes | PKC-η, FAT4, and PDGFRA mRNAs expression rose as a result of the reduction of m6A methylation brought on by METTL3 silencing, which prevented diabetes-related peripapillary cell dysfunction and reduced retinal vascular complications. The protective effect of METTL3 was, however, abrogated by overexpression of YTHDF2 | [43] |
| FAT4 mRNA |
| PDGFRA mRNA |
| YTHDC1 | SQSTM1 mRNA | In the pathophysiology of diabetes, downregulation of YTHDC1 inhibits the initiation of SQSTM1 m6A methylation, which results in lower levels of SQSTM1 expression. This impairs autophagic flux and keratinocyte migration, which ultimately delays the healing of wounds. | [76] |
| IGF2BP1 | SLC7A11 m6A | hepatoblastoma | IGF2BP1 recognizes METTL3-mediated m6A modification of SLC7A11 mRNA and prevents the recruitment of the BTG2/CCR4-NOT complex to PABPC1 by competitive binding to PABPC1 and inhibits the deacetylation of SLC7A11 mRNA, ultimately leading to tumorigenesis in hepatoblastoma. | [44] |
| IGF2BP2 | slug mRNA | head and neck squamous carcinoma (HNSCC) | IGF2BP2 detects the m6A site in the coding sequence (CDS) region of slug and binds to it, increasing the stability of the mRNA. Slug, which is highly expressed, initiates the epithelial-mesenchymal transition and encourages the invasion and migration of HNSCC cells. | [77] |
| TAB3 mRNA | AKI | METTL3 mediates the m6A methylation of TAB3 mRNA. IGF2BP2 improves TAB3's stability by combining the m6A site on termination codec region of TAB3, which induces the inflammatory effect of TAB3. | [78] |
| TIMP2 mRNA | diabetic nephropathy | METTL3 mediates the m6A methylation of TIMP2 mRNA. IGF2BP2 recognizes the m6A site on TIMP2 and improves TAB3's stability, which regulates Notch signaling and induces podocyte injury (inflammation and apoptosis) in diabetic nephropathy. | [79] |

Abbreviations: SLC7A11 (Solute carrier family 7 member 11); FBXW7 (F-box and WD repeat domain-containing 7); ZMYM1 (zinc finger MYM-type containing 1); SOX4 (SRY-related high-mobility-group box 4); TINCR (terminal differentiation-induced non-coding RNA); MXD2 (MAX dimerization protein 2); ETS1 (ETS proto-oncogene 1); mTORC1 (mechanistic target of rapamycin complex 1); GATA3 (GATA Binding Protein 3); SIRT1 (Silencing information regulator 1); CCAT1 (colon cancer associated transcript 1); CCAT2 (colon cancer associated transcript 2); TMBIM6 (transmembrane BAX inhibitor motif containing 6); HK2 (hexokinase 2); GPI (glucose-6-phosphate isomerase); PGK1 (phosphoglycerate kinase 1); SOCS3 (Suppressor Of Cytokine Signaling 3); WIF-1 (Wnt inhibitory factor 1); CNOT7 (CCR4-NOT transcription complex subunit 7); UBXN1 (UBX domain protein 1); Myh7 (beta-myosin heavy chain); SQSTM1 (sequestosome 1); TAB3 [TGF-β-activated kinase 1 (MAP3K7) binding protein 3]; TIMP2 (TIMP Metallopeptidase Inhibitor 2).