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Epitranscriptomic Remodeling of N6-Methyladenosine (m6A) RNA Marks in CRISPR-Edited Genomes: Emerging Implications for Off-Target Genetic Instability and Precision Gene Therapy

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Abstract

With the advent of epitranscriptomics, there is the addition of a regulatory layer of control over gene expression which goes beyond DNA sequence and chromatin-based regulation and encompasses dynamic chemical RNA modification. Of these N6-methyladenosine (m6A) is the most common interior modification of eukaryotic messenger RNA (mRNA) and is crucial in maintaining RNA stability, splicing, nuclear export, and translational efficiency. M6A deposition, removal and functional interpretation are regulated by an extensive system of methyltransferases (writers), demethylases (erasers) and RNA-binding proteins (readers), which allow a rapid and reversible regulation of gene expression in response to cellular signals.

Simultaneously, the emergence of CRISPR-Cas genome editing technologies has transformed the field of molecular biology and provided a new opportunity in the field of precision gene therapy. Although significant focus has been placed on the conceptualization of off-target DNA mutation and genomic instability, the consequences of genome editing on RNA layers



of control, and especially, the epitranscriptomic changes have not been fully investigated. Recent data indicate that, following the formation of CRISPR-induced DNA double-strand breaks and the ensuing activation of DNA damage response pathways, the global state of cells can be changed, with a potential impact on m6A deposition patterns, including: chromatin remodeling, transcriptional reprogramming, and stress signaling.

This review offers the highest possible idea of the m6A epitranscriptomic environment and its regulatory apparatus, and then a deeper discussion of CRISPR-Cas systems and the cellular reactions related to it. We make the mechanistic case of the interaction between genome editing and m6A remodelling, and how the transcriptional dynamics and RNA-binding protein activity perturbation can cause transcriptome-wide changes in m6A distribution. We also compare the existing methods of m6A modifications detection, their advantages, and shortcomings, and address their possibilities of use in CRISPR-based research.

Notably, we discuss the consequences of the CRISPR-based epitranscriptomic variability to precise gene therapy, in which unintended RNA-level regulatory alterations can influence treatment safety, efficacy and reproducibility. Combining the findings of RNA biology, genome engineering, and high-throughput sequencing technologies, this review highlights the importance of taking into consideration epitranscriptomic measurements in genome editing models. The interaction between the CRISPR systems and m6A regulation will need a better insight, as it will be the key to more precise and safer therapeutic approaches.

Keywords: Epitranscriptomics; N6-methyladenosine (m6A); CRISPR-Cas9; Genome Editing; RNA Modification; Off-target Effects; DNA Damage Response; Precision Gene Therapy.

1. Introduction

Over the last few years the central dogma of molecular biology has grown beyond the linear expression of genetic information between DNA and RNA to protein, and many levels of regulatory complexity fine tuning gene expression have been added. Epigenetics is one of these regulatory tiers, and it has been known since ancient times to regulate the chromatin structure and transcription without changing the underlying sequence (1,2,3). Nevertheless, an emerging fast changing area epitranscriptomics has added another layer of post-transcriptional regulation, in which chemical modifications of RNA molecules dynamically affect their fate and function. Of the more than 170 known RNA modifications, the most common and functionally relevant internal modification of eukaryotic messenger RNA (mRNA) has

been N6-methyladenosine (m6A), which is essential in the stability of RNA, alternative splicing, nuclear export and translational efficiency (4,5,6).

The deposition of m6A and removal are controlled by a carefully coordinated group of methyltransferases (also known as writers), demethylases (also known as erasers), and RNA-binding proteins (also known as readers), allowing the fast and reversible regulation of gene expression in response to developmental signals and environmental conditions. It is this dynamism that renders m6A a significant regulatory molecule in numerous biological processes, i.e., cell differentiation, stress responses, and disease pathogenesis (7,8,9). It is worth noting that m6A dysregulation has been associated with a wide range of pathological diseases, such as cancer, neurodegeneration, and immune disorders, which makes its biological and clinical relevance hard to overlook (10,11,12).

At the same time, the introduction of CRISPR-Cas genome editing technologies has completely transformed the world of molecular biology, which has guaranteed more accuracy and effectiveness in targeted manipulation of genes. Particularly, the CRISPR-Cas9 system has found extensive use in functional genomics, as well as in therapeutic-gene correction. Although this has the potential to transform, there is the issue of unintended consequences particularly off-target DNA mutation and genomic instability, which is a significant hindrance in its clinical translation. Although the literature has been much on the characterization of DNA-level off-target effects, limited studies have been done on the possible effects of genome editing on RNA regulatory layers, and epitranscriptomic modifications in particular (13,14,15).

There are new indications that CRISPR-mediated genome editing can cause more profound cellular perturbations than changes in the DNA sequence. These consist of the stimulation of DNA damage response pathways, chromatin remodeling, transcriptional program shifts all of which can indirectly affect the epitranscriptomic landscape. Since m6A deposition is sensitive to transcriptional dynamics and cellular stress cues, it is likely that genome editing actions may cause massive remodelling of m6A patterns, in turn influencing RNA metabolism and downstream gene expression networks (16,17,18).

In this respect, it is of paramount importance to learn about the interaction between CRISPR-induced genomic perturbations and m6A-mediated epitranscriptomic regulation. These interactions could carry far-reaching consequences on cellular homeostasis, phenotypic homeostasis, and the safety of gene-editing based



therapeutic approaches (19,20,21). The current review seeks to review the existing literature in the crossroads of genome engineering and epitranscriptomics to reflect new mechanisms by which CRISPR editing can have an impact on m6A dynamics. In addition, it aims at determining some of the knowledge gaps and suggest future research directions to improve how unintended regulatory consequences are evaluated and mitigated in an effort to further develop safer and more precise gene therapy strategies (22,23,24).

2. The Epitranscriptomic Landscape of m6A RNA Modification

N6-methyladenosine (m6A) is the most common internal modification in eukaryotic messenger RNA (mRNA), and it is an essential part of epitranscriptomic regulatory network (25,26,27). The process is the methylation at nitrogen-6 of adenosine residues, and is largely overrepresented in consensus elements in the form of DRACH motifs (D = A/G/U, R = A/G, H = A/C/U). Transcriptome wide mapping analyses have shown that m6A sites are not randomly distributed, and are very much enriched in 3' end regions (3' UTR), near stop codons, and in long internal splicing and these findings indicate a very strict pattern of deposition that may have a function of great importance (28,29,30).

RNA m6A is a functional regulator of RNA metabolism, with many roles in the mRNA life cycle. It regulates the stability of mRNAs by regulating their decay or lengthening their half-life

based on the reader proteins that it interacts with. Also, M6a can also be important in control of the efficiency of translation, and it frequently promotes the quick production of proteins under cellular stress conditions. It also plays roles in making alternative splicing choices, nuclear export, and localization of RNA thus combining transcriptional products with post-transcriptional control systems (31,32,33).

Dynamicity and reversibility is one of the properties of m6A modification. Unlike the fixed genetic mutations, the m6A marks can be erected and erased promptly depending on the cellular conditions and thus the cells can be adapted to the extended environmental conditions. The plasticity is important in embryonic development, stress adaptation and stem cell differentiation (34,35,36).

It is worth noting that cellular stressors such as oxidative stress, heat shock, and DNA damage have been demonstrated to cause significant changes in m6A patterns of distribution, indicating that it is a responsive regulatory layer (37,38,39).

The m6A epitranscriptomic landscape is very sensitive to transcriptional activity and cellular signaling pathways, therefore it is highly prone to perturbations created by external interventions, such as genome editing technologies. The key to comprehending how CRISPR-mediated genomic changes can indirectly remodel the RNA regulatory networks is therefore in having a basic understanding of the underlying properties and functional implications of m6A (40).

Table 1. Key Features and Functional Roles of m6A RNA Modification (41,42,43).

Feature	Description	Biological Significance
Chemical Nature	Methylation at the N6 position of adenosine	Most abundant internal mRNA modification
Consensus Motif	DRACH sequence (e.g., RRACH)	Determines site-specific deposition
Transcript Distribution	Enriched near stop codons, 3' UTRs, and long exons	Indicates regulatory hotspots
Reversibility	Dynamically added and removed	Enables rapid cellular adaptation
Role in mRNA Stability	Can promote decay or stabilization depending on reader proteins	Controls transcript lifespan
Impact on Translation	Enhances or regulates translation efficiency	Supports rapid protein synthesis
Role in Splicing	Influences alternative splicing events	Contributes to transcript diversity
Response to Stress	Altered under stress conditions (e.g., DNA damage,	Links
Biological Processes	Development, differentiation, immune response	Essential for cellular function and homeostasis

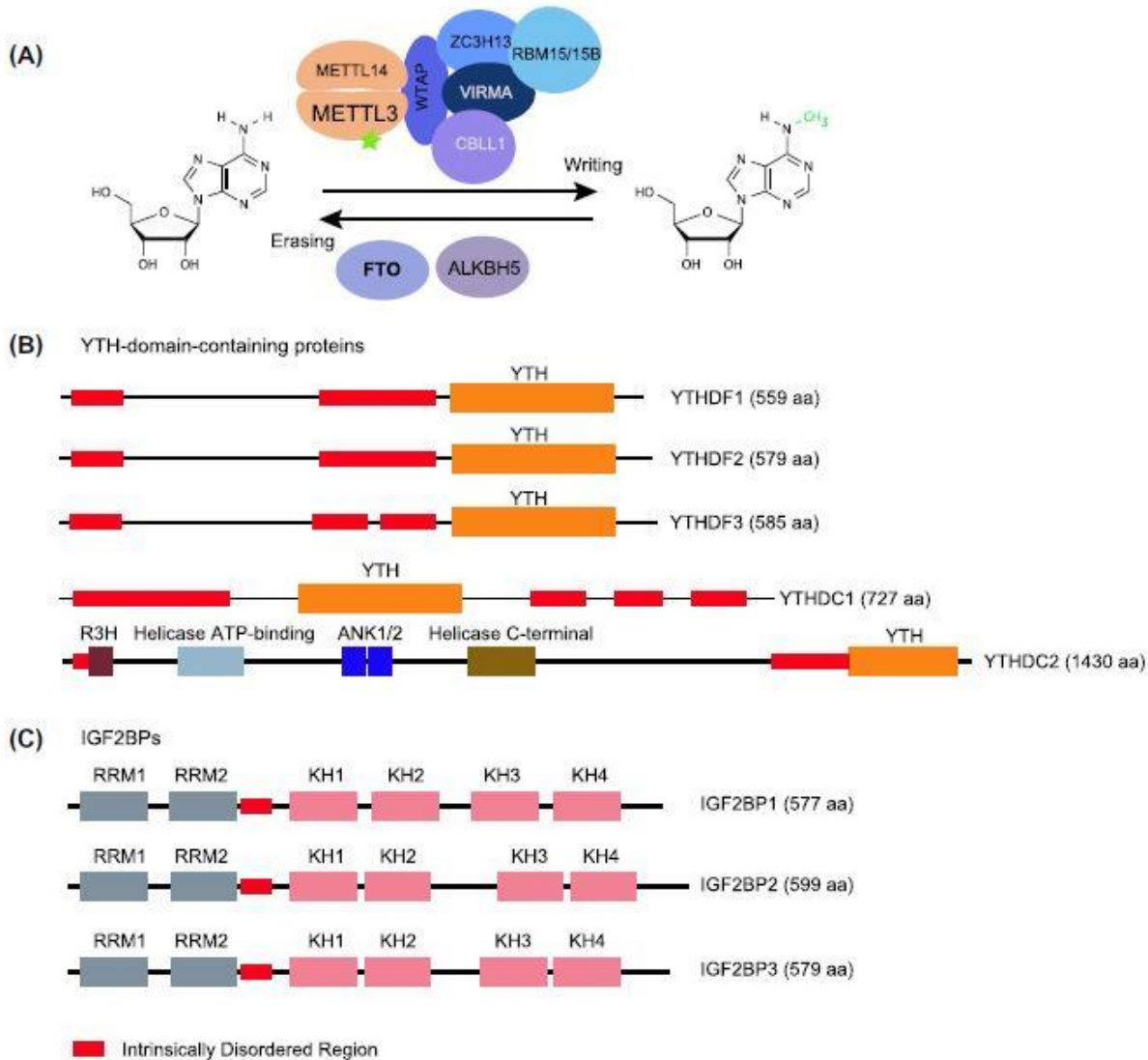


Figure 1. m6A writers, readers, and erasers. (A) The RNA modification m6A is deposited by a methyltransferase complex comprising a heterodimeric core consisting of METTL3 and METTL14, along with additional accessory subunits including WTAP, VIRMA, ZC3H13, CBLL1, and RBM15/15B. METTL3 functions as the only catalytic subunit, converting adenosine (A) to N6-methyladenosine (m6A). Below, two m6A erasers, FTO and ALKBH5, are illustrated. (B) The domain architecture of canonical m6A readers, YTH-domain-containing proteins (YTHDF1/2/3 and YTHDC1/2) which directly recognise m6A through their YTH domain. The protein sizes shown on the right are in accordance with annotations in the human genome. Note: recent evidence suggests that YTHDC2 may bind to RNA independently of m6A [82], contrasting with the original finding [83]. (C) The domain architecture of non-canonical m6A readers IGF2BP proteins (IGF2BP1/2/3) which recognise m6A through their KH domain. The protein sizes shown on the right are in accordance with annotations in the human genome.

3. Molecular Machinery Regulating m6A (Writers, Erasers, and Readers)

A highly coordinated and dynamic regulatory network of three major classes of proteins namely writers, erasers and readers controls the functional role of N6-methyladenosine

(m6A) modification. All these factors are known to control deposition, removal and interpretation of m6A tags, which in turn provides the coordination of post-transcriptional regulation of genes with extraordinary precision (44,45,46).



The installers in the installation process of m6A on RNA molecules are the methyltransferase complexes known as the writers. The key constituents of this complex are the METTL3, which is the catalytic subunit, and METTL14 which is an RNA-binding scaffold. Other such proteins that regulate substrate specificity, localization and efficiency of methylation incorporate other regulatory proteins such as WTAP, VIRMA (KIAA1429) and RBM15. The latter multi-protein complex ensures that the m6A deposition is context-dependent and site-selective and typically linked with transcriptional activity (47,48).

In contrast, the erasers are demethylases that remove m6A posts to underline the reversible nature of the epitranscriptomic mark. Two of the key identified demethylases are FTO and ALKBH5 all of them are members of the AlkB family of dioxygenases. These enzymes enable dynamically reprogramming of RNA methylation patterns in response to physiological and environmental signals, including cellular stress and metabolic reaction (49).

The final action is the functional result of the m6A marks that are mediated by a pool of assorted RNA-binding proteins referred to as readers that selectively binds methylated transcripts. Nuclear readers Nuclear readers, such as YTHDC1, take part in the core action of controlling the destiny of the m6A-modified RNA. Fate determination is also dependent on members of the YTH domain family which include YTHDF1, YTHDF2 and YTHDF3. Depending on the reader to which the m6A is conjugated, the mRNA can either be destroyed, translated, or regulated to be spliced and exported (50,51).

It is these interactions and relationships between writers, erasers and readers that give rise to cellular homeostasis. This regulatory network is susceptible to perturbation that causes the mass change in the expression of genes to become important in both normal physiology and disease states (52,53).

4. CRISPR-Cas Systems and Genome Editing-Induced Cellular Responses

Genome engineering has changed with CRISPR-Cas systems due to the possibility of exact, efficient and programmable manipulation of DNA sequences. The best known of them is CRISPR-Cas9 platform which uses a guide RNA (gRNA) to direct the Cas9 endonuclease to a specific locus in the genome where it causes a double-strand break (DSB). This targeted cleavage may trigger endogenous repair signaling, composed of most parts of non-homologous end joining (NHEJ) and homology-directed repair (HDR), which is the ultimate character of the editing outcome (54,55).

Although the CRISPR technology provides unmatched manipulation of the genetic aspect, the DSB induction is a severe cellular stressor. DNA damage resulting in activation of DNA damage response (DDR) pathways causes a series of molecular events that involve recruitment of repair factors, chromatin remodeling, and transient cell cycle arrest. These reactions are necessary to sustain genome integrity but can also have unintended effects especially when the error-prone repair mechanisms are involved (56).

In addition to direct changes in DNA, the editing via CRISPR has been demonstrated to induce an effect on the general cellular processes. As an example, formation of DSBs may result in the alteration of chromatin accessibility, and consequently transcriptional activity of the target and non-target loci. Also, genome editing can cause oxidative stress and inflammatory signaling pathway changes, which further promote global changes in the profile of gene expression (57).

Notably, these cell responses are not confined to the DNA level but may be extended to the RNA regulation systems. Various modifications in transcription and chromatin organization can have an indirect effect on RNA processing and alteration, such as epitranscriptomic modifications like m6A. Therefore, the CRISPR-induced perturbations can have a cascading effect on not only the genomic stability but also post-transcriptional regulation (58,59).

These inter-relatives help to understand the entire range of CRISPR-related effects, especially in therapeutic situations where accuracy and safety are the most important aspects (60).

5. Interplay Between CRISPR Editing and m6A Epitranscriptomic Remodeling

CRISPR-mediated genome editing and m6A epitranscriptomic regulation is a newly emerging and complicated field of study. Despite the fact that CRISPR-Cas9 is used to target DNA, there is growing evidence that downstream cellular effects of the technology go beyond changes in the genomic context and that it can affect the regulatory landscape of RNA. To be more exact, the activation of DNA damage response (DDR) pathways and the resulting induction of double-strand breaks (DSBs) can provide a cellular environment that facilitates epitranscriptomic remodelling (61,62).

Among the most important processes connecting the CRISPR activity to m6A dynamics is a change in transcriptional programs. RNA polymerase II activity can be modified by DNA damage and chromatin remodelling, and this can control transcription rates and co-transcriptional m6A deposition. Because the



installation of m6A is strictly connected to transcription, any event of disruption to transcriptional kinetics can produce the redistribution of m6A across the transcriptome. In addition, genome editing can trigger stress-responsive signaling pathways, including p53 signaling and oxidative stress response, that have been reported to regulate the expression and activity of m6A regulatory proteins, such as METTL3 and FTO (63,64).

Also, the alterations in chromatin accessibility caused by CRISPR can change the recruitment of RNA-binding proteins and m6A machines to particular genomic loci. It may cause local or global changes in m6A content, which may change the stability

of mRNAs, translation, and the cell phenotype. Notably, the effects can be long-term, after the editing event, which brings up long-term transcriptomic instability (65,66).

Other recent research has also suggested that off-target editing events may play an indirect role in the deposition of aberrant m6A, through the disruption of regulatory genes in RNA metabolism. Despite the fact that this area is still in its infancy the existing evidence suggests that epitranscriptomic implications should be taken into account to improve the analysis of CRISPR effects, especially in delicate processes like stem cell editing and gene therapy (67,68).

Table 2. Potential Mechanisms Linking CRISPR Editing to m6A Remodeling (69,70).

CRISPR-Induced Event	Effect on Cellular Processes	Potential Impact on m6A
DNA Double-Strand Breaks (DSBs)	Activation of DDR pathways	Altered m6A deposition via stress signaling
Chromatin Remodeling	Changes in DNA accessibility	Modified recruitment of m6A machinery
Transcriptional Reprogramming	Altered RNA polymerase II activity	Redistribution of m6A across transcripts
Oxidative Stress	Activation of stress-response pathways	Regulation of writers and erasers
Off-target Mutations	Disruption of regulatory genes	Indirect perturbation of RNA modification pathways
Cell Cycle Arrest	Temporary	Changes in RNA processing dynamics

6. Experimental Approaches for Detecting m6A Changes Post-CRISPR Editing

N6-methyladenosine (m6A) modifications can be accurately detected and measured, which is why the study of their impact on the epitranscriptomic environment requires CRISPR-mediated genome editing. Since m6A is dynamic and context-dependent, a multiplicity of experimental and computational strategies has been established to map these modifications with different degrees of resolution, sensitivity and specificity. Nonetheless, research into m6A changes during genome editing poses special technical problems, especially in trying to identify definitive changes caused by editing and background fluctuations (71,55).

One of the most common types of transcriptome-wide m6A mapping using antibody-based enrichment methods include methylated RNA immunoprecipitation sequencing (MeRIP-seq) and m6A-seq. The techniques are based on immunoprecipitation of fragments of RNA that are methylated and then subjected to next-generation sequencing. They offer a general picture of the m6A distribution globally; however, their comparatively low resolution, which usually identifies regions of 100-200

nucleotides, does not allow them to identify the exact site of modification. Besides, the specificity of antibodies and changes in batches can cause experimental bias (72,44).

To address the limitations, techniques with higher resolution have been invented. Single-nucleotide mapping techniques, like miCLIP (m6A individual-nucleotide-resolution crosslinking and immunoprecipitation), allow introducing a mutagenic signature at the m6A sites during reverse transcription. In the same way, methods aided by photo-crosslinking (ex: PA-m6A-seq) enhance specificity by utilizing covalent RNA-protein interactions. Nanopore direct RNA sequencing is a relatively more recent technology that has become a potent antibody-free technology with the ability to identify RNA modifications in real-time at single-molecule resolution. This approach is especially useful when examining changes in epitranscriptomic responses to CRISPR editing, which are subtler, but issues associated with signal noise, base-calling and data interpretation still exist (73,74).

In complement to approaches based on sequencing, liquid chromatography-mass spectrometry (LC-MS/MS) offers very precise quantification of global m6A abundance, but does not include information about location. Thus, it may be required to



combine various orthogonal methods to obtain both quantitative and site-specific information (75,76).

Other factors to consider in CRISPR-edited systems are cellular heterogeneity, editing efficiency and transcriptional responses to stress, each of which can confound interpretation. Matched

unedited cells and other controls on appropriate experimental conditions are essential to robust analysis and require advanced bioinformatics pipelines. Finally, these technologies will need further refinement before they can be reliably used to characterize epitranscriptomic changes and what they imply in genome editing (77,78,79).

Table 3. Technologies for m6A Detection and Their Key Features (80,81).

Technique	Principle	Resolution	Advantages	Limitations
MeRIP-seq	Antibody-based enrichment of m6A RNA	Low (~100–200 nt)	Widely used, scalable	Low resolution, antibody bias
m6A-seq	Immunoprecipitation followed by sequencing	Low	Global mapping capability	Limited precision
miCLIP	UV crosslinking induces mutation signatures	High (single-base)	Precise site identification	Technically demanding, complex analysis
PA-m6A-seq	Photo-crosslinking for enhanced specificity	Medium–High	Improved signal-to-noise ratio	Requires specialized protocols
Nanopore Sequencing	Direct RNA sequencing without antibodies	Very high	Single-molecule, real-time detection	Higher error rates, computational challenges
LC-MS/MS	Mass spectrometry-based quantification	No site resolution	Highly accurate global quantification	Lacks positional information

Conclusion

This recent movement toward epitranscriptomics has created a new dimension of important cells that should not be controlled by the DNA sequence or chromatin state but by the dynamic and reversible changes in RNA state. N6-methyladenosine (m6A) is one of them, and has been found to be a key regulatory modification that modulates various processes of RNA metabolism, such as stability, translation, and splicing. Simultaneously, the CRISPR-Cas genome editing technologies have transformed the contemporary molecular biology and have colossal potential in gene correction therapy. Nonetheless, the biological implications of genome editing, as highlighted in this review, go beyond the desired alterations in DNA and can feature numerous, multifaceted regulatory changes.

There is mounting evidence indicating that editing using CRISPR can indirectly reorganize the epitranscriptome by activating DNA damage response and chromatin remodeling and transcriptional reprogramming. Such perturbations of cells have the potential to affect the activity and localization of m6A regulatory machinery, resulting in a change in RNA methylation patterns. Such changes are capable of impacting on gene-expression networks, stable phenotype cells and long-term genomic integrity particularly in

sensitive uses such as stem cell engineering and regenerative medicine.

It is interesting to note that CRISPR-related epitranscriptomic variability might also be involved to a further complication in gauging the security and usefulness of accuracy gene therapy. Even though there has been a lot in minimizing the off-target effects at the DNA level, there is a lack of adequate studies at the RNA level to adequately describe the changes in regulation. This amounts to a desperate requirement in the current genome editing evaluation structures, which must be reconciled to ensure the development of truly correct and predictable treatment methods.

It is perceived that the novel high-resolution sequencing schemes, integrative multiple-omics approaches will be instrumental in the disclosing of the entire remodeling of m6A following genome editing. Subsequent studies must consider mapping these changes systematically, determining their functional implications and come up with ways of stemming off these unintended epitranscriptomic effects. Finally, a thorough knowledge of the interaction between CRISPR technologies and RNA modification systems would be necessary to streamline the use of genome



editing and open up their potential as a safe and controlled source of therapeutics.

References

1. Dominissini, D.; Moshitch-Moshkovitz, S.; Schwartz, S.; Salmon-Divon, M.; Ungar, L.; Osenberg, S.; Cesarkas, K.; Jacob-Hirsch, J.; Amariglio, N.; Kupiec, M.; et al. Topology of the human and mouse m6A RNA methylomes revealed by m6A-seq. *Nature* **2012**, *485*, 201–206. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
2. He, P.C.; He, C. m⁶A RNA methylation: From mechanisms to therapeutic potential. *EMBO J.* **2021**, *40*, e105977. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
3. Cusenza, V.Y.; Tameni, A.; Neri, A.; Frazzi, R. The lncRNA epigenetics: The significance of m6A and m5C lncRNA modifications in cancer. *Front. Oncol.* **2023**, *13*, 1063636. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
4. Wang, J.; Wang, L. Deep analysis of RNA N6-adenosine methylation (m⁶A) patterns in human cells. *NAR Genom. Bioinform.* **2020**, *2*, lqaa007. [[Google Scholar](#)] [[CrossRef](#)]
5. Yang, S.; Wei, J.; Cui, Y.H.; Park, G.; Shah, P.; Deng, Y.; Aplin, A.E.; Lu, Z.; Hwang, S.; He, C.; et al. m6A mRNA demethylase FTO regulates melanoma tumorigenicity and response to anti-PD-1 blockade. *Nat. Commun.* **2019**, *10*, 2782. [[Google Scholar](#)] [[CrossRef](#)]
6. Shi, Y.; Fan, S.; Wu, M.; Zuo, Z.; Li, X.; Jiang, L.; Shen, Q.; Xu, P.; Zeng, L.; Zhou, Y.; et al. YTHDF1 links hypoxia adaptation and non-small cell lung cancer progression. *Nat. Commun.* **2019**, *10*, 4892. [[Google Scholar](#)] [[CrossRef](#)]
7. Han, M.; Liu, Z.; Xu, Y.; Liu, X.; Wang, D.; Li, F.; Wang, Y.; Bi, J. Abnormality of m6A mRNA Methylation Is Involved in Alzheimer's Disease. *Front. Neurosci.* **2020**, *14*, 98. [[Google Scholar](#)] [[CrossRef](#)]
8. Dorn, L.E.; Lasman, L.; Chen, J.; Xu, X.; Hund, T.J.; Medvedovic, M.; Hanna, J.H.; van Berlo, J.H.; Accornero, F. The N-Methyladenosine mRNA Methylase METTL3 Controls Cardiac Homeostasis and Hypertrophy. *Circulation* **2019**, *139*, 533–545. [[Google Scholar](#)] [[CrossRef](#)]
9. Wang, H.; Hu, X.; Huang, M.; Liu, J.; Gu, Y.; Ma, L.; Zhou, Q.; Cao, X. Mettl3-mediated mRNA m⁶A methylation promotes dendritic cell activation. *Nat. Commun.* **2019**, *10*, 1898. [[Google Scholar](#)] [[CrossRef](#)]
10. Zhang, Y.; Wang, X.; Zhang, X.; Wang, J.; Ma, V.; Zhang, L.; Cao, X. RNA-binding protein YTHDF3 suppresses interferon-dependent antiviral responses by promoting FOXO3 translation. *Proc. Natl. Acad. Sci. USA* **2019**, *116*, 976–981. [[Google Scholar](#)] [[CrossRef](#)]
11. Liu, J.; Yue, Y.; Han, D.; Wang, X.; Fu, Y.; Zhang, L.; Jia, G.; Yu, M.; Lu, Z.; Deng, X.; et al. A METTL3-METTL14 complex mediates mammalian nuclear RNA N6-adenosine methylation. *Nat. Chem. Biol.* **2014**, *10*, 93–95. [[Google Scholar](#)] [[CrossRef](#)]
12. Bokar, J.A.; Rath-Shambaugh, M.E.; Ludwiczak, R.; Narayan, P.; Rottman, F. Characterization and partial purification of mRNA N6-adenosine methyltransferase from HeLa cell nuclei: Internal mRNA methylation requires a multisubunit complex. *J. Biol. Chem.* **1994**, *269*, 17697–17704. [[Google Scholar](#)] [[CrossRef](#)]
13. Theler, D.; Dominguez, C.; Blatter, M.; Boudet, J.; Allain, F.H.T. Solution structure of the YTH domain in complex with N6-methyladenosine RNA: A reader of methylated RNA. *Nucleic Acids Res.* **2014**, *42*, 13911–13919. [[Google Scholar](#)] [[CrossRef](#)]
14. Rauch, S.; He, C.; Dickinson, B.C. Targeted m6A reader proteins to study epitranscriptomic regulation of single RNAs. *J. Am. Chem. Soc.* **2018**, *140*, 11974–11981. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
15. Sokpor, G.; Xie, Y.; Nguyen, H.P.; Tuoc, T. Emerging Role of m6A Methylome in Brain Development: Implications for Neurological Disorders and Potential Treatment. *Front. Cell Dev. Biol.* **2021**, *9*, 656849. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
16. Huang, H.; Weng, H.; Sun, W.; Qin, X.; Shi, H.; Wu, H.; Zhao, B.S.; Mesquita, A.; Liu, C.; Yuan, C.L.; et al. Recognition of RNA N(6)-methyladenosine by IGF2BP proteins enhances mRNA stability and translation. *Nat. Cell Biol.* **2018**, *20*, 285–295. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
17. Mauer, J.; Sindelar, M.; Despici, V.; Guez, T.; Hawley, B.R.; Vasseur, J.J.; Rentmeister, A.; Gross, S.S.; Pellizzoni, L.; Debart, F.; et al. FTO controls reversible m⁶Am RNA methylation during snRNA biogenesis. *Nat. Chem. Biol.* **2019**, *15*, 340–347. [[Google Scholar](#)] [[CrossRef](#)]
18. Ke, S.; Alemu, E.A.; Mertens, C.; Gantman, E.C.; Fak, J.J.; Mele, A.; Haripal, B.; Zucker-Scharff, I.; Moore, M.J.; Park, C.Y.; et al. A majority of m6A residues are in the last exons, allowing the potential for 3' UTR regulation. *Genes Dev.* **2015**, *29*, 2037–2053. [[Google Scholar](#)] [[CrossRef](#)]
19. Zhang, W.; Qian, Y.; Jia, G. The detection and functions of RNA modification m6A based on m6A writers and erasers. *J. Biol. Chem.* **2021**, *297*, 100973. [[Google Scholar](#)] [[CrossRef](#)]
20. Kostyusheva, A.; Brezgin, S.; Glebe, D.; Kostyushev, D.; Chulanov, V. Host-cell interactions in HBV infection and



- pathogenesis: The emerging role of m6A modification. *Emerg. Microbes Infect.* **2021**, *10*, 2264–2275. [[Google Scholar](#)] [[CrossRef](#)]
21. Hu, L.; Liu, S.; Peng, Y.; Ge, R.; Su, R.; Senevirathne, C.; Harada, B.T.; Dai, Q.; Wei, J.; Zhang, L.; et al. m6A RNA modifications are measured at single-base resolution across the mammalian transcriptome. *Nat. Biotechnol.* **2022**, *40*, 1210–1219. [[Google Scholar](#)]
 22. Zhang, Q.; Dai, Y.; Teng, X.; Li, J. Visualization and Quantification of Single-Base m6A Methylation. *Angew. Chem. Int. Ed. Engl.* **2025**, *64*, e202420977. [[Google Scholar](#)] [[CrossRef](#)]
 23. Liu, Z.; Zou, H.; Dang, Q.; Xu, H.; Liu, L.; Zhang, Y.; Lv, J.; Li, H.; Zhou, Z.; Han, X. Biological and pharmacological roles of m6A modifications in cancer drug resistance. *Mol. Cancer* **2022**, *21*, 220. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
 24. Wang, H.; Xu, B.; Shi, J. N6-methyladenosine METTL3 promotes the breast cancer progression via targeting Bcl-2. *Gene* **2020**, *722*, 144076. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
 25. Ma, J.Z.; Yang, F.; Zhou, C.C.; Liu, F.; Yuan, J.H.; Wang, F.; Wang, T.T.; Xu, Q.G.; Zhou, W.P.; Sun, S.H. METTL14 Suppresses the Metastatic Potential of Hepatocellular Carcinoma by Modulating N6-Methyladenosine-Dependent Primary MicroRNA Processing. *Hepatology* **2016**, *65*, 529–543. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
 26. Panneerdoss, S.; Eedunuri, V.K.; Yadav, P.; Timilsina, S.; Rajamanickam, S.; Viswanadhapalli, S.; Abdelfattah, N.; Onyeagucha, B.C.; Cui, X.; Lai, Z.; et al. Cross-talk among writers, readers, and erasers of m⁶A regulates cancer growth and progression. *Sci. Adv.* **2018**, *4*, eaar8263. [[Google Scholar](#)]
 27. Qin, S.; Mao, Y.; Chen, X.; Xiao, J.; Qin, Y.; Zhao, L. The functional roles, cross-talk and clinical implications of m6A modification and circRNA in hepatocellular carcinoma. *Int. J. Biol. Sci.* **2021**, *17*, 3059. [[Google Scholar](#)] [[CrossRef](#)]
 28. Bray, F.; Ferlay, J.; Soerjomataram, I.; Siegel, R.L.; Torre, L.A.; Jemal, A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J. Clin.* **2018**, *68*, 394–424. [[Google Scholar](#)] [[CrossRef](#)]
 29. Gong, S.; Wang, S.; Shao, M. Mechanism of METTL14-mediated m6A modification in non-small cell lung cancer cell resistance to cisplatin. *J. Mol. Med.* **2022**, *100*, 1771–1785. [[Google Scholar](#)] [[CrossRef](#)]
 30. Zhang, Y.; Liu, S.; Zhao, T.; Dang, C. METTL3-mediated m6A modification of Bcl-2 mRNA promotes non-small cell lung cancer progression. *Oncol. Rep.* **2021**, *46*, 163. [[Google Scholar](#)] [[CrossRef](#)]
 31. Liu, C.; Ren, Q.; Deng, J.; Wang, S.; Ren, L. c-MYC/METTL3/LINC01006 positive feedback loop promotes migration, invasion and proliferation of non-small cell lung cancer. *Biomed. J.* **2024**, *47*, 100664. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
 32. Zhang, D.; Ning, J.; Okon, I.; Zheng, X.; Satyanarayana, G.; Song, P.; Xu, S.; Zou, M.H. Suppression of m6A mRNA modification by DNA hypermethylated ALKBH5 aggravates the oncological behavior of KRAS mutation/LKB1 loss lung cancer. *Cell Death Dis.* **2021**, *12*, 518. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
 33. Xu, X.; Qiu, S.; Zeng, B.; Huang, Y.; Wang, X.; Li, F.; Yang, Y.; Cao, L.; Zhang, X.; Wang, J.; et al. N6-methyladenosine demethyltransferase FTO mediated m6A modification of estrogen receptor alpha in non-small cell lung cancer tumorigenesis. *Oncogene* **2024**, *43*, 1288–1302. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
 34. Sun, Y.; Shen, W.; Hu, S.; Lyu, Q.; Wang, Q.; Wei, T.; Zhu, W.; Zhang, J. METTL3 promotes chemoresistance in small cell lung cancer by inducing mitophagy. *J. Exp. Clin. Cancer Res.* **2023**, *42*, 65. [[Google Scholar](#)] [[CrossRef](#)]
 35. Sharba, M. M., Mohammed, A. A., & Mohammed, S. F. (2022). Isolation and Characterization of tannase from isolated *Bacillus subtilis*. [[Google Scholar](#)].
 36. Zhang, S.; Dou, T.; Li, H.; Yu, H.; Zhang, W.; Sun, L.; Yang, J.; Wang, Z.; Yang, H. Knockdown of IGF2BP2 overcomes cisplatin-resistance in lung cancer through downregulating Spon2 gene. *Hereditas* **2024**, *161*, 55. [[Google Scholar](#)] [[CrossRef](#)]
 37. Wang, X.; Kong, W.; Guo, F.; Sha, R.; Zhao, G.; Qiao, W.; Xu, K.; Feng, Y.; Sun, W.; Ma, X. Identification of Therapeutic Targets and Prognostic Biomarkers of IGF2BPs in the Lung Cancer Microenvironment. *Sci. Rep.* **2021**, *15*, 5681. [[Google Scholar](#)] [[CrossRef](#)]
 38. Yu, M.; Ji, W.; Yang, X.; Tian, K.; Ma, X.; Yu, S.; Chen, L.; Zhao, X. The role of m6A demethylases in lung cancer: Diagnostic and therapeutic implications. *Front. Immunol.* **2023**, *14*, 1279735. [[Google Scholar](#)] [[CrossRef](#)]
 39. Wan, W.; Ao, X.; Chen, Q.; Yu, Y.; Ao, L.; Xing, W.; Guo, W.; Wu, X.; Pu, C.; Hu, X.; et al. METTL3/IGF2BP3 axis inhibits tumor immune surveillance by upregulating N6-methyladenosine modification of PD-L1 mRNA in breast cancer. *Mol. Cancer* **2022**, *21*, 60. [[Google Scholar](#)] [[CrossRef](#)]
 40. Zhao, C.; Ling, X.; Xia, Y.; Yan, B.; Guan, Q. The m6A methyltransferase METTL3 controls epithelial-mesenchymal transition, migration and invasion of breast



- cancer through the MALAT1/miR-26b/HMGA2 axis. *Cancer Cell Int.* **2021**, *21*, 441. [[Google Scholar](#)] [[CrossRef](#)]
41. Pan, X.; Hong, X.; Li, S.; Meng, P.; Xiao, F. METTL3 promotes adriamycin resistance in MCF-7 breast cancer cells by accelerating pri-microRNA-221-3p maturation in a m6A-dependent manner. *Exp. Mol. Med.* **2021**, *53*, 91–102. [[Google Scholar](#)] [[CrossRef](#)]
42. Shi, Y.; Zheng, C.; Jin, Y.; Bao, B.; Wang, D.; Hou, K.; Feng, J.; Tang, S.; Qu, X.; Liu, Y.; et al. Reduced Expression of METTL3 Promotes Metastasis of Triple-Negative Breast Cancer by m6A Methylation-Mediated COL3A1 Up-Regulation. *Front. Oncol.* **2020**, *10*, 1126. [[Google Scholar](#)] [[CrossRef](#)]
43. Wang, S.; Zou, X.; Chen, Y.; Cho, W.C.; Zhou, X. Effect of N6-Methyladenosine Regulators on Progression and Prognosis of Triple-Negative Breast Cancer. *Front. Genet.* **2021**, *11*, 580036. [[Google Scholar](#)] [[CrossRef](#)]
44. Zhang, C.; Samanta, D.; Lu, H.; Bullen, J.W.; Zhang, H.; Chen, I.; He, X.; Semenza, G.L. Hypoxia induces the breast cancer stem cell phenotype by HIF-dependent and ALKBH5-mediated m6A-demethylation of NANOG mRNA. *Proc. Natl. Acad. Sci. USA* **2016**, *113*, E2047–E2056. [[Google Scholar](#)] [[CrossRef](#)]
45. Malek, G. K., Hussein, S. A. M., & Mohammed, A. A. (2024). Effect of Puberty and Gender on Metabolic Hormones Level and Lipid Profile in Patients with Growth Hormone Deficiency. *International Journal of Medical Science and Dental Health*, *11*(11), 63-72. [[Google Scholar](#)].
46. Chang, G.; Shi, L.; Ye, Y.; Shi, H.; Zeng, L.; Tiwary, S.; Huse, J.T.; Huo, L.; Ma, L.; Ma, Y.; et al. YTHDF3 Induces the Translation of m6A-Enriched Gene Transcripts to Promote Breast Cancer Brain Metastasis. *Cancer Cell* **2020**, *38*, 857–871.e7. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
47. Gong, P.J.; Shao, Y.C.; Yang, Y.; Song, W.J.; He, X.; Zeng, Y.F.; Huang, S.R.; Wei, L.; Zhang, J.W. Analysis of N6-Methyladenosine Methyltransferase Reveals METTL14 and ZC3H13 as Tumor Suppressor Genes in Breast Cancer. *Front. Oncol.* **2020**, *10*, 578963. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
48. Bai, X.; Liu, J.; Zhou, S.; Wu, L.; Feng, X.; Zhang, P. METTL14 suppresses the expression of YAP1 and the stemness of triple-negative breast cancer. *J. Exp. Clin. Cancer Res.* **2024**, *43*, 307. [[Google Scholar](#)] [[CrossRef](#)]
49. Schadendorf, D.; Fisher, D.E.; Garbe, C.; Gershenwald, J.E.; Grob, J.J.; Halpern, A.; Herlyn, M.; Marchetti, M.A.; McArthur, G.; Ribas, A.; et al. Melanoma. *Nat. Rev. Dis. Prim.* **2015**, *1*, 15003. [[Google Scholar](#)] [[CrossRef](#)]
50. O'Neill, C.H.; Scoggins, C.R. Melanoma. *J. Surg. Oncol.* **2019**, *120*, 873–881. [[Google Scholar](#)] [[CrossRef](#)]
51. Dahal, U.; Le, K.; Gupta, M. RNA m6A methyltransferase METTL3 regulates invasiveness of melanoma cells by matrix metalloproteinase 2. *Melanoma Res.* **2019**, *29*, 382–389. [[Google Scholar](#)] [[CrossRef](#)]
52. Yue, Z.; Cao, M.; Hong, A.; Zhang, Q.; Zhang, G.; Jin, Z.; Zhao, L.; Wang, Q.; Fang, F.; Wang, Y.; et al. m6A Methyltransferase METTL3 Promotes the Progression of Primary Acral Melanoma via Mediating TXNDC5 Methylation. *Front. Oncol.* **2022**, *11*, 770325. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
53. Wu, H.; Xu, H.; Jia, D.; Li, T.; Xia, L. METTL3-induced UCK2 m6A hypermethylation promotes melanoma cancer cell metastasis via the WNT/ β -catenin pathway. *Ann. Transl. Med.* **2021**, *9*, 1155. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
54. Li, N.; Kang, Y.; Wang, L.; Huff, S.; Tang, R.; Hui, H.; Agrawal, K.; Gonzalez, G.M.; Wang, Y.; Patel, S.P.; et al. ALKBH5 regulates anti-PD-1 therapy response by modulating lactate and suppressive immune cell accumulation in tumor microenvironment. *Proc. Natl. Acad. Sci. USA* **2020**, *117*, 20159–20170. [[Google Scholar](#)] [[CrossRef](#)]
55. Mohammed, A. A., Barale, S. S., Dhotare, P. S., & Sonawane, K. D. (2025). Polymyxin-B as a novel inhibitor of amyloid beta aggregation: Computational insights and experimental validation. *Journal of Molecular Structure*, 143738. [[Google Scholar](#)].
56. Jia, R.; Chai, P.; Wang, S.; Sun, B.; Xu, Y.; Yang, Y.; Ge, S.; Jia, R.; Yang, Y.G.; Fan, X. M6A modification suppresses ocular melanoma through modulating HINT2 mRNA translation. *Mol. Cancer* **2019**, *18*, 161. [[Google Scholar](#)] [[CrossRef](#)]
57. Ozakyol, A. Global Epidemiology of Hepatocellular Carcinoma (HCC Epidemiology). *J. Gastrointest. Cancer* **2017**, *48*, 238–240. [[Google Scholar](#)] [[CrossRef](#)]
58. Chen, M.; Wei, L.; Law, C.T.; Tsang, F.H.; Shen, J.; Cheng, C.L.; Tsang, L.H.; Ho, D.W.; Chiu, D.K.; Lee, J.M.; et al. RNA N6-methyladenosine methyltransferase-like 3 promotes liver cancer progression through YTHDF2-dependent posttranscriptional silencing of SOCS2. *Hepatology* **2018**, *67*, 2254–2270. [[Google Scholar](#)] [[CrossRef](#)]
59. Lin, Y.; Wei, X.; Jian, Z.; Zhang, X. METTL3 expression is associated with glycolysis metabolism and sensitivity to



- glycolytic stress in hepatocellular carcinoma. *Cancer Med.* **2020**, *9*, 2859–2867. [[Google Scholar](#)] [[CrossRef](#)]
60. Qiao, K.; Liu, Y.; Xu, Z.; Zhang, H.; Zhang, H.; Zhang, C.; Chang, Z.; Lu, X.; Li, Z.; Luo, C.; et al. RNA m6A methylation promotes the formation of vasculogenic mimicry in hepatocellular carcinoma via Hippo pathway. *Angiogenesis* **2021**, *24*, 83–96. [[Google Scholar](#)] [[CrossRef](#)]
 61. Chen, Y.; Zhao, Y.; Chen, J.; Peng, C.; Zhang, Y.; Tong, R.; Cheng, Q.; Yang, B.; Feng, X.; Lu, Y.; et al. ALKBH5 suppresses malignancy of hepatocellular carcinoma via m6A-guided epigenetic inhibition of LYPD1. *Mol. Cancer* **2020**, *19*, 123. [[Google Scholar](#)] [[CrossRef](#)]
 62. Li, J.; Zhu, L.; Shi, Y.; Liu, J.; Lin, L.; Chen, X. M6A Demethylase FTO Promotes Hepatocellular Carcinoma Tumorigenesis via Mediating PKM2 Demethylation. *Am. J. Transl. Res.* **2019**, *11*, 6084. [[Google Scholar](#)] [[PubMed](#)]
 63. Zhao, Y.; You, S.; Yu, Y.Q.; Zhang, S.; Li, P.T.; Ye, Y.H.; Zhao, W.X.; Li, J.; Li, Q.; Jiao, H.; et al. Decreased nuclear expression of FTO in human primary hepatocellular carcinoma is associated with poor prognosis. *Int. J. Clin. Exp. Pathol.* **2019**, *12*, 3376–3383. [[Google Scholar](#)] [[PubMed](#)]
 64. Qin, S.; Liu, G.; Jin, H.; Chen, X.; He, J.; Xiao, J.; Qin, Y.; Mao, Y.; Zhao, L. The Comprehensive Expression and Functional Analysis of M6A Modification “Readers” in Hepatocellular Carcinoma. *Aging* **2022**, *14*, 6269. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
 65. Aherkar, V. V., Mohammed, A. A., Al-Shimary, A. A., Kshirsagar, V., Shendage, R., Ubale, P. A., ... & Ovhal, R. M. (2025). Photocatalytic dye degradation efficacy and antimicrobial potency of zinc oxide nanoparticles synthesized via sol-gel method. *Next Materials*, *9*, 100972. [[Google Scholar](#)]
 66. Zhao, L.; Huang, H.; Luo, L.; Huang, Z.; Wu, Z.; Wang, F.; Wen, Z. The m6A reader IGF2BP3 promotes HCC progression by enhancing MCM10 stability. *Sci. Rep.* **2025**, *15*, 8204. [[Google Scholar](#)] [[CrossRef](#)]
 67. Yao, Y.; Xie, J.; Ba, J.; Zhang, M.; Wan, Y.; Jin, Z. The m⁶A methyltransferase METTL3 promotes the stemness and malignant progression of breast cancer by mediating m⁶A modification on SOX2. *JBUON* **2021**, *26*, 444–449. [[Google Scholar](#)]
 68. Chen, S.; Wang, L.; Xu, Z.; Chen, L.; Li, Q.; Zhong, F.; Tang, N.; Song, J.; Zhou, R. YTHDF3-mediated m6A modification of NKD1 regulates hepatocellular carcinoma invasion and metastasis by activating the WNT/β-catenin signaling axis. *Exp. Cell Res.* **2024**, *442*, 114192. [[Google Scholar](#)] [[CrossRef](#)]
 69. Zhong, L.; Liao, D.; Zhang, M.; Zeng, C.; Li, X.; Zhang, R.; Ma, H.; Kang, T. YTHDF2 suppresses cell proliferation and growth via destabilizing the EGFR mRNA in hepatocellular carcinoma. *Cancer Lett.* **2019**, *442*, 252–261. [[Google Scholar](#)] [[CrossRef](#)]
 70. Deng, X.; Qing, Y.; Horne, D.; Huang, H.; Chen, J. The roles and implications of RNA m6A modification in cancer. *Nat. Rev. Clin. Oncol.* **2023**, *20*, 507–526. [[Google Scholar](#)] [[CrossRef](#)]
 71. Bedi, R.K.; Huang, D.; Eberle, S.A.; Wiedmer, L.; Ślędz, P.; Cafilisch, A. Small-Molecule Inhibitors of METTL3, the Major Human Epitranscriptomic Writer. *ChemMedChem* **2020**, *15*, 744–748. [[Google Scholar](#)] [[CrossRef](#)]
 72. Yankova, E.; Blackaby, W.; Albertella, M.; Rak, J.; De Braekeleer, E.; Tsagkogeorga, G.; Pilka, E.S.; Aspris, D.; Leggate, D.; Hendrick, A.G.; et al. Small-molecule inhibition of METTL3 as a strategy against myeloid leukaemia. *Nature* **2021**, *593*, 597–601. [[Google Scholar](#)] [[CrossRef](#)]
 73. Chen, W.; Zhang, J.; Ma, W.; Liu, N.; Wu, T. METTL3-Mediated m6A Modification Regulates the Polycomb Repressive Complex 1 Components BMI1 and RNF2 in Hepatocellular Carcinoma Cells. *Mol. Cancer Res.* **2025**, *23*, 190–201. [[Google Scholar](#)] [[CrossRef](#)]
 74. Cesaro, B.; Iaiza, A.; Piscopo, F.; Tarullo, M.; Cesari, E.; Rotili, D.; Mai, A.; Diana, A.; Londero, M.; Del Giacco, L.; et al. Enhancing sensitivity of triple-negative breast cancer to DNA-damaging therapy through chemical inhibition of the m6A methyltransferase METTL3. *Cancer Commun.* **2024**, *44*, 282–286. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
 75. Khamees, H. H., Mohammed, A. A., Hussein, S. A. M., Ahmed, M. A., & Raoof, A. S. M. (2024). In-Silico Study OF Destabilizing Alzheimer's Aβ42 Protofibrils with Curcumin. *International Journal of Medical Science and Dental Health*, *10*(05), 76-84. [[Google Scholar](#)]
 76. Huang, Y.; Su, R.; Sheng, Y.; Dong, L.; Dong, Z.; Xu, H.; Ni, T.; Zhang, Z.S.; Zhang, T.; Li, C.; et al. Small-Molecule Targeting of Oncogenic FTO Demethylase in Acute Myeloid Leukemia. *Cancer Cell* **2019**, *35*, 677–691.e10. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
 77. Su, R.; Dong, L.; Li, Y.; Gao, M.; Han, L.; Wunderlich, M.; Deng, X.; Li, H.; Huang, Y.; Gao, L.; et al. Targeting FTO Suppresses Cancer Stem Cell Maintenance and Immune Evasion. *Cancer Cell* **2020**, *38*, 79–96.e11. [[Google Scholar](#)] [[CrossRef](#)]
 78. Lai, G.Q.; Li, Y.; Zhu, H.; Zhang, T.; Gao, J.; Zhou, H.; Yang, Z.-G. A covalent compound selectively inhibits RNA



- demethylase ALKBH5 rather than FTO. *RSC Chem. Biol.* **2024**, *5*, 335–343. [[Google Scholar](#)] [[CrossRef](#)]
- 79.** Zhang, H.; Wang, X.; Chen, J.; Su, R. Combating cancer stem cells: RNA m6A methylation and small-molecule drug discovery. *Front. Drug Discov.* **2024**, *4*, 1465222. [[Google Scholar](#)] [[CrossRef](#)]
- 80.** Moroz-Omori, E.V.; Huang, D.; Kumar Bedi, R.; Cheriyankunnel, S.J.; Bochenkova, E.; Dolbois, A.; Rzeczowski, M.D.; Li, Y.; Wiedmer, L.; Caflisch, A. METTL3 Inhibitors for Epitranscriptomic Modulation of Cellular Processes. *ChemMedChem* **2021**, *16*, 3035–3043. [[Google Scholar](#)] [[CrossRef](#)]
- 81.** Dolbois, A.; Bedi, R.K.; Bochenkova, E.; Müller, A.; Moroz-Omori, E.V.; Huang, D.; Caflisch, A. 1,4,9-Triazaspiro[5.5]undecan-2-one Derivatives as Potent and Selective METTL3 Inhibitors. *J. Med. Chem.* **2021**, *64*, 12738–12760. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]