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Role of METTL3 Protein in Asthma: Insights from Transcriptomic Profiling and Molecular Docking Analysis

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ABSTRACT

Asthma is a chronic inflammatory disease characterized byimmune dysregulation. This study aimed to perform unbiased analysis of transcriptomic data to identify differentially expressed m6A-related genes in asthma, with a focus on exploring their potential as biomarkers and therapeutic targets.

Gene Expression Omnibus (GEO) (GSE134544) dataset was analyzed to identify differentially expressed m6A-related genes. Functional enrichment analysis was performed clusterProfiler, immune infiltration profiling was conducted with CIBERSORT, and a competing endogenous RNA (ceRNA, including microRNA [miR] and lncRNA) network was constructed. Drug enrichment analysis was carried out using DSigDB, and molecular docking was utilized to assess the interaction between dabigatran and the METTL3 protein.

From 192 differentially expressed genes, four m6A-related genes (METTL3, HNRNPC, IGFBP2, and RBMX) were identified as the intersecting genes between the m6A-related gene set and differentially expressed genes (DEGs) from the GSE134544 dataset. Gene Ontology (GO) analysis revealed significant enrichment in biological processes related to RNA metabolic processes and post-transcriptional regulation, while Kyoto Encyclopedia of Genes and Genomes (KEGG) analysis identified important pathways such as spliceosome and p53 signaling pathways. METTL3 and HNRNPC were central in the ceRNA network, interacting with miRs such as hsa-miR-93-3p and lncRNAs like LINC01529. Drug enrichment analysis identified dabigatran as a potential METTL3 inhibitor, with molecular docking confirming a stable binding affinity (−5.9 kcal/mol).

This study emphasizes the critical role of m6A-related genes, particularly METTL3 and HNRNPC, as macromolecules in asthma pathophysiology, and provides insights into their potential as biomarkers and therapeutic targets for asthma treatment.

Keywords: Asthma; Biomarker; ceRNA; m6A-related genes; Therapeutic targets

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INTRODUCTION

Asthma is a chronic respiratory disease with a significant global impact, affecting approximately 339 million individuals and contributing to considerable morbidity and mortality.[1,2] It is characterized by airway hyperresponsiveness, inflammation, and episodic symptoms such as wheezing and breathlessness.[3] The disease exhibits substantial heterogeneity, and its development is influenced by complex gene-environment interactions, including genetic predisposition and exposure to allergens, pollutants, and respiratory infections.[4,5] Despite advancements in the understanding of its pathophysiology, asthma remains underdiagnosed and inadequately managed, particularly in regions with limited access to healthcare.[1,6] This highlights the necessity for advanced diagnostic and therapeutic strategies to address diverse phenotypes of asthma.

N6-methyladenosine (m6A), the most abundant internal RNA modification in eukaryotes, plays a critical role in post-transcriptional regulation of gene expression, including mRNA stability, splicing, and translation.[7,8] Recent studies have increasingly linked m6A modifications to the pathogenesis of inflammatory diseases, including asthma, by modulating the key pathways involved in immune responses and airway inflammation.[8,9] Transcriptome-wide analyses using methylated RNA immunoprecipitation sequencing (MeRIP-seq) have revealed significant alterations in the m6A-modified genes in asthma. For example, differentially m6A-modified genes, including B-cell CLL/lymphoma 11A (*BCL11A*) gene, megakaryocyte-associated tyrosine kinase (*MATK*) gene, and CD300a molecule (*CD300A*) gene, have been identified as potential contributors to asthma susceptibility and severity.[10,11] Furthermore, m6A-regulating enzymes such as methyltransferase-like 3 (*METTL3*) and fat mass and obesity–associated (*FTO*) have been shown to influence asthma-related gene expression, highlighting the mechanistic importance of m6A modifications in disease progression.[12,13] However, despite these advancements, the specific role of m6A-related genes in the diverse phenotypes and pathophysiology of asthma remains underexplored.[10,14]

In this study, we systematically investigated m6A-related genes in asthma using bioinformatic analyses. By analyzing publicly available transcriptomic datasets, it aims to identify key m6A-related genes and their roles in the molecular mechanisms underlying asthma pathophysiology. By exploring the expression patterns and potential functional pathways, this study provides valuable insights into the biological significance of m6A modifications in asthma.

MATERIALS AND METHODS

Microarray Data Acquisition and Differentially Expressed Gene Analysis

The microarray gene expression dataset used in this study was retrieved from the Gene Expression Omnibus (GEO) database. A list of 26 m6A-related genes was acquired from the GeneCards database, as detailed in Supplementary Table 1. Differentially expressed genes (DEGs) were identified in the GSE134544 dataset using the limma R package. DEGs were defined as genes meeting the criteria of $p<0.05$ and log fold change (logFC)>1.0. The overlapping genes between DEGs and m6A-related genes were further analyzed to identify hub genes.

Functional Enrichment Analysis

Functional enrichment analyses were conducted to explore the biological significance of the DEGs. Gene Ontology (GO) analysis was performed across three categories: Biological Process (BP), Cellular Component (CC), and Molecular Function (MF). Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis was also carried out to map DEGs to biological pathways. Both analyses were implemented using the cluster Profiler R package, with significance thresholds set at adjusted p values<0.05. The results were visualized using the ggplot2 package, highlighting the enriched GO terms and KEGG pathways.

Immune Infiltration Analysis

Immune cell infiltration was assessed using the CIBERSORT algorithm, which estimates the relative proportions of 22 immune cell types within each sample. The output was normalized so that the sum of all immune cell fractions for each sample was equal to 1, ensuring a comprehensive characterization of immune cell distribution.

Construction of the ceRNA (lncRNA–miR–mRNA) Network

The competing endogenous RNA (ceRNA) (lncRNA–miR–mRNA) network was constructed to

explore potential regulatory interactions of the four m6A-related genes (*METTL3*, heterogeneous nuclear ribonucleoprotein C [*HNRNPC*], insulin-like growth factor binding protein 2 [*IGFBP2*], and RNA-binding motif protein, X-linked [*RBMX*]). Candidate miR–mRNA interactions were obtained from miRTarBase (experimentally validated), TargetScan, and miRDB, and only interactions experimentally supported or consistently predicted by≥2 databases were retained (miRDB score≥80; TargetScan context+ score≤-0.20). Putative miR–lncRNA interactions were retrieved from starBase, miRcode, and DIANA-LncBase, and pairs supported by≥1 CLIP-seq dataset in starBase or present in≥2 databases were considered reliable. Identifiers were standardized to HGNC/miRBase/GENCODE nomenclature, and duplicates were removed. Given the absence of matched miR/lncRNA expression profiles in GSE134544, no correlation filtering was applied, and the resulting ceRNA network represents an evidence-integrated, hypothesis-generating framework. Network visualization was performed in Cytoscape.

Statistical Analysis

Drug enrichment analysis was performed using the clusterProfiler package, and molecular docking was conducted to evaluate binding affinity. All statistical analyses were performed using R software (version 4.1.3). Graphs and visualizations were created using ggplot2 package. Statistical significance was defined as $p<0.05$ (two-tailed). The detailed workflow of this study is shown in Figure 1.

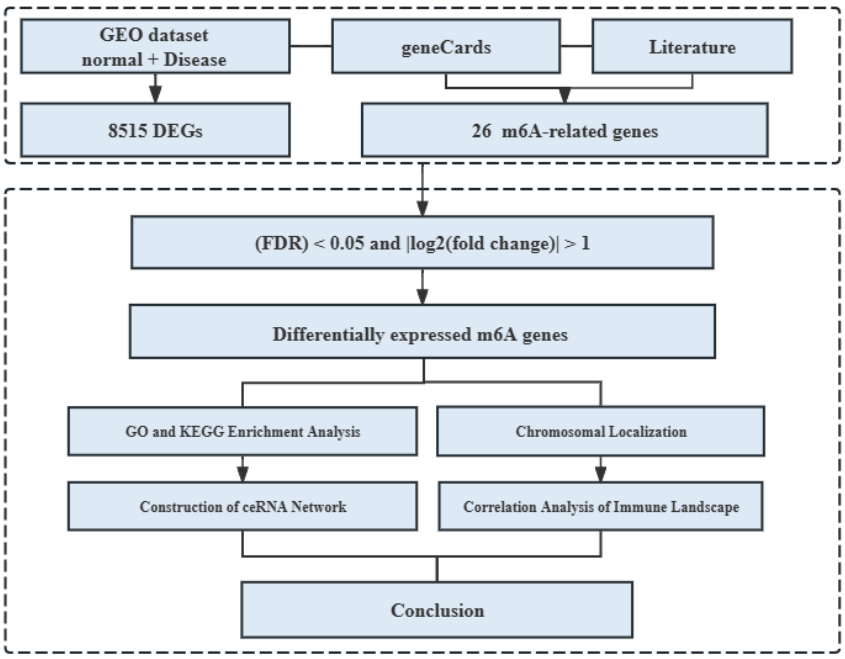

Figure 1. Workflow of the bioinformatics analysis in this study. Overview of the analytical workflow. The study includes transcriptomic data analysis, identification of differentially expressed genes (DEGs), functional enrichment analysis, immune infiltration profiling, and competing endogenous RNA (ceRNA) network construction in asthma.

RESULTS

Differential Expression Analysis (DEGs)

In total, 192 genes were differentially expressed between the disease and control groups. The volcano plot shows the expression pattern of differentially expressed genes ($p<0.05$) among the samples (Figure 2A). Among the upregulated genes were ribonuclease A family member 3 (*RNASE3*) gene, killer cell lectin like receptor C1 (*KLRC1*) gene, granzyme B (*GZMB*) gene, complement C3a receptor 1 (*C3AR1*) gene, and defensin alpha 4 (*DEFA4*) gene, whereas the downregulated genes included megakaryocyte associated tyrosine kinase (*MATK*) gene, carcinoembryonic antigen related cell adhesion molecule 8 (*CEACAM8*) gene, trefoil factor 3 (*TFF3*) gene, histone cluster 1 H2A family member E (*HIST1H2AE*) gene, and pyruvate dehydrogenase kinase 4 (*PDK4*) gene. Expression

analysis of m6A-related genes identified several genes with significant differential expression (p<0.05) (Figure 2B). Genes such as *METTL3*, methyltransferase like 14 (*METTL14*) gene, and Wilms tumor 1 associated protein (*WTAP*) gene were significantly upregulated in asthma patients compared to controls (p<0.05). Similarly, reader genes, including YTH domain containing 1 (*YTHDC1*) gene and YTH N6-methyladenosine RNA binding protein 2 (*YTHDF2*) gene, showed elevated expression levels, whereas alkB homolog 5 (*ALKBH5*) gene was downregulated in asthma samples.

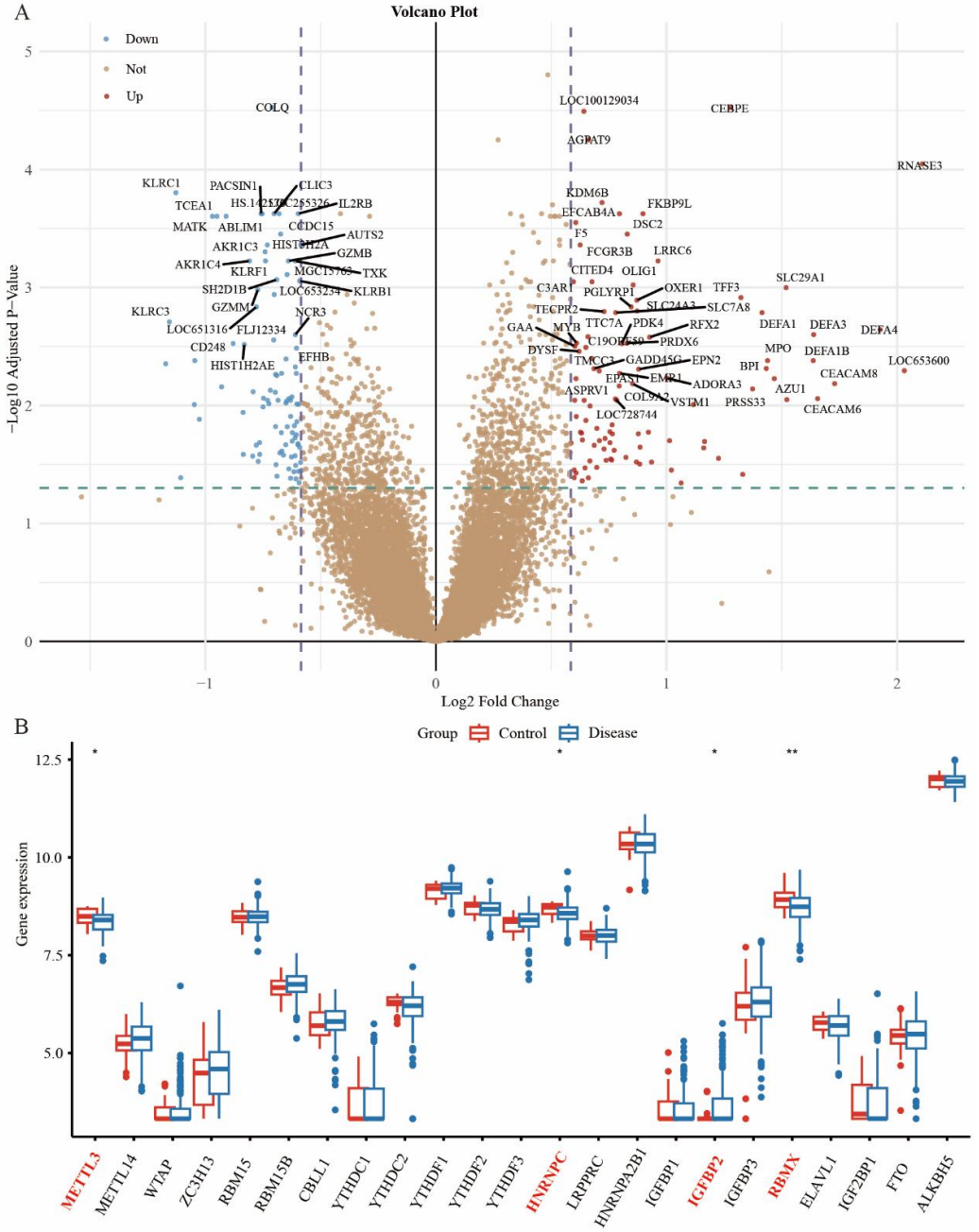

Figure 2. Identification of Differentially Expressed Genes in Asthma. (A) Volcano plot showing the distribution of differentially expressed genes (DEGs) between asthma and normal samples, with significant upregulated (red) and downregulated (blue) genes. (B) Boxplot showing the normalized log$_2$ expression values of representative m6A-related genes in asthma vs control groups.

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Integration of DEGs and m6A-Related Genes with Functional Enrichment Analysis

Venn diagram analysis identified four intersecting genes between DEGs and m6A-related genes, highlighting their potential shared roles in asthma pathophysiology (Figure 3A). Chromosomal mapping of these intersecting genes indicated their distribution across multiple chromosomes, with prominent localization on chromosomes 14, X, and 2 (Figure 3B).

GO enrichment analysis revealed that the intersecting genes were significantly enriched in biological processes such as "RNA modification," "regulation of RNA stability," and "mRNA catabolic process." In the cellular component category, notable enrichment was observed in "nuclear membrane," "spliceosomal complex," and "cytoplasmic stress granule." For molecular functions, the key terms included "mRNA methyltransferase activity," "miR binding," and "demethylase activity" (Figure 3C). KEGG pathway analysis further indicated significant involvement of these genes in pathways such as the "p53 signaling pathway" and "spliceosome" (Figure 3D).

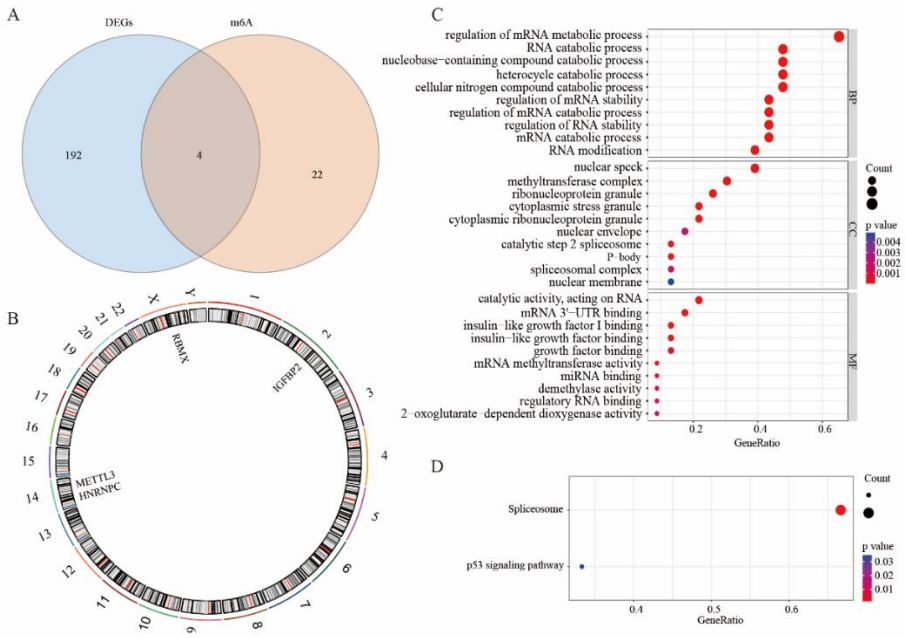

Figure 3. Integration of m6A-related genes with DEGs and functional enrichment analysis. A. Venn diagram showing the overlap between differentially expressed genes (DEGs) and m6A-related genes, identifying 4 overlapping genes. B. Chromosomal location of the overlapping genes. C. GO enrichment analysis showing significant biological processes, molecular functions, and cellular components. D. Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis showing key pathways, including spliceosome and p53 signaling. Enriched terms involving a single gene are displayed for completeness but should be interpreted with caution, as they may represent hypothesis-generating rather than robust multi-gene associations.

Construction of the ceRNA Network

A ceRNA network was constructed to explore the regulatory interactions among the m6A-related genes (*METTL3*, *HNRNPC*, *IGFBP2*, and *RBMX*), miRs, and lncRNAs (Figure 4). The network identified *HNRNPC* as the most interconnected gene, showing extensive interactions with miRs such as hsa-miR-744-5p, hsa-miR-505-5p, and hsa-miR-615-3p, which were further linked to lncRNAs like *RP11-394A14.2* and *RP11-54O7.17*. The network identified multiple key interactions, including *METTL3*-hsa-miR-93-3p, *METTL3*-hsa-miR-126-5p, and *METTL3*-hsa-miR-302a-3p, highlighting *METTL3* as a central node. These miRs were further associated with several lncRNAs, such as *RP5-892K4.1* and *LINC01529*, which act as ceRNAs by regulating *METTL3* through miR binding. In comparison, *IGFBP2* and *RBMX* exhibited fewer connections; *IGFBP2* was primarily associated with

hsa-miR-335-5p and lncRNAs such as *SLC8A1-AS1*, whereas *RBMX* was linked to hsa-miR-196a-5p and lncRNAs like *AC011284.3*. These results reveal the central roles of *HNRNPC* and *METTL3* in ceRNA networks and suggest their involvement in modulating m6A-associated regulatory pathways in asthma.

Immune Landscape Analysis

The immune infiltration landscape in asthma was analyzed for the 4 m6A regulatory genes: *METTL3*, *HNRNPC*, *IGFBP2*, and *RBMX* (Figure 5). Distinct correlations were observed between gene expression and various immune cell types. *METTL3* expression was positively correlated with eosinophils, plasmacytoid dendritic cells, type 17 T helper cells, and immature B cells, while it was negatively associated with CD56dim natural killer cells, T follicular helper cells, and type 1 T helper cells. *HNRNPC* showed strong positive correlations with type 1 T helper cells, activated CD4 T cells, activated CD8 T cells, and T follicular helper cells but was negatively correlated with plasmacytoid dendritic cells, eosinophils, macrophages, and natural killer cells. *IGFBP2* was positively associated with immature dendritic cells and plasmacytoid dendritic cells, while negatively correlated with activated CD4 T cells and T follicular helper cells. Similarly, *RBMX* was positively correlated with T follicular helper cells, activated CD4 T cells, activated CD8 T cells, and T follicular helper cells, while negatively associated with plasmacytoid dendritic cells and eosinophils.

Drug Enrichment and Molecular Docking Analysis

Drug enrichment analysis was performed using the DSigDB database to identify potential compounds targeting key m6A-related genes. A total of 20 drugs were significantly enriched, with the top candidates including dabigatran, flutamide, glycocholic acid, and Spectrum 001666 (Figure 6A). Molecular docking analysis revealed five potential binding cavities between dabigatran and *METTL3*, with binding scores ranging from −4.5 kcal/mol to −5.9 kcal/mol. The most stable binding was observed in cavity 1, with a score of −5.9 kcal/mol, involving interactions with residues GLU450, ARG451, VAL452, ASP453 (chain A), and GLU197, TYR198, ARG200 (chain B). Additional stable interactions were identified in cavity 2 (−5.8 kcal/mol) and cavity 3 (−4.8 kcal/mol), with residues such as CYS376, ASP395, TRP398, and HIS512 (Figure 6B).

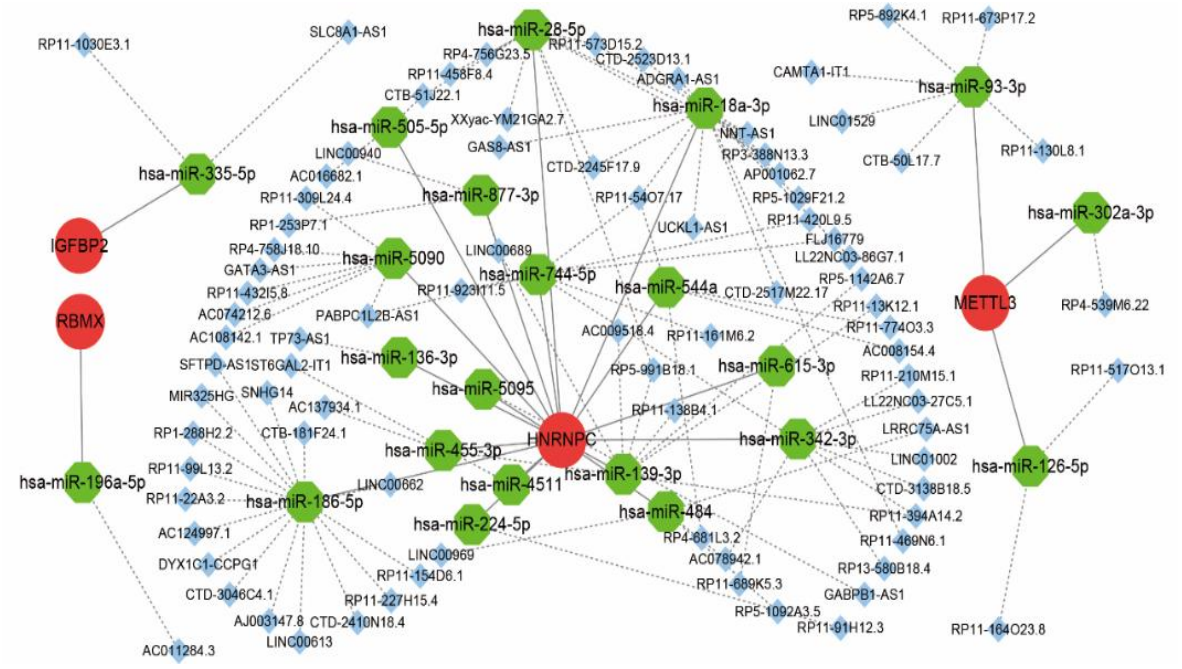

Figure 4. Construction of the competing endogenous RNA (ceRNA) Network. ceRNA network showing interactions among messenger RNAs (mRNAs), microRNA (miRs), and long noncoding RNAs (lncRNAs).

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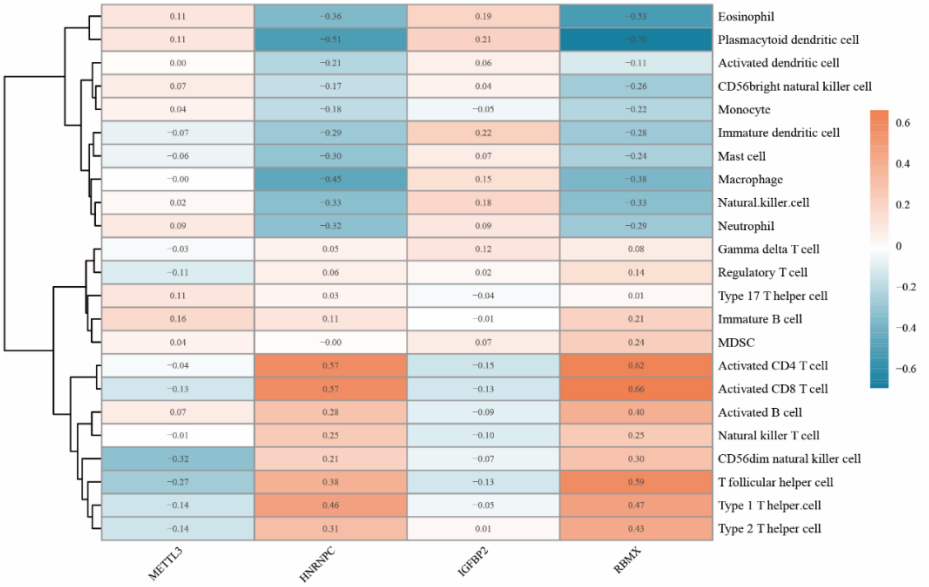
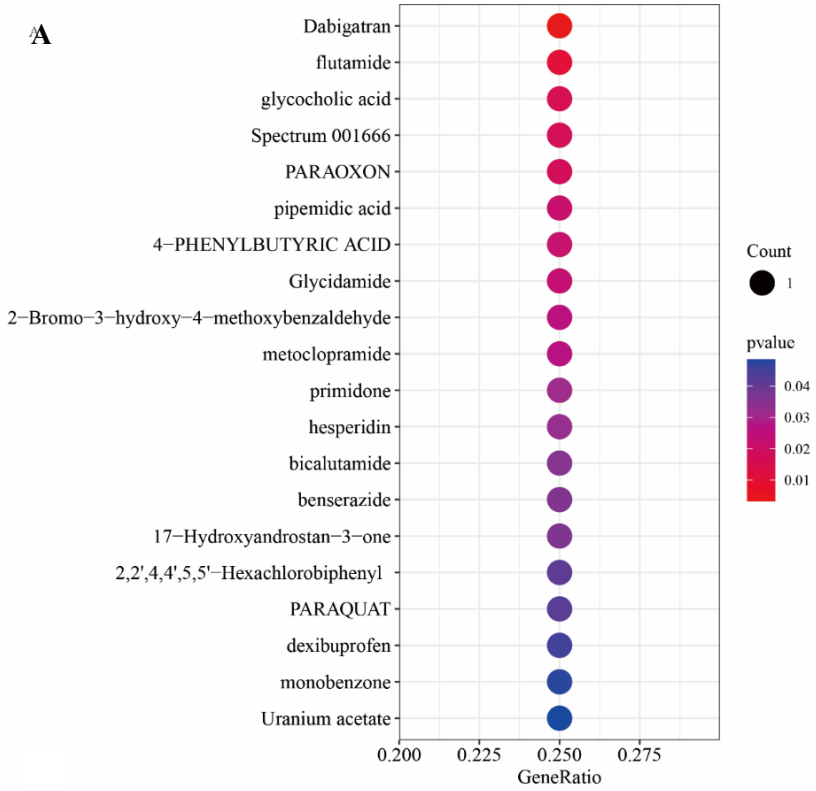


Figure 5. Immune landscape analysis associated with key m6A genes. Immune infiltration profiling based on Cell-type Identification By Estimating Relative Subsets of RNA Transcripts (CIBERSORT) analysis. Correlation plots demonstrate the association between immune cell types and the expression levels of methyltransferase-like 3 (*METTL3)*, heterogeneous nuclear ribonucleoprotein C (*HNRNPC*), insulin-like growth factor binding protein 2 (*IGFBP2*), and RNA-binding motif protein, X-linked (*RBMX*).



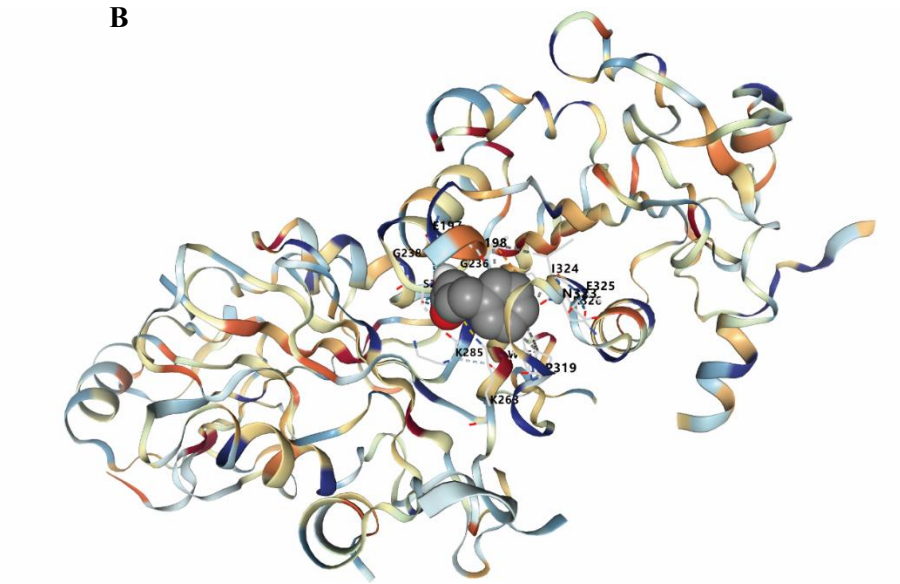


Figure 6. Drug enrichment and molecular docking of dabigatran with methyltransferase-like 3 (METTL3).

DISCUSSION

In this study, we systematically analyzed the role of m6A-related genes in asthma using bioinformatic approaches. Four key m6A-related genes-*METTL3*, *HNRNPC*, *IGFBP2*, and *RBMX*-were identified as significantly differentially expressed in patients with asthma. Functional enrichment analyses revealed that these genes are involved in critical biological processes such as RNA modification, regulation of RNA stability, and mRNA splicing. Additionally, immune infiltration analysis highlighted correlations between these genes and various immune cell populations, suggesting their role in modulating the immune microenvironment in asthma. Drug enrichment analysis identified several compounds potentially targeting these m6A regulators, with molecular docking revealing strong binding interactions with *METTL3*.

The central role of m6A methylation in RNA biology has been extensively documented, with *METTL3* recognized as the primary catalytic subunit responsible for m6A deposition.[15] Our study found that *METTL3* was upregulated in asthma, a finding consistent with its role in stabilizing pro-inflammatory transcripts and enhancing their translation.[16] Structural analyses revealed that *METTL3* works synergistically with *METTL14* to methylate specific RNA substrates, with *METTL14* serving as an RNA-binding platform.[17] Additionally, *METTL3*'s interaction with translation initiation factors such as eIF3h facilitates mRNA looping, which is crucial for the efficient translation of inflammation-related proteins.[16] These results suggest that *METTL3* may amplify inflammatory responses in asthma through enhanced translation of key cytokines and chemokines. *HNRNPC*, another gene identified in our study, acts as an m6A "reader" that recognizes m6A-modified RNAs, altering RNA-protein interactions through a structural switch.[18] In the context of asthma, *HNRNPC* may regulate alternative splicing and the stability of immune-related transcripts, consistent with its known roles in other inflammatory diseases.[19] Similarly, *IGFBP2* has been found to correlate with dendritic and plasmacytoid cells, supporting its involvement in immune regulation.[20] *RBMX*, traditionally linked to RNA splicing, shows strong associations with T follicular helper cells and activated T cells, highlighting its potential role in adaptive immunity within the asthma microenvironment.[21] *METTL3*'s ability to regulate helper T (T_H) cell differentiation via m6A methylation of *SOX5* provides a mechanistic insight into how m6A modification can influence T_H2-associated inflammation. By controlling *SOX5* expression, *METTL3* indirectly impacts T_H2 cytokine production, such as *IL-4* and *IL-13*, thereby playing a pivotal role in the development of asthma. This mechanism highlights the importance of *METTL3* in the

fine-tuning of the immune response in T2 asthma.[22] Additionally, immune infiltration analysis highlighted correlations between these genes and various immune cell populations. Notably, *METTL3* expression was positively correlated with eosinophils and T_H17 cells, both of which are key drivers of airway inflammation in asthma. Previous studies have shown that *METTL3* promotes T_H2 and T_H17 differentiation through m6A-dependent stabilization of lineage-defining transcription factors and cytokine transcripts, such as *SOX5*, *IL-17A*, and *IL-13*. Eosinophilic inflammation, a hallmark of allergic asthma, may thus be exacerbated by *METTL3*-mediated regulation of *IL-5* and *IL-13*. These mechanistic links support the hypothesis that *METTL3* not only serves as a general regulator of RNA metabolism but also plays a direct role in shaping immune cell composition within the asthmatic microenvironment. These findings align with recent studies linking *METTL3* to eosinophilic and T_H17-driven asthma endotypes, underscoring its role as a potential therapeutic target. Importantly, the dysregulation of *METTL3* and *HNRNPC* may hold direct clinical relevance. In pediatric asthma, where immune system maturation coincides with airway remodeling, aberrant *METTL3* activity could amplify T_H2 cytokine responses and thereby serve as both a biomarker for early diagnosis and a candidate therapeutic target. Similarly, in severe or corticosteroid-resistant asthma, persistent airway inflammation may be sustained through *HNRNPC*-mediated splicing of pro-inflammatory cytokine transcripts, highlighting its potential role in identifying high-risk phenotypes and guiding novel treatment strategies. Together, these observations suggest that integrating m6A regulators such as *METTL3* and *HNRNPC* into clinical stratification frameworks may improve risk prediction, enable precision medicine, and facilitate the development of epigenetic therapies tailored to severe and pediatric asthma.

The enrichment of GO terms such as “RNA modification” and “cytoplasmic stress granule” underscores the role of these genes in cellular responses to inflammation and stress. Such processes are critical in asthma, in which airway epithelial cells experience repeated oxidative and inflammatory insults. Additionally, the cellular component enrichment in “spliceosomal complex” and “nuclear membrane” aligns with findings on *HNRNPC*, which facilitates alternative splicing through its m6A reader functions.[18] Functional pathway enrichment highlighted the involvement of m6A-related genes in key signaling cascades, such as the p53 pathway, which regulates apoptosis and immune responses.[7,14] Previous studies have shown that m6A modifications are crucial for balancing cellular stress responses, with SUMOylation of *METTL3* further modulating its activity.[12] Additionally, drug enrichment and molecular docking analyses identified several compounds that target *METTL3*, suggesting its potential as a therapeutic target.[23] Recent preclinical studies have demonstrated the feasibility of pharmacologically inhibiting *METTL3*: STM2457, a selective small-molecule inhibitor, significantly suppressed tumor growth and extended survival in acute myeloid leukemia models.[24] Although no *METTL3*-targeting agents have yet entered clinical evaluation for airway diseases, functional studies in relevant models highlight *METTL3*’s potential therapeutic relevance in asthma: myeloid-specific knockout of *METTL3* exacerbates T_H2-driven allergic airway inflammation,[25] while *METTL3* deficiency reduces airway smooth muscle proliferation and airway remodeling in asthma models.[26] These observations together support *METTL3* as a promising target but underscore the need for further translational research to assess its druggability in human airway disease.

The ceRNA network analysis revealed that m6A-related genes (*METTL3*, *HNRNPC*, *IGFBP2*, and *RBMX*) interact with specific miRs and lncRNAs to regulate immune responses and inflammation in asthma. Among these, miR-126, which regulates T_H2 cell differentiation and allergic airway inflammation, targets *METTL3*. *METTL3* likely stabilizes inflammatory transcripts through m6A methylation, thereby increasing T_H2 response. The lncRNA *NEAT1*, acting as a sponge for miR-126, may further enhance *METTL3*’s role in airway remodeling.[27] Similarly, miR-21 promotes T_H2 polarization and inhibits apoptosis-related gene expression. It interacts with *HNRNPC*, an m6A reader that regulates RNA splicing and stability.[28] This interaction likely affects the splicing of cytokine transcripts such as *IL-4* and *IL-13*, which are crucial in asthma. Additionally, the lncRNA *MALAT1*, by sponging miR-21, indirectly enhances *HNRNPC*’s role in regulating immune cell activation.[29] Furthermore, miR-335-5p, implicated in cell maturation and antigen presentation, is associated with *IGFBP2*, a gene that stabilizes inflammatory mediators critical for immune cell infiltration.[30] The lncRNA *SLC8A1-AS1* functions

as a sponge for miR-335-5p, indirectly regulating *IGFBP2* expression and contributing to immune dysregulation in asthma.[31] Meanwhile, miR-196a-5p, known to maintain the T_H1/T_H2 balance, interacts with *RBMX*, emphasizing its role in regulating the alternative splicing of immune-related transcripts essential for immune homeostasis.[32] This regulatory network is further modulated by the lncRNA *RP11-394A14.2*, acting as a ceRNA for miR-196a-5p and indirectly influencing *RBMX* function and the splicing of pro-inflammatory genes.[33] Regulatory axes such as miR-126-*NEAT1*-*METTL3* and miR-21-*MALAT1*-*HNRNPC* highlight potential therapeutic targets for modulating m6A-dependent pathways, while miRs like miR-335-5p and miR-196a-5p offer insights into asthma heterogeneity and immune dysregulation.[30] While our study primarily focused on *METTL3* due to its central role in m6A-mediated regulation and asthma pathogenesis, we acknowledge that other m6A regulators, such as *FTO* and *ALKBH5*, were also differentially expressed in the asthma samples. However, these genes were not explored further in this study due to several reasons. First, *METTL3* has been extensively documented as a key player in the inflammatory response and RNA regulation in asthma, making it the focus of our investigation. Additionally, while *FTO* and *ALKBH5* are important m6A regulators, their roles in asthma are still not fully defined, and the data available did not provide sufficient evidence to establish a direct link to the disease process.

Based on the results of this study, m6A-related genes, including *METTL3*, *HNRNPC*, *IGFBP2*, and *RBMX*, have emerged as promising biomarkers and therapeutic targets for asthma treatment. These genes are intricately involved in post-transcriptional regulation, including RNA stability, splicing, and immune response modulation, which are critical for the pathophysiology of asthma. The integration of ceRNA network analysis, immune infiltration profiling, and drug enrichment studies highlights their multifaceted roles and provides novel insights into the m6A-driven mechanisms in airway inflammation. These findings offer potential pathways for developing precise diagnostic tools and targeted therapies for asthma, particularly through the modulation of m6A-related signaling pathways.

This study was based on whole-blood transcriptomic data from asthma patients, without specification of inflammatory endotypes (eosinophilic, neutrophilic, or mixed-type). Accordingly, the results should be interpreted with caution, as the regulatory effects of *METTL3* may differ among asthma phenotypes. Further studies using datasets with rigorous endotype classification are warranted to confirm and expand upon our observations. In addition, the dataset analyzed did not provide demographic information such as age, sex, or detailed clinical subtype, precluding subgroup analyses. Given that m6A expression and asthma phenotypes may vary by demographic factors, this represents an important limitation. Future studies, including prospective institutional cohorts currently being planned in our center, will allow validation of these findings in well-characterized patient populations and facilitate exploration of age- and sex-specific effects. The reliance on a single dataset limits the generalizability of our conclusions, and functional validation experiments (such as qRT-PCR, Western blot, and gene knockdown/overexpression) are planned for future studies to confirm the role of these genes in asthma. Another limitation of this study is the reliance on a single GEO dataset (GSE134544). Future studies will incorporate additional datasets for further validation to strengthen the findings. In this study, docking analysis was limited to binding affinities and identification of interacting residues between dabigatran and *METTL3*. Additional structural parameters, such as RMSD values, hydrogen bonding interactions, and comparative docking with known inhibitors, were not included and represent a limitation. Future work will incorporate these metrics to provide a more comprehensive evaluation of binding stability and specificity. Despite these constraints, this study lays a robust foundation for future investigations. The integration of m6A pathway modulation with therapeutic strategies offers a promising avenue for advancing asthma management, paving the way for translational applications in this field.

This study emphasizes the critical role of m6A-related genes, particularly *METTL3* and *HNRNPC*, as biological macromolecules in asthma pathophysiology, and provides insights into their potential as biomarkers and therapeutic targets for asthma treatment.

STATEMENT OF ETHICS

This study utilized publicly available datasets, and no human subjects or animal experiments were involved. All data used in the study were obtained in compliance with relevant ethical standards and international

guidelines, ensuring that no direct intervention or interaction with human or animal subjects occurred.

FUNDING

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

ACKNOWLEDGMENTS

We want to acknowledge the Gene Expression Omnibus (GEO) database for providing access to valuable datasets that significantly contributed to this study.

DATA AVAILABILITY

Data is available on request from the authors.

AI ASSISTANCE DISCLOSURE

Not applicable. No artificial intelligence (AI) tools were used in the preparation of this manuscript.

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