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Research Article

Cross-validated Uncovery of a Diagnostic miRNA-mRNA Regulatory Hub in Osteoporosis

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Abstract

Background: Osteoporosis is a complex skeletal disorder whose pathogenesis involves intricate transcriptional networks. Robust biomarker discovery and mechanistic elucidation remain challenging due to the prevalent use of single-dataset analyses in transcriptomics.

Methods: We integrated four independent datasets from the Gene Expression Omnibus (GEO) to construct a disease-specific miRNA-mRNA regulatory network. Our analytical pipeline included differential expression analysis, target prediction, rigorous cross-dataset validation, diagnostic efficacy assessment (ROC analysis), and in silico drug prediction.

Results: A core regulatory axis was identified, featuring downregulated hsa-miR-30b-5p and its upregulated targets, AP2A1 and CHST1. Additionally, four novel hub genes (PSMD5, GRB7, TRAF7, TTC7A) showed consistent dysregulation across datasets. All core genes exhibited exceptional diagnostic performance (AUC > 0.9).

Conclusions: Through multi-dataset validation, we delineated a novel molecular network in osteoporosis, encompassing a key miRNA-mRNA axis and previously unrecognized hub genes. This work provides a high-potential diagnostic biomarker panel and reveals new mechanistic targets for therapeutic development.

Keywords: *Osteoporosis (OP); Core genes; Biomarkers; hsa-miR-30b-5p; AP2A1; CHST1*

1. Introduction

Osteoporosis (OP) is a systemic skeletal disorder characterized by reduced bone mass and deterioration of bone microarchitecture. Its fundamental pathology lies in the disrupted balance of bone remodeling, leading to compromised bone strength and a significantly increased risk of fractures[1]. Globally, OP affects over 200 million individuals. The resultant fragility fractures are associated with high rates of disability and mortality, imposing a substantial socioeconomic burden[2, 3]. The development of osteoporosis is highly complex, involving multi-level network disturbances spanning from systemic to molecular scales. At the systemic level, estrogen deficiency, age-related chronic low-grade inflammation, and oxidative stress constitute key pathological backgrounds. At the cellular and molecular level, dysregulation of core signaling pathways such as RANKL/RANK/OPG and Wnt/β-catenin directly disrupts the functional balance between osteoblasts and osteoclasts.

Furthermore, the senescence of bone marrow mesenchymal stem cells and their diminished osteogenic potential provide a critical cellular basis for the disease[4-6]. Additionally, epigenetic modifications, non-coding RNA regulatory networks, and genetic susceptibility are deeply implicated in its progression[7, 8]. Consequently, osteoporosis is not a disorder of a single pathway but rather a complex outcome arising from the interplay of genetic, epigenetic, cellular senescence, and systemic factors.

In recent years, transcriptomic analyses leveraging public databases have identified aberrant mRNA and miRNA expression profiles in OP, linking them to processes like cellular senescence and immune dysregulation, thereby offering valuable mechanistic clues[9-11]. However, significant limitations persist in current research. Most findings originate from single datasets, lacking cross-cohort systematic validation, which casts doubt on the robustness and generalizability of candidate biomarkers. Moreover, studies often remain at the level of listing differentially expressed genes, with insufficient exploration of the upstream transcriptional regulatory networks (e.g., key transcription factors) driving these changes, hampering their translation into actionable therapeutic targets. These shortcomings collectively hinder the advancement towards precise diagnosis and targeted therapy for OP. Therefore, there is a pressing need to systematically construct and validate disease-specific, robust gene regulatory networks.

To address these challenges, this study integrated multiple GEO datasets. For the first time, we employed three independent mRNA expression profiles to perform systematic cross-validation of the constructed miRNA-mRNA regulatory network, thereby establishing a highly robust and OP-specific molecular network. Our research not only newly identifies two key regulatory pairs, hsa-miR-30b-5p/AP2A1 and hsa-miR-30b-5p/CHST1, but also discovers four novel core genes—PSMD5, GRB7, TRAF7, and TTC7A—that show highly consistent expression patterns across datasets. These multi-validated core molecules collectively form a reliable diagnostic biomarker panel. More importantly, the hub genes revealed in this study provide novel entry points for deciphering the complex regulatory mechanisms of OP and point to potential directions for developing targeted intervention strategies.

2. Materials and Methods

2.1. Data Acquisition

A schematic workflow of this study is presented in Figure 1. We retrieved and downloaded four transcriptomic datasets related to osteoporosis from the Gene Expression Omnibus (GEO) database. These comprised one miRNA dataset (GSE74209) and three mRNA datasets (GSE35956, GSE35958, and GSE230665). All datasets contained well-defined samples from osteoporosis patients and healthy controls.

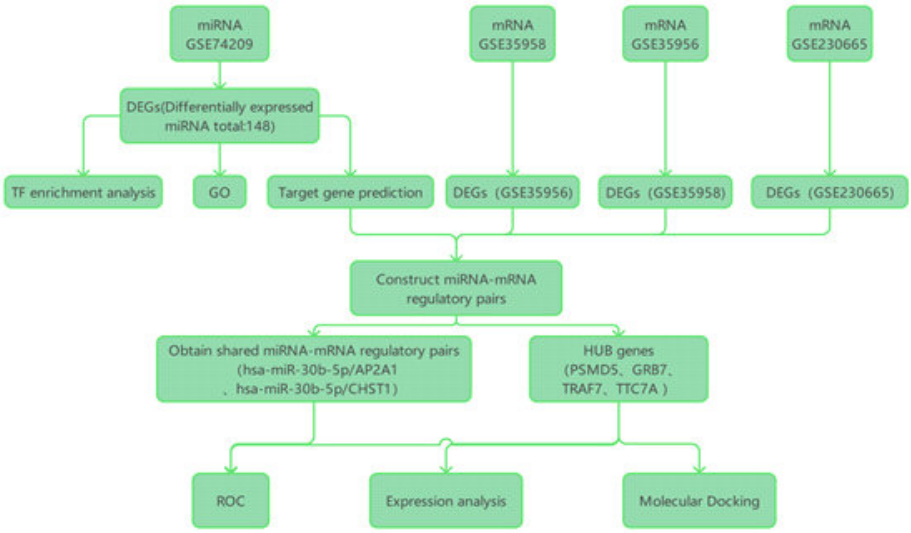

Figure 1. Schematic of the multi-omics analysis pipeline for osteoporosis.
The workflow outlines the integrated bioinformatics strategy for identifying key miRNA-mRNA interactions and hub genes from miRNA and mRNA expression datasets.

2.2. Differential Expression Analysis

Differential expression analysis for miRNAs and mRNAs was performed using the limma package in R. Significance was calculated via its empirical Bayes framework. Genes were considered differentially expressed with a threshold of P.Value < 0.05 and $|\log_2$Fold Change (FC)$| \geq 1$. Volcano plots were generated using the ggplot2 package to visualize the expression profiles.

2.3. miRNA Functional Enrichment Analysis

To investigate the potential functions of the differentially expressed miRNAs, we performed transcription factor enrichment analysis and Gene Ontology (GO) functional enrichment analysis using FunRich software (version 3.1.3). A significance threshold of $P < 0.05$ was applied.

2.4. Construction of the miRNA-mRNA Regulatory Network

Target genes (mRNAs) of the differentially expressed miRNAs were predicted using the built-in target prediction database within FunRich. The predicted target gene sets were then intersected with the differentially expressed mRNAs identified from the three mRNA datasets, respectively, to construct preliminary miRNA-mRNA regulatory pairs. Finally, the regulatory network was visualized using Cytoscape software (version 3.10.2).

2.5. Screening and Validation of Core Regulatory Pairs

miRNA-mRNA pairs that consistently appeared across all three mRNA datasets were defined as core regulatory pairs, and the mRNAs within these pairs were designated as core genes. Additionally, differentially expressed mRNAs that showed consistent expression trends (all up-regulated or all down-regulated) across the three datasets were also defined as core genes. To evaluate their diagnostic potential, Receiver Operating Characteristic (ROC) curves were plotted for the core genes. Their expression distribution between the disease and control groups was visualized using violin plots.

2.6. Targeted Drug Prediction and Molecular Docking

To explore the translational potential of the core mRNAs, we obtained known drug-gene signature relationships from the DSigDB database to screen for potential targeting drugs. Subsequently, three-dimensional structures of the small molecule drugs and their corresponding protein targets were downloaded from the PubChem database and the Protein Data Bank (PDB), respectively. Molecular docking simulations were conducted using the online platform CB-Dock2. Complexes with a predicted binding free energy (ΔG) lower than -5 kcal/mol were considered to have stable binding potential.

3. Results

3.1. Differential Expression Profiles of miRNAs and mRNAs in Osteoporosis

To systematically decipher the transcriptional dysregulation in osteoporosis, we first performed differential expression analysis on the GSE74209 miRNA dataset. A total of 148 differentially expressed miRNAs were identified, comprising 84 upregulated and 64 downregulated miRNAs (Figure 2A). Subsequent independent mRNA analyses corroborated significant transcriptomic disturbances, revealing 1,293 (GSE35956), 2,134 (GSE35958), and 1,790 (GSE230665) differentially expressed genes (DEGs) in the respective datasets (Figures 2B-D). Notably, the number of upregulated genes surpassed that of downregulated ones across all mRNA datasets, suggesting a potential state of widespread transcriptional activation in osteoporotic bone tissue.

3.2. Upstream Transcriptional Factor Regulation Profile of Differentially Expressed miRNAs

Transcription factor enrichment analysis of the 148 differentially expressed miRNAs uncovered a highly significant ($P < 0.001$) upstream regulatory network (Figure 3A). SP1 emerged as the most central regulator, with its binding motifs present in the promoter regions of 57.8% of the dysregulated miRNAs. EGR1 (31.4%) and SP4 (37.0%) also demonstrated broad regulatory potential. Other significantly enriched transcription factors included POU2F1, ZFP161, LHX3, RORA, FOXA1, MEF2A, and NKX6-1 (Figure 3B).

These findings indicate that the perturbed miRNA expression landscape in osteoporosis is likely not stochastic but may be governed by a coordinated transcriptional program steered by key factors such as SP1.

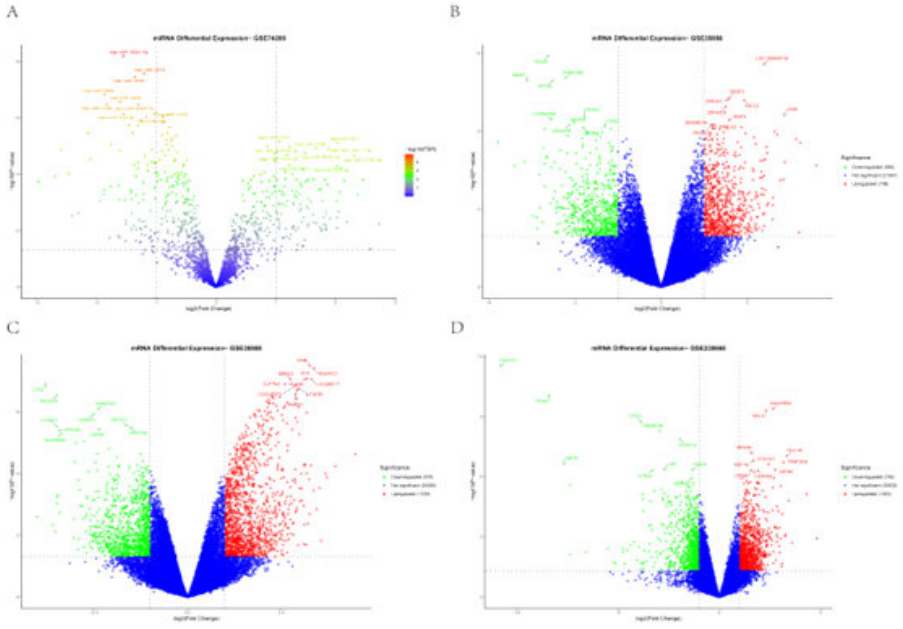

Figure 2. Identification of differentially expressed miRNAs and mRNAs.
(A)Volcano plot of 148 dysregulated miRNAs from GSE74209. (B-D) Volcano plots of differentially expressed mRNAs from three independent cohorts: GSE35956 (B), GSE35958 (C), and GSE230665 (D).

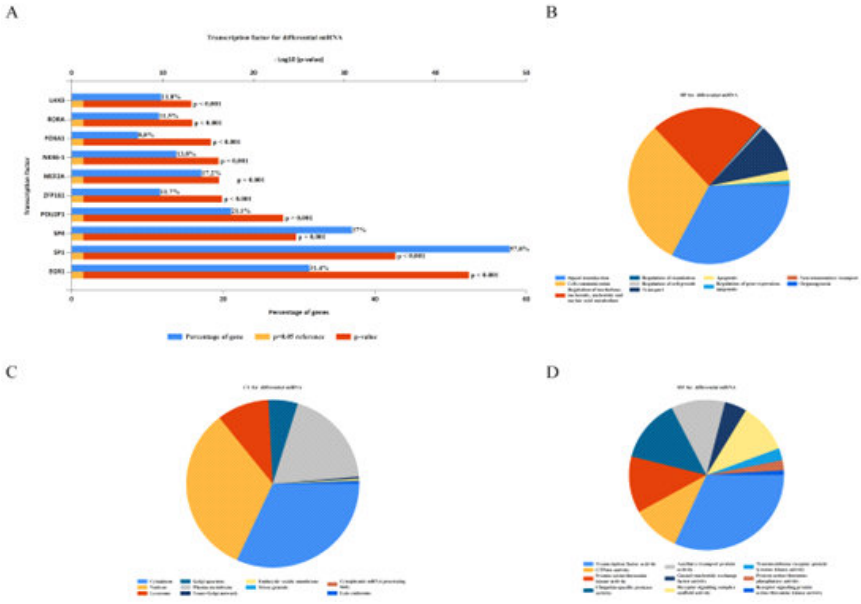

Figure 3. Upstream regulators and functional roles of dysregulated miRNAs.
(A) Enrichment network of transcription factors predicted to regulate the promoter regions of differentially expressed miRNAs. (B-D) GO term enrichment analysis of the predicted target genes of these miRNAs, shown for molecular function (B), cellular component (C), and biological process (D).

3.3. Functional Enrichment Landscape of Target Genes for Differentially Expressed miRNAs

Gene Ontology (GO) enrichment analysis of the predicted target genes for the differentially expressed miRNAs systematically outlined their potential biological involvement in osteoporosis (Figures 3B-D). Within the Molecular Function (MF) category, target genes were most prominently enriched in "transcription factor activity," suggesting these miRNAs might regulate upstream transcription factors, forming an amplifying regulatory cascade. Concurrent enrichments in "GTPase activity" and various "protein kinase/phosphatase activity" terms indicated a broad influence on intracellular signal transduction pathways.

Cellular Component (CC) localization analysis revealed that target gene products were primarily located in the "cytoplasm" and "nucleus," with significant enrichment also in membranous compartments such as the "plasma membrane," "Golgi apparatus," and "endosome," hinting at functions related to transmembrane signal reception, intracellular trafficking, and membrane-associated metabolism. These molecular functions and cellular localizations collectively underpinned the Biological Process (BP) enrichment results, where target genes were significantly involved in the core processes of "signal transduction" and "cell communication."

3.4. Identification of Cross-Dataset Robust miRNA-mRNA Regulatory Pairs

Through integrated analysis, we constructed three independent miRNA-mRNA regulatory networks (Figures 4A, B; 5A). These networks delineated high-confidence interactions based on the differential miRNAs from GSE74209 and the DEGs from the GSE35956, GSE35958, and GSE230665 datasets, respectively.

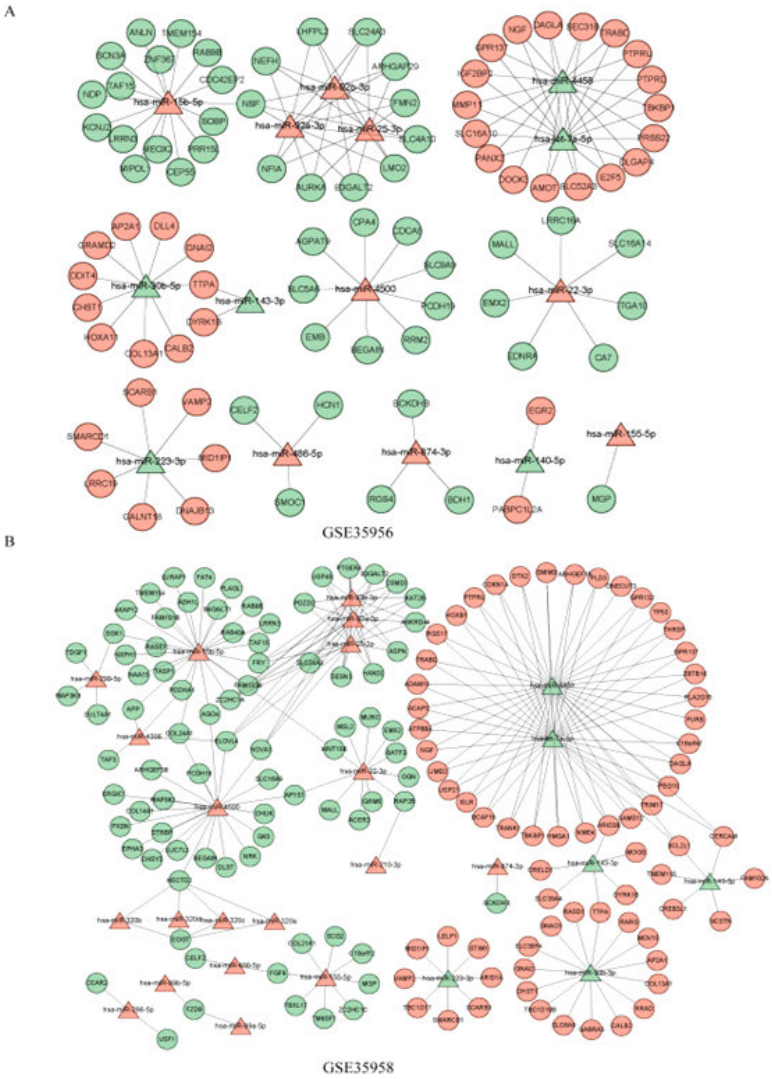

Figure 4. Construction of miRNA-mRNA regulatory networks. Networks were built by pairing differentially expressed miRNAs (GSE74209) with differentially expressed mRNAs from (A) GSE35956 and (B) GSE35958 datasets.

Cross-network comparison identified a set of core regulatory pairs that recurrently appeared across all three datasets, representing highly robust post-transcriptional regulatory events in osteoporosis. Among these, the axis mediated by hsa-miR-30b-5p was most prominent. This miRNA was significantly downregulated in GSE74209, while its predicted target genes, AP2A1 and CHST1, were consistently upregulated across all three mRNA datasets. This expression pattern perfectly aligns with the canonical negative regulatory logic of miRNAs. This discovery strongly suggests that hsa-miR-30b-5p may play a pivotal role in osteoporosis pathology, potentially by derepressing AP2A1 and CHST1.

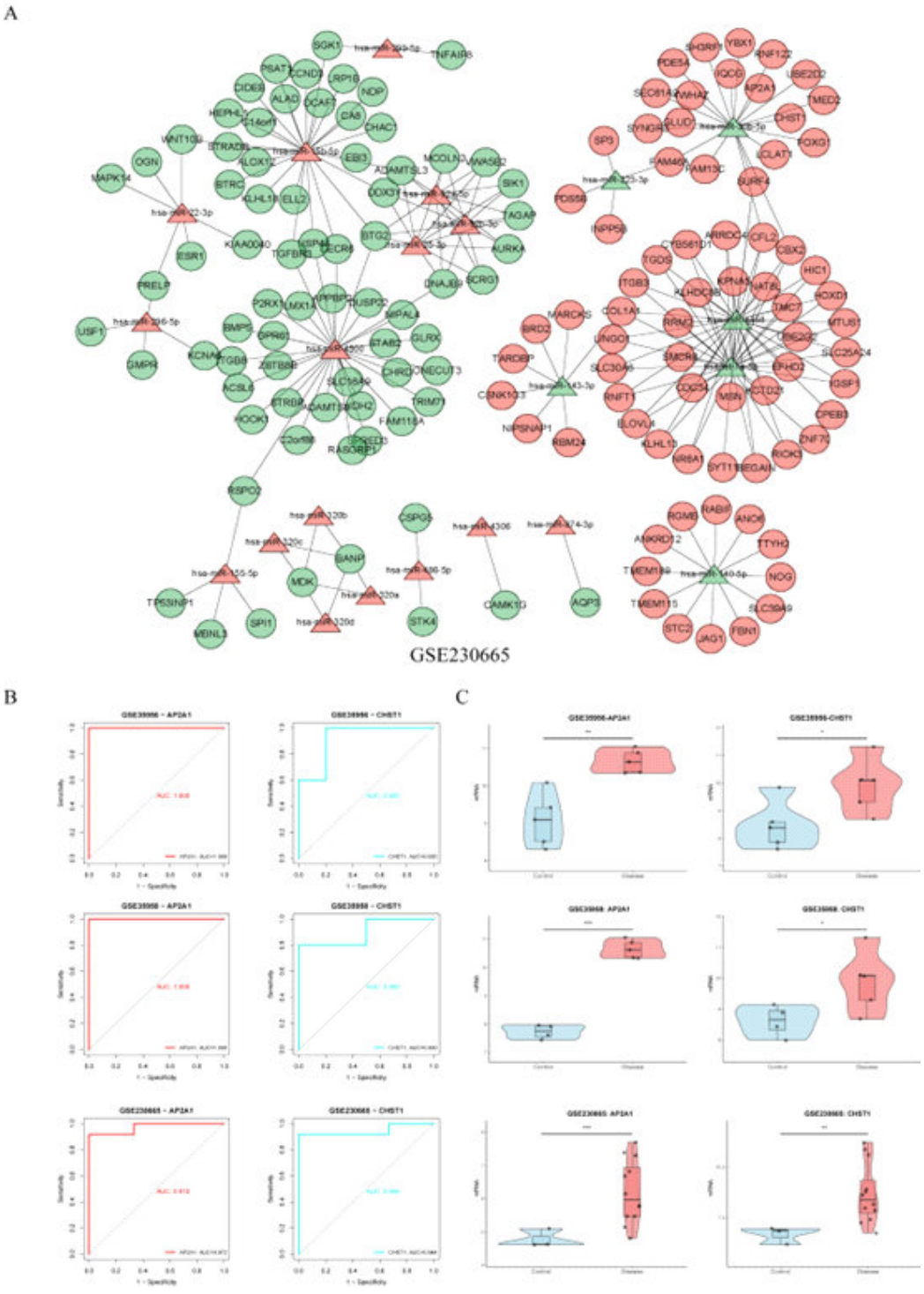

Figure 5. Diagnostic potential of core target genes AP2A1 and CHST1. (A) Regulatory network integrating miRNAs (GSE74209) and mRNAs (GSE230665). (B) ROC curves evaluating the diagnostic efficacy of AP2A1 and CHST1 across three mRNA datasets. (C) Violin plots comparing AP2A1 and CHST1 expression between osteoporosis and control groups (GSE230665).

3.5. Diagnostic Potential and Expression Validation of Core Genes

To assess the translational value of the core genes, we analyzed the diagnostic efficacy and expression patterns of genes from the core regulatory pairs (AP2A1, CHST1) and those showing consistent expression trends across datasets (PSMD5, GRB7, TRAF7, TTC7A). All core genes demonstrated excellent diagnostic capability in distinguishing osteoporotic from control samples. As shown in Figure 5B, the Area Under the Curve (AUC) values for AP2A1 and CHST1 were > 0.9 across the three independent datasets (GSE35956, GSE35958, GSE230665). Remarkably, PSMD5, GRB7, TRAF7, and TTC7A achieved an AUC of 1.0 in all datasets (Figures 6A-C), confirming their robust discriminatory power as potential biomarkers.

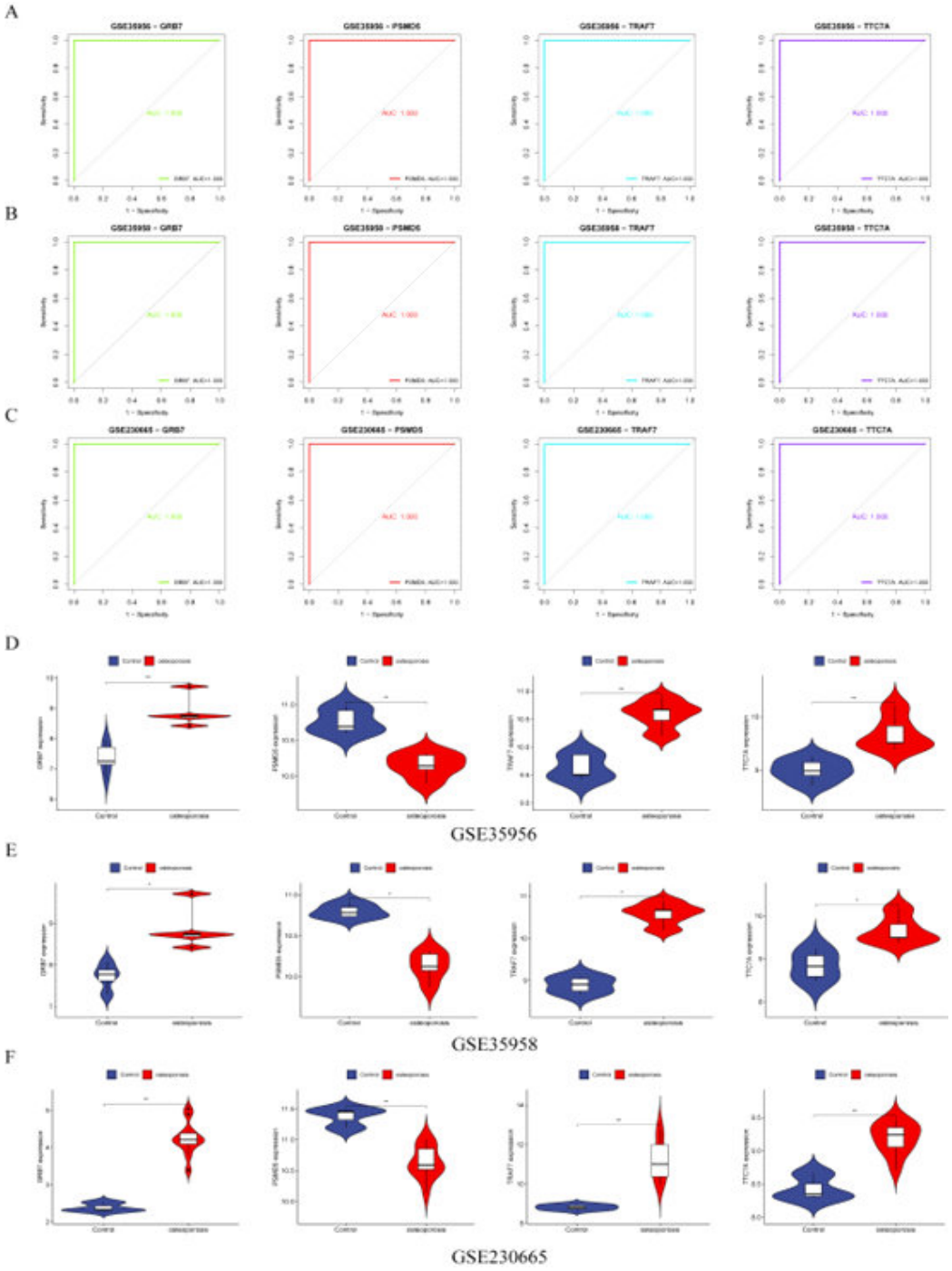

Figure 6. Four additional hub genes exhibit perfect diagnostic performance.
(A-C) ROC curves showing perfect discrimination (AUC = 1.0) by PSMD5, GRB7, TRAF7, and TTC7A across all datasets. (D-F) Violin plots confirming their consistent dysregulation in osteoporosis samples.

Expression analysis further validated these findings. Violin plots (Figure 5C; Figures 6D-F) showed that expression levels of AP2A1 and CHST1 were significantly higher in the osteoporosis group compared to controls ($P < 0.001$), consistent with their upregulated pattern and the prediction of negative regulation by hsa-miR-30b-5p. Additionally, PSMD5, GRB7, TRAF7, and TTC7A exhibited consistent expression trends across all datasets (Figures 6D-F). This high degree of cross-cohort consistency validates the reliability of the core regulatory pairs at the expression level and reinforces the likelihood that these core genes are critically involved in osteoporotic pathology.

3.6. Targeted Drug Prediction and Molecular Docking Validation for Core Targets

Leveraging the six core genes, we further explored their therapeutic targeting potential. Interrogation of the DSigDB database identified several candidate compounds with known associations to these targets. Molecular docking simulations for top-ranked drug-target pairs revealed several complexes with favorable binding potential. Stable docking conformations were formed for CHST1 with S-1,2-Dichlorovinyl-N-acetylcysteine; for PSMD5 with meclofenoxate, sulfaguanidine, and tolazoline; and for GRB7 with 5,6-BENZOFLAVONE and 8-HYDROXYQUINOLINE (Figure 7). All validated complexes had predicted binding free energies (ΔG) < -5 kcal/mol, indicating spontaneous and stable binding characteristics. These computational results provide preliminary structural biology evidence supporting CHST1, PSMD5, and GRB7 as targetable nodes, suggesting that existing or novel compounds acting on these targets could potentially modulate the osteoporotic process.

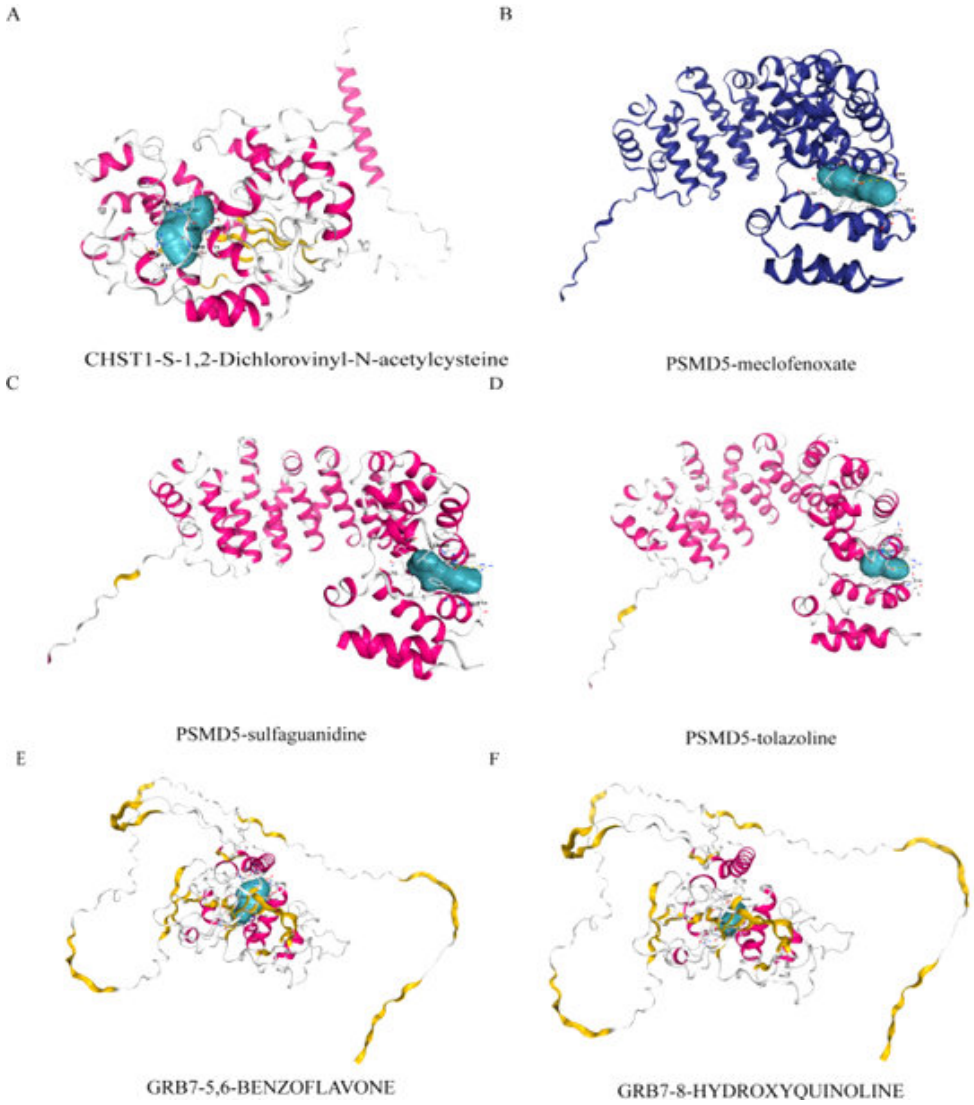

Figure 7. In silico screening identifies potential therapeutics targeting core genes.
Molecular docking models reveal high-affinity binding (predicted ΔG < -5 kcal/mol) between core target proteins (CHST1, PSMD5, GRB7) and candidate small-molecule compounds from the DSigDB database.

4. Discussion

This study integrated a miRNA dataset with three independent mRNA datasets to systematically construct and validate a robust miRNA-mRNA regulatory network in osteoporosis, overcoming limitations inherent to single-data-source analyses. We identified core regulatory axes, exemplified by hsa-miR-30b-5p/AP2A1 and hsa-miR-30b-5p/CHST1, which exhibit the classic negative regulatory expression pattern. Furthermore, we discovered four novel core genes (PSMD5, GRB7, TRAF7, TTC7A) with highly consistent dysregulation across all datasets. Diagnostic analysis revealed that all six core genes possess exceptional discriminatory power (AUC up to 1.0), highlighting their biomarker potential. Finally, in silico drug prediction and molecular docking provide a computational foundation for exploring therapeutic strategies targeting these hubs.

Notably, the core molecules identified in this study play key roles in various other pathophysiological processes, suggesting their regulatory functions may be universal rather than unique to osteoporosis. As the central hub of the key regulatory axis in this study, dysregulated expression of hsa-miR-30b-5p has been significantly associated with synovial lesions in rheumatoid arthritis[12], circulating profiles in heart failure[13], genetic risk for type 2 diabetes and peripheral arterial disease[14], sperm quality in male infertility[15], progression of head and neck squamous cell carcinoma[16], and exosome-based diagnostic models for amyotrophic lateral sclerosis[17]. Particularly in RA and cancer, it has been explicitly integrated into the long non-coding RNA/circular RNA-miRNA-mRNA competitive endogenous RNA (ceRNA) regulatory network. This cross-disease evidence strongly implies that hsa-miR-30b-5p may be a "pleiotropic" regulatory molecule involved in fundamental biological processes such as cell proliferation, apoptosis, inflammation, and stress responses. Therefore, the hsa-miR-30b-5p/AP2A1 and hsa-miR-30b-5p/CHST1 axes identified in this study for OP may reveal new links between bone metabolism disorders and the aforementioned shared pathological mechanisms.

The core genes AP2A1 and CHST1, identified in this study, demonstrate multifaceted and crucial mechanisms across different diseases. AP2A1 has been confirmed as a hub regulating cellular state and signal transduction: during aging, its upregulation directly drives cytoskeleton reorganization and abnormal adhesion, thereby locking the senescent phenotype[18]; in Alzheimer's disease, it binds to and activates Rab7 GTPase to regulate autophagosome trafficking, restoring autophagic flux[19]; in lung adenocarcinoma, as an interactor of DNAJC5, it enhances the endocytosis and recycling of the epidermal growth factor receptor, sustaining pro-oncogenic signaling[20]; in diabetic retinopathy, it is identified as a key epigenetic node co-regulated by DNA methylation and miRNA networks[21]. On the other hand, CHST1 primarily functions as a regulator of cell proliferation and the immune microenvironment: its high expression significantly promotes tumor cell proliferation, migration, and is closely associated with immune cell infiltration and poor prognosis in gastric and prostate cancers[22, 23]; in ovarian cancer, it is confirmed to sulfate specific galactose residues on cell surface O-glycans[24]. Collectively, AP2A1 and CHST1 broadly influence cell fate and tissue homeostasis from two distinct levels: intracellular trafficking and signal integration (AP2A1), and extracellular matrix modification and intercellular communication (CHST1). We hypothesize that in osteoporosis, they may synergistically act on core processes such as osteocyte senescence, autophagy imbalance, and bone immune microenvironment dysregulation, collectively contributing to the homeostatic imbalance between bone formation and resorption

Furthermore, the core genes PSMD5 and GRB7 identified in this study also exhibit complex functions as key regulatory nodes across various disease contexts. As a crucial regulatory subunit of the 26S proteasome, aberrant expression of PSMD5 is closely linked to cell cycle dysregulation and disease progression. Its expression is upregulated in high-grade pancreatic tumors[25]. In glioblastoma, its high expression is not only an independent risk factor for poor prognosis but also correlates with malignant phenotypes like cell cycle progression and invasion/migration[26]. A cross-population transcriptome-wide association study also found that the antisense transcript PSMD5-AS1 is a potential risk gene for juvenile idiopathic arthritis, suggesting its involvement in immune regulation[27]. These findings collectively point to the central role of PSMD5 in maintaining proteostasis and cell cycle control. On the other hand, the adaptor protein GRB7 is a key amplifier in cellular signal transduction, particularly in growth factor pathways. In HER2-positive breast cancer, GRB7 is directly driven to high expression by the transcription factor TCF12, subsequently promoting tumor cell proliferation, migration, and epithelial-mesenchymal transition by activating Wnt/β-catenin and ERK pathways[28]. In ovarian cancer, high GRB7 expression also correlates with poor prognosis and can influence disease progression by modulating the tumor immune microenvironment (e.g., M2 macrophage infiltration)[29]. Its oncogenic function is also confirmed in colorectal cancer, where it is transcriptionally regulated by the long non-coding RNA LINC02320, forming a pro-tumorigenic positive feedback loop[30]. Additionally, GRB7 is integrated into the ceRNA network mediated by circular RNA circDOCK1, promoting breast cancer progression[31].

In summary, PSMD5 and GRB7 profoundly and broadly impact cellular fate from two fundamental aspects: protein degradation homeostasis and growth factor signal transduction, respectively. Based on this, we speculate that in osteoporosis, PSMD5 might disrupt the fine regulation of bone remodeling by interfering with protein degradation balance in bone cells, while GRB7 might abnormally amplify growth factor signals in osteoblasts or osteoclasts.

The core genes TRAF7 and TTC7A, identified in this study, have revealed their key mechanisms in regulating cellular homeostasis in other disease models. TRAF7 is a RING-type E3 ubiquitin ligase with complex biological functions. In basic cell biology, it directly regulates circadian rhythm oscillation by mediating K48-linked polyubiquitination and degradation of the transcription factor DBP[32]. In oncology, its role is context-dependent: in glioma and hepatocellular carcinoma, TRAF7 acts as an oncogene with high expression, driving tumor progression by inducing KLF4 degradation or promoting P53 ubiquitin-mediated degradation, respectively, and suppressing cellular senescence[33, 34]; conversely, in acute myeloid leukemia, TRAF7 functions as a tumor suppressor, where its overexpression inhibits glycolysis and induces cell cycle arrest via activating the KLF2-PFKFB3 axis[35]. These findings collectively establish TRAF7's central role in protein stability, cell cycle, and metabolic regulation. On the other hand, the function of TTC7A is clearly linked to cytoskeletal dynamics and immune cell migration. Loss-of-function mutations in TTC7A are the primary cause of combined gastrointestinal defects and immunodeficiency syndrome, characterized by severe intestinal malformations, immunodeficiency, and inflammatory bowel disease in patients[36]. Mechanistic studies indicate that TTC7A deficiency, through impairing phosphoinositide signaling, leads to abnormal lymphocyte migration, impaired deformability, and dysregulated actin cytoskeleton dynamics, resulting in progressive immunodeficiency[37]. This deficiency can be accompanied by diverse skin manifestations clinically[38]. In summary, TRAF7 and TTC7A profoundly influence cell function and tissue homeostasis from two dimensions: post-translational modification and signal integration (TRAF7), and cytoskeletal rearrangement and cell motility (TTC7A). TRAF7 might regulate osteoblast or osteoclast activity and cycle by ubiquitinating specific substrates, while dysregulation of TTC7A could affect the recruitment and positioning of immune cells or bone progenitor cells within bone tissue, both contributing to the dysregulation of the bone remodeling microenvironment.

Methodologically, this study differs from most existing research by being the first to systematically cross-validate the constructed miRNA-mRNA regulatory network using three independent mRNA expression datasets. This strategy significantly enhances the robustness and generalizability of the conclusions. On this basis, we not only systematically identified and validated two novel regulatory pairs, hsa-miR-30b-5p/AP2A1 and hsa-miR-30b-5p/CHST1, but also discovered four hub genes—PSMD5, GRB7, TRAF7, and TTC7A—that have not been fully characterized in OP. These findings collectively fill a gap in the current understanding of the post-transcriptional regulatory network in OP. It is noteworthy that these novel molecules possess broad potential connections to classic pathological mechanisms of OP (such as RANKL/RANK/OPG pathway-mediated bone resorption and Wnt/β-catenin pathway-regulated bone formation), providing new connecting points for understanding the complexity of OP within a broader mechanistic landscape. However, it is crucial to acknowledge the limitations of this study: its conclusions are derived from bioinformatics analyses of public databases, and the specific tissue origin of the samples used limits the direct extrapolation of the results to broader clinical scenarios; the predicted miRNA-target relationships and upstream regulatory networks (e.g., SP1) lack experimental validation of causality; simultaneously, the computationally based drug prediction results urgently require rigorous validation through subsequent wet-lab experiments, including functional cellular assays, animal models, and preclinical efficacy evaluations. These represent the boundaries of the present study and also point the way for future in-depth exploration.

5.Conclusion

Through integrated analysis of multiple transcriptomic datasets, this study established and cross-validated a robust miRNA-mRNA regulatory network specific to osteoporosis. We identified two key regulatory axes—hsa-miR-30b-5p/AP2A1 and hsa-miR-30b-5p/CHST1—along with four novel hub genes (PSMD5, GRB7, TRAF7, TTC7A) that show consistent dysregulation. Together, these molecules represent a promising diagnostic signature and provide a new molecular framework for understanding the dysregulated interplay of cellular processes in osteoporosis.

In summary, PSMD5 and GRB7 profoundly and broadly impact cellular fate from two fundamental aspects: protein degradation homeostasis and growth factor signal transduction, respectively. Based on this, we speculate that in osteoporosis, PSMD5 might disrupt the fine regulation of bone remodeling by interfering with protein degradation balance in bone cells, while GRB7 might abnormally amplify growth factor signals in osteoblasts or osteoclasts.

Abbreviations

AUC – Area Under the Curve
BP – Biological Process
CC – Cellular Component
ceRNA – Competitive Endogenous RNA
DEGs – Differentially Expressed Genes
FC – Fold Change
GEO – Gene Expression Omnibus
GO – Gene Ontology
MF – Molecular Function
miRNA – MicroRNA
mRNA – Messenger RNA
OP – Osteoporosis
PDB – Protein Data Bank
ROC – Receiver Operating Characteristic
TF – Transcription Factor

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

The datasets analyzed during the current study are publicly available in the National Center for Biotechnology Information (NCBI) Gene Expression Omnibus (GEO) repository (https://www.ncbi.nlm.nih.gov/geo/).The drug-gene interaction data were sourced from the Drug SIGnatures Database (DSigDB, https://dsigdb.tanlab.org/). The three-dimensional structures of small-molecule compounds and target proteins were retrieved from PubChem (https://pubchem.ncbi.nlm.nih.gov/) and the Protein Data Bank (PDB, https://www.rcsb.org/), respectively. Molecular docking was performed using the online server CB-Dock2 (https://cadd.labshare.cn/cb-dock2/php/index.php).

Competing Interests

All the authors declared that they had no competing interests.

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Authors' contributions

Bufan Li: Writing – Original Draft, Data Curation, Formal Analysis,Visualization.
Jiaxing Zeng : Methodology, Investigation, Validation,Funding Acquisition,Software.
Mao-Lin He: Conceptualization, Writing – Review & Editing, Project Administration.
Qifan Chen: Methodology,Original Draft,Writing – Review & Editing.

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