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| **Recent research on mechanisms of osteoarthritis (OA)** |
| **Literature** | **Study Objectives** | **Methodology** | **Key Findings** | **Strengths** | **Limitations** |
| Identification and validation of aging related genes in osteoarthritis(Du et al. 2025) | To identify OA associated genes and elucidate molecular pathways, focusing on CX3CR1 as a potential diagnostic biomarker and therapeutic target. | Integrated bioinformatics analysis (GEO datasets, WGCNA, PPI networks) with qPCR, Western blot (WB) and immunohistochemistry (IHC) to explore CX3CR1's role in OA pathogenesis. | CX3CR1 was significantly upregulated in OA, correlating with lipid metabolism, extracellular matrix degradation, and immune cell infiltration (e.g., activated mast cells), and showed diagnostic potential (AUC = 0.806). | Combined multi-omics approaches with robust experimental validation, highlighting CX3CR1's mechanistic link to OA progression and immune modulation. | Reliance on public datasets; lack of detailed molecular mechanism exploration and in vivo therapeutic validation. |
| Identification of WDR74 and TNFRSF12A as biomarkers for early osteoarthritis using machine learning and immunohistochemistry(Chen et al. 2025) | To identify ubiquitination-related genes as diagnostic biomarkers for early OA using machine learning and validate their clinical relevance. | Integrated scRNA-seq, bulk RNA-seq, machine learning (XGBoost), and IHC analyze OA datasets and validate candidate genes (WDR74, TNFRSF12A). | WDR74 and TNFRSF12A were identified as core OA biomarkers, with diagnostic model AUC >0.9, and validated via qRT-PCR/IHC in human OA cartilage and IL-1β-stimulated chondrocytes. | Multi-modal approach combining scRNA-seq, ML, and experimental validation; high diagnostic accuracy and subgroup stratification potential. | Requires larger cohort validation; functional roles of WDR74/TNFRSF12A in OA pathogenesis need further mechanistic studies. |
| Identification of Energy Metabolism-Related Subtypes and Diagnostic Biomarkers for Osteoarthritis(Xu et al. 2025) | To identify energy metabolism-related genes as diagnostic biomarkers for OA and explore their association with immune infiltration | Integrated bioinformatics (GEO datasets, differential expression analysis, PPI networks) with machine learning (LASSO, SVM-RFE, RF) and immune infiltration analysis (CIBERSORT, ssGSEA). | Identified NUP98 and RPIA as diagnostic biomarkers (AUC >0.9), validated in training (GSE51588) and test sets (GSE63359), with distinct immune infiltration patterns in OA subtypes. | Multi-modal approach combining transcriptomics, machine learning, and immune profiling; robust diagnostic performance validated across datasets. | Limited clinical validation; mechanistic roles of NUP98/RPIA in OA pathogenesis require further experimental investigation. |
| Identification of Genes Linked to Meniscal Degeneration in Osteoarthritis: An In Silico Analysis(Papageorgiou et al. 2025) | To identify key genes and pathways involved in meniscal degeneration during (OA progression through computational analysis of transcriptomic data. | Integrated bioinformatics (DESeq2, PPI networks, GO/KEGG enrichment) with comparative analysis of OA meniscus, synovium, and cartilage datasets (GSE185064, GSE114007, GSE143514). | Identified 85 mRNAs (e.g., MMP13, RUNX2, ITGB2) and 8 lncRNAs (e.g., XIST, H19) dysregulated in OA meniscus;GJB, PAQR5, and CLEC12A were shared across all OA-affected tissues. | Multi-tissue comparative approach revealing shared pathogenic mechanisms; robust functional enrichment linking genes to inflammation, ECM degradation, and lipid metabolism. | Small cohort size; lack of experimental validation; age/gender metadata gaps in datasets may confound results. |
| Identification of Key Chondrocyte Apoptosis-Related Genes in Osteoarthritis(Wang et al. 2025) | To identify key chondrocyte apoptosis-related genes (CARGs) in OA through bioinformatics and experimental validation, focusing on their diagnostic and therapeutic potential. | Integrated WGCNA, PPI network analysis, and in vitro assays (IL-1β-stimulated C28/I2 chondrocytes) to validate hub genes (NFKB1, ICAM1) from GEO datasets (GSE32317, GSE55235). | Identified NFKB1 and ICAM1 as hub CARGs in OA, upregulated in IL-1β-induced chondrocytes and correlated with apoptosis, ECM degradation, and inflammation (AUC: 0.9 for ICAM1). | Multi-modal approach combining bioinformatics (WGCNA, ROC analysis) with experimental validation (qRT-PCR, WB) to confirm gene roles in OA pathogenesis. | Lack of in vivo validation; clinical relevance of NFKB1/ICAM1 as therapeutic targets requires further preclinical studies. |
| Identification of ZNF652 as a Diagnostic and Therapeutic Target in Osteoarthritis Using Machine Learning(Chen et al. 2024) | To identify key chondrocyte apoptosis-related genes (CARGs) in OA through bioinformatics and experimental validation, focusing on their diagnostic and therapeutic potential. | Integrated WGCNA, PPI network analysis, and in vitro assays (IL-1β-stimulated C28/I2 chondrocytes) to validate hub genes (NFKB1, ICAM1) from GEO datasets (GSE32317, GSE55235). | Identified NFKB1 and ICAM1 as hub CARGs in OA, upregulated in IL-1β-induced chondrocytes and correlated with apoptosis, ECM degradation, and inflammation (AUC: 0.9 for ICAM1). | Multi-modal approach combining bioinformatics (WGCNA, ROC analysis) with experimental validation (qRT-PCR, Western blot) to confirm gene roles in OA pathogenesis. | Lack of in vivo validation; clinical relevance of NFKB1/ICAM1 as therapeutic targets requires further preclinical studies. |
| Identification and Validation of Aging-Related Genes in Osteoarthritis(Du et al. 2025) | To identify aging-related genes (ARGs) linked to osteoarthritis (OA) pathogenesis using bioinformatics and experimental validation, focusing on synovial tissue to uncover diagnostic and therapeutic targets. | Integrated GEO datasets (GSE55235, GSE55457, GSE82107) for DEG screening, ARG intersection, PPI networks, machine learning (LASSO/RF), and qRT-PCR validation in OA synovial tissues. | Identified ATF3, KLF4, NFKBIA, and SOD2 as downregulated ARGs in OA, correlating with immune infiltration (e.g., altered Mast cells, M1 macrophages) and oxidative stress pathways (AUC: 0.967 for diagnostic model). | Multi-dataset validation, machine learning robustness, and experimental confirmation via qRT-PCR, highlighting translational potential for OA biomarkers. | Small clinical sample size; lack of in vivo mechanistic studies and single-cell resolution for synovial cell-type-specific gene expression. |
| Identification of Key Genes in Osteoarthritis Development: Biomarker Discovery and Therapeutic Targets(Wu et al. 2025) | To identify synovial tissue-derived diagnostic biomarkers (CXCL8, CXCL2, DUSP5, TNFSF11) for OA through multi-dataset bioinformatics analysis and experimental validation, addressing the limitations of single-biomarker approaches. | Integrated GEO datasets (GSE1919/GSE55235/GSE82107) for DEG screening, PPI network construction (Cytoscape), machine learning (ROC AUC >0.8), and qRT-PCR validation in 5 OA/control synovial samples. | Identified 4 hub genes: CXCL8 (AUC=1.0), CXCL2 (AUC=0.901), DUSP5 (AUC=0.851), and TNFSF11 (AUC=0.810), linking synovial inflammation (CXCL8/2) and bone remodeling (TNFSF11/DUSP5) pathways. | Multi-dataset validation (training + GSE29746), synergistic biomarker clusters overcoming single-target limitations, and drug prediction (e.g., acetaminophen-DUSP5 interaction). | Small clinical cohort (n=5/group), lack of mechanistic studies, and platform heterogeneity across GEO datasets. |
| Identification of MEG3 and MAPK3 as Potential Therapeutic Targets for Osteoarthritis Through Multiomics Integration and Machine Learning(Ma et al. 2025) | To identify causal genes for knee osteoarthritis (KOA) using Mendelian randomization (MR), transcriptomics, and machine learning, focusing on synovial tissue biomarkers with diagnostic and therapeutic potential | Identified MEG3 (protective, OR=0.962) and MAPK3 (risk, OR=1.094) as diagnostic biomarkers, linked to immune infiltration (e.g., Tfh/mast cells) and validated in synovial tissues (AUC >0.7 in training/validation sets). | Identified MEG3 (protective, OR=0.962) and MAPK3 (risk, OR=1.094) as diagnostic biomarkers, linked to immune infiltration (e.g., Tfh/mast cells) and validated in synovial tissues (AUC >0.7 in training/validation sets). | Multi-modal integration (MR + transcriptomics + machine learning), robust cross-validation, and non-invasive biomarker potential via blood-based eQTL associations. | Small clinical validation cohort (n=3/group), lack of mechanistic studies, and unaddressed subclinical OA in controls. |
| Integrating Bioinformatics and Machine Learning to Identify Biomarkers of Branched Chain Amino Acid Related Genes in Osteoarthritis(ZhaYang et al. 2025) | To identify BCAA-related biomarkers (SLC3A2 and SLC7A5) in OA through multi-omics integration, machine learning, and experimental validation, addressing gaps in early diagnosis and metabolic dysregulation. | Combined GEO transcriptomics (GSE114007/GSE51588), differential expression analysis, WGCNA, three machine learning algorithms (LASSO/SVM-RFE/Boruta), and experimental validation (qPCR/IHC/WB) to screen and validate biomarkers. | Identified SLC3A2 and SLC7A5 as diagnostic biomarkers (AUC >0.7), linked to ribosome/insulin pathways and regulated by XIST/OIP5-AS1 miRNAs; nomogram model achieved 98.1% accuracy in OA prediction. | Multi-algorithm cross-validation, robust nomogram predictive performance, and experimental validation (qPCR/IHC) supporting clinical relevance of BCAA metabolism in OA. | Small clinical cohort (n=10/group), reliance on cartilage-specific datasets, and unvalidated mechanistic roles of SLC3A2/SLC7A5 in BCAA transport. |
| Identification of Ferroptosis-Related Genes and Potential Drugs in Osteoarthritis(Song et al. 2025) | To identify ferroptosis-related biomarkers (GPX4, TFRC, SLC7A11, EGFR, IL1B) in OA and elucidate resveratrol’s therapeutic mechanism via ferroptosis modulation. | Integrated GEO transcriptomics (GSE55235/GSE77298/GSE82107), WGCNA, PPI networks, immune infiltration analysis, molecular docking, and in vitro validation (qPCR/WB) to screen targets and validate resveratrol’s effects. | Identified 462 ferroptosis-related genes in OA; resveratrol ameliorated OA by targeting GPX4/SLC7A11 to suppress ferroptosis and inflammation via PI3K-Akt/mTOR pathways (p<0.001). | Multi-omics validation (bioinformatics + in vitro experiments), robust immune infiltration insights, and molecular docking confirming resveratrol-target interactions. | Small clinical cohort (n=10/group), lack of in vivo validation, and unaddressed subclinical OA in controls. |
| Screening of Potential Biomarkers of Osteoarthritis: A Bioinformatics Analysis(Hou et al. 2024) | To identify novel diagnostic biomarkers (JUN, ATF3, DUSP1) and regulatory mechanisms (hsa-mir-26b-5p) in OA through integrative bioinformatics analysis. | Analyzed GEO datasets (GSE55457/GSE55235/GSE114007) for DEGs, performed GO/KEGG enrichment, constructed PPI networks, validated hub genes via ROC curves, and predicted miRNA interactions (hsa-mir-26b-5p). | Identified JUN, ATF3, and DUSP1 as downregulated hub genes (AUC >0.95) linked to MAPK signaling and mitochondrial dysfunction; hsa-mir-26b-5p potentially regulates all three genes. | Multi-dataset validation, robust ROC performance (AUC up to 1.00), and integration of miRNA-mRNA networks revealing hsa-mir-26b-5p as a therapeutic target. | Lack of in vitro/in vivo validation and clinical cohort data to confirm biomarker specificity in diverse OA subtypes. |

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