NAMPT

Ferroptosis and necroptosis are two recently identified forms of non-apoptotic cell death. Their dysregulation plays a critical role in the development and progression of Psoriasis (PsD) and Atherosclerosis (AS).

Fan et al. explored shared Ferroptosis and necroptosis-related genes and elucidates their molecular mechanisms in PsD and AS through the analysis of public databases.

Methods: Data sets for PsD (GSE30999) and AS (GSE28829) were retrieved from the GEO database. Differential gene expression (DEG) and weighted gene co-expression network analysis (WGCNA) were performed. Machine learning algorithms identified candidate biomarkers, whose diagnostic values were assessed using Receiver Operating Characteristic (ROC) curve analysis. Additionally, the expression levels of these biomarkers in cell models of AS and PsD were quantitatively measured using Western Blot (WB) and real-time quantitative PCR (RT-qPCR). Furthermore, CIBERSORT evaluated immune cell infiltration in PsD and AS tissues, highlighting the correlation between characteristic genes and immune cells. Predictive analysis for candidate drugs targeting characteristic genes was conducted using the DGIdb database, and an lncRNA-miRNA-mRNA network related to these genes was constructed.

They identified 44 differentially expressed ferroptosis-related genes (DE-FRGs) and 30 differentially expressed necroptosis-related genes (DE-NRGs). GO and KEGG enrichment analyses revealed significant enrichment of these genes in immune-related and inflammatory pathways, especially in NOD-like receptor and TNF signaling pathways. Two ferroptosis-related genes (NAMPT, ZFP36) and eight necroptosis-related genes (C7, CARD6, CASP1, CTSD, HMOX1, NOD2, PYCARD, TNFRSF21) showed high sensitivity and specificity in ROC curve analysis. These findings were corroborated in external validation datasets and cell models. Immune infiltration analysis revealed increased levels of T cells gamma delta, Macrophages M0, and Macrophages M2 in PsD and AS samples. Additionally, we identified 43 drugs targeting 5 characteristic genes. Notably, the XIST-miR-93-5p-ZFP36/HMOX1 and NEAT1-miR-93-5p-ZFP36/HMOX1 pathways have been identified as promising RNA regulatory pathways in AS and PsD.

Conclusion: The two ferroptosis-related genes (NAMPT, ZFP36) and eight necroptosis-related genes (C7, CARD6, CASP1, CTSD, HMOX1, NOD2, PYCARD, TNFRSF21) are potential key biomarkers for PsD and AS. These genes significantly influence the pathogenesis of PsD and AS by modulating macrophage activity, participating in immune regulation, and mediating inflammatory responses [1)].

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Fan J, Zhu T, Tian X, Liu S, Zhang SL. Exploration of ferroptosis and necroptosis-related genes and potential molecular mechanisms in psoriasis and atherosclerosis. Front Immunol. 2024 Jul 12;15:1372303. doi: 10.3389/fimmu.2024.1372303. PMID: 39072329; PMCID: PMC11272566.