Atherosclerosis

Atherosclerosis is a chronic cardiovascular disease associated with oxidative stress damage, which is caused by excessive oxidation of low-density lipoprotein (ox-LDL).

(Also known as arteriosclerotic vascular disease or ASVD) is a specific form of arteriosclerosis in which an artery wall thickens as a result of invasion and accumulation of white blood cells (WBCs).

The accumulation of the WBCs is termed “fatty streaks” early on because of appearance being similar to that of marbled steak. These accumulations contain both living, active WBCs (producing inflammation) and remnants of dead cells, including cholesterol and triglycerides. The remnants eventually include calcium and other crystallized materials, within the outer-most and oldest plaque. The “fatty streaks” reduce the elasticity of the artery walls. However, they do not affect blood flow for decades, because the artery muscular wall enlarges at the locations of plaque. The wall stiffening may eventually increase pulse pressure; widened pulse pressure is one possible result of advanced disease within the major arteries.

Atherosclerosis is therefore a syndrome affecting arterial blood vessels due to a chronic inflammatory response of WBCs in the walls of arteries. This is promoted by low-density lipoproteins (LDL, plasma proteins that carry cholesterol and triglycerides) without adequate removal of fats and cholesterol from the macrophages by functional high-density lipoproteins (HDL). It is commonly referred to as a “hardening” or furring of the arteries. It is caused by the formation of multiple atheromatous plaques within the arteries.

Studies have revealed the important role of CD137 in human atherosclerosis

see Intracranial atherosclerosis.

Pathogenesis

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.