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MAFB Expression in LPS-Induced Exosomes: Revealing the Connection to sepsis-trigerred Hepatic Injury

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Abstract : Sepsis poses a significant global health threat, necessitating extensive exploration of indicators tied to its pathological mechanisms and multi-organ dysfunction. While murine studies have shed light on sepsis, the intricate cellular and molecular landscape in human sepsis remains enigmatic. Exploring the influence of activated monocyte-derived exosomes in sepsis sheds light on a promising pathway for understanding the intricate cellular and molecular mechanisms involved in this condition in humans. In sepsis, exosome-borne mRNA and miRNA orchestrate immune response gene expression in recipient cells. Yet, the specifics of exosome-mediated cell-to-cell communication, especially how mRNA cargoes modulate gene expression in recipient cells, remain poorly understood. This study aims to elucidate the precise molecular pathways through which exosomal mRNA cargo, particularly MAFB, contributes to the developing sepsis-induced molecular aberrations in liver tissues, employing rigorously defined cell culture conditions. THP-1 cells were treated with LPS to induce changes in exosomal RNA profiles. Exosomes were isolated and characterized using microscopy and mass spectrometry. RNA was extracted from exosomes and sequenced. The most abundant exosomal mRNAs were subjected to GO analysis for functional annotation analysis and KEGG database analysis to identify the involved enriched pathways. PCR (Polymerase Chain Reaction), RNA sequencing, and Western blotting were involved to analyze changes in gene expression, protein levels, and signaling pathways within the liver cells(HepG2) after exposure to exosomal MAFB. This study pinpoints exosomal MAFB as a potential key regulator linked to liver cell damage during sepsis, along with associated genes (miR155HG, H3F3A, and possibly JARD2) forming a crucial molecular pathway contributing to liver cell injury, Together, these elements indicate a vital molecular pathway that plays a significant role in the emergence of liver cell injury during sepsis.. These findings suggest the importance of further research on these components for potential therapeutic interventions in managing acute liver damage in sepsis.

Keywords : sepsis, exososome, exosomal MAFB, LPS-induced THP-1 cells, RNA profiles, sepsis-triggered liver injury
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