[BIOINFO 2025]

LAMA2 downregulation via the circRNA–hsa-miR-224 axis facilitates immune evasion and metastasis in non-small cell lung cancer

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The understanding of the molecular mechanisms underlying immune evasion and progression in non-small cell lung cancer (NSCLC) remains limited. However, dysregulation of the competing endogenous RNA (ceRNA) network, which involves circular RNAs (circRNAs), microRNAs (miRNAs), and messenger RNAs (mRNAs), is increasingly recognized as a critical factor in tumorigenesis. We conducted an integrated bioinformatics analysis using multiple public datasets (GEO, TCGA) to construct and validate a regulatory network involving circRNA–miRNA–mRNA in NSCLC. Functional enrichment, protein–protein interaction, survival, and drug sensitivity analyses were performed to elucidate the roles of key network components. Our analysis identified a key regulatory axis initiated by five consistently downregulated circRNAs. The downregulation of these circRNAs promoted the upregulation of hsa-miR-224, which in turn suppressed its target gene, laminin alpha 2 (LAMA2). Subsequently, LAMA2 has been identified as a critical hub gene; reduced LAMA2 expression is significantly associated with poor patient prognosis. Functional analysis revealed that LAMA2 downregulation correlated with a dual phenotype of profound immune suppression and enhanced metastatic potential, characterized by the inhibition of key immune signaling pathways (TNFα/NF-κB, and IL-2/STAT5), impaired T cell function, and the disruption of cell adhesion. Importantly, the mediation of the LAMA2 downregulation was driven by hsa-miR-224, rather than somatic mutations, and also correlated with differential sensitivity to several anticancer drugs. This study established LAMA2 as a central regulator of immune evasion and tumor progression in NSCLC. Our findings highlight the LAMA2-centered ceRNA network as a source of promising prognostic and predictive biomarkers for guiding personalized therapeutic strategies.

Keywords: non-small cell lung cancer; circRNA–miRNA–mRNA network; hsa-miR-224; LAMA2; prognostic biomarker; bioinformatics