Notification Number: 588/2025

Date of award: 24-10-25

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Topic: **Integrated multi-omics approach to identify novel prognostic biomarkers associated with apoptosis-autophagy crosstalk and therapeutics against lung cancer**

Keywords: Lung adenocarcinoma; multi-omics integration; apoptosis; autophagy; prognostic biomarkers

Findings

This study elucidates the complex crosstalk between apoptosis and autophagy in lung adenocarcinoma (LUAD) using a comprehensive multi-omics and network biology approach. By integrating transcriptomic, survival, and immune profiling data, distinct molecular subgroups of LUAD were identified, each displaying unique patterns of cell death regulation and clinical outcomes.

Among these, the high-risk subgroup exhibited concurrent upregulation of autophagy and apoptosis-related genes, suggesting a compensatory survival mechanism that promotes tumor persistence despite cellular stress. Weighted Gene Co-expression Network Analysis (WGCNA) and protein interaction mapping pinpointed CHEK1, BIRC5, and GAPDH as central regulatory nodes. These genes play dual roles in cell cycle control, DNA repair, and metabolic adaptation, collectively driving LUAD progression and therapeutic resistance.

Immune infiltration analysis further revealed that the high-risk subgroup displayed increased proportions of regulatory T cells (Tregs) and exhausted $CD8^+$ T cells, signifying an immunosuppressive tumor microenvironment. This suggests that overexpression of CHEK1, BIRC5, and GAPDH not only promotes tumor survival but also contributes to immune evasion : a hallmark of advanced LUAD. Integration of gene expression, pathway enrichment, and protein–protein interaction (PPI) data revealed six master regulators (NLRC4, CHEK1, IL6,

BIRC5, PMAIP1, and TP63) coordinating apoptosis-autophagy balance through p53, PI3K/AKT, and HIF-1 signaling axes.

Network pharmacology identified curcumin as a potent small-molecule modulator targeting CHEK1 and BIRC5. Experimental validation in A549 LUAD cells demonstrated dose-dependent inhibition of cell viability and significant suppression of CHEK1 expression, validating the computational predictions.

Collectively, these findings establish that integration of multi-omics analysis with functional validation provides a strong foundation for developing precision therapies that co-regulate cell death pathways, offering new directions for diagnosis, prognosis, and targeted treatment of lung adenocarcinoma.