Huh7, p63 downregulation was observed. In both cell lines, miR-203a-3p overexpression attenuated DOX-induced antiproliferative and apoptotic effects and increased oxygen consumption rates.

Conclusions: Chemotherapeutic drug resistance remains a major challenge in cancer treatment. Our findings demonstrate that miR-203a-3p modulates DOX resistance in HCC cells by regulating the expression of p53 family members, reprogramming mitochondrial metabolism, and altering apoptotic response. These results highlight miR-203a-3p as a promising therapeutic target in HCC, independent of p53 status, and support the potential of miRNA-based strategies to overcome chemoresistance and improve treatment outcomes.

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109eP Identification of potential novel therapies of leukemia

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Background: Acute lymphoblastic leukemia (ALL) is characterized by the malignant proliferation of immature lymphoid progenitors, resulting in hematopoietic suppression and clinical manifestations such as anemia, immunodeficiency, and hemorrhage. Resistance to glucocorticoids (GCs), which are essential agents in the treatment of ALL, presents a significant therapeutic challenge. This study aims to investigate alternative and combinatorial treatment regimens that target the glucocorticoid receptor (GR) axis, calcium signaling, and kinase-mediated survival pathways to overcome this GC resistance.

Methods: T-cell ALL cell lines, CEM-C7 (GC-sensitive) and CEM-C1 (GC-resistant), were exposed to Perifosine, Ulixertinib, Dasatinib, dexamethasone (Dex), and calcium channel modulators (e.g., Verapamil). Cell viability was quantified via MTS assays, and apoptosis was evaluated using propidium iodide-based flow cytometry. Bioinformatic enrichment analyses were performed to identify convergence nodes across hormone-responsive and oncogenic signaling pathways.

Results: Perifosine, Ulixertinib, and Dasatinib chosen through bioinformatics analysis significantly reduced metabolic activity across both cell lines. Flow cytometry confirmed elevated apoptosis rates, with Perifosine demonstrating pronounced cytotoxicity. Combination treatments (e.g., Perifosine + Dex + Verapamil) exhibited enhanced efficacy in CEM-C1 cells, indicating more cytotoxic effects. Pathway enrichment highlighted GR signaling, PI3K-Akt, JAK-STAT, and FoxO pathways as central regulatory hubs.

Conclusions: Perifosine-based combination therapies exhibit potent anti-leukemic activity, particularly in GC-resistant phenotypes, and warrant further translational exploration. Targeting intersecting nodes in hormone and survival signaling pathways may offer a viable strategy to circumvent therapeutic resistance in ALL.

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