

عنوان مقاله:

Safe Combination of Cisplatin and Metformin Reverts the Malignant Ascites in a Mouse Model to a Solid Tumor by Downregulation of $\Delta Np63$ and Induces Tumor Dormancy via mTOR/ p21 Mechanism

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خلاصه مقاله:

Background: Currently, combination therapy has become the cornerstone of cancer treatment. The combination of different anticancer mechanisms can induce tumor cell quiescence. However, toxicity to normal tissue is the major limitation of existing combined drugs. Method: In this experimental study, Ehrlich ascites carcinoma (EAC) inoculated into mice was targeted with just one dose of cisplatin and later doses of metformin, a safe antidiabetic drug with an anticancer effect, to maintain EAC cells in the quiescent state and secure a longer survival time without tumor recurrence. Results: The group that underwent dual therapy developed a delayed solid tumor instead of a malignant ascites. The induction of chemo-quiescence in the EAC cells was proven by the downregulation of mechanistic target of rapamycin and the upregulation of cyclin-dependent kinase inhibitor 1 (p21) expressions. Intriguingly, the conversion of free neoplastic cells into a solid tumor was associated with a significant decrease in $\Delta Np63$ immunostaining in EAC cells. Conclusion: Taken together, a single dose of cisplatin followed by metformin doses could overcome the aggressiveness of malignant ascites by the conversion into a solid tumor, induction of chemo-quiescence, and the extension of survival time.

کلمات کلیدی:

Chemo-quiescence, Ehrlich ascites carcinoma, Mechanistic target of rapamycin (mTOR), Metformin, Cisplatin, $\Delta Np63$

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