Short Communication

iMedPub Journals
http://www.imedpub.com

Clinical Immunology and Infectious Diseases

2022
Vol 6. No. 2

Safe Combination of Cisplatin and Metformin Reverts the Malignant Ascites in a Mouse Model to a Solid Tumor by Downregulation of ΔNp63 and Induces Tumor Dormancy via m TOR/ p21 Mechanism

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Abstract

Currently, combination therapy has become the cornerstone of cancer treatment. The combination of different anti-cancer mechanisms can induce tumor cell quiescence. However, toxicity to normal tissue is the major limitation of existing combined drugs. In this study, Ehrlich ascites carcinoma (EAC) inoculated into mice was targeted with just one dose of cisplatin and later doses of metformin, a safe anti-diabetic drug with an anti-cancer effect, to maintain EAC cells in the quiescent state and secure a longer survival time without tumor recurrence. The group that underwent dual therapy had developed a delayed solid tumor instead of a malignant ascites. Induction of chemo-quiescence in the EAC cells was proven by downregulation of mechanistic target of rapamycin (mTOR) and 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 ΔNp63 immunostaining in EAC cells. 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 extension of survival time

Keywords: Chemo-quiescence; Ehrlich ascites carcinoma; mTOR; Metformin; Cisplatin; Np63.

Received: April 12, 2022; **Accepted:** April 18, 2022; **Published:** April 25, 2022

Biography

The Sara Gebril is a senior research fellow at the University Hospital Basel, Switzerland. The Sara Gebril has published so many articles different journals. He won so many honariums for his researchworks.