

Enhancing low dose doxorubicin-induced MCA-fibrosarcoma killing through an immunomodulator-mediated natural killer activation

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The combination of cytotoxic drugs with immunotherapy should be more effective than monotherapy alone since both therapeutic modalities may target different toxic mechanisms. Doxorubicin (Dox) is an effective and high potency anticancer drug. Dox use, however, is limited because of dose-related cardiomyopathy and increasing congestive heart failure risk. Thus, cytokine modulating agents may enhance Dox actions on tumor cells and lower Dox side effects on normal tissues. *Eriobotrya japonica* water extract (EJ-WR) was found to modulate cytokines by enhancing IL-12, IFN- γ and TNF- α in vitro and in vivo and within tumor microenvironment. This was associated with enhancing survival of mice bearing intra-peritoneal MCA-fibrosarcoma. Therefore, the present study is conducted to show if the combination of Dox and EJ-WR will increase death to tumor cells in the presence of natural killer (NK) lymphocytes. The results showed that Dox exhibited 15% toxicity on healthy spleen cells and EJ-WR reduced such toxicity. In addition, increasing concentration of Dox caused a 40% killing to MCA fibrosarcoma cells which is significantly increased when fibrosarcoma cells is co-cultured with healthy NK, but not with NK cells from tumor-bearing mice, cells at low concentrations of Dox. However, the % killing by Dox and NK cells from tumor bearing mice was enhanced significantly when co-cultured with EJ-WR. This enhancement of Dox-induced MCA fibrosarcoma killing via NK cells was highly associated with significant production of TNF- α from NK cells lysates. This concluded that the immunomodulator, EJ-WR, mediates NK activation and enhances Dox- induced MCA fibrosarcoma killing.

Biography

Khalid Matalka has completed his Ph.D from Ohio State University and postdoctoral studies from Harvard Medical School in 1994. He joined Petra University, Faculty of Pharmacy and Medical Sciences in 1995. He has been promoted to Professor in 2004 and became the Dean of the Faculty in 2006 till 2009. Prof. Matalka is now heading a newly established Pharmaceutical Center at the University (PUPC) and has published 45 papers in reputed journals and serving as an editorial board member of several reputed journals.

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