

SYNERGISTIC ANTI-TUMOR EFFECT OF COMBINATION OF RADIOTHERAPY AND IMMUNOTHERAPY BY ELECTRO-GENE THERAPY PLUS INTRA-TUMOR INJECTION OF DENDRITIC CELLS

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Purpose : Intra-tumoral (i.t.) injection of dendritic cells (DC) has been demonstrated to be able to evoke the systemic immunological response. Nevertheless, the injected DC are prone to be apoptotic in tumor site. Local secreted IL-2 and GM-CSF help the maturation and functioning of injected DC.

Experimental Design : We developed a method of creating an immunological favorable microenvironment by in situ electroporation of IL-2 and GM-CSF genes followed by injection of DC at tumor site. Necrotic and apoptotic cells from electrical shock may provide antigen source for DC to promote cross-priming of cytotoxic T cells and activate NK cells. PSA/CT-26 cells was used in this study.

Results : 4 repeated cycles of double gene EGT plus i.t. DC significantly inhibited the tumor growth and produced systemic immunity. The combination of double gene EGT and DC treatment induced heavy T cell infiltration inside tumor. Mice successfully treated by the combination of immunotherapy & radiotherapy can induce a systemic immunity to prevent the contralateral tumor challenge. Interestingly, the immunological favorable micro-environment established in the tumor site by this protocol created a highly effective condition for subsequent radiotherapy.

Conclusions : Our findings may have clinical implications in achieving better local control and prevention of systemic relapse through the combination of immunotherapy and radiotherapy. Further study for the mechanism is warranted.

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Key words: Dendritic cells, Electroporation, Immunotherapy, Radiotherapy