Alpha-tocopheryloxyacetic acid (αTEA) induced immune activation synergizes with radiation therapy to treat murine mammary carcinoma

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Abstract

Immunotherapy has emerged as a promising treatment for metastatic cancer. However, immunotherapy for advanced stage breast carcinoma remains an unmet need. Here we demonstrate that the novel immunomodulator alpha-tocopheryloxyacetic acid (αTEA) synergizes with radiation therapy (RT) in a metastatic murine mammary carcinoma model to improve tumor control, and we propose a mechanism based on the stimulation of type I interferons by αTEA.

Materials/Methods

For in-vivo studies, BALB/c mice bearing 4T1 murine mammary carcinoma lesions were treated with dietary αTEA, ionizing radiotherapy, or the combination of αTEA/RT. Immune activation in animals treated with dietary αTEA was determined by analyzing the percentage of proliferating CD4 and CD8 T cells using a Ki-67 assay. Pulmonary metastatic burden was determined using a DCFDA assay and treatment with 30-60 μM αTEA.

Radiotherapy performed using an Xstrahl small animal radiation platform

Animals received 20 Gy x 2 or 12 Gy x 5 fractions (BED₁₀ of 120-132)

Treatment of 4T1 bearing mice with oral αTEA results in increased T cell activation and decreased pulmonary metastases

Conclusions

These preliminary results suggest that the combination of αTEA and ionizing radiation may be a viable therapy for the treatment of metastatic breast carcinoma. This therapeutic combination may provide more durable response to radiotherapy while simultaneously reducing further metastatic spread.

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