عنوان مقاله:

Down-regulation of immune checkpoints by doxorubicin and carboplatin-containing neoadjuvant regimens in a murine breast cancer model

محل انتشار:

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خلاصه مقاله:

Objective(s): Immune checkpoint expression on tumor-infiltrating lymphocytes (TILs) has a correlation with the outcome of neoadjuvant chemotherapy (NAC) in breast cancer. However, the reciprocal effect of these regimens on the quality and quantity of immune checkpoints has hitherto not been addressed. We aimed to evaluate the impact of three NAC regimens on TILs and immune checkpoints in a murine triple-negative breast cancer model.Materials and Methods: Syngeneic model of locally-advanced breast cancer was established in immunocompetent mice using a ۴T۱ cell line. Tumor-bearing animals were treated with human-equivalent dosages of doxorubicin, paclitaxel, paclitaxel and carboplatin combination, and placebo. Infiltration of CD۳+, CD۸+, and FoxP۳+ cells into the tumor was assessed by immunohistochemistry. Expression of immune checkpoints, including PD-۱, CTLA-۴, and TIM-۳, was evaluated by real-time PCR.Results: Doxorubicin led to a significant ($p < ۰.۰۱$) increase in the percentage of the stromal infiltrating CD۳+ and CD۸+ lymphocytes. Doxorubicin also suppressed significantly ($p < ۰.۰۵$) the relative expression of PD-۱ compared with the placebo. PD-۱ expression was significantly ($p < ۰.۰۵$) lower in the group treated with paclitaxel and carboplatin combination as compared with the placebo. The relative expression of TIM-۳ was significantly ($p < ۰.۰۵$) suppressed in doxorubicin-treated mice in comparison with other interventions.Conclusion: Our findings hypothesize

that NAC with doxorubicin may potentiate antitumor immunity not merely by recruitment of TILs, but via down-regulation of PD-۱ and TIM-۳ checkpoints. Carboplatin-containing NAC may suppress PD-۱ as well.

کلمات کلیدی:

Animal model Breast neoplasms Immune checkpoints Neoadjuvant chemotherapy Tumor, infiltrating, Lymphocytes

لینک ثابت مقاله در پایگاه سیویلیکا: