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Immunotherapy vaccines for triple-negative breast cancer and its influence on the tumor microenvironment

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Objective: Cancer is still a complex and debilitating disease even though advances in treatment have occurred. Triplenegative breast cancer (TNBC) is an aggressive subtype of breast cancer with a poor prognosis and occurs more frequently in young women. Due to its metastatic features and unique tumor microenvironment, TNBC treatment is limited. In this study, we evaluated how three chemotherapy drugs could be used to produce vaccines with cells under immunogenic cell death. **Methodology**: For that, 4T1-luc2 cells were treated with cisplatin (100 μ M), mitoxantrone (MTX) (15 μ M), and doxorubicin (DOX) (50 µM) for 24 h. Then, the treated cells were injected subcutaneously in tumor-bearing Balb/c female mice, after the tumor challenge. The treatment occurred three times, once a week. During and after the treatment, primary tumor and metastatic progression were followed using the chemiluminescence technique. After 5 weeks of the tumor challenge, mice were euthanized and organs (liver, tumor, lungs, and spleen) were collected for analysis. Additionally, the spleens were processed for flow cytometry for regulatory T lymphocyte and myeloid-derived suppressor cells analysis. **Results:** Cisplatin and MTX vaccines slowed the primary and metastatic tumor growth as well as the decreased tumor, liver, and spleen weight, while the DOX vaccine slowed the metastatic tumor progression in the lungs but did not alter tumor and other organs' weight. Moreover, cisplatin and MTX vaccine increased the ratio of lymphocytes in the spleen but not the DOX vaccine. All comparison was done regarding the tumor-bearing mice treated with PBS. Conclusion: Taken together, both MTX and cisplatin vaccines treated primary and secondary tumors probably by the increase of lymphocyte recruitment, and the cisplatin vaccine also has an influence on the tumor microenvironment. Finally, the therapeutical vaccine might be an interesting approach as a treatment for TNBC due to its positive effect on metastasis and tumor microenvironment, especially with cisplatin.

Keywords: vaccine; breast cancer; immunogenic cell death.