COMBINED CHEMOTHERAPY AND NATURAL KILLER T CELL IMMUNOTHERAPY ENHANCES PROTECTION FROM BREAST CANCER METASTASIS.

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Breast cancer is the most common cancer in Canadian women and the second leading cause of cancer related deaths. Given that most mammary tumours are surgically resectable and over 90% of breast cancer-associated deaths are due to metastasis, new therapeutic strategies targeting metastasis are required. Natural killer T (NKT) cells are a rare population of immune cells that have been shown to limit primary tumor growth and target distant metastatic disease in various animal models. We have shown that NKT cell activation improves survival in a model of post-surgical metastatic breast cancer. We are now expanding this work to determine whether NKT cell activation can be combined with chemotherapies to improve outcomes. In our model, 4T1 mammary carcinoma cells were injected into the mammary fatpad of syngeneic BALB/c mice. Tumours were resected at day 12, and mice were treated with cyclophosphamide or gemcitabine. On day 17, NKT cells were activated by transfer of dendritic cells loaded with the glycolipid antigen α-GalCer. Chemotherapeutics did not affect NKT cell activation as measured by serum IFNγ levels. Treatment with cyclophosphamide, gemcitabine, or α-GalCer-loaded dendritic cells alone reduced metastasis and prolonged survival. Combined treatments significantly enhanced survival. NKT cell activation decreased the frequency and immunosuppressive function of myeloid derived suppressor cells (MDSCs). Treatments resulted in enhanced tumor specific immunity as surviving mice exhibited slower tumour growth following secondary tumour challenge. This work provides a clear rationale for combining chemotherapy with NKT cell immunotherapy to target metastatic disease.