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DETERMINING EFFICACY OF BREAST CANCER THERAPY BY PET IMAGING OF HER2 MRNA

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Objective: Monitoring the effectiveness of therapy early and accurately continues to be challenging. We hypothesize that determination of HER2 mRNA in malignant Breast Cancer cells by PET imaging, before and after treatment, would reflect therapeutic efficacy.

Materials and Method: Peptide Nucleic Acid (PNA) that would hybridize with HER2 mRNA was synthesized together with D (CSKC), a cyclic peptide, that facilitated internalization of the PNA via IgFR expressed on breast (BC) cancer cells and DOTA that chelated Cu-64. Mice (n=8) with BT474 ER+/HER2+ human BC received doxorubicin (DOX), 1.5 mg/kg intraperitoneally, three times a week. Mice (n=3) without DOX treatment served as controls. All mice were PET imaged with F-18-FDG and 24-48 hrs later with Cu-64-PNA. PET imaging was performed before and 72 hrs after each treatment. Standard uptake values (SUV) for tumors were determined and % change calculated. Animal body weight (BW) and tumor volume (TV) were measured.

Results: Following each of the three DOX treatments, tumor SUV for Cu-64-PNA declined to 54±17%, 41±15%, and 29±7% of pretreatment SUV (P<0.05), as compared to 42±22%, 31±18%, 13±9% (P<0.05), SUVs respectively for F-18-FDG. In control mice the corresponding % SUVs for Cu-64-PNA were 145±82%, 165 ±39 and 212±105%, and for F-18-FDG 108±28%, 151±8 and 152±35%. In treated mice, at the end of three DOX treatments, BW was 101.7±12.7% while TV declined to 35.1±35%. In control mice, BW remained 107.8±9.3% and TV averaged 181.3±51.5%.

Conclusion: Effectiveness of therapy can be better determined by PET-imaging measurements of genomic biomarkers targeted specifically, than by PET imaging of metabolic activity of a tumor. Cu-64-PNA PET-imaging provides a genetic tool for evaluation of therapeutic efficacy.

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