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Targeting HER2 Positive Breast Cancer Cells by Affibody Labeled, Gefitinib Loaded Apoferritin Nanoparticles

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Breast cancer is the most prevalent type of cancer diagnosed among females globally. HER2 positive breast cancer accounts for 25% of all breast cancers. Overexpression of HER2 has been associated with an aggressive phenotype and decreased survival. The HER2 receptor is capable of forming dimers with other receptors, such as EGFR/HER1. The dimerization activates uncontrolled cell growth and survival through PI3K/AKT and MAPK signal transduction when HER2 is overexpressed. Gefitinib is a small molecule that acts as an inhibitor of the intracellular tyrosine kinase domain of EGFR that blocks EGFR/HER2 signalling, and it is used for the treatment of breast cancer. However, there are adverse effects associated with this drug. Herein we report, enhanced targeted delivery of gefitinib to the HER2 receptor using an affibody labeled apoferritin with encapsulated gefitinib. These affibodies can specifically target the HER2 receptor with a high affinity that will ultimately increase cancer cell selectivity and reduce toxicity to healthy cells in the human body. We found that gefitinib, encapsulated *via* the nanoreactor route was 100- fold potent compared to free gefitinib in SKBR3 cells. Further, this agent showed a cytotoxic effect in SKBR3 clonogenic assays compared to gefitinib alone. Results also showed cell cycle inhibition along with cell apoptosis. Our results are encouraging as the newly designed agent showed a potent effect against the HER2 overexpressing SKBR3 cells. Further, a nanomolar concentration of gefitinib can be administered in the encapsulated affibody labeled apoferritin form, thereby reducing the toxicities and increasing patient safety in the clinic.

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