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Amrita Hari-Raj

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Investigation of the Use of Zr-89 Radiolabeled Desferrioxamine Conjugated Antibodies in Imaging Her2 Positive Breast Cancer

Amrita Hari-Raj

Mentor: Suzanne Lapi

Human epidermal growth factor 2 (Her2) dimerization with other growth factor receptors normally leads to cell division. However, Her2 gene over-expression is seen in approximately 20% of invasive types of breast cancer, and it is often resistant to conventional therapy. Herceptin, a prevalent treatment, is a monoclonal antibody that attaches to Her2 receptors and prevents them from signaling cells to divide. Imaging of Her2 expression is difficult for patients undergoing Herceptin therapy, though, because excess amount of this antibody blocks binding sites and does not allow for the true level of Her2 expression. Therefore, we study two antibodies, called 2H9 and 7D8, which target different epitopes of Her2. They are chelated with Desferrioxamine (DFO), purified with desalting columns, and labeled with Zr-89. Cell uptake of these antibodies is much higher in Her2 positive cancer cell lines, and 2H9 is consistently taken up more than 7D8. Cell competition binding assays examine the binding affinities of the antibodies conjugated with and without DFO, and we find that there is a 4.2 fold decrease in binding affinity between the modified and unmodified 2H9, versus a 1.2 fold decrease with 7D8. A saturation experiment determines the point at which cells take up 50% of the antibody, and the resulting saturation curves show that more antibodies must be added to the cells to further clarify the saturation points. A cell internalization experiment examines the rate at which Her2 positive cells internalize 2H9 and 7D8, and we find that half of the 2H9 quantity is internalized in six hours, versus fifteen hours for 7D8. Ultimately, the goal is to maximize the amount of radioactive agent and minimize the amount of antibody necessary to image Her2 positive cancer tumors in vivo.