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In vitro/in vivo assessment of novel 99mTc-bombesin conjugates in human cancer tissue

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Receptor-specific, radiolabeled peptides are becoming increasingly popular as targeting vectors for the development of new diagnostic radiopharmaceuticals. The over-expression of certain receptors such as the gastrin releasing peptide receptor (GRPr) on human cancer cells makes this method of drug development a viable tool for tumor targeting in vivo. Breast, pancreatic, prostate, gastric, colon, and small-cell lung cancer have demonstrated GRPr expression. In this project, we have conjugated a diaminoproionic acid (DPR) bifunctional chelator to bombesin (BBN) peptide targeting vector by solid phase peptide synthesis. BBN is an analogue of human gastrin releasing peptide (GRP) that binds to the GRPr with high affinity and specificity. Conjugates of the general structure [DPR-(X)-BBN(7-14)NH2] (X = a series of amino acid pharmacokinetic modifiers) were purified by reverse-phase high-performance liquid chromatography and characterized by electrospray-ionization mass spectrometry. Radiolabeling investigations of with fac-[99mTc(CO)3(H2O)3]+ (Isolink®) provided for metallated conjugates of the following general structure: [99mTc(CO)3-DPR-(X)-BBN(7-14)NH2]. These new conjugates demonstrated the ability to target specific human tumors in rodent models. Subsequent radiolabeling studies of [DPR-(X)-BBN(7-14)NH2] with fac-[188Re(CO)3(H2O)3]+, the therapeutic surrogate precursor of Tc-99m, have given us the potential to treat specific human tumors via these new targeting vectors. Detailed radiolabeling protocols, in vitro cell binding studies, and in vivo biodistribution assays will be reported.