IN VIVO AND IN VITRO EVALUATION OF ^{64}Cu-LABELED BOMBESIN ANALOGS FOR TARGETING GASTRIN-RELEASING PEPTIDE RECEPTORS ON HUMAN PROSTATE CANCER

Stephanie R. Lane (Doctoral Candidate)

(Charles "Jeff" Smith, PhD)
School of Medicine, Department of Radiology

Introduction: Gastrin-releasing peptide receptors (GRPr) are expressed in high numbers on human prostate cancer. The bombesin peptide derivative, BBN(7-14)NH_2, has high affinity and selectivity to GRPr. Therefore, Copper-64 (^{64}Cu) radiolabeled bombesin conjugates could have potential in positron-emission tomography (PET) of human prostate cancer.

Methods: In vitro assays of the NO2A bombesin conjugates and non-radioactive ^{63}Cu-NO2A bombesin conjugates were performed in human PC-3 cells. In vivo pharmacokinetic studies of the radiolabeled ^{64}Cu-NO2A bombesin conjugates were performed in normal CF-1 and PC-3 tumor-bearing SCID mice. In vivo, multimodal, molecular images were obtained of the radiolabeled ^{64}Cu-NO2A bombesin conjugates in PC-3 tumor-bearing SCID mice *via* microPET/CT.

Results: In vitro studies indicated idea uptake of the NO2A bombesin conjugates (1.99-6.24 nM), and ^{63}Cu-NO2A bombesin conjugates (3.16-51.81 nM) in PC-3 cells. In vivo results of the ^{64}Cu-NO2A bombesin conjugates at 1, 4, and 24 h p.i. showed affinity towards GRPr-positive tissue and effective clearance properties. Due to the favorable in vivo pharmacokinetic properties of ^{64}Cu-NO2A bombesin conjugates, high-resolution multimodal, molecular imaging was performed via microPET/CT in a PC-3 tumor-bearing SCID mouse model. High-quality target to non-target images were obtained, with the tumors clearly visible.

Conclusions: The ^{64}Cu-NO2A bombesin conjugates showed affinity and specificity towards GRPr-positive tissues. High quality microPET images of PC-3 xenografted tumors in SCID mouse model were obtained, demonstrating the potential for PET imaging of GRPr-positive human prostate cancer tumors.