

RADIOLABELED BIVALENT PEPTIDE LIGANDS FOR  
PROSTATE CANCER IMAGING

Zongrun Jiang

Dissertation Advisors: Dr. Silvia S. Jurisson, Dr. C. Jeff Smith

ABSTRACT

The usage of radiolabeled peptides as the targeting vector that selectively target cancer biomarkers or cell-surface receptors has been an active field and investigated for decades. However, the radiotracer equipped with more than one type of peptide targeting motif for two distinct biomarkers that are co-expressed in human tumors has not been exploited thoroughly. This dissertation is focused on the so-called bivalent ligand, a radiotracer that has two types of targeting motifs for two different biomarkers. Several bivalent ligands composed of combinations of different targeting vectors are discussed.

The first bivalent ligand, [DUPA-6-Ahx-K-5-Ava-BBN(7-14)NH<sub>2</sub>], for targeting both GRPR (gastrin releasing peptide receptor) and PSMA (prostate specific membrane antigen) was synthesized, and conjugated with NODAGA ([2-(4,7-biscarboxymethyl)-1,4,7-(triazonan-1-yl)pentanedioic acid]). The NODAGA conjugate, [DUPA-6-Ahx-(NODAGA)-5-Ava-BBN(7-14)NH<sub>2</sub>], was radiolabeled with <sup>64</sup>Cu, and evaluated biologically. The study demonstrated the capability of the bivalent ligand to target both biomarkers.

The second bivalent ligand was [RGD-Glu-6-Ahx-RM2], which has the capability of targeting both GRPR and  $\alpha_v\beta_3$  integrin. [RGD-Glu-6-Ahx-RM2] was conjugated with NOTA (1,4,7-triazacyclononane-1,4,7-triacetic acid) and DOTA (1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid), respectively. The NOTA conjugate, [RGD-Glu-(NO2A)-6-Ahx-RM2], and DOTA conjugate, [RGD-Glu-(DO3A)-6-Ahx-RM2], were characterized, radiolabeled with <sup>64</sup>Cu/<sup>67</sup>Ga, and investigated biologically. The study indicated the potential of the ligand for targeting prostate cancer *in vivo*. However, further optimizations of the ligands are warranted for superior pharmacokinetics *in vivo*.