LeighAnn Jordan, Biochemistry

University: Westminster College
Year in School: Junior
Hometown: Pittsburgh, PA
Faculty Mentor: Dr. Susan Lever, Chemistry
Funding Source: NSF-REU/NIH Program in Radiochemistry

Exploring protocols for synthesis of bombesin peptides derivatives to be used as GRP cancer receptor biomarkers

LeighAnn Jordan, Wael R. Abd-Elgaliel, Fabio Gallazzi, and Susan Lever

Bombesin (BBN) is a fourteen amino acid peptide that binds to cancer cells overexpressing the gastrin-releasing peptide (GRP) receptor. Only the final eight amino acid chain, BBN[6-13], is responsible for the binding to the cancer receptors. Converting BBN[6-13] to a diagnostic imaging agent or one for radiotherapy includes radiolabeling of a chelating agent that is coupled to the peptide through a spacer. The carbon-based spacer is important for the affinity between the receptor and the peptide along with the efficiency of the chelating agent to form a conjugate with the peptide. To explore the efficiency, the acetyl (C2) and hexanoyl (C6) spacers were coupled to BBN[6-13]. BBN[6-13] was first manually synthesized through solid phase peptide synthesis. The N-terminus of BBN[6-13] was then reacted with either the activated ester of bromohexanoic acid or bromoacetyl bromide to yield derivatized peptides A and B. The couplings were confirmed by LC-MS analysis. The reactivity of the derivatized peptides were then examined by coupling with the commercially available chelate building block, 1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane (DO3A), that yields product C and D. As expected, the bromoacetyl moiety proved more reactive than the bromohexanoyl moiety. The versatility of the bromoacetyl spacer was further evaluated through coupling with a novel in-house-prepared tetradentate-diaminodithioether (N2S2) chelate. Future biological evaluations will determine which spacer is preferred.