

Amanda Meyer

Major: Chemistry
University: University of Missouri-Rolla
Faculty Mentor: Dr. Susan Z. Lever
Mentor Department: Chemistry
Funded by: Molecular Imaging Program

The synthesis of peptide-PNA conjugates

Amanda E. Meyer, Fabio Gallazzi, Michael R. Lewis and Susan Z. Lever

In two long term studies of non-Hodgkin's Lymphoma (NHL), the only clinical feature associated with a high relapse rate and treatment resistance is the presence of the *B-cell lymphoma/leukemia-2(bcl-2)* proto-oncogene in an over-active state. Regulation of this gene has shown promise as a means for better treatment in patients with relapsed NHL. At MU, in the past, many antisense and nonsense peptide-peptide nucleic acid (PNA) conjugates that target the *bcl-2* proto-oncogene were synthesized and radiolabeled for mRNA binding evaluations.

This summer, we synthesized two new peptide-peptide nucleic acid conjugates. The first of these was a nonsense sequence of PNA monomers attached to the peptide Tyrosine-3-Octreotate (1), and the second was the anti-*bcl-2* sequence attached to Alanine-box Octreotate (2). The PNA sequences attached to the peptides correspond to the first fourteen bases of the *bcl-2* proto-oncogene (ccagcgtgcgccat) in the case of the anti-*bcl-2* compound (2) and correspond to no matching sequence in the human genome in the case of the nonsense sequence (1). They are both for later use as a negative control in mRNA binding evaluations (the previously synthesized positive agent being anti-*bcl-2* attached to Tyrosine-3-Octreotate). The peptides were synthesized using standard Fmoc solid phase peptide synthesis on a resin using a very low substitution level. The peptides were synthesized in an automatic peptide synthesizer, and then elongated with the addition of the PNA monomers manually in a reaction vessel. Each peptide-PNA construct was then coupled to DOTA (1, 4, 7, 10-tetraazacyclododecane-*N*, *N'*, *N''*, *N'''*-tetraacetic acid), a ligand to provide a site for subsequent radiometal chelation. The correct molecular weight with a high purity was observed in the LC-MS results for the peptide-PNA compound 1 after two attempts, and compound 2 was successful after the first attempt. The amount of each construct synthesized should be enough for the later mRNA binding study.