Exploring Alternative Bioconjugation Methods for Covalent Linkage of DNA and Peptides

Jen Kahn was born and raised in Albuquerque, NM. She received her bachelor’s degree with honors in Biosystems Engineering in 2008 from the University of Arizona, Tucson, AZ. While there, she spent two years in the lab of Dr. Mark Riley, first studying colorimetric ethylene detection devices and later, high throughput ethanol determination methods for the study of sweet sorghum bioethanol. During her time at Purdue, she has been involved with the ABE Graduate Student Association and the Women in Engineering Graduate Mentoring Program. Her future plans are to remain at Purdue and pursue a doctoral degree in the ABE Department.

Abstract:
The field of bioconjugation focuses on creating combinations of biological and non-biological molecules for novel or increased functionality. Although this encompasses a myriad of chemical structures, we are primarily interested in the conjugation of oligonucleotides and peptides. Oligonucleotide-peptide bioconjugate applications include biological assays, cellular delivery, protein immobilization, and specialized electrophoresis techniques. Current bioconjugate techniques are tedious, expensive, or introduce undesired chemical groups. In order to increase the feasibility of current applications and to open new avenues for bioconjugates, we have attempted to develop two new bioconjugation techniques, one using L-DOPA crosslinking chemistry and one using EDC crosslinking chemistry.

Using RP-HPLC, UV/vis spectrometry, MALDI mass spectrometry, and 2D ESI mass spectrometry, we have explored the efficacy of both methods. Under the reaction conditions employed, periodate-mediated DOPA crosslinking chemistry is not an appropriate method for covalently linking DNA and peptides, although the DOPA peptide does undergo changes upon oxidation; no conjugates were formed. Using a two-step reaction with intermediate purification, EDC was shown to be effective in creating conjugates between phosphorylated DNA and neutral or positively charged peptides, but it was unable to form a conjugate between phosphorylated DNA and a negatively charged peptide. This opens the door for further bioconjugation research using EDC crosslinking chemistry.

Application:
Development of a new method for linking DNA and peptides has the potential to expand all applications that use these particular bioconjugate molecules and to open the door for new ones. Current applications include enhanced protein function, oligonucleotide delivery, biological assays, protein arrays, and specialized electrophoresis methods. A new general method would have implications in the fields of pharmaceuticals, analytical chemistry, and especially materials science.