Synthetically Functionalized DNA-Oligonucleotides for Protein Binding

Mentor: Janarthanan Jayawickramarajah, Ph.D.
Assistant Professor, Department of Chemistry
Member of the Tulane Cancer Center
Tulane University
2015 Percival Stern Hall
New Orleans, LA 70118
Phone: 504-862-3580
Email: jananj@tulane.edu

Overview of Research

DNA-based oligonucleotides (ODNs) are well-known for their biological functions including the storage of genetic information. However chemists are quickly realizing that synthetic ODNs can be used as a tool for a variety of other applications in materials development (e.g., building exquisite nanostructures)[1] and in medicine (e.g., as antisense agents)[2]. We are interested in using synthetically functionalized ODNs as agents that can inhibit the function of clinically important protein targets in a regulable manner (i.e., can be controlled by exogenous or endogenous stimuli).[3,4]

Research Objectives The specific objectives for the 10 week research training period will be to:

1) Use organic chemistry to synthesize ODNs containing a variety of small organic molecule head groups.

2) Analyze the synthesized conjugates *via* spectroscopic and analytical techniques. These techniques include high-pressure liquid chromatography (HPLC), Matrix assisted laser desorption ionization (MALDI) mass spectrometry, circular dichroism (CD) spectroscopy and gel electrophoresis).

3) Investigate the protein binding and inhibiting ability of these ODNs.

Prerequisites or Experience

This is a highly interdisciplinary project where the students will be immersed in a) synthetic chemistry (to prepare synthetic ODNs), b) biological chemistry (to detect protein-ligand interactions) and c) analytical chemistry (to study DNA folding and protein interactions).

The students must have taken at least one semester of organic chemistry and an introductory biology or biochemistry course. A GPA of 3.0 or higher is preferred.

References

(1) Aldaye, F. A.; Palmer, A. L.; Sleiman, H. F. *Assembling materials with DNA as the guide*. **Science 2008**, *321*, 1795-1799.

(2) Wilson, C.; Keefe, A. D. *Building oligonucleotide therapeutics using non-natural chemistries* **Curr. Opin. Chem. Biol. 2006**, *10*, 607-614.

(3) Harris, D. C.; Chu, X; Jayawickramarajah, J. *Protein recognition via oligonucleotide-linked small molecules: Utilization of the hemin-binding aptamer*. **Supramol. Chem. 2009,** *21*, 316-323.

(4) Harris, D. C.; Chu, X; Jayawickramarajah, J. *DNA-small molecule chimera with responsive protein-binding ability.* **J. Am. Chem. Soc. 2008,** *130*, 14950-14951.