

Project Title: Real-Time Interactions Between SV40 T-Antigen and a Stream of Analytes

Investigator: Wendi David

Department: Chemistry & Biochemistry

Project Summary:

The primary goal of the funded research involved using surface plasmon resonance (SPR) for determining real-time interactions between viral SV40 large T-antigen (T-ag), DNA, and a stream of quadruplex DNA-interactive small molecules. We successfully developed an SPR-based assay for monitoring the ability of T-ag to unwind both normal duplex DNA and quadruplex DNA and characterized the ability of several small molecules to inhibit the helicase activity of T-ag. The ability to monitor unwinding of quadruplex DNA in real-time is an advance for investigating the inhibitory effects of quadruplex-interactive agents and this work was published recently in *Cell Biochemistry and Biophysics* (Feb. 2009). Our results will aid in future characterization of potential therapeutic approaches involving G-quadruplex interactive small molecules and in understanding the structural basis for selective targeting of different families of G-quadruplex DNA helicases. These results form the basis for a recent NIH ARRA grant in collaboration with UT-Austin. In addition, data generated in this research was presented at poster presentations for three national biochemistry meetings. A total of 4 undergraduate students and 1 graduate student were involved in the research.

Publications:

Jasheway, K.; Plyler, J.; Brennan, J. S.; Karr, J.; Kerwin, S. M.; David, W. M.* "Real-time Investigation of Simian Virus 40 Large T-antigen Helicase Activity by Surface Plasmon Resonance," *Cell Biochem. Biophys.*, 2009, 53, 43-52.

Presentations:

- 1) David, W. M.; Karr, J.; Brennan, J.; Jasheway, K.; Kerwin, S. M. Real-time Investigation of SV40 T-antigen Helicase Activity Using SPR Abstracts of the 235th ACS National Meeting, Biological Chemistry Div.; New Orleans, LA, 2008, BIOL-101.
- 2) Brennan, J.; Jasheway, K.; David, W. M. Characterization of SV40 T-antigen G-quadruplex Helicase Activity Using SPR Abstracts of the Experimental Biology National Meeting, Biochemistry/ Molecular Biology (ASBMB); San Diego, CA, 2008, 2391.
- 3) David, W. M.; Plyler, J.; Kerwin, S. M. Monitoring SV40 T-antigen Activity and Inhibition in Real Time Using Surface Plasmon Resonance Abstracts of Papers, 236th ACS National Meeting, Biological Chemistry Div., Philadelphia, PA, 2008, BIOL-077.

External Grants Applied:

NIH, ARRA, grant entitled "G-quadruplex DNA Helicase Inhibition and Telomere Maintenance", April 2009

Student Number: 5