Oral Defense Announcement
University of Missouri – St. Louis Graduate School

An oral examination in defense of the dissertation for the degree
Doctor of Philosophy in Chemistry with an emphasis of Organic Chemistry

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M.S in Chemistry, May 2021, University of Missouri-Saint Louis
B.S in Biochemistry and Biotechnology, May 2016, University of Missouri-Saint Louis

Synthesis of Novel DNA-binding Polyamides to Prevent Cancer-related Gene Overexpression

Date: November 15th, 2022
Time: 2:00 p.m. to 4:00 p.m.
Place: 233 Benton Hall

Abstract
Pyrrole-imidazole polyamides (PIPs) are nanomolecular compounds designed to fit in the tight space of DNA minor grooves. As analogs of Netropsin and Distamycin A, PIPs are specifically designed to recognize the base pairs of DNA sequences. PIPs have many biological applications, such as regulating gene expression, biochemistry pathway regulations, and suppressing the development of cancer cells. SETMAR gene is the chimeric fusion of the SET domain with the mariner transposase. SETMAR protein has the functions of DNA repairs in the NHEJ pathway, regulating gene expression, DNA decatenation, etc. Despite not having an active transposable element, SETMAR still has an unknown function in cancer development. Some reports show that SETMAR mRNA increases by 70 times in glioblastoma cancer cells, as well as in other types of cancer cells. It is essential to understand the mechanism of SETMAR in the cancer cell, and suppressing the overexpression of SETMAR is a goal for anti-cancer development.

Our goal in this project was to design new sequences of polyamides based on the previously discovered conserved TIR (Terminal Inverted Repeat) binding locations on the SETMAR gene. We tested the DNA binding affinity and ability to compete for the protein’s DNA binding site with our collaborators’ assistance through surface plasmon resonance, fluorescence anisotropy, and competitive DNA binding. We modified the polyamide sequence by substituting pyrrole with β-alanine to reduce the rigidity of the continuous chain of heterocycles and introduced an additional charge to the N-terminus of new polyamides.

Defense of Dissertation Committee
James K. Bashkin, Ph.D.- Chairperson
James S. Chickos, Ph.D.
Alexei V. Demchenko, Ph.D.
Eike B. Bauer, Ph.D.