

JMU Chemistry and Biochemistry Seminar

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3:35pm in ISAT 159

Probes of Biological Methylation

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Methylation is an important biomolecular modification occurring on proteins and/or DNA that are pivotal in the dynamic regulation of cellular processes. It has been demonstrated that changes in the methylation state of specific biomolecules can lead to gene mis-regulation and a variety of diseases. One challenge that still remains is the identification and characterization of the exact site(s) responsible for altering these cellular fates. Although methods for detecting methylation have improved tremendously over the last decade, such analytical methodologies display high specificity for specific biomolecules and lack an overall generality. Faced with this shortfall, we seek to develop a more universal approach to identify sites of biological methylation. Our approach exploits a combination of organic chemistry to synthesize analogs of S-adenosyl-L-methionine (SAM) and their subsequent biochemical evaluation to generate easily identifiable biological complexes. Specifically, analogs of SAM are derivatized with a panel of reactive functionalities, containing either an azide or alkyne, and subjected to cellular methyltransferases to covalently derivatized proteins and/or DNA in an enzyme-dependent fashion. Once incorporated, the appended handle can be modified through highly selective reactions, such as the Staudinger ligation and the Huisgen [2+3] cyclo-addition. The research presented here discusses the synthetic generation of functionalized SAM analogs and the evaluation of their biological utility in functionalizing DNA and proteins.