

## BCH 252 Seminar Series



**Dr. Humaira Gowher, Associate Professor,  
Department of Biochemistry, Purdue  
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**Seminar Title:** “Regulation of DNMT Activity in  
Development and Disease”

**Abstract:** The timing and location of DNA methylation are critical parameters controlling cell differentiation. Dysregulation of these processes has widespread consequences ranging from developmental disorders to cancer. DNMT3A and 3B methyltransferases (MTases) that catalyze de novo DNA methylation have essential, distinct roles in embryonic development and differentiation. The focus of the Gowher laboratory is to understand how DNA methyltransferases efficiently use their reader and writer domains to coordinate their activity with TFs and chromatin modifiers, at specific locations, in response to environmental signals, including those of cellular differentiation.

Our recent findings elucidated mechanisms that regulate target site recognition and catalytic activity of DNMT3A and 3B in the normal and diseased states. Our lab discovered that during embryonic stem cell differentiation, DNA methylation by DNMT3A is regulated by the upstream activity of the Lsd1-Mi2/NuRD complex at the enhancers of pluripotency genes, and this mechanism is disrupted in cancer cells. Similarly, in normal cells, the cooperative catalytic mechanism, which supports the high catalytic turnover and DNA sequence preference of DNMT3A, is disrupted by DNMT3A R882H mutation in AML cancer cells, and the variant enzyme gains DNMT3B-like properties. In our current work, we elucidated how lncRNA, Dnmt3bas, controls the inducible expression and alternative splicing of Dnmt3b. Our data suggest that Dnmt3bas coordinates alternative splicing and transcriptional induction of Dnmt3b by facilitating the interaction of PRC2 and hnRNPL at the Dnmt3b promoter. This two-pronged mechanism regulates the expression of catalytically active DNMT3B, potentially ensuring fidelity and specificity of de novo DNA methylation.

**Tuesday, May 2nd, 2023 | 12:00 p.m. - 12:50 p.m. PST**

**In-Person: Genomics Auditorium 1102A**

**Hosts: Dr. Jikui Song & Dr. Maria Ninova**