UC RIVERSIDE

BCH 252 Seminar Series

Dr. Linlin Zhao, Assistant Professor, Department of Chemistry, UC Riverside

Seminar Title: "Exploiting Abasic Site Chemistry to Decipher Mitochondrial Genome Biology"

Abstract: Human mitochondrial DNA (mtDNA) encodes 37 essential genes and plays a critical role in mitochondrial and cellular functions. Compared to nuclear DNA (nDNA), mtDNA is more susceptible to chemical modifications by endogenous and exogenous factors partly due to its proximity to the oxidative phosphorylation system and the lack of certain DNA repair pathways. Our research aims to understand the chemical and molecular mechanisms by which DNA modifications are processed in the mitochondrial genome and their implications in human diseases. In this seminar, I will discuss our recent efforts to probe the role of mitochondrial transcription factor A (TFAM) in damaged mtDNA degradation. We have focused on a prevalent type of DNA modification, i.e., abasic (AP) sites, formed by the loss of nucleobases during natural depurination or depyrimidination and DNA repair. We used biochemical and cellular assays to demonstrate that TFAM accelerates DNA scission at AP sites. The reaction produces chemically reactive entities at the DNA terminus and leads to secondary products, such as TFAM-DNA cross-links and glutathionylated DNA single-strand breaks, which could serve as triggers for mtDNA degradation and the recruitment of additional proteins. We have also identified the cross-linking amino acids of TFAM using mass spectrometry. Together, our research demonstrates the involvement of TFAM in processing AP DNA damage in mitochondria. In the second part of my talk, I will discuss how we exploit the chemistry of AP sites to develop specific chemical probes to label and enrich AP-DNA. We have successfully used the workflow to map AP sites and DNA alkylation modifications using next-generation sequencing in cultured human cells.

Biography: Dr. Zhao earned his B.S. in Chemistry from Jilin University in 2005 and Ph.D. in Bioanalytical Chemistry from the University of Connecticut in 2010. He was a postdoctoral fellow from 2010-2013 in the Department of Biochemistry at Vanderbilt University School of Medicine. He started his independent career in the Department of Chemistry and Biochemistry at Central Michigan University in 2013 and then relocated to the University of California, Riverside in 2019. He is currently an assistant professor in the Department of Chemistry and the Environmental Toxicology Graduate Program.
Dr. Zhao's research focuses on the enzymology and chemical biology of DNA damage and repair with an emphasis on the human mitochondrial genome. His lab was the first to establish the role of mitochondrial transcription factor A in degrading damaged mitochondrial DNA containing abasic sites. His lab also develops next-generation sequencing-based methods to map DNA modifications. Dr. Zhao is a dedicated teacher and research mentor. He enjoys working with students at different levels to nurture next-generation scientists.

Tuesday, March 7th, 2023 | 12:00 p.m. - 12:50 p.m. PST

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Hosts: Dr. Richard Debus & Dr. Russ Hille