# Spring 2025

## Biochemistry and Molecular Biology Brown Bag Series

# Sri Yerrapragada

# Graduate Student

***"Elucidating the biological effects of cell-free platinum adduct-containing DNA"***

**Tuesday, February 25, 2025**

**11:00 AM**

**Location 103 Biological Sciences Building**

**Lab: Mike Kemp, Ph.D.**

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Boonshoft School of Medicine
WRIGHT STATE UNIVERSITY

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https://science-math.wright.edu/biochemistry-and-molecular-biology

## Abstract

**Cisplatin is a widely used chemotherapeutic agent for cancers such as lung, breast, esophageal, ovarian, and pancreatic. However, its effectiveness is constrained by its cytotoxicity to healthy tissues and the rapid development of cancer cell resistance. Cisplatin binds to the N7 position of purines in DNA, forming intra- and inter-strand crosslinks, which are potentially mutagenic and lethal if not removed by the nucleotide excision repair (NER) system. When DNA repair mechanisms are overwhelmed, cisplatin-DNA adducts can trigger caspase-dependent apoptosis, leading to degradation of the damaged DNA.**

**Interestingly, the ultimate fate of this damaged DNA remains unclear. Our study, using differential centrifugation and DNA immunoblotting, has identified that cisplatin-adduct-containing DNA are released into extracellular spaces upon treating with lethal doses of cisplatin. Notably, caspase inhibition blocks this release, while inhibition of NER enhances it.**

**Further, our research demonstrates that non-damaged bystander cells can uptake the cisplatin-DNA adducts, potentially activating DNA damage checkpoints or innate immune responses. This process can also alter the sensitivity of bystander cells to cisplatin. Given the role of cell-free DNA (cf-DNA) in intercellular communication, our findings suggest that damaged DNA could be transferred to distant organs, contributing to cisplatin resistance, toxicity, and systemic side effects. Understanding the mechanism by which cisplatin-DNA adducts influence cell signaling and treatment outcomes could open new avenues for using cf-DNA as biomarkers to monitor therapeutic responses and minimize long-term genomic risks associated with chemotherapy.**