# *Glutathione Prodrugs and Oxidative Stress-related Disorders*


## Dr. Nuran Ercal

**Chancellor's professor**

**Chemistry, Missouri S&T**


**Chemistry Seminar on *Glutathione Prodrugs and Oxidative Stress***

**Monday February 2 at 4 pm in 126 Schrenk**

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**Abstract**: Disruption of redox homeostasis contributes to the pathogenesis of numerous diseases, and thiol-containing antioxidants play a central role in maintaining cellular redox balance. Over the past several decades, the Ercal group has investigated a wide range of oxidative stress–related disorders using thiol-based therapeutic strategies. Among these efforts, studies focused on acetaminophen (APAP)-induced hepatotoxicity and cataract formation have produced particularly robust and translationally significant outcomes. Therefore, due to both the strength of these findings and time constraints of the present presentation, we will focus exclusively on these two disease models. APAP overdose remains a leading cause of acute liver failure, driven by depletion of hepatic glutathione (GSH) following excessive formation of the reactive metabolite N-acetyl-p-benzoquinone imine (NAPQI). While N-acetylcysteine (NAC) is the standard antidote, its limited bioavailability and prolonged dosing regimen present clinical challenges. Our work demonstrates that N-acetylcysteine amide (NACA), a thiol antioxidant with enhanced bioavailability, more effectively restores hepatic GSH, improves survival, and reduces oxidative damage compared to NAC in both HepaRG cell culture and murine models of APAP toxicity. Cataract formation similarly results from oxidative stress–induced damage to lens crystallin proteins, exacerbated by age-related depletion of lens GSH. Using multiple experimental cataract models, we have shown that thiol-based antioxidants preserve lens transparency, maintain redox balance, and reduce oxidative injury. Recent collaborative studies with Dr. Hu Yang's group, employing highly sensitive HPLC-based thiol analysis in ocular tissues, have further strengthened mechanistic understanding of thiol antioxidant distribution and efficacy in the lens. Collectively, these findings underscore the therapeutic promise of thiol-based antioxidants—particularly NACA—in APAP toxicity and cataract prevention and justify their focused discussion in this presentation.


**About the speaker:** Dr. Nuran Ercal began her career at Missouri S&T as a research associate in 1990, becoming assistant professor in 1993, associate professor in 1999, and professor of chemistry in 2005. She served as the Richard K. Vitek/Foundations for Chemical Research Endowed Chair in Biochemistry from 2009 to 2023 and currently holds the title of Chancellor's Professor following her retirement in 2023. Dr. Ercal's research has focused on oxidative stress–related diseases since 1995, with particular emphasis on glutathione (GSH), metal toxicity—especially lead poisoning—and thiol-containing antioxidants. She was among the early researchers at Missouri S&T whose work received sustained support from the National Institutes of Health (NIH). Her recent work includes cataract prevention using thiol-based eye drops and nanocarrier delivery systems. She has advised 21 Ph.D. and 11 M.S. students and authored over 120 peer-reviewed publications, with an h-index of 59.