



**Pharmaceutical Sciences Seminar Series**  
Hybrid

Wednesday, October 26, 2022

4:00-4:30pm

2548 NUB

<https://umich.zoom.us/j/95228641097>

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**“Mechanistic Analysis and Quantification of Clofazimine (CFZ)  
Accumulation in Skeletal Muscle”**

Presented by:

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**Abstract:** The skeletal muscle (SM) experiences age-related changes that lead to structure and function loss. Long-term medication exposure can lead to drug accumulation in the host and impact SM physiology. The objective of my work was to investigate how age affects SM composition, metabolic function, its ability to sequester drugs, and its immune responses following long-term treatment with the antimicrobial riminophenazine dye, clofazimine (CFZ).

C57BL/6J male mice were allocated into two groups based on age. Groups included young mice (4 weeks old) and old mice (61 weeks old). Mice in each group were randomized to receive either CFZ (36 mg/kg/day), a known immune-stimulating molecule, or vehicle (equivalent sesame oil) for 8-weeks. Muscle strength and performance were tested via a grip strength and treadmill study. At the end of treatment, mice were placed in metabolic cages to track their food consumption, after which blood, organs, and SM samples were collected. CFZ concentration was measured in blood and organs, and muscle cryosections were trichrome stained and assessed for composition. Raman-microscopy was performed to determine CFZ distribution. Since CFZ is known to disrupt mitochondrial function, L-carnitine and acetyl-L-carnitine were measured in the SM. Cytokine array assays were used to measure SM immune response.

CFZ treatment in young (Y+) and old (O+) mice did not result in different CFZ concentrations in the blood, but both groups accumulated 3-times more CFZ-HCl than CFZ-freebase. However, CFZ distribution patterns were different in Y+ and O+ mice. Notably, older mice experienced greater accumulation of CFZ in SM, which was accompanied by a trend towards downregulation in several SM cytokine levels compared to young mice. I will discuss these results and their implications for age-related SM responses, which shed light on adverse drug reactions attributable to drug bioaccumulation in off-target sites.