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Pharmaceutical Sciences Seminar

Wednesday, March 17, 2021
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4:00-5:00 pm

"L-Carnitine as a biomarker for adverse drug reactions"

Presented by:

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Abstract: Most small molecule drugs on the market are designed to enter the organism following oral administration, via gastrointestinal absorption. Once they reach the blood stream, drug molecules circulate and distribute throughout the body before reaching their intended, target site(s). In this process, many different biochemical pathways and mechanisms can be perturb causing alterations of mitochondrial function, predisposing patients to adverse drug reactions (ADRs). ADRs are considered to be an inherent risk of medication use, yet they pose a major burden on the United States' health care system and the drug development process, with the FDA withdrawing many approved drug products from the market every year because of ADRs. Based on a systematic analysis of drug-induced alterations in mitochondrial metabolites as reported in the scientific literature and the results of a clinical trial in critically-ill patients, L-carnitine has emerged as a candidate, metabolic stress biomarker that can be used to identify individuals predisposed to drug-induced ADRs caused by perturbations in mitochondrial function. Preliminary studies in humans and animals support L-carnitine as a functional biomarker of mitochondrial health status that can be informative of patient outcomes. The study proposes to establish the physiological basis for which variations in the regulation of L-carnitine levels in the blood can serve to identify individuals at increased risk of ADRs. We will test the usefulness of an L-carnitine "challenge test" to serve as a "probe" to interrogate the metabolic adaptiveness of the organism and its connection to drug-related toxicological manifestations. We envision using an L-carnitine challenge to differentiate patients based on their predisposition to metabolic stress-related ADRs.

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