

# IEM SEMINAR SERIES

TUESDAY  
October 25<sup>th</sup>, 2016

## Human on a Chip - Exploring Metabolic Dynamics



Institute for  
Engineering in Medicine

UNIVERSITY OF MINNESOTA

Driven to Discover<sup>SM</sup>

Dr. Yaakov (Koby) Nahmias  
Director of the Center of Bioengineering  
Center of Bioengineering  
Hebrew University of Jerusalem



FREE event, no registration required.

Pizza and Beverages will be  
provided from 11:45 am

12:00PM - 1:00PM  
Mayo Memorial  
Building  
Room 3-100

For additional information on  
Dr. Nahmias' presentation  
please contact:  
scot0353@umn.edu

The Institute for Engineering in Medicine (IEM) is pleased to announce a seminar by Dr. Yaakov (Koby) Nahmias, "Human on a Chip - Exploring Metabolic Dynamics."

Microfluidic organ-on-a-chip technology aims to replace animal toxicity testing, but thus far has demonstrated few advantages over traditional methods. Mitochondrial dysfunction plays a critical role in the development of chemical and pharmaceutical toxicity, as well as pluripotency and disease processes. However, current methods to evaluate mitochondrial activity still rely on end-point assays, resulting in limited kinetic and prognostic information. Here, we present a liver-on-chip device capable of maintaining human tissue for over a month in vitro under physiological conditions. Mitochondrial respiration was monitored in real time using two-frequency phase modulation of tissue-embedded phosphorescent microprobes. A computer-controlled microfluidic switchboard allowed contiguous electrochemical measurements of glucose and lactate, providing real-time analysis of minute shifts from oxidative phosphorylation to anaerobic glycolysis, an early indication of mitochondrial stress. We show a hereto-unknown mechanism of acetaminophen (Tylenol<sup>®</sup>) toxicity that is independent of CYP450-metabolism, and thus might be responsible for clinically observed nephrotoxicity and dermatitis. We also show that the anti-diabetic drug Troglitazone (Rezulin<sup>®</sup>) shifts metabolic fluxes at concentrations previously regarded as safe, suggesting a mechanism for its observed idiosyncratic toxicity. Our work marks the importance of tracing toxicity effects in real-time, demonstrating specific advantages of human-on-chip technology in predictive toxicology. (1. Prill et al. Archives of Toxicology 2016, 2. Bavli et al. PNAS 2016, 3. Levy et al. Nature Biotechnology 2016).

Dr. Yaakov Nahmias received his B.Sc. from the Technion, Israel Institute of Technology, Magna Cum Laude. He did his PhD at the University of Minnesota and postdoctoral training at Massachusetts General Hospital. In 2006, he became a faculty member of Harvard Medical School, winning a prestigious National Institute of Health (NIH) Career Award. In 2009, Dr. Nahmias, at the Hebrew University of Jerusalem, won a major European Research Council (ERC) Starting Grant. Dr. Nahmias is the head of the microLiver Technologies ( $\mu$ LT) Laboratory with over \$5.2 million in independent research funding.

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