“Is the impact of endocrine disrupting compounds on metabolism confounded by the molecular clock?”

Aalim M. Weljie, Ph.D.
Research Assistant Professor of Systems Pharmacology and Translational Therapeutics

Abstract

Endocrine disrupting chemicals (EDCs) disrupt hormone action and are linked to the development of metabolic disease. EDCs found to significantly alter adipose physiology and adipogenesis are termed “obesogens,” yet to date, few specific molecular mechanisms of EDC-induced obesity have been delineated. In parallel, the circadian clock is a critical contributor to energy homeostasis and regulates glucose and lipid metabolism. Indeed, circadian disruption is strongly associated with metabolic disease which leads to a simple, but unanswered question: do EDCs disrupt metabolism in part through actions on the circadian clock?

The *long-term goal* of this research is to understand how exposure to EDCs may contribute to the development of metabolic disease through disruptions in energy handling. The *central hypothesis* is that EDC exposure leads to changes in cycling cellular metabolites involved in bioenergetic pathways and is a common mechanism of metabolic dysfunction through dysregulated glucose and lipid metabolism. This will be tested with two *Aims*:

Aim 1. **Characterize global and circadian metabolic effects of EDC exposure *in vitro***. *Aim 1a:* Characterize global metabolic output in unsynchronized hepatocyte and adipose cell lines exposed to BPA, DEPH and NP. *Aim1b:* Test whether molecular clock function and metabolic rhythms are disrupted as a result of exposure to EDCs. Rationale: Our preliminary work shows that EDCs have heterogeneous effects on liver metabolism. **Aim 2**. **Characterize global metabolic output in liver, adipose tissue and serum from BPA-exposed C57BL/6J mice and their first generation offspring**. Rationale: Gender-specific metabolic changes following direct and developmental BPA exposure have been reported. Comprehensive metabolomic analysis of liver, adipose tissue and serum following direct or developmental BPA exposure will aid understanding of the effects of BPA exposure on whole body metabolism as well as liver and adipose physiology *in vivo*.