

Use of cross-omics to identify metabolic control points for therapeutic intervention in diabetes

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Advances in genetics, molecular and cellular biology, and *in vivo* tracer methodologies have made it possible to interrogate metabolic pathways in unprecedented detail. This convergence of investigational opportunities is especially attractive to scientists in the field of diabetes and metabolic disorders, as they attempt to identify metabolic control points for therapeutic intervention. In this regard, the ability to leverage advanced mouse models of insulin resistance and sensitivity by appropriate *in vivo* techniques to determine the fate of substrates in different metabolically active tissues is the mainstay of discovery. Our premise is that insulin resistance and sensitivity affect the pool and patterns of acetylated proteins, and that these alterations in turn are reflected into metabolic changes that are either conducive to, or protective from, diabetes. We have developed a framework for the step wise interrogation of complex models of hepatic insulin resistance, using fluxomics as a primary tool for examining the functionality of hepatic acetylome changes that occur in the fasting/re-feeding transition. Additional “layers” of-omic information, such as metabolomics, lipidomics, and transcriptomics, are obtained in a hypothesis driven manner, guided by our fluxomic framework, considering only the-omic data that “weaves” together as a whole, to explain the phenotype characterized by fluxomics. The goal is to identify tissue specific altered metabolic control steps that can be targeted for the development of insulin sensitizers.

Biography

Irwin J Kurland, MD, Ph.D. is an Associate Professor of Medicine, and Director of the Stable Isotope and Metabolomics Core Facility at the Albert Einstein College of Medicine. Dr Kurland's laboratory has helped, for over a decade, to establish stable isotope phenotyping methodology for assessing inter-organ fuel switching. Recent papers by the Kurland laboratory illustrate the regulatory role of lysine acetylation on enzymes in tissue specific metabolic networks (Yang et al., *J. Proteome Res.* 2011), and the linkage between disturbances in fasted/re-fed acetyl CoA levels and dysregulated global lysine acetylation, on the fasted/re-fed metabolic network response (Vaitheesvaran et al., *PLoS One* 2012).

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