BIOCHEMISTRY SEMINAR

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"Chemical Control of DGAT2 Reveals Lipid Droplet Remodeling and Metabolic Heterogeneity"

Diacylglycerol acyltransferase 2 (DGAT2) catalyzes a critical step in triacylglycerol biosynthesis and plays a central role in regulating lipid droplet size, stability, and function. Owing to its importance in lipid storage, DGAT2 has been widely studied as a therapeutic target for metabolic disease, primarily through small-molecule enzymatic inhibitors. However, these approaches have shown limited clinical success, as inhibition suppresses catalytic activity without eliminating the DGAT2 protein itself, allowing residual scaffolding or compensatory functions to persist. This highlights the need for strategies that directly modulate DGAT2 protein abundance.

To address this gap, we designed and screened DGAT2-targeting proteolysis-targeting chimeras (PROTACs) that enable selective and tunable degradation of DGAT2. DGAT2 depletion was validated by immunoblotting and enables tunable chemical control over DGAT2 levels in cells. Loss of DGAT2 induces marked changes in lipid droplet morphology, lipid composition, and associated protein networks, as revealed by integrated lipidomics, proteomics, and imaging. These findings establish DGAT2 protein abundance, rather than enzymatic activity alone, as a key determinant of lipid droplet organization and downstream lipid metabolism.

To extend these observations across biological contexts, we characterized lipid droplets from 5XFAD mouse models, a widely used Alzheimer's disease model that recapitulates amyloid pathology and lipid droplet accumulation associated with neurodegeneration, using complementary omics and imaging strategies. Recognizing that lipid metabolism exhibits substantial cell-to-cell heterogeneity, we further developed a single-cell lipidomics platform combining charge-switch derivatization with targeted multiple reaction monitoring. Application across numerous cancer cell lines reveals pronounced fatty acid heterogeneity that is masked in bulk analyses. Together, this work links targeted protein degradation to organelle remodeling and single-cell metabolic diversity, providing a framework for understanding how chemical control of a single enzyme can reshape lipid metabolism across biological scales.

BIOCHEMISTRY SEMINAR

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"Investigation of Undergraduate Problem-Solving at the Interface of Biology and Chemistry"

To prepare a chemical workforce capable of interdisciplinary problem solving and systems thinking, undergraduate instructors at large academic institutions widely utilize short-term assessment tasks requiring the incorporation and connection of knowledge from multiple disciplines, particularly at the interface of biology and chemistry. Prior work conducted by researchers developing interdisciplinary curriculum combining biology and physics have provided guidelines for the evaluation of interdisciplinary short-term assessment tasks. However, this evaluation is solely from the instructor's perspective; furthermore, how these assessments are experienced by students in various contexts beyond those involving biology and physics remain understudied. To address this gap, retrospective interviews and student work were collected after active learning sessions during the Fall 2024 semester of a bioanalytical chemistry course. Informed by the Resource and Framing theoretical framework, an initial inductive analysis of the materials collected was conducted. This seminar will focus on emergent findings from this initial analysis, including examples of how the disciplinary context presented within a problem can influence the information students believe to be important in problem solving and the knowledge they integrate. The findings from this work will inform instructional strategies aimed at cultivating interdisciplinary problem solving, especially in contexts requiring the integration of biological and chemical knowledge.