that will explore mechanisms of mitochondrial dysfunction in T2DM.

Pancreatic islet beta-cells are sensitive to plasma nutrients in the body. Excess levels of glucose and fatty acids lead to glucolipotoxicity, resulting in declined beta-cell function and survival—a major component of type 2 diabetes mellitus (T2DM). Despite significant knowledge of glucose-stimulated insulin secretion, the effect of fatty acids remains uncertain. Here we show a novel way to measure a response from fatty acids in ex vivo pancreatic islets using quantitative and autofluorescence imaging of a Complex II flavin, electron transfer flavoprotein (ETF). Together with two-photon imaging of NAD(P)H and our previously reported liposome dehydrogenase (LipDH) autofluorescence, we found that the electron transport chain is nutrient supply-driven and dominated by Complex I rather than Complex II. These data are consistent with beta-cells being predominantly glucose responsive. Furthermore, we found an oxidized ETF redox response in the presence of excess glucose-stimulation, suggesting a shift in lipid partitioning from fatty acid oxidation to synthesis above 10 mM glucose. Our results demonstrate that ETF autofluorescence can in part be used as readout of islet response to fat. Overall, we anticipate our ETF imaging to platform to be a starting point for more sophisticated biological studies that will explore mechanisms of mitochondrial dysfunction in T2DM.

Biophysics Education

Membranes, Ions, and Signals: An Integrated, Multimedia, Biophysics Module for First-Year Medical Students

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First-year medical students, unlike typical graduate students, include many non-science majors with varying prior exposure to mathematics or physical sciences. To provide a common substrate for medical education that acknowledged these disparate backgrounds, an introductory Molecules to Cells course was designed in 1996 by D.G., O.S.A., and colleagues. Now Molecules, Genes, and Cells (MGC), this spans protein structure, lipids, cellular genetics, metabolic biochemistry, cell division, and more. We now report design and implementation of a Membranes, Ions, and Signals (MIS) module for MGC, covering cellular biophysics, physiology, and pharmacology. Building on membrane lipid structure and function, MIS incorporates:

- plasma membrane and compartments
- properties of those compartments important to electrochemistry, signaling, and biophysics,
- structure and function of membrane channels, transporters and receptors
- electrophysiology of excitable tissue
- signals and information transmission, synaptic, cellular, cytoplasmic, and nuclear
- signals in disease contexts
- signals into actions: structure and function of skeletal and smooth muscle

This material is both essential and conceptually difficult, and MIS is designed to offer students an optimal sequence, schedule, and presentation forms and formats to aid understanding. As an integrated module, MIS relates these topics and makes them relevant to contemporary work and translational promise. Staffing is interdepartmental, via Physiology & Biophysics, Pharmacology, Biochemistry, and Cardiology. MD-PhD students take the course and module in their first year, then participate as journal club instructors. A signals-and-inference-learning environment for providing a comprehensive introduction for biologists to physical and mathematical scientists, which can be accessed from anywhere using a networked laptop. This paper proposes such an environment. The didactic portion is organized according to the flow of information among biomolecular systems, starting with the genome and continuing with the processes of transcription, translation, and post-translational modification, and the interaction of gene products to give rise to the cellular phenotype and to interactions among cells. Reverse information flow via influence of the environment on the cell completes the information loop, with dynamic responses ranging in time scales from fractions of a second for an emergency response to thousands or millions of years for evolutionary change. The textbook level of understanding can be assembled from the NCBI bookshelf. The ability of students to dig deeper in all subjects is achieved through training in the use of Google Scholar and PubMed to assemble functional bibliographies beginning with seminal papers (early papers with many citations) leading up to the most recent advances, punctuated with review papers. Hands-on interaction with the concepts can be introduced with the use of bioinformatics and molecular modeling tools accessible online, leading to an early experience in computational research and in framing meaningful problems to be attacked.