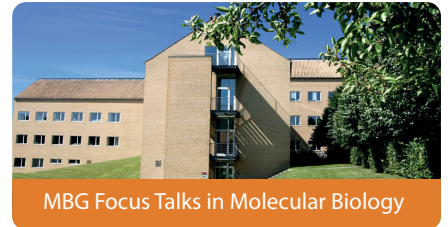


MBG FOCUS TALK

hosted by Erik Østergaard Jensen



Thursday August 15, 2019 at 9:15-10:00

Conference room at the science park (3130-303)

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Ceramide induced lipotoxicity in metabolic diseases

The ectopic deposition of lipid molecules in tissues not suited for fat storage drives the tissue dysfunction that underlies diabetes and heart disease. Of the numerous lipid subtypes that accumulate, ceramides and dihydroceramides, show particularly tight associations with these metabolic disorders. Indeed, clinics recently began quantifying serum ceramides as diagnostic measures of risk for major adverse cardiac events. Studies in rodents further suggest that these sphingolipids play causative roles in the pathologies. Ceramides further serve as signals of lipid overload, altering cellular metabolism and rigidifying membranes in order to prevent dissolution of lipid bilayers that could result from the deluge of excess, detergent-like fatty acids. These actions, when prolonged, elicit the tissue dysfunction (e.g. insulin resistance, decreased mitochondrial efficiency, enhanced triglyceride synthesis, apoptosis, fibrosis, etc.) that underlies diabetes and heart disease. Attempts to develop safe therapeutics targeting these enzymes have been problematic, however, owing to negative consequences of global sphingolipid depletion. The presentation will review the history of research on these enigmatic molecules, exploring (a) their mechanism of action, (b) the evolutionary pressures that gave them their unique attributes, and (c) the potential of ceramide-reduction therapies as treatments for cardiometabolic disease.