

Guest lecture

Emerging roles of glial cells in the central control of energy balance by lipids



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Date: 13 June 2019

Time: 10:30

Place: BMB Seminar room

Host: Nils J. Færgeman, BMB, SDU.

Abstract:

Emerging roles of glial cells in the central control of energy balance by lipids

In the brain, the hypothalamus plays a key role in the control of appetite and body weight. This control relies on neuronal populations that sense circulating metabolic signals including lipids and activate neuroendocrine and behavioral responses to maintain body weight.

Long time though to be the “glue” that holds the brain together, glial cells are now recognized for their key roles in brain energetics, neuronal activity and plasticity. Astrocytes, the most abundant glial cells, are implicated in complex and fundamental behaviours such as breathing and sleeping and have recently emerged as key players in energy homeostasis.

However, the mechanisms by which hypothalamic astrocytes affect energy balance neurocircuitry remain largely unknown. We identified Acyl-CoA Binding Protein (ACBP) as a protein strongly expressed in hypothalamic astrocytes where it regulates the intracellular metabolism of unsaturated fatty acids. ACBP is also secreted and cleaved to generate endozepines including the octadecaneuropeptide which modulate GABA_A receptor signaling. We demonstrated that targeted ACBP loss-of-function in astrocytes promoted diet-induced hyperphagia and obesity in both male and female mice, an effect prevented by genetic rescue of ACBP in arcuate astrocytes. Interestingly, mice with astroglial ACBP deficiency were unresponsive to the anorectic effect of oleic acid. The ACBP-derived octadecaneuropeptide selectively activated anorectic pro-opiomelanocortin neurons in the arcuate nucleus via a GABA_A-independent mechanism and suppressed feeding while increasing carbohydrate utilization via the melanocortin system, and induced weight loss in obese mice. These findings uncovered ACBP as a hypothalamic gliopeptide playing a key role in energy balance and exerting strong anorectic effects via the central melanocortin system.