KJELDGAARD Lecture - Professor Joost Holthuis

Monday 6 December 2021 at 13:15—14:00

Followed by PhD-session at 14:30—15:00

(Coffee and cake will be served between lecture and PhD-session)

Merete Barker Auditorium, Lakeside Lecture Theatres (1253-211)

Bartholins Allé 3, 8000 Aarhus C

Host: Joseph Lyons

Professor Joost Holthuis, PhD

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Organellar lipid codes

A slowly emerging but fundamental concept in lipid cell biology is that the identity and function of cellular organelles critically rely on information encoded in their lipid bilayers (1). Work in my group focuses on the functional implications of, and compensatory cellular responses to disease-induced imbalances in organellar lipid codes, with a main focus on aberrant distributions of sphingolipids. As approach, we exploit disease-relevant cell models and photoactivatable lipid analogs to interrogate organellar lipid codes and capture novel lipid effector proteins. In this seminar, I will highlight how these efforts helped elucidate the mechanism by which ceramides, a class of putative tumor suppressor lipids, commit cells to death (2). I will also describe how pathogenic mutations in a key sphingolipid biosynthetic enzyme erode the contrasting lipid codes of ER and plasma membrane, culminating in a rare bone disorder. Finally, I will discuss the identification of a sphingolipid-operated membrane repair pathway by which cells preserve the functional integrity of lysosomes. Our findings indicate that a calcium-activated sphingolipid scrambling and turnover drives an ESCRT-independent mechanism to clear minor lesions from the lysosome-limiting membrane and prevent lysosome damage-induced cell death (3).

1. Holthuis JC, Menon AK (2014) Lipid landscapes and pipelines in membrane homeostasis. *Nature* 510, 48-57
2. Dadsena S, et al. (2019) Ceramides bind VDAC2 to trigger mitochondrial apoptosis. *Nature Communications* 10, 1832
3. Niekamp P, et al. (2021) Ca^{2+}-activated sphingomyelin scrambling and turnover mediate ESCRT-independent lysosomal repair. *bioRxiv* 2021.03.12.435146

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