MBG FOCUS TALK

hosted by Section for Structural Biology

MBG Focus Talks in Molecular Biology

Thursday 14. June 2018 from 10:15-11:00

Biomedicine auditorium (1170-347), Ole Worms Allé 3, 8000 Aarhus C

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Flippase-gate: Explorations Into How P4-ATPases Recognize Their Lipid Substrate

Phospholipid flippases (P4-ATPases) transport phospholipids across the membrane bilayer and play crucial roles in establishing an asymmetric membrane structure important for signal transduction, cell division, and vesicular transport. P4-ATPases are thought to specifically transport glycerol-based phospholipids to the cytosolic leaflet while leaving sphingolipids in the extracellular leaflet. However, we have identified P4-ATPases from yeast (Dnf1, Dnf2) and humans (ATP10A and ATP10D) that flip glucosylceramide, and establish structural determinants for recognition of this substrate. For example, a conserved glutamine in the center of transmembrane segment 4 is essential for GlcCer recognition in fungal and human P4-ATPases. Prior studies have shown that human ATP10D variants are associated with elevated levels of glucosylceramide in the plasma, increased risk of diabetes, obesity, and myocardial infarction. Our observations clarify the relationship between ATP10D and human disease, and provide further insight into the mechanism of substrate recognition by P4-ATPases.

Host: Prof. Poul Nissen, Dept. Molecular Biology and Genetics

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