BRAINSTRUC & DANDRITE
Topical Seminar

Tuesday 17 September 2019
From 14:15 – 15:00

The conference room, building 3130, 3rd floor
Gustav Wieds Vej 10C, 8000 Aarhus C

Cristina Paulino

Assistant Professor
Head of the cryo-Electron Microscopy Unit
Department of Structural Biology and Enzymology
University of Groningen, The Netherlands

The flips and flops of a scramblase story – proteins in nanodiscs and electrons at 200kV

The TMEM16 family of membrane proteins encompasses members that work as calcium-activated chloride channels, calcium-activated lipid scramblases or both. By solving several cryo-EM structures of TMEM16 members and contrasting the results with functional properties, we demonstrate the relationship between ion conduction and lipid scrambling. Albeit activated by the same mechanism, they appear to be mediated by either distinct structural entities or different protein conformations, suggesting that both processes might be less coupled than previously anticipated. For this study, target proteins were reconstituted into detergent micelles or lipid nanodiscs and data was acquired in absence and presence of its ligand. Reconstitution of nhTMEM16 into lipid nanodiscs, but not into detergent micelles, allowed to sample the conformational plasticity present under activating conditions. Additionally, we show how nhTMEM16 distorts the bilayer, thereby channeling lipids into the 'subunit cavity' and lowering the energy barrier for lipid transport. Our study, describes the interaction of scramblases with its membrane environment and highlights pitfalls and advantages of working with lipid nanodiscs. Notably, this work among others performed in the lab show the potential of 200 kV TEM machines for the structure determination of small and challenging membrane proteins.

For more information about the research in Cristina Paulino's group, visit:
www.paulinolab.com

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