DANDRITE

Topical Seminar

Beyond individual protein conformations – How multimodal conformational landscapes underpin the function and pharmacology of pumps and G protein coupled receptors

Our lab is developing fluorescence-based bioassays to elucidate the function and pharmacology of primary active transporters and G protein coupled receptors on the nanoscale.[1-7]

Our measurements have revealed the existence of modes. Modes are ultrastable assemblies of conformational and functional states that persist over unpresented spatiotemporal scales.

In this presentation, I will focus on pumps and G protein coupled receptors. I will introduce the methods that allowed us to observe modes on the nanoscale and at the single molecule level and showcase how modes underpin macroscopic measurements of function and regulation. I will argue that modes comprise a novel mechanistic foundation for drug discovery and development.

References

1. Mathiasen, S. *et al.* Nanoscale high-content analysis using compositional heterogeneities of single proteoliposomes. *Nat Meth* 11, 931–934 (2014).
2. Rosholm, K. R. *et al.* Membrane curvature regulates ligand-specific membrane sorting of GPCRs in living cells. *Nat Chem Biol* 13, 724–729 (2017).
3. Kockelkoren, G. *et al.* Molecular mechanism of GPCR spatial organization at the plasma membrane. Front Cover Page. *Nat Chem Biol,* 20, 142–150 (2024).
4. Patent pending.
5. Manuscript under review.
6. Kosmidis, E. *et al.* Regulation of the mammalian-brain V-ATPase through ultraslow mode-switching. Front Cover Page. *Nature* 611, 827–834 (2022).
7. Veshaguri, S. *et al.* Direct observation of proton pumping by a eukaryotic P-type ATPase. *Science* 351, 1469–1473 (2016).

Hosted by Poul Nissen group (DANDRITE)

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Date: **Wednesday 11 September 2024**
Time: **14:00 – 14:45**
Venue: **Nucleus, 1871-120**
Address: **Universitetsbyen 81, 8000 Aarhus**

OPEN TO ALL INTERESTED.

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