MBG FOCUS TALK

hosted by Erik Østergaard Jensen

MBG Focus Talks in Molecular Biology

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The conference room, building 3130-303, Gustav Wieds vej 10c

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Aquaporin water channels: players in water balance regulation and cell migration

Aquaporins (AQPs) are transmembrane proteins facilitating passive transport of water following an osmotic gradient. AQP2 and AQP3 in the renal collecting duct facilitate hormone regulated urine concentration and dysregulation of AQP2 expression and/or targeting to the plasma membrane, as well as genetic mutations in AQP2, are key in many water balance disorders. Moreover, AQPs are necessary for cell migration and AQP5 has recently been implicated as a major player in breast cancer metastasis. Thus, it is essential to study the regulation of AQPs to promote fundamental insights in cell biology and to develop therapeutic interventions targeting dysregulation of water balance disorders and cancer.

It is well known, that AQP2 shuttles to and from the apical plasma membrane in response to stimulation with the antidiuretic hormone vasopressin, and it is now recognized that a key regulatory mechanism occurs in the actual plasma membrane via regulation of AQP2 endocytosis rates to either stabilize or exclude AQP2 from the membrane. Several direct phosphorylations of AQP2 have been determined to play a role for AQP2 plasma membrane stability, but the actual mechanisms of how AQP2 stability in the plasma membrane is regulated nanoscopically, are unknown. To investigate this, we have employed recently developed super resolution microscopy, for which the Nobel Prize in Chemistry 2014 was awarded. Super resolution microscopy has enabled imaging below the spatial resolution of fluorescence microscopy, and revolutionized studies of protein localization and interactions at the nanoscale, revealing that many receptors are organization into functionalized nanodomains. However, little is known regarding the biogenesis, stability, function and regulation of these nanodomains and also, it is unknown if constitutively open channels, like AQPs, organize into functional nanodomains and how this organization controls AQP plasma membrane stability, which ultimately determines water permeability of the epithelium.

In my talk, I will present two research areas from our laboratory concerning hormone regulated nanoscale organization of renal aquaporins studied by Photoactivatable Localization Microscopy and studies of how AQP5, a key player in breast cancer metastasis, regulates epithelial cell migration.