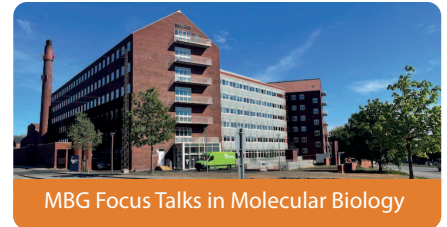


# MBG FOCUS TALK

hosted by Section of Protein Science - Bjørn Panyella Pedersen



**Monday 22nd May 2023 from 14.00 - 14.45**

MBG Faculty Club (1870-816)

**By Postdoc Jonathan Flores**

Oregon Health & Science University

## **Structural & Functional Effects of the Ageing Cellular Environment on Native Lens Gap Junctions**

Gap junctions are large-pore ion channels that forms direct conduits for intercellular communication in virtually every human tissue. In the ocular lens for instance, Connexin-46 and Connexin-50 (Cx46/50) oligomerize to form gap junctions essential for ionic homeostasis and maintenance of transparency.

Various signals regulate solute permeation through gap junctions, including voltage, pH, Ca<sup>2+</sup>, and lipids. Because the mature lens is devoid of cell or protein turnover, a lifetime of chemical changes ultimately reduce intercellular coupling through Cx46/50. The inevitable decline in Cx46/50 function is accompanied by cataract formation, which remains the leading cause of blindness worldwide.

Despite a body of work spanning five decades, atomic-level descriptions for how these channels respond to dynamic cellular conditions are scarce. To rectify this scarcity, my doctoral work exploited advances in membrane protein biochemistry and single-particle cryoEM to visualize how native lens gap junctions respond to age-related changes in the lens environment.

In my talk, I will describe how my colleagues and I established an approach to obtain routine ~2 Å resolution structures of native Cx46/50 isolated from lens tissue, and how we exploited this approach to visualize the dynamic structural response of Cx46/50 to membrane cholesterol enrichment and aberrant Ca<sup>2+</sup> accumulation.