Press release

Unfolding the blindness proteins through fly eyes

ITQB NOVA and IGC researchers identify a new production mechanism for a critical protein for vision in Drosophila *fruit flies*

Oeiras, 17 December 2021 – Every 6 minutes someone is told they're going blind. One of the major causes of human blindness is a disease called **Retinitis Pigmentosa** (RP), which causes progressive degeneration of the retina and vision loss. Approximately one-tenth of Retinitis Pigmentosa cases worldwide are caused by mutations in the **rhodopsin** gene. Researchers from ITQB NOVA and IGC had now **identified a crucial mechanism for the production of Rhodopsin**, the light-sensitive protein of photoreceptors, using fruit flies (*Drosophila melanogaster*) and human cells as models.

Rhodopsin is a membrane protein which detects photons of light and is involved in the initial events of vision. Membrane proteins are essential for many functions in our cells and are produced by an organelle called Endoplasmic Reticulum (ER), our cell's protein factory. When the proper structure of the proteins cannot be attained, it can lead to several diseases, including retinitis pigmentosa.

The research, now published in *EMBO Reports*, identifies a new mechanism that is required for the production of Rhodopsin. The production of membrane proteins entails that these are **folded and inserted into the lipid membrane of the endoplasmic reticulum by specific molecular machineries**. *"In our study we developed a method to predict and identify membrane proteins that use a recently identified protein production machinery called the ER Membrane Complex, or EMC, for their biogenesis",* explains Catarina Gaspar, first author of the study developed during her PhD.

Through the analysis of the *Drosophila* proteome, the researchers bioinformatically identified proteins that could depend on the EMC for their biogenesis. From 254 predicted proteins, researchers were then able to identify two proteins that require the ER Membrane Complex for their biogenesis, after some genetic screening done in the eyes of *Drosophila* larvae.

One of these proteins, **Xport-A, turned out to be key for the proper folding of Rhodopsin**. The results also reveal that the EMC acts as a machine to insert Xport-A into the ER membrane. "We can now better understand how production of Rhodopsin, crucial for animal vision, is regulated and the role of Xport-A in this process", adds Pedro Domingos, ITQB NOVA Principal Investigator.

Since fruit flies and humans share many genes, the study could help open new avenues to enlighten rhodopsin production and the degeneration of the retina in humans. *"This study ignited further research that we are pursuing in mammalian systems, which will lead to a greater understanding of the role of EMC in membrane protein biogenesis",* concludes Colin Adrain, Principal Investigator at IGC and Queen's University Belfast.

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The work led by ITQB NOVA principal investigator Pedro Domingos and IGC principal investigator Colin Adrain, in collaboration with researchers from University of Oxford (UK) and Czech Academy of Sciences (Czech Republic), was supported by La Caixa Foundation.

Original paper:

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EMC is required for biogenesis of Xport-A, an essential chaperone of Rhodopsin-1 and the TRP channel

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