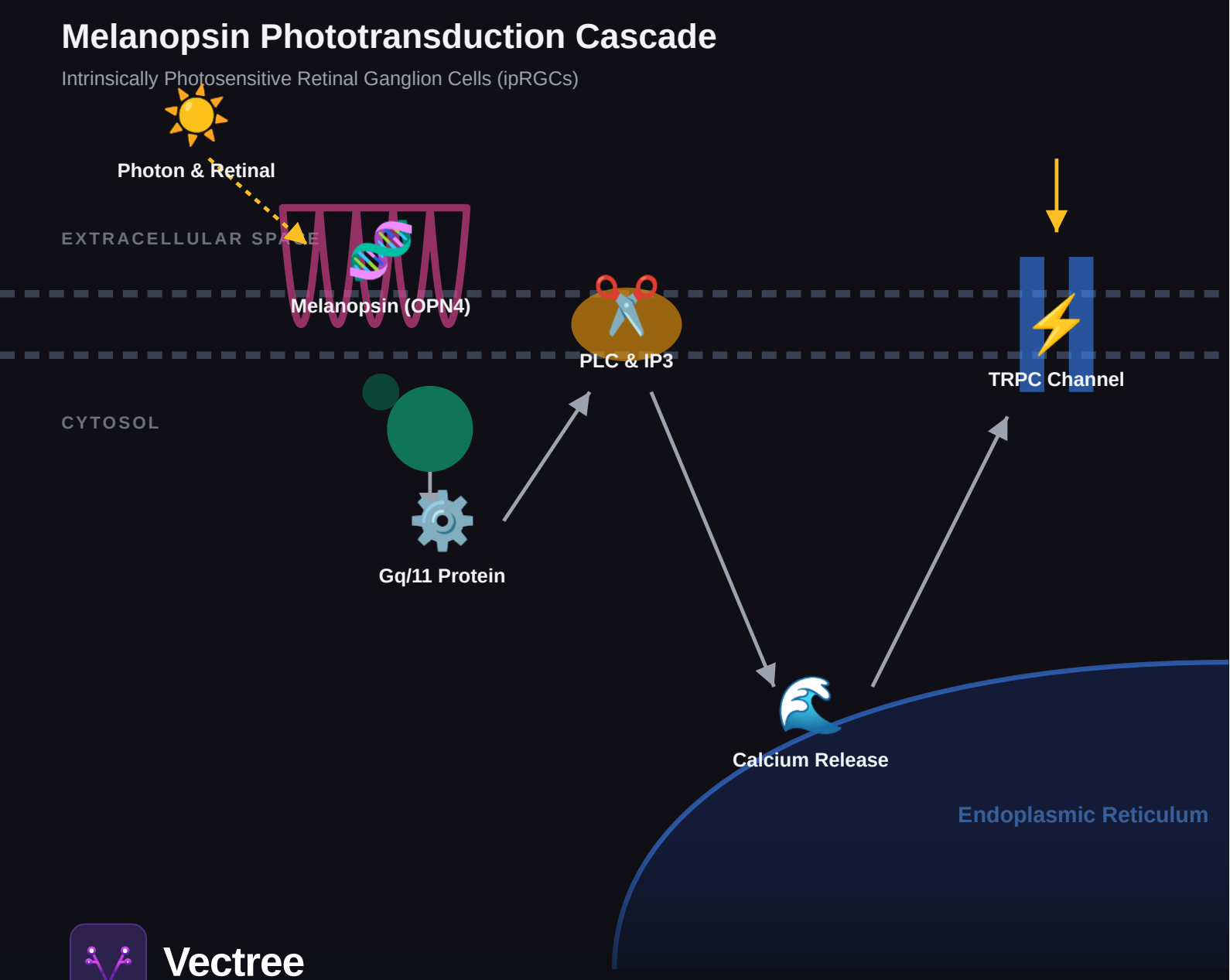

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Molecular structure of melanopsin and its phototransduction cascade

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VECTREE · KNOWLEDGE MAP

Molecular structure of melanopsin and its phototransduction cascade

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☀️ Photon & Retinal

The phototransduction cascade is initiated when an environmental photon strikes the intrinsically photosensitive retinal ganglion cell (ipRGC). Unlike typical rod and cone cells, this system depends heavily on a specific covalently bound chromophore, normally 11-cis-retinal.

When the photon hits the chromophore, it undergoes rapid photoisomerization, transforming from its 11-cis state into an all-trans structural form. This rapid physical transformation converts raw electromagnetic light energy into mechanical tension within the core of the receptor protein.

🧬 Melanopsin (OPN4)

Melanopsin, designated as OPN4, is a specialized seven-transmembrane G-protein-coupled receptor (GPCR) embedded in the plasma membrane of ipRGCs. It serves as the master photoreceptor for non-image-forming visual responses, such as circadian photoentrainment and the pupillary light reflex.

Evolutionarily, melanopsin is more closely related to invertebrate rhabdomeric opsins than to classic vertebrate visual opsins. The isomerization of its bound retinal forces the melanopsin molecule into an active conformational state, exposing its intracellular binding loops to cytosolic G-proteins.

⚙️ Gq/11 Protein Complex

Upon binding to active melanopsin, the intracellular Gq/11 protein complex undergoes a structural shift that triggers a vital nucleotide exchange, discarding GDP in favor of energy-rich GTP. This initiates the breakdown of the heterotrimeric complex.

Once GTP is bound, the alpha subunit (Gαq) violently dissociates from its beta-gamma dimer. By utilizing the Gq/11 pathway rather than the transducin (Gt) pathway used by traditional photoreceptors, the ipRGC signals light levels similarly to how mammalian cells process olfaction or how insect eyes detect light.

✂️ Phospholipase C & IP3

The newly liberated Gαq subunit traverses the inner surface of the plasma membrane until it encounters and activates Phospholipase C (PLC), a critical membrane-bound effector enzyme.

PLC acts as a molecular scissors, forcefully hydrolyzing the membrane lipid phosphatidylinositol 4,5-bisphosphate (PIP2). This catalytic cleavage produces two essential secondary messengers: Diacylglycerol (DAG), which remains anchored in the lipid bilayer, and Inositol 1,4,5-trisphosphate (IP3), a water-soluble molecule that freely diffuses into the deep cytosol.

🌊 ER Calcium Release

The diffusing IP3 molecules act as key messengers, traversing the cellular fluid to reach the Endoplasmic Reticulum (ER), a vast organelle that actively sequesters high concentrations of intracellular calcium.

Upon arriving, IP3 binds directly to specialized ligand-gated calcium channels known as IP3 Receptors located on the ER surface. This binding event forces the channels open, unleashing a massive torrent of Ca2+ ions into the cytosol, severely amplifying the downstream cellular response.

⚡ TRPC Channel Depolarization

The ultimate endpoint of the melanopsin cascade is the activation of Transient Receptor Potential Canonical (TRPC) channels on the plasma membrane. These ion channels are forced open by a combination of the membrane-bound DAG and the sudden spike in intracellular calcium.

The opening of the TRPC pores allows a rapid, overwhelming influx of extracellular sodium (Na+) and calcium (Ca2+) ions into the cell. This rush of positive charge powerfully depolarizes the ipRGC membrane, firing action potentials down the optic nerve directly to the suprachiasmatic nucleus (SCN) to report ambient light intensity to the brain.