Popular science abstract [English]

The eye is a spectacular organ, but despite its importance, eyes and eye diseases are notoriously understudied in medicine and diagnostics compared with other health issues although, many diseases affect them. Recently functional imaging devices have been gaining popularity, but still, for some, the molecules responsible for the changes observed are unknown, and the full potential of a diagnostic tool can only be unleashed when the biology behind it is fully understood. Of the many cell types necessary to build an eye, photoreceptors are among the most remarkable. Their outer segments, composed of a stack of about 800 membrane discs, receive light stimulus from an extensive range of intensities and convert that stimulus into an electrical impulse that travels to the brain to generate images. Between these two stages, light arrival and the perception of an image, a series of proteins execute a cascade of events in which phosphodiesterase 6 (PDE6) plays a central role and is known to contribute to some eye illnesses. When all is well, PDE6 hydrolyzes a small molecule from its circular form to an open form in a process that happens at or close to the atomic scale. Upon receiving light, photoreceptors have been noticed to change length on a much larger scale that still cannot be detected without specialized instruments. The atomic-scale molecular details that form the basis of larger-scale observations remain unknown. Several scientific studies suggest that PDE6 could be the protein responsible for that large-scale change. We propose that PDE6 causes such large changes because the photoreceptor outer segment's peculiar organization of stacks of discs allows minute changes per disc to build up to larger changes across the entire stack. To test this hypothesis and provide a biological explanation for the observations in functional imaging diagnostics, we will use a new microscope technology that allows us to measure such small changes within a reconstituted system that enables precise control of the players involved. Our results will contribute towards objective and impartial diagnostics in ophthalmology and will help extend our structural knowledge on how such important proteins work in their natural environment, between membrane discs, and help advance science and medicine in drug design, diagnostics, and functional imaging, for example.