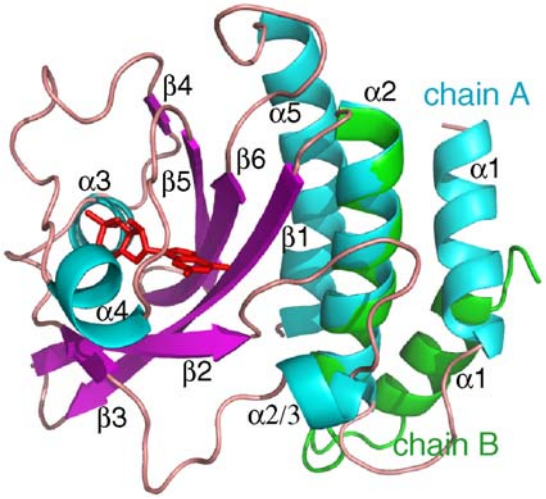
Illuminating Photoreceptors

Fundamental studies give insight into ocular function

The eyes house the elegant machinery that responds to photons and triggers the neural impulses that allow us to visualize our environment. Researchers from the University of Washington have used EMSL's nuclear magnetic resonance spectrometers and sophisticated probe technologies to gain new knowledge about the complex visual system at the molecular level. The team is the first to determine a high-resolution structure of the regulatory domain of the photoreceptor phosphodiesterase (PDE6) bound to its ligand, cyclic guanosine monophosphate (cGMP). Studies such as this one are the first steps toward a fundamental understanding of the how the visual system works and how to fix it when it goes awry.



Structure of PDE6 GAF A bound to cGMP (red).

The interaction between PDE6 and cGMP affects how *quickly* the eye can see. When it is activated by light, the regulatory region of PDE6, referred to as GAF A, activates PDE6. PDE6 in turn degrades cGMP, ultimately allowing the brain to receive information from the retina. Previous attempts to learn more about the ligand-free PDE6 GAF A domain via crystallization and diffraction studies were unsuccessful because crystals of the ligand-free protein are not easily prepared. So, the team turned to EMSL's NMR spectrometer and probe capabilities to investigate the conformational change of recombinant PDE6 while binding cGMP in real time and confirmed, at the atomic level, that GAF A is indeed the PDE6 binding site of cGMP.

Scientific impact: Determining the first structure of this essential photoreceptor regulator is an important step for understanding ocular function. In addition, studies such as this one support EMSL's goals to measure dynamic interactions in native environments and to predict biological functions from molecular and chemical data.

Societal impact: Studies that allow a fundamental, molecular-level understanding of eye function could lead to insights about maintaining ocular health and to targeted drug design based on protein structures.

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