Beginning to see the light

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Molecular mechanisms of vision

(PhysOrg.com) -- Scientists have detailed the active form of a protein which they hope will enhance our understanding of the molecular mechanisms of vision, and advance drug design.

Writing in the journal *Nature,* the team, including Dr Norbert Krauss from Queen Mary's School of Biological and Chemical Sciences, has detailed the active structure of a G-protein coupled receptor for the first time.

G-protein coupled receptors are found in the cell membranes of many different animals, and are involved in sensing light and a range of chemical signals including hormones, odours, pheromones and flavours. A huge variety of therapeutic drugs, such as alpha and beta blockers, antihistamines, dopamine agonists and opioids, work by regulating the behaviour of these receptors, and any information about their structure, particularly in an active form, is of valuable use to the pharmaceutical industry.

The team, lead by academics from the Charité (Medical School of Berlin) in Germany and Chonbuk National University in South Korea, studied a G-protein coupled receptor protein called Opsin, which is found in the rod cells of our eyes.

Opsin is the first link in a chain of chemical reactions which allow us to process images and see. First it joins together with another molecule called retinal, forming a protein called Rhodopsin. This in turn reacts with particles of light called photons to join with another protein, the G-protein and stimulate vision.

The team used a technique called X-ray crystallography to analyse the structure of Opsin when it was joined together with the G-protein. They found that Opsin had adopted an active structure, significantly different from its normal inactive state. This explains why Opsin can only bond with the G-protein in its active form, and provides a picture about how Rhodopsin is activated by light, like a mechanical switch.

Dr Krauss explains: “Our findings contribute to our understanding of the primary processes underlying vision. They might also help to model the interactions of other pairs of G-protein coupled receptors and G-proteins. As Rhodopsin/Opsin is now the first example of a G-protein coupled receptor where structures of both the active and inactive forms are known, it might also serve as a model system for selectively designing therapeutic drugs which function as agonists or antagonists of G-protein coupled receptor activity.”

Citation: 'Crystal structure of opsin in its G-protein-interacting conformation' by Patrick Scheerer, Jung Hee Park et al. will be published in the journal Nature on Thursday, 25th September.

Provided by Queen Mary, University of London