immune to prion infection, thus establishing that the PrP protein is an essential component of the disease. Finally, because no posttranslational chemical modification could be found to distinguish the two prion protein isoforms, it was proposed that they differed only in their conformations.

The attention received in the media and by scientists (both believers and nonbelievers alike) ensures that prions will continue to be the focus of much research. Lines of investigation will include experiments to address the function of PrP^c, the development of effective rapid diagnostic techniques, and molecular studies on the mechanisms of propagation to provide targets for the development of effective chemotherapeutic agents. Given its history, the prion will no doubt continue to surprise us.

Boyana Konforti

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Rhodopsin structure sees the light of day

Light is a powerful source of energy that is used for various biological purposes. Some organisms harness light to produce ATP, the energy currency of cells, while others use light to interpret their environment. Although the outcomes of these two processes are very different, both utilize similar proteins — ones that have seven membrane spanning segments and are coupled to the chromophore retinal, which is capable of changing shape upon absorption of a photon.

In certain archeabacteria, light activates a ~26 kDa proton pump called bacteriorhodopsin, which generates a proton gradient across the membrane that drives the synthesis of ATP. In vertebrates, light activates ~40 kDa photoreceptors called rhodopsins in the retina, and this leads to stimulation of G-protein signaling cascades and ultimately to the firing of specific neurons in the brain. In both cases, a photon of light causes the retinal chromophores to isomerize (from either the all-*trans* to the 13-*cis* conformation, in the case of bacteriorhodopsin, or from the 11-*cis* to the all-*trans* conformation, in the case of rhodopsin). This in turn causes conformational changes in the proteins leading to the particular biological outcomes.

Both bacteriorhodopsin and rhodopsin have been studied intensively from a biochemical perspective, in large part because of excellent sources for each protein, such as the purple membranes of certain archaebacteria for bacteriorhodopsin, and bovine retina for rhodopsin. Both have also been used as models for G-protein coupled receptors, even though only rhodopsin has this activity and two proteins are not terribly similar at the sequence level. Recently, we have been treated to structures of bacteriorhodopsin in its 'dark state', and to structures of presumed intermediates in its photocycle (see *Nature* **406**, 645–657, 2000, for the three newest structures). However, high-resolution structural investigations of rhodopsin have been less successful — until now.

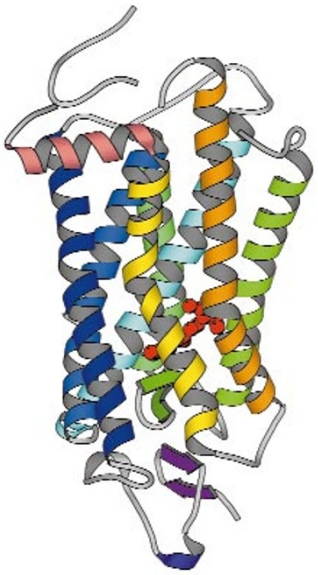

Figure courtesy of R. Stenkamp

In a recent issue of *Science* (**289**, 739–745, 2000), Palczewski *et al.* present the structure of bovine rhodopsin at 2.8 Å resolution. This is the first high-resolution structure of a member of the G-protein-coupled receptor family, which also includes receptors for ligands such as hormones, odorants and neurotransmitters. As is sometimes the case with 'difficult' proteins, the new structural work does not clarify why rhodopsin has been so recalcitrant, nor does it really explain why this group was ultimately successful. Nevertheless, we can hope that more structures of rhodopsin, in various intermediate states of its photocycle, will soon follow.

The structure of rhodopsin clearly shows the seven membrane spanning helices as well as the extracellular (bottom) and cytoplasmic (top) domains. The extracellular domain appears to act as a 'plug' that may prevent the retinal from protruding from the protein upon isomerization, thereby forcing the protein to adapt to the all-*trans* conformation of the chromophore. Several of the membrane spanning helices are distorted near the chromophore (red), and it is likely that these are some of the key regions that change shape in response to light.

The large body of structural and biochemical work on bacteriorhodopsin and rhodopsin has indicated that the conformational changes in the seven transmembrane helices surrounding the retinal are fairly subtle — on the order of one or a few angstroms. It is now fairly well understood, at the level of individual atoms, how such changes in bacteriorhodopsin facilitate a unidirectional path for protons through the protein. In contrast, how such changes in rhodopsin lead to the activation of G-proteins is less well defined. Clearly, the conformational changes that occur in the transmembrane region are somehow transmitted to the cytoplasmic domain, which then alters its shape to one suitable for interaction with G-proteins. The new structure of rhodopsin is a strong step toward describing this pathway at atomic resolution.

Tracy Smith