Opsins

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1.22.0 Introduction

Visual pigments comprise a large family of G protein-coupled receptors. They share homology with other G protein-coupled receptor types; however, there is significant specialization in visual pigments not found in other receptor families (Dohiman et al., 1991; Fryxell and Meyerowitz, 1991; Hargrave, 1991; Hargrave and McDowell, 1992). The visual pigments of many species of vertebrates and invertebrates have been studied by absorption spectroscopy or microspectrophotometry of visual organs. Therefore, historically vertebrate visual pigments have been classified on the basis of photoreceptor cell type of the retina in which they were detected (Bowmaker and Dartnall, 1980). Rod cells, responsible for dim-light vision, contain rhodopsin (“red” opsin). Cone cells, responsible for bright-light and color vision, contain iodopsins (“violet” opsin), also known as cone pigments or color vision pigments. Cloning of opsins from a variety of species has allowed more detailed comparisons and phylogenetic classifications based on structural, spectral, and biochemical properties of visual pigments (Applebury and Hargrave, 1986; Findlay and Pappin, 1986; Nathans, 1987).

Pigments are made up of opsin apoprotein plus chromophore. The chromophore is a cofactor and not a ligand as in other seven helix receptors. It is linked covalently via a Schiff base bond to a specific lysine residue. The chromophore-binding pocket resides in the membrane-embedded domain of the protein. One of two retinoids serves as the chromophore for all visual pigments. The chromophore in most vertebrate pigments is the aldehyde of vitamin A, 11-cis-retinal. The chromophore in some fishes and amphibians is the aldehyde of vitamin A₂, 11-cis-3-dehydroretinal, which contains an additional carbon-carbon double bond in the β-ionone ring (Figure 1).

Photoisomerization of the 11-cis to all-trans form of the chromophore is the primary event in visual signal transduction, and it is the only light-dependent step (Schoenlein et al., 1991; Wald, 1968). Retinal isomerization activates the pigment, allowing it to interact with a specific heterotrimeric G protein. In the case of the vertebrate visual system, G protein activation leads to the activation of a cyclic-GMP phosphodiesterase (Fung et al., 1981), and the closing of a cyclic-GMP-gated cation channel (Kaupp et al., 1989; Kaupp, 1991). In short, light causes a graded hyperpolarization of the photoreceptor cell. The amplification, modulation, and regulation of the light response is of great physiological importance and has been discussed in detail (Chabre, 1985; Koch, 1992; Stryer, 1991).
FIGURE 1. Photoisomerization of 11-cis-retinal to all-trans-retinal is the only light-dependent event in vision. All vertebrate visual pigments contain one of two chromophores, vitamin A aldehyde (11-cis-retinal), or vitamin $A_2$ aldehyde (11-cis-3-dehydroretinal), which contains an additional carbon-carbon double bond in the $\beta$-ionone ring. The chromophore is covalently linked as a cofactor to a specific opsin lysine residue via a Schiff base bond.

All pigments are tuned to a characteristic wavelength of maximal absorption ($\lambda_{\text{max}}$). Despite the fact that retinal is the universal chromophore, the $\lambda_{\text{max}}$ values of visual pigments span the visible spectrum, i.e., from near ultraviolet at about 400 nm to far visible red at about 600 nm. Distinct chromophore-protein interactions are responsible directly or indirectly for spectral tuning in visual pigments. Thus, differences in primary structure result in differences in spectral properties.

As pigment genes from a variety of species have been cloned and characterized, models of pigment evolution have been proposed (Okano et al., 1989; Wang, S. et al., 1992; Yokoyama and Yokoyama, 1989, 1990a). The homology in the opsin family of genes indicates that divergent evolution occurred from a single precursor retinal-binding protein to form long- and short-wavelength absorbing prototypes. The long-wavelength prototype diverged to form red and green pigments. The short-wavelength prototype then diverged to form a blue pigment and the family of rhodopsins and rhodopsin-like green pigments. Details of sequence comparisons are discussed below.

It is interesting to note that retinal-based pigments are found in unicellular algae and prokaryotes. It is possible that these pigments are the precursors of the superfamily of G protein-coupled receptors (Yokoyama and Yokoyama, 1989). One of the most widely studied membrane proteins has been bacteriorhodopsin (br), the light-driven proton pump of *Halobacterium halobium*. Detailed spectroscopic studies of mutants and a high resolution structure for br have led to a basic understanding of the mechanism of light-driven proton pumping (Henderson et al., 1990; Khorana, 1988). Some structural aspects of br are relevant to understanding the structures of visual pigments (Henderson and Schertler, 1990).

A number of structural features are shared by visual pigments. Like all G protein-coupled receptors, they consist of seven hydrophobic domains (Dratz and Hargrave, 1982). A Glu or Asp/Arg/Tyr tripeptide sequence is found at the cytoplasmic border of the third transmembrane domain. This domain is conserved in most G protein-
coupled receptors and has been shown to be involved in G protein interaction (Franke et al., 1990; Sakmar et al., 1989). A lysine residue that acts as the linkage site for the chromophore is conserved within the seventh transmembrane segment in all pigments. A pair of highly conserved cysteine residues is found on the extracellular surface and may form a disulfide bond. In many pigments, a carboxylic acid residue that acts as the counterion to the protonated, positively charged Schiff base is conserved within the third transmembrane segment (Nathans, 1990; Sakmar et al., 1989; Zhukovsky and Oprian, 1989). Sites of light-dependent phosphorylation (serine and threonine residues) are found at the carboxyl-terminal of most visual pigments. These sites may be analogous to phosphorylation sites found on the carboxyl-terminal domains of other G protein-coupled receptors (Benovic et al., 1986).

1.22.1 Rhodopsins

1.22.1.1 Human Rhodopsin and Cone Pigments

Rhodopsin is the pigment of the retinal photoreceptor rod cell that is responsible for dim-light vision. The gene for human rhodopsin was cloned from a genomic library and sequenced (Nathans and Hogness, 1984). The gene is located on chromosome 3. It codes for a protein with 348 amino acid residues and contains four introns. The primary structure is 93.4% homologous to that of bovine rhodopsin. The key structural, spectral, and biochemical features of rhodopsins in general are discussed in Section 1.22.1.4.

Retinitis pigmentosa is a group of hereditary progressive blinding diseases with variable clinical presentations. One form of the disease, autosomal dominant retinitis pigmentosa (ADRP) was linked to a mutation in the gene for rhodopsin (Dryja et al., 1990; Farrar, 1990). About 30 different rhodopsin gene mutations have been reported in ADRP patients (Dryja et al., 1990; Dryja et al., 1991; Gal et al., 1991; Humphries et al., 1992; Inglehearn et al., 1991; Keen et al., 1991; Sung et al., 1991a). The mutations reported would result in alterations in all domains of rhodopsin; extracellular, membrane-embedded, and cytoplasmic. A study was carried out in which site-directed mutant opsin genes corresponding to ADRP genotypes were prepared (Sung et al., 1991b). When expressed in 293S cells in tissue culture, the mutant opsins displayed a heterogeneity of spectral properties and cellular transport behavior. Some mutants were defective in chromophore binding, others in cellular transport and insertion into the plasma membrane. However, some mutations had no apparent effect. One mutation linked to ADRP is a replacement of the Schiff base lysine by glutamic acid. This mutation should prevent chromophore Schiff base formation. Interestingly, a similar mutant of bovine rhodopsin was shown to have constitutive activity without chromophore addition in in vitro transducin activation assays (Robinson et al., 1992). The molecular pathophysiology of ADRP remains to be fully elucidated.

Human trichromatic color vision, at the level of the photoreceptor, requires the presence of three cone pigments with broad overlapping spectral absorption. Three genomic and cDNA clones encoding the opsin apoproteins of these pigments were cloned and characterized (Nathans et al., 1986b). The amino acid sequences of these opsins are about 41% identical to that of human rhodopsin. The green and red opsins are about 96% identical to each other and about 43% identical to the blue opsin. The spectral properties of human cone pigments have been studied by a variety of techniques ranging from psychophysical color matching to microspectrophotometry (Bowmaker and Dartnall, 1980; Winderickx et al., 1992). Recently, however, the human cone pigment genes were
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expressed in tissue culture cells, reconstituted with 11-cis-retinal, and studied by ultraviolet-visible spectroscopy (Merbs and Nathans, 1992a; Oprian et al., 1991). The \( \lambda_{\text{max}} \) values reported in the two studies were as follows: blue, 426 nm; green, 530 nm; red, 552 and 557 nm for polymorphic variants (Merbs and Nathans, 1992a); and blue, 424 nm, green, 530 nm, and red, 560 nm (Oprian et al., 1991). These studies confirmed the assignments based on genetic analysis of the cloned pigment genes.

Analysis of the arrangement of the cone opsin genes on the X chromosome has led to a detailed understanding of the molecular genetics of inherited variations in color vision (Nathans et al., 1986a). In males with normal color vision, a single red opsin gene resides with one or more green opsin genes in a head-to-tail tandem array. In one type of color vision defect, anomalous trichromacy, unequal intragenic recombination can result in an opsin gene that is a hybrid between green and red opsin genes. It was proposed that these hybrids would have anomalous spectral properties (Nathans et al., 1986a; Neitz et al., 1989). Recently, this genetic hypothesis was confirmed experimentally by obtaining absorption spectra for heterologously expressed hybrid pigments responsible for anomalous trichromacy (Merbs and Nathans, 1992b). The molecular genetics of blue cone monochromacy has also been elucidated (Nathans et al., 1989).

A genetic model to account for the absence of the green and red genes has been tested in transgenic mice (Wang et al., 1992). The results suggest that a conserved 5’ region interacts with the green or red gene promoter to determine which gene is expressed in a given cone cell.

Comparisons of amino acid residues in the chromophore binding pocket of rhodopsin, cone pigments, and hybrid cone pigments has led to a number of proposals regarding the specific amino acid residues responsible for spectral tuning in the visual pigments (Kosower, 1988; Nathans et al., 1986b; Neitz and Jacobs, 1986; Neitz et al., 1989). Of the 15 amino acid differences between green and red pigments, three hydroxyl-bearing amino acid residues may be predominantly responsible for the spectral shift: Ser-180, Tyr-277, and Thr-285 (Chan et al., 1992; Merbs and Nathans, 1992b; Neitz et al., 1991).

1.22.1.3  Monkey Rhodopsin

Partial nucleotide sequence information from polymerase chain reaction nucleotide sequencing of monkey visual pigment exons has led to models of spectral tuning and to predictions about the identity of specific amino acids involved in human red-green color vision (Neitz et al., 1991; Williams et al., 1992). New world monkeys, such as marmosets (Callithrix jacchus jacchus), tamarins (e.g., Saguinus fuscicollis), and squirrel monkeys (e.g., Saimiri sciureus) have dichromatic vision with a blue pigment and a single long-wavelength pigment. However, there is a striking polymorphism in the long-wavelength pigment, such that females with two X-linked opsin genes are effectively trichromatic. Using pairwise comparisons of opsin gene sequences from a number of individual male monkeys with a range of pigment \( \lambda_{\text{max}} \) values, a model was proposed in which amino acid residues at three sites account for the spectral variation between human green and red cone pigments: positions 180, 277, and 285 (Neitz et al., 1991). This model was tested by introducing mutations at these sites in bovine rhodopsin (Chan et al., 1992) and by expression of hybrid human pigment genes (Merbs and Nathans, 1992b).

1.22.1.4  Bovine Rhodopsin

Bovine rhodopsin is the most extensively studied G protein-coupled receptor. A large amount of pigment (as much as 0.4 mg) can be obtained from a single bovine retina
by a sucrose density gradient centrifugation preparation of rod outer segment disk membranes. The pigment can be further purified by lectin affinity chromatography on conconavalin A Sepharose resin. Rhodopsin is stable in solubilized form in a variety of detergents, including digitonin, dodecylmaltoside, and octyl glucoside. Bovine rhodopsin was the first G protein-coupled receptor to be sequenced by amino acid sequencing (Hargrave et al., 1983; Ovchinnikov, 1982) and the first to be cloned (Nathans and Hogness, 1983). The cloning of a β-adrenergic receptor (Dixon et al., 1986) led to the identification of the structural homologies that now define the superfamily of G protein-coupled receptors.

Bovine rhodopsin is 348 amino acid residues in length, and is identical to human rhodopsin at all but 23 positions. Hydrophobicity profiles are consistent with seven transmembrane segments (Dratz and Hargrave, 1983). The amino-terminal domain is remarkable for two N-linked glycosylation sites. The carboxyl-terminal domain is rich in serine and threonine residues, which are phosphorylated in a light-dependent manner by rhodopsin kinase. The retinal Schiff base linkage is at Lys-296.

Bovine rhodopsin has a broad absorption maximum ($\lambda_{\text{max}}$) at about 500 nm (Figure 2). Upon photoisomerization of the chromophore, the pigment is converted to metarhodopsin II (MII) with an $\lambda_{\text{max}}$ value of 380 nm. The MII intermediate is characterized by a deprotonated Schiff base chromophore linkage. MII is the active form of the receptor that catalyzes guanine nucleotide exchange by transducin (Ganter et al., 1989; Longstaff et al., 1986).

Recent work on the structure and function of bovine rhodopsin focusing on molecular biology has been reviewed (Nathans, 1992; Khorana, 1992). These studies have elucidated the role of the extracellular domain in structure, key retinal-protein interactions, and the domains involved in transducin activation. The extracellular loops of bovine rhodopsin have been shown in a deletion analysis to be important for proper folding of the peptide that allows cellular processing and chromophore binding (Doi et al., 1990). In addition, two保守 cysteine residues on the extracellular domain, Cys-110 and Cys-187, were shown to be essential for proper folding of opsin (Karnik et al., 1988). These two residues were shown to form a disulfide linkage (Karnik and Khorana, 1990).

A number of studies have been carried out to investigate the retinal-binding domain of bovine rhodopsin. Several spectroscopic methods such as resonance Raman spectroscopy, Fourier-transform infrared difference spectroscopy, and nmr spectroscopy have been employed (Birge, 1990; Sawatzki et al., 1990; Siebert, 1990). Other approaches have included reconstitution of opsin apoprotein with synthetic retinal analogs (Honig et al., 1980) and photochemical cross-linking (Nakayama and Khorana, 1990). Recently, site-directed mutagenesis in combination with ultraviolet-visible spectroscopy and other spectroscopic and biochemical techniques has provided useful information about the retinal binding pocket (Bhattacharya et al., 1992; Nakayama and Khorana, 1991). One important result from the study of mutant bovine rhodopsin pigments was the identification of the retinylidene Schiff base counterion as Glu-113 (Nathans, 1990; Sakmar et al., 1989; Zhukovsky and Oprian, 1989). A model for the retinal binding pocket in bovine rhodopsin has been proposed based on a study of mutant pigments by microprobe resonance Raman spectroscopy (Figure 3) (Lin et al., 1992).

The domains of rhodopsin that interact with transducin have also been studied by site-directed mutagenesis of bovine rhodopsin. Relatively large segments of cytoplasmic loops are required for proper rhodopsin-transducin interaction (Franke et al., 1992; König et al., 1989). However, single amino acid substitutions within these domains can have dramatic effects on transducin activation (Franke et al., 1988; Gurevich et al., 1992).
FIGURE 2. An ultraviolet-visible absorption spectrum of purified bovine rhodopsin shows a characteristic broad visible absorbance with a $\lambda_{\text{max}}$ value of 500 nm. The 280-nm peak represents the protein component. After exposure to light, the pigment is converted to a peak with a $\lambda_{\text{max}}$ value of 380 nm characteristic of metarhodopsin II. This is the active form of the receptor that interacts with the rod cell G protein, transducin.

1990; Sakmar et al., 1989). In addition, transducin binding, and activation of bound transducin were shown to be discrete steps involving different surface domains of the receptor (Franke et al., 1990).

Recently, bovine rhodopsin mutants with substitutions at the site of the Schiff base linkage (Lys-296) and the counterion (Glu-113) were employed to show that a covalent bond to the 11-cis-retinal chromophore is not required for light-dependent activation of transducin (Zhukovsky et al., 1991). Furthermore, rhodopsin mutants were reported that have constitutive activity. They activate transducin in the absence of chromophore (Robinson et al., 1992). In this context, the main physiological reason for a covalent linkage between opsin and chromophore may be to reduce dark noise and to provide an extremely rapid light-dependent activation. These results emphasize

FIGURE 3. A schematic representation of the retinal-binding pocket of bovine rhodopsin (Lin et al., 1992). The pigment is viewed from above the plane of the membrane bilayer. Selected amino acid side chains are displayed and numbered.
similarities among the opsins and other receptors in terms of the mechanism of G protein activation.

1.22.1.11 Mouse Rhodopsin

The complete nucleotide sequence of the mouse opsin gene including introns and flanking sequences was reported (Al-Urbaidi et al., 1990). Evidence was also presented that the heterogeneity of mouse opsin transcript was due to the use of multiple polyadenylation sites in the 3'-flanking region. The existence of this clone is especially important because of the potential for using transgenic mice in studies of vertebrate visual development and of the molecular pathophysiology of human retinitis pigmentosa. The gene for rhodopsin is located on chromosome 6 (Elliott et al., 1990).

Ultraviolet retinal sensitivity has been identified in rodent retinas (Jacobs et al., 1991), but the cloning of a vertebrate ultraviolet pigment gene has not been reported.

1.22.1.15 Chicken Rhodopsin

Chicken retinas contain an abundance of cone cells compared with other vertebrate retinas, and the chicken visual system has been studied in detail using a number of approaches in addition to molecular biology. Five chicken visual pigments have been partially purified and characterized spectrally (Chen et al., 1989; Okano et al., 1989). The cloned DNA sequences of three chicken opsins have been reported: chicken rhodopsin (Takao et al., 1988), chicken red iodopsin (Kuwata et al., 1990; Tokunaga et al., 1990; Yoshizawa and Kuwata, 1991), and a chicken opsin that is likely to correspond to the chicken green iodopsin (Wang et al., 1992). The latter pigment is of particular interest because it displays an $\lambda_{\max}$ value (495 nm) similar to that of rhodopsin (500 nm), yet it is sensitive to hydroxylamine bleaching. This opsin was reported to define a new branch of the visual pigment gene family that is now known to contain the goldfish green pigment and the gecko rhodopsin (see below).

1.22.1.18 Octopus and Squid Rhodopsin

The primary structures of octopus (Paroctopus defleini) rhodopsin (Dergachev et al., 1989; Ovchinnikov et al., 1988) and squid (Logligo forbesi) rhodopsin (Hall et al., 1991) have been reported. The amino acid sequences of the octopus and squid rhodopsin are homologous and are most similar to the Drosophila opsin (see below). Several features of these invertebrate pigments distinguish them from vertebrate pigments. For example, in place of a glutamic acid identified to serve as the Schiff base counterion at position 113 in bovine rhodopsin, both of these pigments have a tyrosine residue. Some features of invertebrate rhodopsins such as the stability and acidity constant (pKₐ) values of their photoproducts are suggestive of bovine rhodopsin mutants with replacements of Glu-113. However, replacement of Glu-113 in bovine rhodopsin by Tyr does not result in a mutant pigment with properties similar to those of invertebrate rhodopsins (Sakmar, unpublished results).

The carboxyl-terminal region of octopus rhodopsin and squid rhodopsin consists of two domains. The first domain is a charged region that may contain a calcium binding site in addition to multiple threonine and serine residues. The second domain is a proline-rich region that consists of a multiple (8 to 10 times) repeat of a pentapeptide with the following consensus sequence: Pro-Pro-Gln-Gly-Tyr. This structure may be involved in regulating rhodopsin-rhodopsin and rhodopsin-cytoskeleton interactions within the visual microvilli of cephalopods (Hall et al., 1991).
1.22.1.21 Drosophila Rhodopsin

The invertebrate visual transduction system has been elucidated by biochemical, electrophysiological, and genetic studies. There are fundamental differences between vertebrate and invertebrate signaling. For example, at the level of the photoreceptor, the chromophore in some higher orders of insects is likely to be 11-cis-3-hydroxyretinal, rather than 11-cis-retinal (Goldsmith et al., 1986). Photoactivation of the pigments results in a stable meta (M) state that displays a red-shifted absorption maximum relative to that of the dark form of the pigment. The heterotrimeric G protein activated by the pigment in turn activates a visual phospholipase C, resulting in increases in cellular inositol-3-phosphate and diacylglycerol. Calcium is mobilized and ultimately sodium channels are opened resulting in a depolarization of the photoreceptor cell (Smith et al., 1991a; Smith et al., 1991b).

The visual system of the fruit fly (Drosophila melanogaster) has proven especially valuable for the study of invertebrate visual pigments and visual system development. The Drosophila compound eye is made up of about 800 ommatidia. Each ommatidium contains 8 photoreceptor cells: 6 outer cells (R1-R6) and 2 central cells (R7 and R8). In addition, simple eyes called ocelli are found on the top of the fly head. The cells fall into one of 3 spectral classes: R1-R6 are blue-sensitive photoreceptors with absorption peaks at about 470 nm, R7 and R8 are ultraviolet receptors, and the ocelli are violet sensitive with absorption peaks at about 420 nm (Feiler et al., 1988; Harris et al., 1976).

Four opsin genes (Rh1-Rh4) have been cloned and characterized. The ninaE gene was shown to be the structural gene for Rh1, which is found in the R1-R6 cells (O’Toosa et al., 1985; Zuker et al., 1985). Although the Rh1 rhodopsin shares only about 22% homology at the amino acid level with bovine rhodopsin, the seven transmembrane segment motif and a number of other structural features are conserved. The Rh2 gene encodes the ocelli opsin (Cowman et al., 1987; Feiler et al., 1988; Fryxell and Meyerowitz, 1987). The Rh3 and Rh4 opsins are expressed in the pair of central ommatidial cells (Montell et al., 1987; Zuker et al., 1987). The Rh2 gene is 67% homologous, and the Rh3 and Rh4 genes are only about 38% homologous to the Rh1 opsin.

An opsin of the larger fly species (Calliphora erythrocephala) was also cloned and displayed an 86% amino acid identity with the Drosophila Rh1 opsin (Huber et al., 1990).

1.22.1.22 Fish Rhodopsin and Iodopsins

The visual systems of fish have evolved to adapt to a variety of specific underwater environments (Loew and Lythgoe, 1978). For example, the visual spectrum in fish is somewhat shifted to longer wavelengths from that of other vertebrates because of the use of the chromophore 11-cis-3-dehydroretinal, which contains one additional carbon-carbon double bond. Some species of fish exhibit ultraviolet spectral sensitivity, as well as sensitivity to polarized light (Bowmaker et al., 1991; Hárosi and Hashimoto, 1983). Recently, a number of fish opsins have been cloned and characterized. Of particular interest has been the cloning of long-wavelength sensitive visual pigments from fish. Comparison of fish long-wavelength pigments with mammalian long-wavelength pigments allows insights regarding the evolutionary mechanism of visual development.

The Mexican blind cave fish (Astyanax fasciatus) shows rhodopsin and green-spectral responses in its pineal organ. Three opsin genes have been cloned from a genomic library that have been tentatively assigned to be a red-like opsin and two related green-like opsins (Yokoyama and Yokoyama, 1990a, 1990b). A rhodopsin has also been cloned from lamprey (Lampetra japonica) (Histomi et al., 1991).
Table 1. Opsin

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Goldfish (Carassius auratus) show rod and cone spectral sensitivities similar to those of humans. Five opsin genes from goldfish have been cloned and expressed (Johnson et al., 1992). The clones were assigned to a rod opsin, a red cone opsin that may be a polymorphic variant, a blue cone opsin that shows homology to both human blue and human rod opsins, and two green opsins that share some biochemical properties with chicken green opsins.

An evolutionary model has been described that takes into account the sequence information from human, chicken, fish, and gecko opsin sequences (Johnson et al., 1992; Yokoyama and Yokoyama, 1989). In summary, short- and long-wavelength sensitive opsins diverged from a common ancestor. The short-wavelength opsin precursor then diverged into blue opsins and a family of rhodopsin. The rhodopsin family includes goldfish green, chicken green, and gecko rod opsins that share biochemical properties with rhodopsins such as resistance to hydroxylamine reaction. The physiological roles of the rhodopsin-like green opsins is not understood. The long-wavelength opsin precursor went on to form human red and green iodopsins, cave fish red and green opsins, and chicken and goldfish red opsins.

1.22.4 Other Retinal-Based Pigments

Bacteriorhodopsin (br) is a light-driven proton pump found in Halobacterium halobium (Stoeckenius and Bogomolni, 1982). Like visual pigments, br is an integral membrane protein and employs a Schiff base-linked retinal (all-trans-retinal) as a chromophore. Br has been studied extensively by spectroscopic, biochemical, and genetic methods (Khorana,
In addition, a high resolution structure from cryoelectron microscopy has been reported for br (Henderson et al., 1990). This structure confirmed that seven segments transverse the membrane bilayer and that they are predominantly α-helical in secondary structure. A number of molecular models of visual pigments and other G protein-coupled receptors have been based on the structure of br and the relevance of structural comparisons has been discussed (Birge, 1990; Henderson and Schertler, 1990).

Other retinal-based pigments have been identified in prokaryotes (Duschil et al., 1990; Scharf et al., 1992; Stoeckenius and Bogomolni, 1982) and in unicellular algae (Beckmann and Hegemann, 1991; Foster et al., 1991; Gualtieri et al., 1992). These pigments are involved in phototactic and photophobic responses, and are thus a part of primitive sensory systems. For example, rhodopsin has been shown to regulate calcium currents in Chlamydomonas (Harz and Hegemann, 1991). The primary structures of prokaryotic sensory rhodopsins have been reported (Blanck et al., 1989; Lanyi et al., 1990).

FIGURE 4. Primary structures of cloned opsins. Primary structures of prokaryotic sensory rhodopsins have been reported (Blanck et al., 1989; Lanyi et al., 1990).
FIGURE 4b.
FIGURE 4c.
FIGURE 4e.
### FIGURE 4f.

#### REFERENCES


Opsins


Opsins


