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The Opsins: Lies Between Image Forming and Non-image Forming Process

Naseem Asma* and Malik Shalie

Centre for Biological Timekeeping, Department of Zoology, University of Lucknow, Lucknow 226007, India

*Corresponding Author

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Abstract: Light, the most abundant and important stimuli, can be sensed by a single photon by the photoreceptors. These photoreceptors are usually a group of protein of GPCR (G protein-coupled receptor) family. Opsins, a group of this family absorb these photons and processes both image forming and non-image forming phototransduction. Initially, their role was only limited to image formation, but recent studies reveal their importance in non-image forming functions also. In this review, we discussed various roles of opsins other than image formation, such as in photorelaxation of blood vessels, mechanoreception of skin, temperature regulation, hearing, immune system, thermotaxis of sperms, photosensation as well as in reproduction. These various functions of opsins show their immense importance in non-image forming functions as well as their evolutionary importance.

Keywords: Opsins, Image forming, Non-image forming, GPCR, Phototransduction

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Introduction

Light as well as its sensitivity was so important that it can be understood by the fact that even a single photon can be detected by photosensors. Various physical, chemical and biological stimuli were detected by a group of protein, commonly known as GPCR (G protein-coupled receptor). Opsin, which absorb light and processes both image forming and non-image forming transduction is a part of this family. For instance, rodopsin, after absorption of a single photon of light, changes the role of many cGMP (cyclic guanosine monophosphate) or TRP (tryptophan metabolic pathway) channels. The existing literature on opsin was first depicted on rodopsin.

After its discovery, various types of opsin have been discovered. The central dogma has been that opsins have their role in light absorption and phototransduction only, but recently opsins shows their presence in different fields. Because of their functional diversity, the focus now has been shifted towards their non- image forming roles. The primary structure of opsin consists of seven transmembrane alpha helices (Fig. 1) (Palczewski *et al.*, 2000).

Classification:

The most convincing classification of opsin was done on the basis of their photoreceptor

Fig. 1: (A) Structural model of Opsin molecule showing seven membrane components and the attachment site for the chromophore (retinal); (B) Photoactivation of opsin molecule from 11-cis- to all-trans, which initiates phototransduction cascade (Yau and Hardie, 2009).

Fig. 2: Graphical representation of phototransduction of opsin.

cell type in which the photopigment resides (Fig. 2). Ciliary (c-opsins) and rhabdomeric (r-opsins) are basic types of photoreceptor cells (Yau and Hardie 2009). Ciliary photoreceptors have stacked and flattened membranous discs, whereas rhabdomeric photoreceptors consist of densely packed membranous microvilli projections. Rods and cones of human and compound eye of flies

and other invertebrates are example of ciliary rhabdomeric photoreceptors. The phototransduction cascade was accomplished by hyperpolarization and depolarization of photoreceptor of c-opsin and r-opsins respectively (Fig. 3). The most striking difference between c-opsin and r-opsin is that upon activation by light, chromophore dissociates, upon which the all-trans retinal is

Fig. 3: Phylogenetic classification of opsin family based on photoreceptor cells: r- and c-opsin (Feuda *et al.*, 2012, 2014; Ramirez *et al.*, 2016).

regenerated to 11-cis retinal in the neighbouring retinal pigment epithelium (RPE) (Wright *et al.*, 2015). On contrary, in r-opsins all-trans retinal do not dissociates, rather, it was converted back into 11-cis retinal after absorption of second photon of light. Along with c- and r-opsins, there is another class of opsin known as RGR/ G_0 -opsins that function as photoisomerases or coupled to different signalling cascade. There are G protein-coupled receptor opsins (RGR), peropsin, and neuropsin.

Some Extraordinary Function of Opsins (Table 1):

Photorelaxation of blood vessels:

Interestingly, cascade of photorelaxation involves a G_0 type G protein coupled receptors which is similar to phototransduction as seen in some invertebrates (Kojima *et al.*, 1997; Gotow and Nishi, 2007). Blood vessels of mice contain melanopsin and help in vasorelaxation induced by light. Melanopsin knockout mice show its importance in dilation of blood vessels, representing melanopsin's role in extra-ocular light detection. Circadian control of blood flow and pressure in mammals may be under control of melanopsin

(Sikka *et al.*, 2014.) There is a possibility of involvement of some other opsins (Opn3, Opn5) in photorelaxation of blood vessels.

In mechanoreception of skin:

After discovery of melanopsin in skin of *Xenopus* (Provencio *et al.*, 1998), almost all opsins have been found in human skin (Tsutsumi *et al.*, 2009; Kojima *et al.*, 2011; Haltaufderhyde *et al.*, 2015). Rodopsin knockout (RNAi) of human epidermal melanocytes reduces Ca^{++} increase in response to ultraviolet A light (Wicks *et al.*, 2011). The best example of adjustment of pigmentation can be seen in fishes as they have specialized dermal light receptors. Vibrant color modification is observed in molluscs (octopus, cuttlefish, squid) mediated by chromatophores (Mäthger *et al.*, 2010; Kingston *et al.*, 2015; Ramirez and Oakley, 2015). Wavelength of light directs the migration of pigment in tilapia erythrophores (red pigment cells). Green and red opsin co-expressed in erythrophores, so as to control the contrasting effect of pigment dispersion and aggregation (Ban *et al.*, 2005). There is a possibility of r-opsin's function in mechanoreception (Ramirez and Oakley, 2015).

Table 1: Different opsins and the tissue from which they are isolated

Photopigments	First isolated from	Function
Rod and cone opsin	vertebrate retina (Bridges 1959)	Nightvision and a wide spectrum of light photons and are responsible for colour vision
Pinopsin	chick pineal (Okano et al. 1994, Kieta Sato 2018)	extraocular photoreception
Encephalopsin, panopsin (OPN3)	human, mouse (Blackshaw and Snyder 1999.)	non-visual photic processes
Peropsin (RRH)	<i>Amphioxus</i> (Sun et al. 1997.)	RPE physiology either by detecting light directly or by monitoring the concentration of retinoids or other photoreceptor-derived compounds.
<i>Ciona</i> opsin	tunicate: <i>Ciona intestinalis</i> (Kusakabe et al. 2001.)	retinal protein is responsible for the action spectrum of the swimming response.
Neuropsin (OPN5)	human, mouse (Tarttelin et al. 2003.)	mediate seasonal reproduction
Parapinopsin (PP-opsin)	cat fish: <i>Ictalurus punctatus</i> (Blackshaw and Snyder 1997.)	It has two color states with absorption spectra at two different wavelengths.
Melanopsin (OPN4)	<i>Xenopus laevis</i> (Provencio et al. 1998.)	pupil constriction to circadian phase shifting and to the acute light induction of sleep.
RGR opsin (Peropsin)	vertebrate retinal pigment epithelium (RPE) (Sun et al. 1997.)	play a role in transportation of small molecules between the RPE and the photoreceptor and also in phagocytosis of RPE layer
Teleost multiple tissue opsin (tmt-opsin)	teleost fish: <i>Danio rerio</i> , <i>Fugu rubripes</i> (Moutsaki et al. 2003.)	
Vertebrate Ancient (VA) opsin	Fish: Atlantic salmon (<i>Salmo salar</i>) (Soni and Foster 1997)	light sensitive and regulate melatonin synthesis and have role in photic responses.

In temperature regulation:

Animals have a tendency to adapt themselves according to their surrounding temperature. Poikilotherms are the organisms which synchronizes their body temperature with the environment. The requirement for opsin changes in drosophila larval stages (Sokabe *et al.*, 2016). The cascade for temperature regulation in Drosophila larvae, which distinguishes difference of fraction in temperature (Klein *et al.*, 2015) was initiated by an opsin (Rh1) (Shen *et al.*, 2011).

In hearing:

Interestingly, opsins were found in Drosophila auditory system (Senthilan *et al.*, 2012). Screening of Johnston's organ, a sensory organ help in hearing, shows the involvement of four different opsins in it-- Rh3, Rh4, Rh5 and Rh6. Mutation in these Rh opsins, results in disfunctioning of the Johnston's organ (Senthilan *et al.*, 2012).

In immune system:

Presence of OPN3 mRNA in T-cells, B-cells,

and bronchiolar epithelial cells has been reported (White *et al.*, 2008). OPN3 is concerned as asthma susceptibility gene. Secretion of interleukin-2 (IL-2) is inhibited in knockdown of OPN3 in Jurkat cells, T-cell line which indicates the importance of OPN3 in immune system.

In thermotaxis of sperms:

For sperm to reach its destination, thermotaxis, rheotaxis and other mechanisms are used. Opsin dependent signaling cascade has been found to be involved in mammalian sperm thermotaxis (Pérez -Cerezales *et al.*, 2015). A number of opsins were found to be present in human sperm as well as in mouse testis, these are mRNA of OPN3, OPN5, OPN1-SW, OPN1-MW and OPN4. Among all opsins OPN3 and OPN5 are abundantly present in mammalian sperm and rhodopsin in mouse. Rhodopsin contributes to thermotaxis which was confirmed by knockout experiments (Pérez -Cerezales *et al.*, 2015).

In photosensation:

During embryogenesis of zebrafish, impulsive activity of spinal central pattern generator promotes coiling behaviour, and the receptor involve in this behaviour is opsin, VALopA (Friedmann *et al.*, 2015). Another behaviour of zebrafish involves opsins in later larval stage. The light was sensed by preoptic area having deep brain photoreceptors that contributes to the hunt for light behaviour, initiated by failure of light and Opn4 may be involve in this dark photokinesis (Fernandes *et al.*, 2012).

In reproduction:

A number of brain regions, such as, medio-basal hypothalamus, septal region of telencephalon, and pineal gland help in extra-

ocular light sensation that influences seasonal reproductive behaviour (García-Fernández *et al.*, 2015; Surbhi and Kumar, 2015). Among the brain regions mediobasal hypothalamus is the most important region for regulation of seasonal behaviour (García-Fernández *et al.*, 2015). VA opsin may be the light receptor which is expressed in hypothalamus (García-Fernández *et al.*, 2015). Opn5 mRNA was expressed in paraventricular organ (PVO), brain area related to photo transduction in many songbirds. Its neurons extended to the external zone of median eminence adjoining to the pars tuberalis of the pituitary gland that translate information from light into neuroendocrine responses. The action spectra of Opn5 shows its maximum spectra approximately at 420 nm which coincides with blue wavelength and UV-B light, that induce photoperiodic responses in pinealectomized quail. This shows that Opn 5 is a deep brain photoreceptor and helps in seasonal reproduction in birds (Nakane *et al.*, 2010).

Conclusion

The diverse function of opsin gives an idea of their role in both image forming and non-image forming field. They were not restricted only to image processing task, their role is emerging in other fields too. However, to understand the photoreceptor types and their function in evolutionary context, we need to have a better understanding of the sensory ecology of both mammalian and non-mammalian vertebrates.

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