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### **LIGHT RESPONSE PROPERTIES OF INTRINSICALLY PHOTOSENSITIVE RETINAL GANGLION CELLS IN NON-IMAGE-FORMING VISION**

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The discovery of intrinsically photosensitive retinal ganglion cells (ipRGCs) as the third retinal photoreceptor has produced the concept of non-image-forming vision in contrast to image-forming vision, that is, the visual system by rods and cones. Sensation of light and darkness by ipRGCs is unconscious but induces physiological actions such as circadian entrainment and regulation of release of some hormones. Studies in rodents have shown that ipRGCs project to hypothalamic and thalamic regions as well as to the suprachiasmatic nucleus (SCN) where the biological clock is localized (Fu et al., 2005; Hattar et al., 2006; Nayak et al., 2007). Those regions in the brain control sleep-wake regulation, pupillary light reflex and other photoadaptive responses. Although the discovery of ipRGCs has been led by efforts to understand mechanisms of circadian entrainment, now the primary role of ipRGCs and non-image-forming vision is recognized as adaptation to changes in environmental light. Understanding of the non-image-forming visual system implies the potential of new luminous environment design in terms of light and health.

The aim of this research work is to investigate light response properties of ipRGCs with the intention of developing new metrics for non-image-forming vision. Similarly to rods and cones, ipRGCs have the spectral sensitivity, but their light responses are different from those of rods and cones in some respects. For example, ipRGCs respond to light slowly and depolarize in response to light, while rods and cones respond to light rapidly and hyperpolarize in response to light (Berson et al., 2002; Berson, 2003). Recent studies in the field of neuroscience have shown that ipRGCs exhibit light and dark adaptation, and receive inputs from rods and cones (Wong et al., 2005; Dacey et al., 2005; Wong et al., 2007). The authors have started a series of studies on non-image-forming vision, and first, are investigating the spectral sensitivity that is a fundamental characteristic of vision. Careful consideration should be given to define luminous quantities of non-image-forming vision due to distinctive light response properties of ipRGCs.

It is known that ipRGCs drive the pupillary light reflex as well as circadian entrainment (Lucas et al., 2001; Lucas et al., 2003). A new measurement system was devised in order to obtain spectral responses of human ipRGCs through the pupillary light reflex. It was composed of a goggle with a built-in CCD camera, a light stimulation device, and recording units. The light stimulation device was capable of monochromatic and dichromatic stimulation. The wavelength of the stimulus was selected between 400 nm and 600 nm. The stimulus of different intensities was presented to one eye, and the pupil diameter in the other eye was continuously monitored. Measurement time was set at 25 seconds (5



second pre-stimulation, 5-second stimulation and 15-second post-stimulation). Pupil responses were measured at scotopic levels.

This paper shows measurements on one female subject (23 yr, normal vision). In the first measurement, monochromatic stimuli were presented to the subject. The spectral sensitivity curve was derived from pupillary constriction ratios by fitting a template for vitamin A1-based visual pigments (Govardovskii et al., 2000). The pupillary constriction ratio was calculated from average pupil diameters over the pre-stimulation and stimulation periods. The resultant curve almost agreed with spectral sensitivity curves shown by other studies (Gamlin et al., 2007; Zaidi et al., 2007), and was also close to the spectral sensitivity of ipRGCs electrophysiologically shown in rodent and primate retinae (Berson et al., 2002; Dacey et al., 2005). In the second measurement, dichromatic stimuli were presented to the subject. The dichromatic stimuli were combinations of shorter-wavelength and longer-wavelength stimuli. Post-stimulus pupillary constriction was obviously prolonged in comparison with the measurements for monochromatic stimulation. This indicates that the light response of ipRGCs is enhanced by polychromatic light or possibly modified by cone input.