Molecular characteristics of mammalian melanopsins for non-visual photoreception

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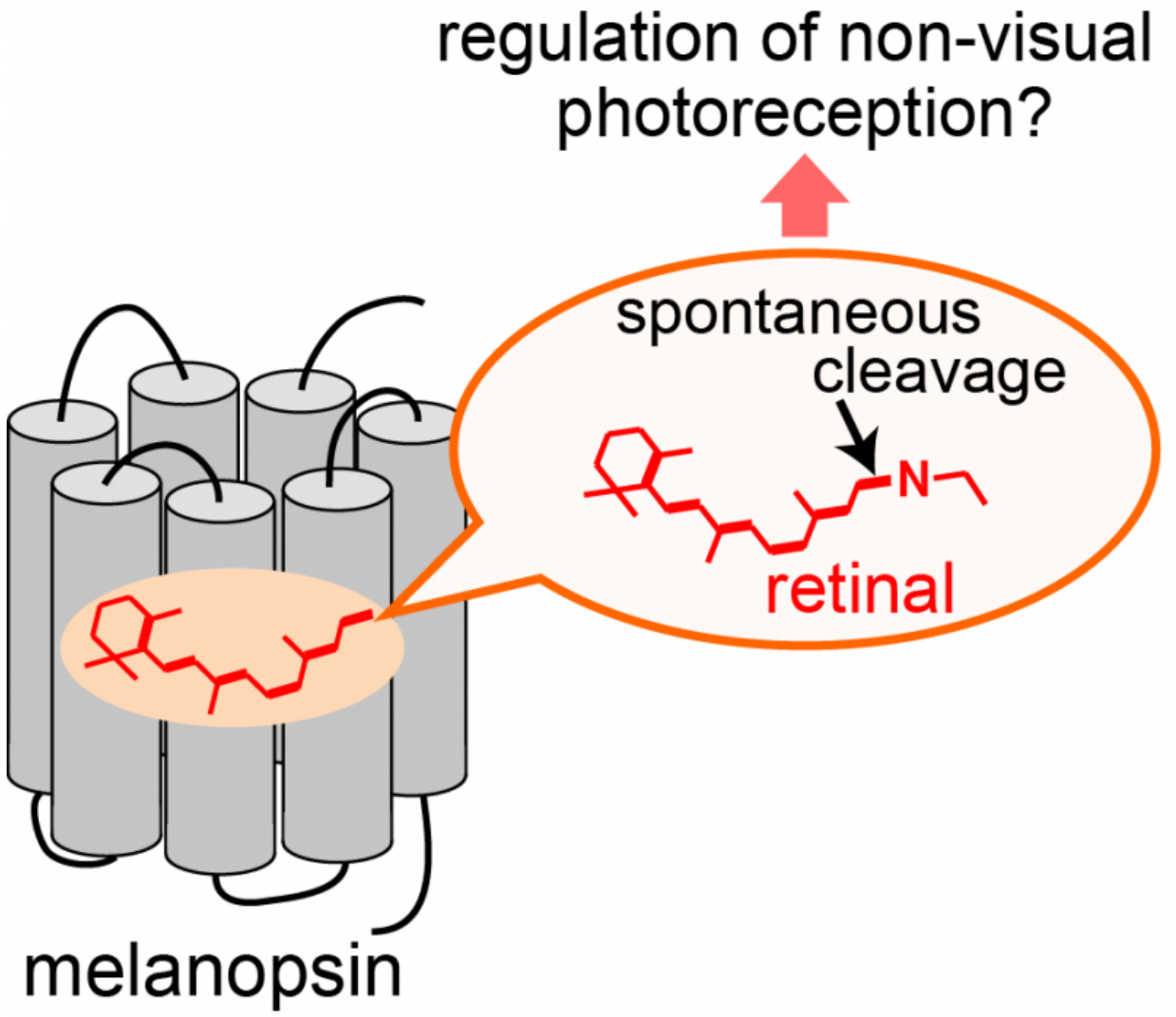

A mammalian photoreceptive protein melanopsin spontaneously releases the chromophore retinal. The property would be important to regulate non-visual photoreception in mammals. Credit: IMS/NINS

Researchers at Institute for Molecular Sciences reported that a mammalian photoreceptive protein melanopsin spontaneously releases the chromophore retinal. The property would be important to regulate non-visual photoreception in mammals. This work was carried out as a collaborative work of Drs. Hisao Tsukamoto and Yuji Furutani (Institute for Molecular Science) with Yoshihiro Kubo (National Institute for Physiological Sciences), David Farrens (Oregon Health and Science University), Mitsumasa Koyanagi and Akihisa Terakita (Osaka City University). This study was published online in the *Journal of Biological Chemistry* on September 28, 2015.

Mammals receive light signals for not only visual but non-visual photoreception such as photoentrainment of circadian clock and pupil constriction. Previous studies have revealed that a photopigment melanopsin receives and transmits light signals in intrinsically photoreceptive retinal ganglion cells (ipRGCs), and the melanopsin-mediated light transmission plays an important role in non-visual photoreception of mammals. Melanopsin is a member of the opsin family, and is more closely related to photopigments in invertebrate visual cells than to pigments in vertebrate visual (rod and cone) cells. The researchers speculated that mammalian melanopsins have acquired different molecular properties from closely related invertebrate visual pigments in order to function in the non-visual photoreception. To identify such properties, they compared biochemical and spectroscopic properties of mammalian melanopsins with those of invertebrate melanopsin and visual pigment.

The researchers found that mammalian melanopsins possess a less stable bond with the chromophore retinal, a vitamin A derivative, than the closely related photopigments. This property of mammalian melanopsin would contribute to lower photosensitivity of ipRGCs to detect

environmental light intensity without saturation. Furthermore, the stability of the retinal attachment is highly diversified among mammalian melanopsins, and human melanopsin possess a much weaker attachment than mouse one. Through further analyses of various primate melanopsins as well as mutagenesis analyses, the researchers showed that amino acid substitutions at particular positions are mainly responsible for the diversity of the retinal attachment stability. Comparison of amino acid residues at these positions among various mammalian melanopsins suggests that melanopsins in apes including humans have acquired and kept two residues destabilizing the bond with retinal in molecular evolution. The destabilized bond would make apes' melanopsin less photosensitive and might be important for these animals living under brighter light environment.

This study revealed that mammalian melanopsins possess characteristics suited for the non-visual photoreception, and their characteristics are diversified among mammalian species. Such insights will help us to understand non-visual photoreception in various mammals and to develop therapies and research tools using melanopsin molecules.

More information: Hisao Tsukamoto et al. Retinal attachment instability is diversified among mammalian melanopsins, *Journal of Biological Chemistry* (2015). DOI: 10.1074/jbc.M115.666305

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