Could retinal be a major factor in blue light-induced vision damage?

Kasun Ratnayake and Ajith Karunarathne

Kasun Ratnayake – PhD student, Department of Chemistry and Biochemistry, University of Toledo, Toledo, OH, USA

Ajith Karunarathne – Assistant Professor, Department of Chemistry and Biochemistry, University of Toledo, Toledo, OH, USA

Blue light possesses the highest energy in visible spectrum. With the increased use of devices such as smartphones, tablets, laptops and TVs, occupational exposure as in dental procedures and cosmetic exposures including tanning procedures, the public is increasingly conscious and worried about blue light-induced health hazards including vision damages and skin cancer. A growing body of research has also demonstrated blue light’s impact on vision-related diseases including age-related macular degeneration, insomnia, and even obesity. Though the connection of blue light with human health is evident, molecular level mechanisms of blue light-induced damage were lacking.

When the cis form of the retinal chromophore is bound, photoreceptors sense light and trigger visual signaling in the eye. During this process, cis-retinal is converted to trans retinal and released from photoreceptors to the disk-membranes of the rod and cone photoreceptor cells. Although free retinal absorbs both Ultra Violet (UV) and blue light, in the eye, the majority of UV light is blocked by the lens and the cornea. Authors anticipated that free trans retinal, before the removal from membranes of cells in the eye by the retinal clearance mechanism, absorbs blue light and undergo photoexcitation. The authors of this study exhibited retinal absorbs blue light, intercepts cellular signaling by introducing irreversible changes to signaling molecules that are crucial for cell survival.

Cell types were selected to represent both visual and non-visual cells since retinal is found both in the retina as well as in the rest of the body. Since retinal is lipophilic, authors anticipated that it can accumulate in the lipid membranes of cells and therefore examined whether blue light-excited retinal damages membrane interacting signaling molecules. Authors selected one such representative molecule named Phosphatidylinositol bisphosphate (PIP2), a major regulator of cell membrane properties and a key signaling lipid, in living cells for the investigation. Using a biosensor that binds PIP2, authors observed severe and permanent damage to PIP2 molecules. This damage was universal for all the visual and non-visual cells tested. Since cell membranes are composed of many lipids and dock lipid anchors of many signaling proteins, authors speculated that the cellular damage elicited by photoexcited retinal is way beyond PIP2 and likely perturb many vital molecules, compromising cell survival. The PIP2 damage was followed by an upsurge of calcium levels in cells, another signaling event that can damage sustainable cellular signaling. Interestingly, neither retinal nor blue light alone did not show any effect on cells. As an extension to this study, authors also demonstrated a profound death of cells that are exposed to retinal and blue light. Incubation of cells with a bioavailable vitamin-E derivative called alpha-tocopherol significantly reduced the blue light and retinal induced damage to PIP2. Interestingly, alpha-tocopherol is a lipid-soluble antioxidant and water-soluble glutathione antioxidant was unable to circumvent this blue light and retinal cellular toxicity.

To elucidate how retinal upon blue light excitation damages cells, response signatures of this process were compared with a known photosensitizer, rose bengal. Photosensitizers absorb light and known to generate reactive oxygen species. Blue light excited retinal and photoexcited rose bengal elicited identical cellular responses with the exception that rose bengal-triggered cellular changes were faster and larger. During this investigation, authors also eliminated the possibility of direct blue light exposure, retinal without photoexcitation or previously suspected mechanisms such as retinal activating G-protein coupled receptors (GPCR), as potential mechanisms of blue light-induced cellular damage. Authors anticipate advancement of treatment options for light-induced cellular damages and the development of new preventive measures to avoid excessive light exposures. Nevertheless, authors emphasize the need for further investigations to see if the observed toxic mechanism are feasible in the human eye and whether low intense and prolonged blue light exposures from digital devises are a genuine human health concern.