16th International Congress on Photobiology

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Light, Lipids and Photoreceptor Survival: Live or Let Die?

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Due to its constant exposure to light and its high oxygen consumption the retina is highly sensitive to oxidative damage, which is involved in the death of photoreceptors in retinal neurodegenerative diseases such as retinitis pigmentosa and age related macular degeneration. A peculiar characteristic of retina lipids, their high content of polyunsaturated fatty acids, mainly docosahexaenoico acid (DHA), has also been proposed to contribute to this sensitivity. However, the role of DHA in the retina is still controversial. Its six double bonds make it highly prone to peroxidation and it has been shown to increase retina vulnerability to photo-oxidative damage. However, DHA has also a protective role on photoreceptors. Our lab has shown that DHA protects photoreceptors from oxidative stress by activating the ERK/MAPK pathway. We now investigated how DHA activated this pathway and if it also activated antioxidant defense mechanisms in photoreceptors. Addition of retinoid X receptors (RXR) antagonists to rat retinal neuronal cultures inhibited DHA protection during early development in vitro and upon oxidative stress. Inhibition of an alternative pathway, involving tyrosine kinase (Trk) receptors, did not affect DHA prevention of photoreceptor apoptosis. These results imply that activation of RXR was required for DHA protection. H_2O_2 treatment increased reactive oxygen species (ROS) production in retinal neurons, inducing photoreceptor apoptosis. DHA prevented H_2O_2-induced apoptosis, simultaneously decreasing ROS formation. Analysis of enzymatic activity evidenced that DHA addition increased glutathione peroxidase activity in cultures treated with or without H_2O_2.
Our results provide the first evidence that DHA activates RXR to prevent photoreceptor death. They also suggest that DHA activation of antioxidant defense mechanisms is at least in part responsible of protecting photoreceptors from oxidative stress.