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Prologue: My Experience with Photoreceptors - The Peroxidation of Lipids

Angel Catala

1. Introduction

In this chapter, I described several studies on the lipid peroxidation of membrane phospholipids in retina. Particular emphasis is placed on the molecular modifications of very long chain polyunsaturated fatty acids associated with protein changes during peroxidation of photoreceptor membranes. Retina possesses membranes with high content of polyunsaturated fatty acids. Reactive oxygen species begins chain reactions of lipid peroxidation which damage the retina, especially the membranes that play important roles in visual function. Furthermore, biomolecules such as proteins or amino lipids can be covalently modified by lipid decomposition products. In retinal membranes, peroxidation of lipids is also usually accompanied by oxidation of membrane proteins. In consequence, lipid peroxidation may alter the arrangement of proteins in bilayers and by that it interferes with their physiological role on the membrane function.

2. Brief description of photoreceptor

The photoreceptors are the only cells that can convert incoming light into an electrical signal that can be carried to the brain (via the optic nerve) to generate conscious vision. Photoreceptors (rods and cones) are highly polarized and specialized neurons with distinct compartments: cell body, inner segment (IS), and outer segment (OS). Although both rods and cones share a similar overall arrangement of the different compartments, they are diverse in their shape, size, and light-detecting capacities. Rods are highly sensitive to light (only active in starlight vision at night) and show long cylindrical structures with the ciliary OS membrane including many membranous discs, which are loaded with the photopigment rhodopsin and other proteins that participate in the phototransduction cascade.

3. Photoreceptor cell damage

Retina is very rich in membranes containing polyunsaturated fatty acids. Reactive oxygen species initiates chain reactions of lipid peroxidation which injure the retina, especially the membranes that play important roles in visual function. Furthermore, biomolecules such as proteins or amino lipids can be covalently modified by lipid decomposition products. In retinal membranes, peroxidation of lipids is also usually accompanied by oxidation of membrane proteins. In consequence,

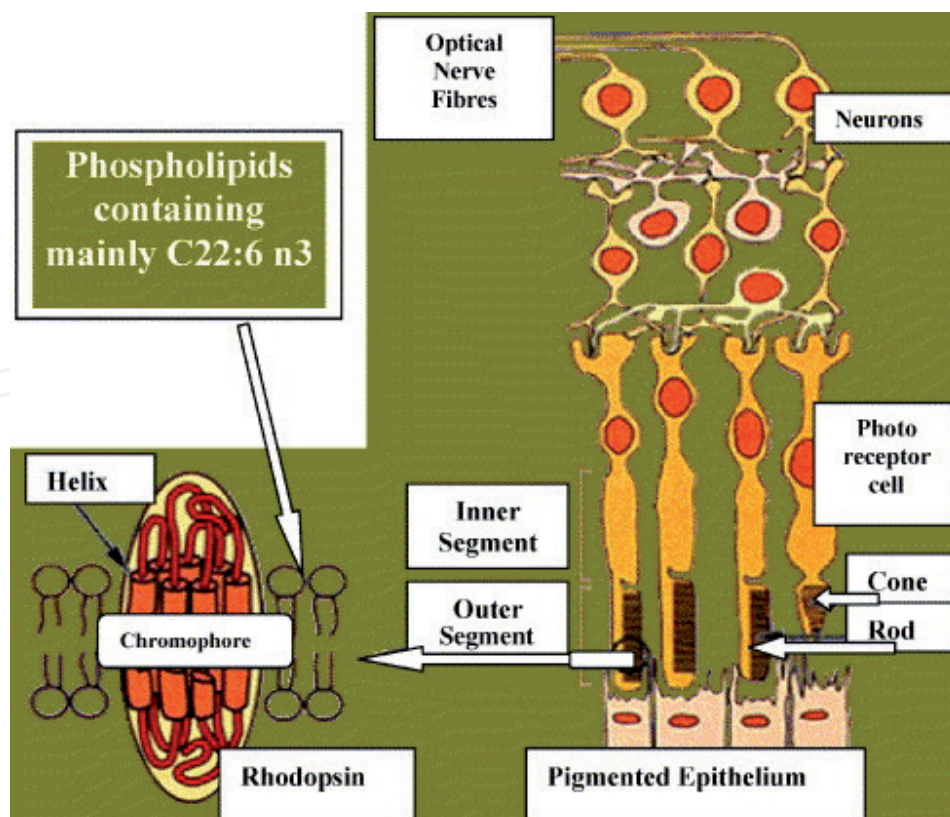


Figure 1.
Schematic diagram of rhodopsin in the membrane of the photoreceptor cell. Taken from: *The International Journal of Biochemistry & Cell Biology*. 2006; 38(9):1482-95.

lipid peroxidation may alter the arrangement of proteins in bilayers and by that it interferes with their physiological role on the membrane function. Here, we review several studies on the lipid peroxidation of membrane phospholipids in retina. Particular emphasis is placed on the molecular changes of very long chain polyunsaturated fatty acids associated with protein modifications during peroxidation of photoreceptor membranes **Figure 1**.

4. My participation in studies with photoreceptor

I started researching lipids almost six decades ago. My main interest was focused on the study of fatty acids. From 1990 up to now, our laboratory has been interested in the lipid peroxidation of biological membranes from various tissues and different species as well as liposomes prepared with phospholipids rich in PUFAs, as a consequence and considering that the retina is a tissue with enormous amounts of polyunsaturated fatty acids, our studies focused on the lipid peroxidation of photoreceptor membranes. In our first study, it was investigated if soluble-binding proteins for fatty acids (FABPs) present in neural retina show protection from in vitro lipoperoxidation of rod outer segment membranes (ROS). [1] Also we studied the effect of alpha-tocopherol, all-trans retinol, and retinyl palmitate on the nonenzymatic lipid peroxidation of rod outer segments [2].

Retina is highly susceptible to oxidative damage due to its high content of polyunsaturated fatty acids (PUFAs), mainly docosahexaenoic acid (22:6 n3). Lipid peroxidation process is thought to be involved in many physiological and pathological events. Many model membranes can be used to learn more about issues that cannot be studied in biological membranes. Sonicated liposomes (SL) and non-sonicated liposomes (NSL) prepared with lipids isolated from bovine retina and characterized

by dynamic light-scattering were submitted to lipid peroxidation, under air atmosphere at 22°C, with Fe(2+) or Fe(3+) as initiator, in different aqueous media. We verified that peroxidation of liposomes made of retinal lipids is affected not only by type of initiator but also by aqueous media. This model constitutes a useful system to study formation of lipid peroxidation intermediaries and products in an aqueous environment [3]. Furthermore, using rod outer segments and/or liposomes made of retinal lipids, we have analyzed the effect of alpha-tocopherol, all-trans retinol, and retinyl palmitate on the nonenzymatic lipid peroxidation of rod outer segments [2]; the selective inhibition of the nonenzymatic lipid peroxidation of phosphatidylserine in rod outer segments by alpha-tocopherol [4]. We have studied also how retinal fatty acid binding protein reduces lipid peroxidation stimulated by long chain fatty acid hydroperoxides on rod outer segments [5], the protective effect of indoleamines on in vitro ascorbate-Fe²⁺-dependent lipid peroxidation of rod outer segment membranes of bovine retina [6], and lipid-protein modifications during ascorbate-Fe²⁺ peroxidation of photoreceptor membranes—protective effect of melatonin [7]. In addition, we have determined that melatonin and structural analogues do not possess antioxidant properties on Fe (2+)-initiated peroxidation of sonicated liposomes made of retinal lipids [8]; for reviews, see [9, 10].

5. General remarks, conclusions, and perspectives

It has been attractive to follow the field of photoreceptor cell damage research during almost three decades. Quantitative proteomics and lipidomics analysis are now accessible for measurement of the main components of the photoreceptor cell. From my experience, it is impossible to predict which aspects of photoreceptor cell damage research will dominate in the future.

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