Review

Analysis the effect of plasmalogens on biofilm homeostasis

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Abstract

Plasmalogens are a class of membrane glycerophospholipids with unique properties. They contain a vinyl-ether linked alkyl chain at the sn-1 position of the glycerol backbone and, typically, a polyunsaturated fatty acyl chain at the sn-2 position. The chemical structure gives it its unique properties. These lipids were widely thought to be involved in the membrane bilayer formation and anti-oxidant function. However, extensive studies revealed that Pls are a reservoir for second messengers, and alos be involved in membrane fusion, ion transport, an cholesterol efflux. A lot of researches have revealed plasmalogen deficiencies associated with more common disorders and allow us to tease out additional functions about plasmalogens. In this review, we present current limited research reports of plasmalogen biological function.

Keyword

Plasmalogens, Biological function, biomembranes, oxidation, biosynthesis, immune

Abbreviations

Pls, plasmalogens;
GPL, glycerophospholipid;
PUFA, polyunsaturated-fatty-acyl;
DHA, docosahexaenoic-acid;
AA, arachidonic-acid;
PE, phosphatidylethanolamine;
PC, phosphatidylcholine;
POPC, palmitoyl-oleyl-phosphatidylcholine;
PLA2, phospholipase A2;
ROS,reactive oxygen species;
SQLE, squalene monooxygenase;

Introduction:

The plasmalogens are a class of glycerophospholipids， and the sn-1 and sn-2 positions of the glycerol main chain contain ethylene ether and ester bonds, respectively, in the glycerol backbone.[1] The head group of Pls is mainly of two kinds, choline and ethanolamine, but the other head group is also present found in the human retina, such as serine-pls. Besides their enrichment in cell membrane, Pls are found to be secreted from the cells including glial and neurons.[2] Pls are not only structural membrane components and a reservoir for second messengers, but may also be involved in membrane fusion, ion transport, and cholesterol efflux. The enol ether double bond at the sn-1

position makes Pls more susceptible to oxidative stress than the corresponding ester-bonded glycerophospholipids. Therefore the Plsmay also act as antioxidants, thus protecting cells from oxidative stress.[3] The pathophysiological roles and their possible metabolic pathways are not fully understood since they present unique structural attributes for the different tissue types.[1] In this review， we present the current limited knowledge of the biological function of plasmalogens.

1. General structure and chemical properties

Plasmalogens with a choline or ethanolamine (polar) head group at the sn-3 position of the glycerol backbone predominate in the majority of biological membranes. More obvious diversity is coming from the apolar residues at the sn-1 and sn-2 positions. Ether GPL species differ from the more common diacyl GPL in having a fatty alcohol or aldehyde bound at the sn-1 position, rather than a fatty acyl chain. The related fatty alcohols are normally restricted to saturated C16 (C16:0), or mono-unsaturated (C18:1) chains and are linked by an 1-O-alkyl ether bond, also termed a plasmanyl GPL, or contain a vinyl ether, or 1-O-(1Z-alkenyl) bond, termed a plasmenyl GPL or plasmalogen. At the sn-2 position, plasmalogens are often enriched in PUFA residues, specifically docosahexaenoic, C22:6 ω−3, or arachidonic acid, C20:4 ω−6.[4] Usually at low levels of these metabolites have nutritional effects, but at high concentrations they are cytotoxic and may be involved in allergic response, inflammation, and trauma.[3]

2. Biological roles attributed to plasmalogens

2.1. Membrane components

Plasmalogens are an important component of cell membranes and influence membrane dynamics.[5] They are mainly distributed in the "lipid raft" structure of biofilms, and are involved in cell fusion, ion transport and cholesterol transport.[6] The "lipid raft" microdomains are lateral membrane domains, enriched in cholesterol and sphingomyelin, and form a ‘liquid ordered phase’ combining the higher order and melting temperatures of a solid with the higher translational mobility of a liquid. These domains contain proteins required for cell signaling, cell–cell interactions, and endocytosis. [7]

Recently Rog and Koivuniemi using molecular dynamics simulations to study a lipid membrane comprised of PE-plasmalogens. Results show that PE-plasmalogens form more compressed, thicker, and rigid lipid bilayers in comparison with the PE-diacyl and POPC membranes.[8] PE-plasmalogens also comprise a major lipid constituent in membranes and cells that undergo rapid membrane fusion such as synaptic vesicles.Vesicles having equimolar mixtures of PE and PC plasmalogens have been found to allow more rapid membrane fusion events than those containing equimolar mixtures of their diacyl analogues(i.e.PE and PC). [7]

2.2. Reservoir of polyunsaturated fatty acids

Since plasmalogens are enriched in AA and DHA, they may function as reservoirs for these biologically active lipid mediators, released by PLA2 hydrolysis.[7] Arachidonic acid serves as

a precursor for the synthesis of eicosanoids and metabolites of these eicosanoids such as thromboxane, prostaglandins, and leukotrienes which are essential for immune regulatory functions [9]. Docosahexaenoic acid is a precursor for the anti-inflammatory lipid mediators resolvins and protectins, which help to terminate acute inflammation in tissues by removal of chemokines and regulation of leukocyte infiltration.[5] DHA has also been suggested to play a role in vesicle formation during the release of neurotransmitters.[3]

2.3. Antioxidation

The characteristics of plasmalogens that make them potent anti-oxidants are: (1) the enhanced electron density of the vinyl ether bond at the sn-1 position that makes it susceptible to cleavage by ROS; (2) the position of the vinyl ether linkage, which is proposed to be in the hydrophilic domain of the membrane and hence accessible to ROS attack; and (3) the suggested slow propagation of the plasmalogen hemiacetal hydroperoxy radicals.[5]

In contrast to ester-bonded phospholipids, vinyl-ether bond present in plasmalogens contribute to oxidation/antioxidant activityas vinyl-ether bond preferentially decomposes during oxidation .[10] It has been proposed that plasmalogens could play a protective role against lipid peroxidation as a sacrificing/scavenger agent. In a study carried out by, oxidative stress was applied to brain phospholipids with and without the presence of plasmalogens in separate liposomal systems.[11] The results revealed that biomarkers for lipid peroxidation were significantly decreased in brain phospholipids with plasmalogens. Further, upon exposure to high oxidative conditions in normal cells, the plasmalogen levels were shown to decrease, suggesting a possible function as scavengers .[10]

2.4. Cholesterol biosynthesis

Plasmalogens have been found to regulate cholesterol metabolism by different mechanisms in several contexts. Having both plasmalogens and cholesterol enriched in the lipid rafts.[6] According to the study of Masanori Honsho et al show that elevation of the cellular plasmalogens can reduce cholesterol biosynthesis without Affecting the Isoprenylation of Proteins. Plasmalogen levels altered the expression of SQLE, Due in the composition of 2,3-epoxysqualene, which is required for cholesterol synthesis.[12]

2.5. The immune function

According to the report that cells deficient in membrane ethanolamine plasmalogen demonstrate a reduced capacity to phagocytize opsonized zymosan particles. Amelioration of plasmalogen deficiency in these cells by incubation with lysoplasmalogen results in a significant augmentation of the phagocytic capacity of the cells. In parallel with these increases, restoration of plasmalogen levels in the cells also increases the number and size of lipid rafts in the membrane, reduces membrane fluidity down to levels found in cells containing normal plasmalogen levels, and improves receptor-mediated signaling. [13]

Lipidomic analysis has shown a profound change in the plasmalogen composition during in

vitro differentiation of human monocytes to macrophages, suggesting a role of plasmalogens in preparing these cells for their phagocytic and inflammatory roles. Decreases in PE plasmalogens with polyunsaturated species and concurrent increases in monounsaturated species containing PE plasmalogens have been observed in macrophages compared to monocytes. These changes rendered monocyte derived macrophages more similar to mature granulocytes in their plasmalogen profile.[5] Furthermore, a recent study observed a reduction of PE plasmalogens in patients with systemic lupus erythematosus which a chronic inflammatory autoimmune disease.[14] While this was proposed to result from the elevated oxidative stress in this condition, it is also suggestive of the immunomodulatory functions of plasmalogens.[5]

3. Conclusion：

Plasmalogens, by virtue of their vinyl ether bond and enrichment in AA and DHA, play a critical role in cell membranes providing unique structural attributes, facilitating signaling processes, protecting membrane lipids from oxidation and regulate cholesterol metabolism and immune function.Although many useful studies have been conducted at the cellular level to investigate the function of acetalophosphatide, its pathophysiological and cellular biological mechanisms remain poorly understand and require further investigation.

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