Research Article

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Articular Cartilage: The Destruction of Bilayers and Deactivation of Phospholipid Molecules

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Abstract

To our knowleadge the coaugulation by interacton of β_2-Glycoprotein I (β_2-GP I) with the phospholipid membrane is required to verify this hypothesis. The open hockey stick-like conformation occurs when protonated amino acid functional group ($-NH_3^+$) β2-GP I is complexed to negatively charged phospholipids functional group ($-PO_4^-$) resulting in the destruction of bilayers and the deactivation of phospholipid molecules.

Keywords: Phospholipid; Deactivation of phospholipid; β_2-Glycoprotein I as deactivator

Introduction

Phospholipids (PLs) comprise an important class of biological molecules that play both structural and functional roles in the human body. Almost everywhere in the body, there are phospholipids, not only building the lipid bilayer of membranes but also in the Free State. The human body naturally produces phospholipids. Phospholipids support most functions of organs, such as cardiovascular health, nerve health, liver function, digestion and, most importantly, certain phospholipids might act as boundary lubricants [1].

A surface-active phospholipid (SAPL, phosphatidylcholines (over 40%) sphingomyelin (~30%) and phosphatidylethanolamines (~30%)) covers normal articular surfaces in a multi-bilayer structure [1-4]. The bilayers serve to integrate interfacial functions between surfaces and have been a subject of several inquiries due to their tribological features [5]. Surface-active phospholipids play a vital role in the joint tissue systems in a large part due to their amphoteric nature that allows for varied structural properties. This amphoteric nature of phospholipids allows them to self-assemble into a classic arrangement which represents the basics of all biological membranes. However, at sites of articular cartilage damage, the SAPL is absent, because a suitable substrate upon which this vital lipid layer can form does not exist [6-8].

Deterioration of cartilage surface

The mechanism of osteoarthritis (OA) is still not fully understood, but it has been established that this debilitating disease is often accompanied by a change in the synovial fluid composition, reduction in viscosity and deterioration of cartilage surface [5]. Well-defined outermost bilayers were clearly visible on healthy cartilage surface but OA may involve in the depletion of important joint molecules and SAPLs on the articular surface [7]. Further, evidence for SAPL lining depletion was demonstrated by the cartilage wettability contact angle change from 103 to 65 degrees [8]. This insight led to the hypothesis that the SAPL is deactivated in the pathologic state of OA and remains present in synovial fluid but in an inactive state (see Fig. 3).

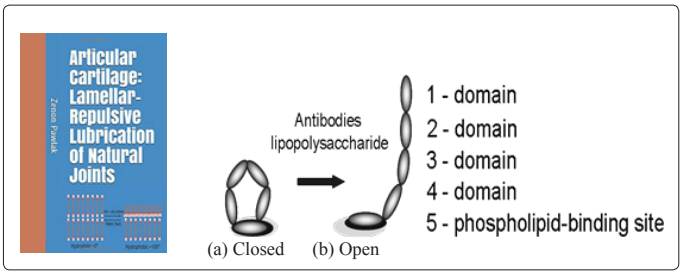

Figure 1: Book cover "Articular cartilage: Lamellar-repulsive lubrication of natural joints" and conversion of β2-Glycoprotein I of the (a) circular conformation into (b) an open hockey-stick-like conformation, each molecule has five domains (1-5) [4]. Note that the antibody-binding site is accessible to the autoantibodies in the (b) open conformation.

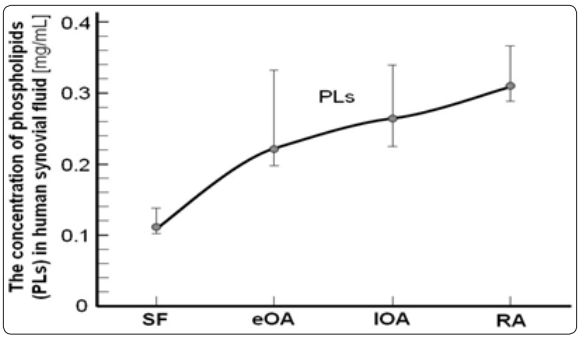

Figure 2: Influence of cartilage damage on concentration of phospholipid (PLs) in synovial fluid from (PLs) controls samples, (PLs) acquired from patients with early (eOA), (PLs) from patients with late (lOA) and (PLs) from patients with rheumatoid arthritis (RA).

Destruction of bilayers and deactivation of phospholipid molecules

The pathological synovial fluid contains three times more phospholipids (PL) (see Figure 2) [6, 7] but the cartilage structure changes and its ability to lubricate, is remarkably poor. During normal functioning, the SAPL serves as a sacrificial perturbation bilayer, whereby it can improve by self-assembly mechanisms. Additionally, phospholipid molecules lose their surface active properties to form vesicles, lamellar phases, and bilayers spontaneously. The active role played by PLs in OA and RA SF as compared with that of control SF and their functions in cartilage boundary lubrication remains still poorly understood.

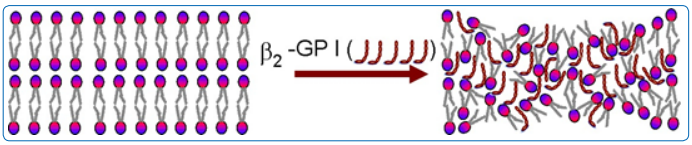

Figure 3: The open hockey stick-like conformation when β2-GP I is complexed to negatively charged phospholipids (-PO4-) resulting in the destruction of bilayers and deactivation of phospholipid molecules.

Cartilage destruction in most rheumatic diseases and osteoarthritis has generally been accepted as a mechanism of deactivation of phospholipid bilayers [11]. An acid-base interaction occurs between protonated amino acid group ($-NH_3^+$) of β_2-Glycoprotein I and the phospholipid ($-PO_4^-$) group: ($-NH_3^+$) + ($-PO_4^-$) → ($-NH_3^+ PO_4^-$) that is strong enough to deactivate the PLs bilayer surface.

β2-Glycoprotein I (β2-GPI) transformation

β_2-Glycoprotein I (β_2-GPI) is a protein that circulates in blood at variable levels (50–500 μg mL^{-1} with a molecular weight of 50 kDa. β_2-Glycoprotein I (β_2-GP I) can exist in (a) closed conformation and (b) the open hockey stick-like conformation. β_2-GP I in its hockey stick-like conformation is a strongly adhesive protein and binds to different receptors on cells. Binding of β_2-GP I to anionic charged phospholipid ($-PO_4^-$) groups at pH ~ 7.4, results in a change in conformation and exposure of the epitope for the autoantibodies [10-14].

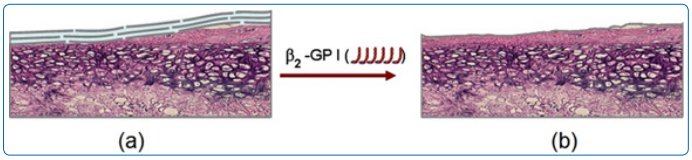

Figure 4: Cartilage surface deterioration with deactivation of surface-active phospholipids bilayers by the open hockey stick-like conformation β_2-Glycoprotein I, β_2-GP I.

Softening of the cartilage is the first phase of cartilage deterioration [9]. The classic morphological changes of osteoarthritic articular cartilage begin with fibrillation and a local surface disorganization involving splitting of the superficial layers of the cartilage, Fig.4. The early splitting is tangential with the cartilage surface, following the axes of' the predominant collagen bundles. Continued deterioration of articular cartilage leads to an exposure of the subchondral bone and more generalized synovial change.

Conclusion

To understand the processes leading to cartilage failure, it is important to look at the cellular processes and biochemical structure of the normal cartilage.

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