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Mimicking the interface between mammalian plasma membrane and extracellular matrix: chondroitin sulfate-decorated supported lipid bilayers

Many vital processes, such as the interaction with pathogens or drugs, take place at the interface between the plasma membrane (PM) and the extracellular-matrix (ECM). The zwitterionic phosphatidylcholine (PC) and the negatively charged phosphatidylserine (PS) are among the most abundant lipids in the PM [1]. The ECM is made of flexible carbohydrates and proteins and is responsible for the cell organisation within tissues. Chondroitin sulphates (CSs) are present in the ECM of animal cells and are composed of a disaccharide unit (i.e. glucuronic acid and galactosamine), which can be sulfonated at different positions. Mono-sulfonation at position 4 or 6 is the most common, resulting in CS-A and CS-C species, respectively. Typically, CS-A is the most abundant form in human cells, however CS-C is overexpressed in cancer cells [2]. There is few information on the structural arrangement of CS molecules onto the PM surface and how this is affected by the status of the cell, e.g. healthy cells vs cancer cells vs inflammation response. This project is aimed at developing supported lipid bilayers (SLB) functionalised with CS molecules to investigate the impact of the bilayer lipid composition on the structural arrangement of CS. To produce said bilayers, we optimised a recently reported protocol [3], which consists in adding a modified phospholipid that bears an ammino group exposed to the bulk solvent (18:1 Dodecylamine PE, DOPE-NH₂) to the SLB to form an amide bond with CS-C. We investigated the CS-SLBs interaction for SLBs composed of either pure PC lipids or a mixture of PC and the negatively charged PS. These systems let us investigate the response of the CS layer structure to the exposure of PS lipids on the PM surface, which occurs in case of inflammation. The produced samples were characterized with quartz crystal microbalance with dissipation monitoring (QCM-D) and neutron reflectometry (NR).

References

- [1] - Harayama, T. et al., Nat Rev Mol Cell Biol, 19, 281-296, 2018.
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- [3] - Altgärde, N. et al., JCIS, 390 (1), 258-266, 2013

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Biological membranes and interfaces

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