LIPID MEMBRANE DESTABILIZATION INDUCED BY AMYLOID-BETA PEPTIDE IN THE SYSTEMS MIMICKING PRECLINICAL ALZHEIMER'S DISEASE

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The amyloid-beta (Aβ) peptide is considered a key factor in Alzheimer's disease (AD) ever since the discovery of the disease. The understanding of its damaging influence has however shifted recently from large fibrils observed in the inter-cellular environment to the small oligomers interacting with a cell membrane.

By means of small angle neutron scattering (SANS), we have observed for the first time a spontaneous reformation of extruded unilamellar vesicles (EULVs) to discoidal bicelle-like structures (BLSs) and small unilamellar vesicles (SULVs). These changes in the membrane self-organization happen during the thermodynamic phase transitions of lipids and only in the presence of Aβ [1]. The complementary experimental data and molecular dynamics (MD) simulations results revealed further the structural arrangements of the observed morphologies. We show by using solid-state ^{31}P nuclear magnetic resonance (NMR) spectroscopy that lipids are found located not only in the flat bilayered part of BLS but also around its perimeter, which is corroborated by the results of coarse-grained (CG) MD simulations. Peptides, on the other hand, appear to mix randomly with lipids in ULVs, while colocalizing with the lipids at the perimeter of BLS and aiding thus a formation of stable bicelle-like object consisting of a single type of lipids and Aβ peptides [2]. Importantly, despite Aβ peptides affecting the elasto-mechanical properties of membrane itself, the observed morphological transformations caused by their disruptive effect were not prevented by the additional presence of cholesterol or melatonin [3], nor by the presence of charged lipids in the membrane [4] or calcium ions in solution [5]. The scattering methods used in these studies provided instrumental information on a level of supramolecular assemblies, while spectrometry allowed obtaining information on the molecular level. Finally, molecular dynamics simulations provided details unachievable by experimental approaches, though the validation role of the latter cannot be undermined. Altogether, the recent advances in research results prove these complementary approaches the most appropriate for tackling the complex issues of biomembrane interactions [6].

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