Bilayers at the ILL

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Role of membrane sphingolipids in the interaction with amyloid beta-peptide

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The early impairments appearing in Alzheimer's disease are related to neuronal membrane damage. Both,aberrant Aβ species and specific membrane components play a role in promoting aggregation, deposition and signal dysfunction. Ganglioside GM1, present with cholesterol and sphingomyelin in lipid rafts, seems to be able to initiate Aβ aggregation on membrane [1]. In general, sphingolipids have a crucial role both in the physico-chemical properties of the membrane matrix and in the signaling paths. Based on our previous studies highlighting the fundamental role of GM1 embedded in large unilamellar vesicles (LUV) in the interaction with Aβ, the dependence of this interaction on GM1 fraction was investigated by SAXS at 20℃ [2,3]. LUV containing different amount of ganglioside in the presence of sphingomyelin were extruded and their structure as a function of the matrix composition, per se and with the addition of the Aβ-peptide, was monitored using SAXS. The analysis of the SAXS spectra by a multi-gaussian model evidences structural differences in the bilayer electron density among the liposomes of different composition. Results show the expected asymmetry due both to the natural membrane curvature and to the different matrices. While the presence of sphingomyelin as well as ceramide, without GM1, does not prompt significant interaction of the bilayers with the Aβ-peptide, results confirm the fundamental role of the ganglioside for such interaction. Moreover, the analysis highlights the concentration-dependent effect of GM1 in the interaction with the Aβ-peptide. However, the co-presence of sphingomyelin, probably due to the higher rigidity of the matrix, has an inhibiting effect on GM1- Aβ interaction, increasing the concentration of GM1 needed to appreciate a perturbation on the bilayer, which propagates down to the interior of the membrane.

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