GANGLIOSIDES- COULD BE A NEW THERAPEUTIC AGENT AGAINST ALZHEIMER’S DISEASE?

H. Ahyayauch¹, A. Alonso¹, M. Masserini², F.M. Goñi¹

¹Biochemistry, Unidad de Biofísica (Centro Mixto CSIC-UPV/EHU) and Departamento de Bioquímica, Universidad del Pais Vasco, Bilbao, Spain, ²Department of Experimental Medicine, University of Milano Bicocca, Monza, Italy

GM1 and other gangliosides are present in highly organized and functionally essential microdomains of neuronal membranes, together with cholesterol and phospholipids. The mechanisms of the neuroprotective effect of GM1 and related gangliosides, however, are still obscure. These gangliosides have been shown to facilitate repair of neuronal tissue after mechanical, biochemical or toxic injuries. Continuous intraventricular infusion of GM1 has recently been shown to have a significant beneficial effect in Alzheimer disease of early onset. In our work, isothermal titration calorimetry (ITC) and Langmuir monolayer experiments have been performed to investigate the interaction of Aβ1-42 with membranes containing 5% gangliosides (GM1, GT1b and a total ganglioside extract). The experiments have been carried out both with toxic (aggregate) and non-toxic (monomer) Aβ. Our ITC results indicate that the peptide interacts significantly with membranes containing gangliosides with binding affinities ranging from $10^{-4}$ to $10^{-5}$ M. No dependence on the type of the ganglioside sugar moiety has been observed. The same results were obtained in experiments with lipid monolayers extended over air-water interfaces. The Aβ insertion is higher in bilayers containing gangliosides. We conclude that ganglioside-based vesicles could be a good and suitable system to develop novel therapeutic and diagnostic tools for Alzheimer disease.

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