Experimental report

17/05/2016

Proposal: 8-02-733 **Council:** 10/2014

Title: Interaction of mutated A-beta peptides with single 'raft' model membrane

Research area: Soft condensed matter

This proposal is a continuation of 8-02-652

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Samples: AB peptides, phospholipids, cholesterol, glycolipids

Instrument	Requested days	Allocated days	From	To
FIGARO	3	3	22/06/2015	25/06/2015
D17	3	0		

Abstract:

A-beta oligomers were identified as the main cause of synaptic dysfunction leading to alterations in both neuronal activity and cognitive function in Alzheimer's Disease. A-beta oligomers, are "membrane-active" species that can promote membrane punctuation and increase its permeability. A putative site on the plasma membrane for amyloid-membrane interaction are the lipid "raft", enriched in cholesterol and sphingolipids.
We identified a more fibrillogenic analogue of A-beta; carrying Ala-to-Val substitution, that promotes a peculiar pathway of oligomerization, forming a connected system similar to a polymer network. The heterotypic interaction between the mutated and wild-type A-beta affects nucleation-dependent A-beta polymerization, preventing amyloid fibril formation.
Aim of this proposal is the study of the structural details of the interaction between the oligomeric species of A-beta amyloid and a raft-mimicking model membrane in the case of the A2V mutant A-beta peptide. Moreover we plan to investigate in detail if the mutated + wild type A-beta mixture displays a different propensity to interact with model membranes.

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We found that wild type and mutated peptide interact differently with different membranes, and that interaction depends in a different manner from the presence or not of GM1 ganglioside inside the approached membrane. As an example we report the spectra referring to the interaction of the two peptides with floating DPPC membranes.

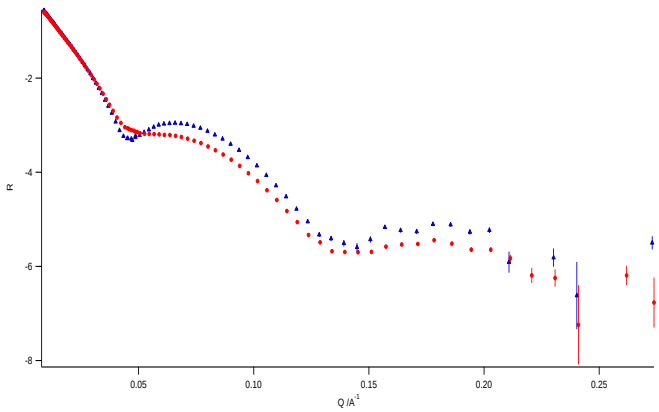

Fig 1: Neutron reflectivity spectra of a double membrane system (dDSPC supporting, dDPPC floating) before (blue) and after(red) the interaction with mutated A2V A-beta1-40 peptide. T=22°C.

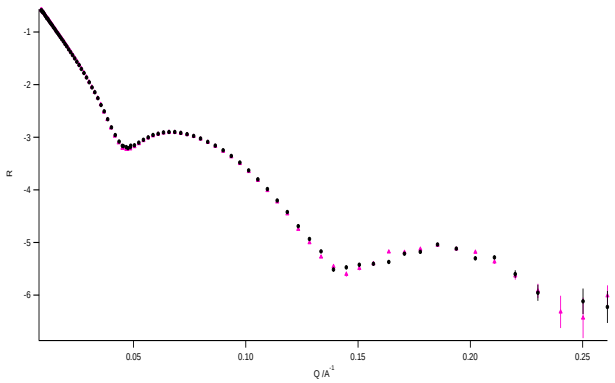

Fig 2: Neutron reflectivity spectra of a double membrane system (dDSPC supporting, dDPPC floating) before (black) and after(pink) the interaction with A-beta1-40 peptide. T=22°C.