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(G*) (POS-52) Atomic Force Microscopy and Molecular Dynamics to Study the Structure of Nanodomains of Model Lipid Membranes in Relation to Alzheimer's Disease.

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Alzheimer's disease (AD) is a progressive neurodegenerative disorder that causes loss of memory. In AD neuronal cell dysfunction and death are caused by amyloid aggregates which are toxic to the cellular membrane and cause membrane damage. The cellular membrane is a complex non-homogeneous bilayer and plays an important role in the amyloid toxicity. We previously showed that model lipid membranes mimicking healthy neurons and AD are different in their interactions with amyloid [1]. In this work, we studied the structure of membrane nano-domains in model membranes composed of DPPC, POPC, cholesterol, SM and GM1 mimicking healthy neuronal membrane and that at an early stage of AD using Atomic force microscopy (AFM) and Molecular Dynamics (MD) simulations. AFM was used to image the morphology of the membrane nanoscale domains and MD provided details on the domain structure and lipid composition that results in the formation of domains in each model membrane. We found that GM1 lipids preferably cluster with GM1, DPPC and cholesterol, while SM does not show a great preference for clustering. These findings help to understand how changes in lipid composition may alter the domain structure in model lipid membranes, and serve to understand their role in amyloid toxicity in AD.

Reference:

[1] Drolle, E., A. Negoda, K. Hammond, E. Pavlov, and Z. Leonenko, "Changes in lipid membranes may trigger amyloid toxicity in Alzheimer's disease", PLoS ONE, vol. 12, issue 8, pp. e0182194, 08/2017.

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