The role of lipid surfaces in molecular mechanism of Alzheimer's disease.

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Abstract

Alzheimer's disease (AD) is a neurodegenerative disease characterized by dementia and memory loss for which no cure or prevention is available. Amyloid toxicity is a result of the non-specific interaction of toxic amyloid oligomers with the surface of plasma membrane. We studied amyloid aggregation and interaction of amyloid beta (1-42) peptide with lipid model membranes using atomic force microscopy (AFM), Kelvin probe force microscopy (KPFM) and surface Plasmon resonance (SPR). Using AFM-based atomic force spectroscopy (AFS) we measured the binging forces between two single amyloid peptide molecules. Using AFM imaging we showed that amyloid binding and aggregation are affected by charge and polarity of the surfaces (we studied chemically modified inorganic surfaces, phospholipid monolayers and bilayers (membranes)). Furthermore, we demonstrated that lipid membrane surfaces play an active role in amyloid binding and toxicity and thus in molecular mechanism of AD: changes in membrane composition and properties increase amyloid binding to the membrane and membrane damage. Effect of lipid composition, the presence of cholesterol and melatonin are discussed. We discovered that membrane cholesterol creates nanoscale electrostatic domains which induce preferential binding of amyloid peptide, while membrane melatonin reduces amyloid-membrane interactions, protecting the membrane from amyloid attack. These findings contribute to better understanding molecular mechanisms of Alzheimer's disease and aid to the developments of novel strategies for cure and prevention of AD.

References

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