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## Biophysics approaches to study molecular mechanism of Alzheimer's disease.

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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 plasma membrane.

We studied amyloid aggregation and interaction of amyloid beta (1-42) peptide with lipid membrane using atomic force microscopy (AFM), Kelvin probe force microscopy and surface Plasmon resonance (SPR). Using AFM-based atomic force spectroscopy (AFS) we measured the binding forces between two single amyloid peptide molecules. Using AFM imaging we showed that oligomer and fibril formation is affected by surfaces, presence of metals and inhibitors. We demonstrated that lipid membrane plays an active role in amyloid binding and toxicity: changes in membrane composition and properties increase amyloid binding and toxicity. 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. Using AFS we that novel pseudo-peptide inhibitors effectively prevent amyloid-amyloid binding on a single molecule level, to prevent amyloid toxicity. These findings contribute to better understanding of the 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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