Canadian Association of Physicists
Association canadienne des physiciens et physiciennes

Contribution ID: **2252** Type: **Oral (Non-Student) / Orale (non-étudiant(e))**

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

Monday 11 June 2018 12:00 (15 minutes)

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 binging 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:

1. E.Drolle, K.Hammond, A.Negoda, E.Pavlov, Z.Leonenko, Changes in lipid membranes may trigger amyloid toxicity in Alzheimer's disease. PLOS ONE, 2017, 12(8), e0182194.
2. B.Mehrazma, M.Robinson, S.K.A.Opare, A.Petoyan, J.Lou, F.T.Hane, A.Rauk, Z.Leonenko. Pseudo-peptide amyloid-β blocking inhibitors: molecular dynamics and single molecule force spectroscopy study. Biochimica et Biophysica Acta (BBA)-Proteins and Proteomics 1865 (11), 1707-1718.
3. M.Robinson, B.Y.Lee, Z.Leonenko, Drugs and Drug Delivery Systems Targeting Amyloid-β in Alzheimer' s Disease. AIMS Molecular Science, 2015, 2(3): 332-358.
4. E.Drolle, R.M.Gaikwad, Z.Leonenko, Nanoscale electrostatic domains in cholesterol-laden lipid membranes create a target for amyloid binding. Biophysical Journal, 2012, 103(4), L27-L29.
5. F.Hane, E.Drolle, R.Gaikwad, E.Faught, Z.Leonenko. 2011. Amyloid-β aggregation on model lipid membranes: an atomic force microscopy study. J. Alzheimer's Dis. 26: 485-494.
6. E.Drolle, F.Hane, B.Lee, Z.Leonenko, Atomic force microscopy to study molecular mechanisms of amyloid fibril formation and toxicity in Alzheimer's disease. J. of Drug Metabolism Reviews, 2014, 46(2): 207-223.
7. E.Drolle, N. Kučerka, M.I.Hoopes, Y.Choi, J. Katsaras, M. Karttunen, Z.Leonenko, Effect of melatonin and cholesterol on the structure of DOPC and DPPC membranes, Biochimica & Biophysica Acta: Biomembranes, 2013, 1828 (9): 2247-2254.
8. F.T.Hane, S.J.Attwood, Z.Leonenko. Comparison of three competing dynamic force spectroscopy models to study binding forces of Amyloid-β 1-42. Soft Matter, 2014, 10(1): 206-213.
9. F.T. Hane, B.Y. Lee, A.Petoyan, A.Rauk, Z.Leonenko, Testing Synthetic Amyloid-β Aggregation Inhibitor Using Single Molecule Atomic Force Spectroscopy. Journal of Biosensors and Bioelectronics, 2014, 54, 492–498.

Authors: Dr DROLLE, Elizabeth (University of Waterloo); Mr ROBINSON, Morgan (University of Waterloo); Prof. LEONENKO, Zoya (University of Waterloo)

Presenter: Prof. LEONENKO, Zoya (University of Waterloo)

Session Classification: M1-6 Biophysics, microscopy and diseases (DPMB) / Biophysique, microscopie et maladies (DPMB)

Track Classification: Physics in Medicine and Biology / Physique en médecine et en biologie (DPMB-DPMB)