

Joint iNANO-DANDRITE Workshop

with visitors

Dr Celiné Galvagnion and Prof. Alexander K. Buell

Tuesday 29th October 2019 at 14:00 - 16:00 Auditorium 1170-347, Ole Worms Allé, 3, 8000 Aarhus C
following Working Pizza Dinner from 16:00 to 18:00 in the Meeting Room 340

Amyloid protein – membrane interactions: the influence of the lipid composition on the kinetics of protein aggregation

Dr Céline Galvagnion, Department of Drug Design and Pharmacology, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen

The conversion of soluble proteins into toxic oligomers and fibrils is the hallmark of a range of diseases including Alzheimer's and Parkinson's Diseases (AD and PD). Each neurological disorder of this type is characterised by the loss of function and/or the gain of toxicity of a given protein: the amyloid- β peptide (A β 42) and tau for AD and α -synuclein for PD. In addition, these proteins show strong interactions with membranes and these protein-membrane interactions have been shown to significantly modulate the kinetics of amyloid formation. Finally, changes in the levels of specific lipids such as cholesterol, sphingolipids and glycolipids, have been associated to several diseases, including PD and AD. In this presentation, I will discuss our latest findings on the influence of membrane composition on the kinetics of amyloid formation of α -synuclein and A β 42. In addition, I will describe how intrinsic (disease associated mutations and truncations) and extrinsic (homologous proteins and small molecules) factors can modulate the lipid-induced aggregation of α -synuclein. Finally, I will discuss our latest results on the characterisation of the dynamics and thermotropic properties of lipid molecules within α -synuclein proto-fibrils. These findings contribute to a better understanding of the, currently undefined, role of lipids in the initiation and/or progression of protein aggregation in the context of neurodegenerative diseases.

Mechanistic insight into the growth and autocatalytic amplification of amyloid fibrils

Prof. Alexander K. Buell, Department of Biotechnology and Biomedicine, DTU

Amyloid fibrils are filamentous assemblies of proteins that are associated with biological function and disease. In our research, we try and dissect the complex overall mechanism of amyloid fibril formation into individual molecular steps and we try to determine the kinetics and thermodynamics of these steps. In recent years, it has emerged that some amyloid fibrils are able to efficiently self-replicate through secondary nucleation, i.e. the fibrils catalyse their own formation. In this seminar I will present some progress on the mechanistic understanding of secondary nucleation of both the amyloid beta peptide and alpha-synuclein. Furthermore, I will present recent results on the efficient inhibition of secondary nucleation of alpha-synuclein amyloid fibrils. I will also briefly mention our efforts to develop quantitative methods to assess the thermodynamic stability of amyloid fibrils. The latter property is probably crucial to the resilience of these structures in a biological context, but very little is known about the molecular origin of this stability. The accurate measurements of aggregate stability can also be used to obtain an unprecedented level of insight into the growth of amyloid fibrils, i.e. the addition of a protein monomer onto the end of a fibril.

To join the workshop and the dinner, please inform Prof. Poul Henning Jensen at 15:00 **Tuesday 29th October 2019**.

