

MEMBRANES & MOLECULES

Mardi 7 Novembre 2017, 11h30

Céline Galvagnion

German Center for Neurodegenerative Diseases (DZNE) Sigmund-Freud-Str. 27, 53127, Bonn, Germany

Amyloid Protein – Membrane Interactions: The influence of the Lipid composition on the kinetics of Aggregation

Abstract

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 and tau proteins for AD and alpha-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 alpha-synuclein and amyloid- β -peptide. In addition, I will describe how intrinsic (disease associated mutations) and extrinsic (homologous proteins and small molecules) factors can modulate the lipid-induced aggregation of alpha-synuclein. 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.

References:

1. Galvagnion C, Buell AK, Meisl G, Michaels TC, Vendruscolo M, Knowles TP, Dobson CM. Lipid vesicles trigger α -synuclein aggregation by stimulating primary nucleation. *Nat Chem Biol*. 2015 Mar;11(3):229-34.
2. Galvagnion C, Brown JW, Ouberai MM, Flagmeier P, Vendruscolo M, Buell AK, Sparr E, Dobson CM. Chemical properties of lipids strongly affect the kinetics of the membrane-induced aggregation of α -synuclein. *Proc Natl Acad Sci U S A*. 2016 Jun 28;113(26):7065-70.
3. Flagmeier P, Meisl G, Vendruscolo M, Knowles TP, Dobson CM, Buell AK, Galvagnion C. Mutations associated with familial Parkinson's disease alter the initiation and amplification steps of α -synuclein aggregation. *Proc Natl Acad Sci U S A*. 2016 Sep 13;113(37):10328-33.
4. Brown JW, Buell AK, Michaels TC, Meisl G, Carozza J, Flagmeier P, Vendruscolo M, Knowles TP, Dobson CM, Galvagnion C. β -Synuclein suppresses both the initiation and amplification steps of α -synuclein aggregation via competitive binding to surfaces. *Sci Rep*. 2016 Nov 3;6:36010.
5. Perni M, Galvagnion C, Maltsev A, Meisl G, Müller MB, Challa PK, Kirkegaard JB, Flagmeier P, Cohen SI, Cascella R, Chen SW, Limboker R, Sormanni P, Heller GT, Aprile FA, Cremades N, Cecchi C, Chiti F, Nollen EA, Knowles TP, Vendruscolo M, Bax A, Zaslhoff M, Dobson CM. A natural product inhibits the initiation of α -synuclein aggregation and suppresses its toxicity. *Proc Natl Acad Sci U S A*. 2017 Feb 7;114(6):E1009-E1017.

Institut de Biologie Physico-Chimique
13, rue Pierre et Marie Curie
75005 PARIS
Invitée par Laurent Catoire

