Membrane Biophysics Spring Lectures

May 7 and 15, 2019

Dear Colleague,

we are excited to host two world leading personalities in membrane biophysics research:

- Katsumi Matsuzaki *(Kyoto University, Japan)*
  May 7, 2019, 4 pm
  GM1 CLUSTER AS A PLATFORM OF FORMATION OF TOXIC AMYLOID FIBRILS BY ALZHEIMER'S ABETA
  HS 44.22 (Humboldtstr. 48)

and

- Gerald Feigenson *(Cornell University, Ithaca, NY)*
  May 15, 2019, 11 am
  LINE TENSION AT THE MEMBRANE RAFT INTERFACE
  Workstation Room (Humboldtstr. 50/ 3rd floor, room# 004503)

In addition to attending their presentations we would like to encourage you to meet with both of them in person and discus your research. To do so please sign up using the following links

→ Doodle Link for Matsuzaki

→ Doodle Link for Feigenson

Abstracts

GM1 CLUSTER AS A PLATFORM OF FORMATION OF TOXIC AMYLOID FIBRILS BY ALZHEIMER'S ABETA

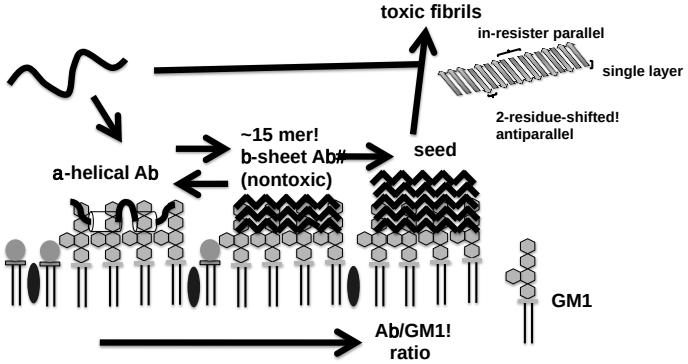
Katsumi Matsuzaki

Graduate School of Pharmaceutical Sciences, Kyoto University, Kyoto, Japan

Abstract:

It is widely accepted that Abeta composed of typically 40 and 42 amino acid residues is central to the development of Alzheimer's disease. However, the mechanisms by which Abeta self-aggregates are not well understood. Accumulating evidence suggests that membranes play an important role in this

process. Yanagisawa et al. discovered a specific form of Abeta bound to GM1 ganglioside from the brain of early AD patients, and proposed that it acts as a template for the formation of Abeta aggregates [1]. We have studied interactions of Abeta with GM1-containing lipid bilayers as well as neuronal membranes using various physicochemical techniques. Abeta specifically binds to cholesterol-induced clusters of GM1, forming an alpha-helix rich conformation at lower Abeta-to-GM1 ratios. At higher ratios, it is converted to a beta-sheet-rich oligomer composed of ~15 Abeta molecules. A further increase in Abeta density leads to the formation of toxic amyloid fibrils (Fig. 1) [2]. In contrast to aggregation in aqueous phase, oligomers were nontoxic, but amyloid fibrils induced apoptosis [3]. The toxic fibrils were found to possess a novel unique 'tape-like' structure composed of a single layer of mixted in-resister parallel and 2-residue-shifted antiparallel beta-sheet structures [4].



Figur 1: Schematic representation of GM1 cluster-mediated amyloidogenesis by Abeta

[1] Yanagisawa, K. et al. (1995) *Nat. Med.,* **1**, 1062–1066.

[2] Matsuzaki, K. (2014) *Acc. Chem. Res.*, **47**, 2397–2404.

[3] Itoh, N. et al. (2018) *ChemBioChem*, **19**, 430-433.

[4] Okada, Y. et al. (2019) *ACS Chem. Neurosci.*,**10**, 563–572.

LINE TENSION AT THE MEMBRANE RAFT INTERFACE

Gerald W. Feigenson

Department of Molecular Biology and Genetics, Cornell University, Ithaca, NY

Abstract:

In the plasma membrane of mammalian cells, lipid composition and temperature are favorable for the separation of the lipid bilayer into two distinct phases. One phase is less ordered, the other, sometimes termed a membrane raft, is more ordered. The properties of these liquid-disordered (Ld) and liquid-ordered (Lo) phases depend on their lipid composition, and determine the bending energy and the tendencies of other lipids, and membrane proteins, to partition between these Ld and Lo phase domains. However, the size of these phase domains seems to depend entirely on the energy where Ld and Lo phases meet, termed the "line tension", which is the 2-dimensional analogue of surface tension. The size of these phase domains would control e.g. the number of proteins that could fit into the domain, and perhaps the influence of the domains across the bilayer. How a cell might control this domain size must depend on the molecular-level origin of the line tension. Here, we propose a model for line tension that is based entirely on the lipid-lipid pairwise interaction energies.