

Quantitative analysis of amyloid nucleation from droplets

Applicable to the screening of amyloid nucleation inhibitor

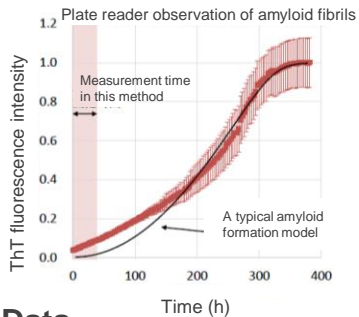
Overview

Recently, amyloid fibrils, which relate to various diseases (Alzheimer's diseases, ALS, etc.), is considered to generate in liquid-like droplets of amyloid precursor proteins (APP).

The quantitative and high-throughput analysis of the amyloid nucleation from the droplets is important for finding inhibitors of amyloid formation. However, there was only qualitative discussion on nucleation process from droplets so far.

This invention provides the method of calculating the quantitative nucleation rate J in a short time by a fluorescence dye and statistical image analysis. The thermodynamic parameter J makes it possible to evaluate amyloid nucleation inhibition capacity of drug candidates regardless of the experimental system, so, this indicator is superior to conventional indicator (lag time).

Advantage of this method for screening inhibitors of amyloid fibrillation



【Previous method】

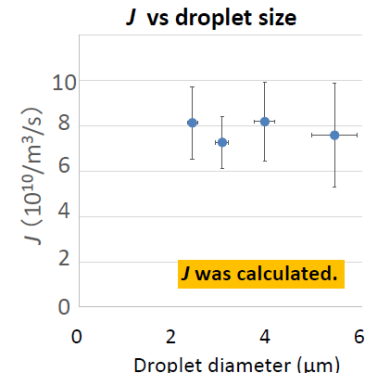
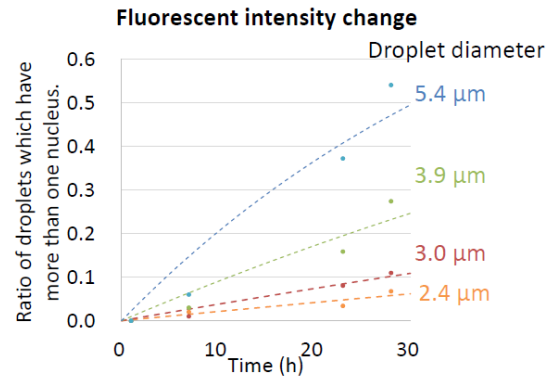
- It takes time because the plot should reach plateau phase ※ (400 h in this case)
- It is estimated by fitting time variation of fluorescence intensity based on the heuristics (Not theoretical) ※T. P. Knowles *et al. Nature Protocols*, 2016.

【This method】

- It saves time because you analyze each droplet statistically. (<30 h in demonstration test)
- You can get thermodynamic parameter; nucleation rate.

Application

1. Preparation of droplets of amyloid precursor proteins (either in vitro or in vivo)
2. Incubation with inhibitor candidates and amyloid dye
3. Image analysis (time variation of fluorescence intensity and droplet volume)
4. Fitting of the experimental data to the formula for statistical analysis
5. Calculate nucleation rate J



IP Data

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[We have the results of inhibitor evaluation \(confidential\).](#)