Supporting Information for

Distinct microscopic mechanisms for the accelerated aggregation of pathogenic Tau mutants revealed by kinetic analysis

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Supporting Information includes:

1. Figure S1-S2
2. Table S1

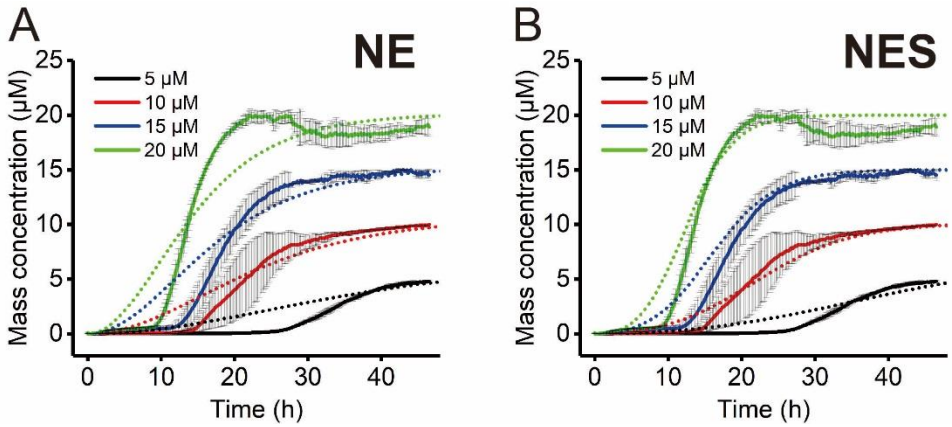

Fig. S1 Global fitting of fibrillation curves for P301S measured by ThT assay. NE indicates a nucleation-elongation model, and NES indicates a nucleation-elongation-secondary nucleation model. Neither of the above models give a satisfactory fit to the data compared to a nucleation-elongation-fragmentation-annealing model (Fig. 2).

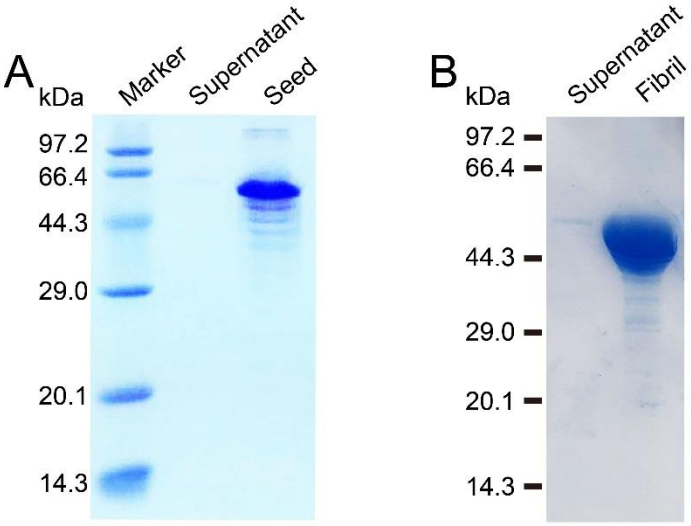

Fig. S2 SDS-PAGE detection of soluble Tau after sonication and after fibrillization reaches plateau. (A) The seed solution of P301S was centrifuged at 13,000 rpm for 60 min. A volume of 6 µl supernatant and resuspended seeds were each subjected to SDS-PAGE analysis. The result shows that there is no detectable free monomer in solution. **(B)** The P301S sample was centrifuged at 13000 rpm for 30 min after the fibrillization reaction reached plateau. An equal volume of supernatant and resuspended fibrils were subjected to SDS-PAGE analysis. Only a trace amount of soluble protein is present in the supernatant indicating that the equilibrium strongly favors fibril formation.

Table S1. Fluorescence lifetime of AF488 for AF488/AF594-labeled Tau and its mutants before and after fibril formation.

Proteins	A488 Lifetime (ns)	
	Long lifetime	Short lifetime
WT Tau40 monomer	4.2 ±0.1 (16.4%)	2.0 ±0.1 (83.6%)
P301L monomer	4.1 ±0.1 (17.1%)	1.9 ±0.1 (82.9%)
P301S monomer	4.2 ±0.1 (17.3%)	2.0 ±0.1 (82.7%)
WT Tau40 fibril	4.1 ±0.2 (7.0%)	1.9 ±0.1 (93.0%)
P301L fibril	3.8 ±0.1 (7.2%)	1.5 ±0.1 (92.8%)
P301S fibril	4.1 ±0.2(10.6%)	1.9 ±0.1 (89.4%)