Table 2. Modulations of α-Synuclein Aggregation[a] by Various Physiological/Pathological Factors and Effectors in Vitro

factors/effectors	effects on fibrillation kinetics[b]	main species	refs
macromolecular crowding and viscosity:			
PEG (150 g/L)	enhancement (~10-fold)	amyloid fibrils	661, 663
dextran (150 g/L)	enhancement (~2-fold)	amyloid fibrils	661, 663
Ficoll 70 (150 g/L)	enhancement (~5-fold)	amyloid fibrils	661, 663
Ficoll 400 (150 g/L)	enhancement (~5-fold)	amyloid fibrils	661, 663
BSA (60 g/L)	enhancement (~7-fold)	amyloid fibrils	661, 663
lysozyme (50 g/L)	enhancement (~5-fold)	amyloid fibrils	661, 663
glycerol (40%)	enhancement (~3-fold)	amyloid fibrils	661, 663
glycerol (50%)	enhancement (~1-fold)	amyloid fibrils	661, 663
glycerol (60%)	no fibrillation	n.d.[h]	661, 663
post-translational modifications:			
Ser87 phosphorylation	no fibrillation	monomers/ amorphous aggregates	675
Ser129 phosphorylation	no fibrillation	monomers/ amorphous aggregates[c]	678
Tyr125 phosphorylation	no change	amyloid fibrils	679
Met-oxidation	no fibrillation	soluble oligomers	700
Tyr-nitration	no fibrillation	spherical aggregates	696, 697
monoubiquitination:			694
Lys10	no change	amyloid fibrils	
Lys6, Lys12, Lys21, Lys23	inhibition (>3-fold)	amyloid fibrils/ proto-fibrils	
Lys32, Lys34, Lys43, Lys96	no fibrillation	monomers/ amorphous aggregates	
poly ubiquitination:			
Tetra-Ub- Lys12	no fibrillation	large, nonfibrillar aggregates	692
Sumoylation[d]	no fibrillation	amorphous aggregates	693
4-hydroxy-2-nonenal[e]	no fibrillation	monomers/soluble oligomers	695
N-terminal acetylation	no change	amyloid fibrils	508
truncation:			
α-synuclein (aa1−108)	enhancement (~10-fold)	shorter amyloid fibrils	52
α-synuclein (aa1−124)	enhancement (~7-fold)	shorter amyloid fibrils	
ligand and protein interactions:			
metal ions[f]:			
Cu(II) (1:1)	enhancement (~2-fold)	amyloid fibrils	687, 722
Mn(II), Fe(II), Zn(II) (1:1)	no change	amyloid fibrils	721
Ca(II) (10:1)	n.d.[h]	spherical oligomers	730
Cu(II), Mn(II), Fe(II), Zn (II) (50:1)	enhancement (>5-fold)	amyloid fibrils	659
polyamines:			
putrescine (3000:1)	enhancement (~4-fold)	shorter amyloid fibrils	
spermidine (300:1)	enhancement (~4-fold)	shorter amyloid fibrils	75
spermine (15:1)	enhancement (~4-fold)	shorter amyloid fibrils	
polyphenols:			
EGCG (1:1)[g]	no fibrillation	spherical aggregates	746
theaflavins	no fibrillation	spherical aggregates	753
dopamine	no fibrillation	amorphous aggregates	734
β-synuclein (2:1)	inhibition (~2-fold)	amyloid fibrils	
γ-synuclein (2:1)	inhibition (>4-fold)	amyloid fibrils	331
chaperones:			
Hsp20 (1:1)	inhibition (~2-fold)	amyloid fibrils	362
Hsp27 (1:1)	inhibition (~1.5-fold)	shorter amyloid fibrils	
HspB8 (1:1)	no fibrillation	spherical aggregates	
Hsp 70 (1:10)	no fibrillation	monomers	
Hsp104 (1:400 -ATP)	no change	amyloid fibrils	758
Hsp104 (1:400 +ATP)	inhibition (~2-fold)	amyloid fibrils	
Hsp104 (1:40 + ATP)	no fibrillation	amorphous aggregates	757

[a]Aggregation is defined as the formation of Thioflavin-T (ThT) positive amyloid fibrils. [b]Quantification based on the half-time ($t_{1/2}$) of in vitro aggregation. Each condition was compared to the aggregation rates of α-synuclein control samples. [c]Longer incubations produced ThT positive aggregates that were morphologically different from non phosphorylated control samples. [d]Complete sumoylation at Lys96 and Lys102. [e]Addition of up to six 4-hydroxy-nonenal molecules. [f]Metal:protein ratios are given in parentheses. [g](−)-Epigallocatechin-gallate. [h]n.d. = not determined