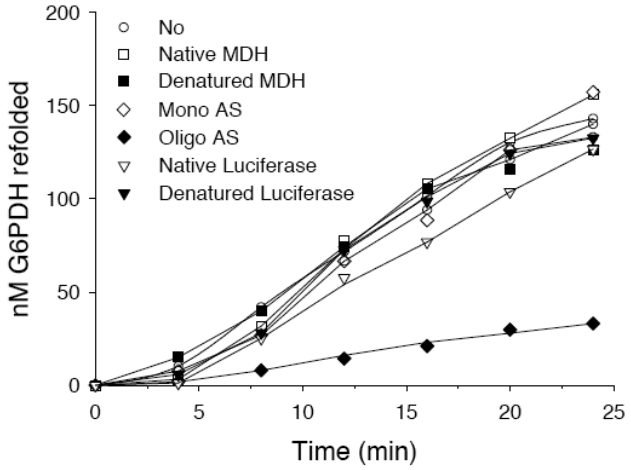
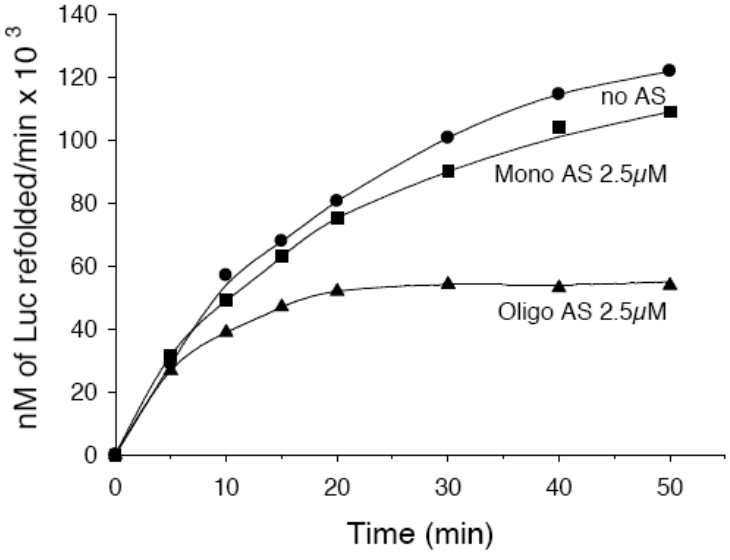
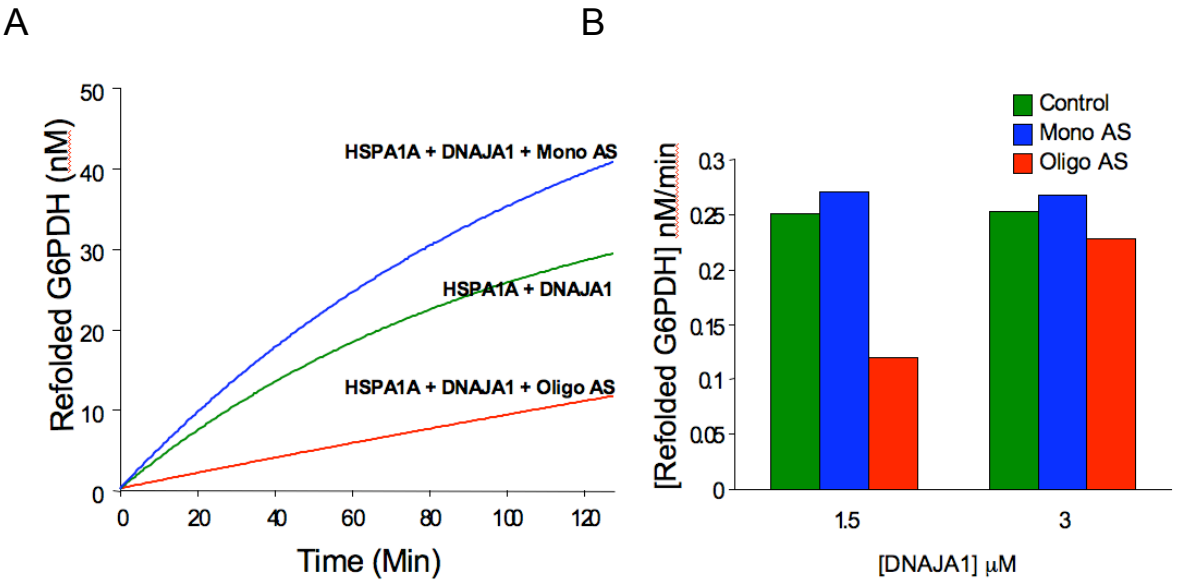
SUPPLEMENTARY FIGURES



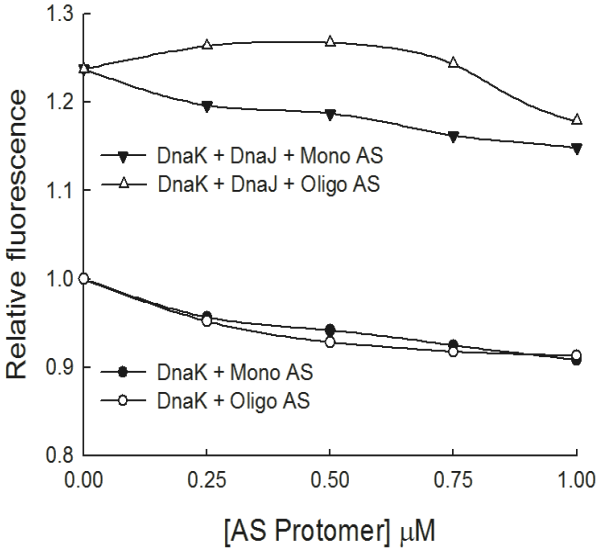
SUPPLEMENTAL FIG. S1. The inhibition of the G6PDH refolding is specific to oligomeric species. Time-dependent reactivation of heat pre-aggregated G6PDH by the DnaK chaperone machinery was performed as in Figure 4. Heat pre-aggregated G6PDH (0,75 µM, ie 38 µg/mL) was incubated in absence (opened circles) or in presence of 58 µg/mL Malate dehydrogenase (MDH) (native or heat-denatured, (squares)), or with 58 µg/mL Luciferase (native or cold-denatured, (triangles)), or with 58µg/mL α-synuclein (monomeric or oligomeric, (diamonds)).



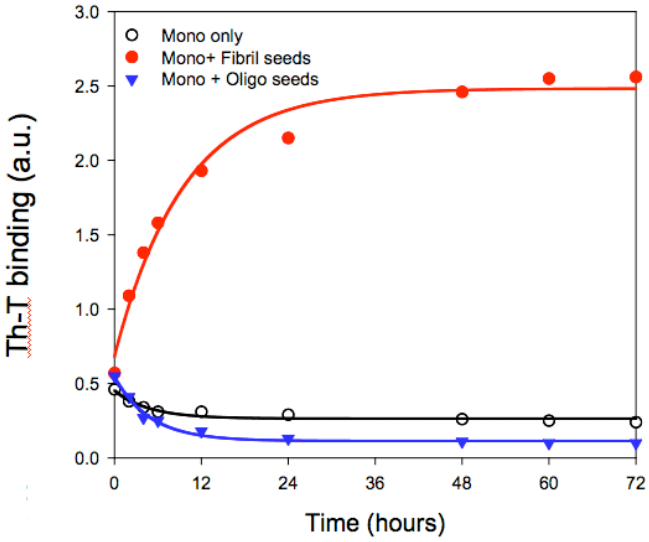
SUPPLEMENTAL FIG. S2. The oligomeric species of α-synuclein inhibit the refolding of freeze-inactivated luciferase mediated by the DnaK chaperone system. Time-dependent reactivation of freeze-inactivated luciferase (0,5µM) by the DnaK chaperone system (2.5µM DnaK, 0.5 µM DnaJ, 0.5 µM GrpE), in absence (circles) or in presence of either 2.5µM oligomeric α-synuclein (triangles) or 2.5µM monomeric α-synuclein (squares). 5 mM ATP were supplemented at time 0min, and aliquots were assayed for Luciferase activity at the indicated time points, as described in Sharma *et al,* 2008.



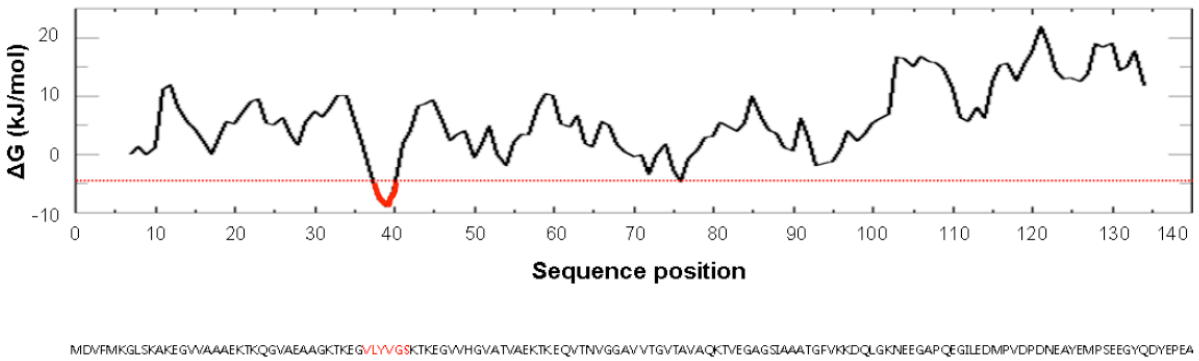
SUPPLEMENTAL FIG. S3. α-Syn oligomers inhibit human Hsp70/40 chaperone mediated refolding of heat denatured G6PDH. G6PDH (750 nM) was heat-denatured 7 minutes at 52°C without chaperones, as in Diamant et al., 2000, then supplemented with purified recombinant human HSP70 (HSPA1A, 5 µM) and Hsp40 (DNAJA1, 1 µM), without (green line), or with 4µM monomeric α-syn (blue line) or 4 µM oligomeric α-syn (red line). The reaction was initiated by addition of 5 mM ATP. *A,* time-dependent refolding of G6PDH at 30°C. *B,* refolding rates in the presence of 5 µM HSPA1A and 1.5 or 3.0 µM DNAJA1.



SUPPLEMENTAL FIG. S4: Steady-state tryptophan fluorescence using a LS50 spectrofluorimeter from Perkin Elmer. 1 µM DnaK in refolding buffer was incubated at 25°C in the presence of 1 mM ATP, 5 µg/ml pyruvate kinase and 4 mM PEP, without or with of 0.5 µM DnaJ and increasing concentrations of monomeric or oligomeric α-syn, as indicated (concentrations expressed in protomers). Excitation was at 300 nm and emission at 348 nm.



SUPPLEMENTAL FIG. S5. α-Syn oligomers do not seed the fibrilization of α-Syn monomers. α-Syn monomers (50 µM; black line) were incubated at **37°C** for the indicated time without or with freshly sonicated α-syn fibrils (10 µM protomers; red line) or α-Syn oligomers (1 µM protomers; blue line)**.** At indicated times, fibril formation was measured by fluorescence in the presence of 60 µM ThT (excitation: 450 nm; emission: 485 nm) and expressed in arbitrary units (a.u.).



SUPPLEMENTAL FIG. S6. α-synuclein possess a single Hsp70 binding site. Free energies of binding shown as a function of the residue number within the α-synuclein primary sequence, as deduced from the algorithm of Rudiger and co-workers (Rudiger *et al*, 1997), using a sliding window approach. The red dotted line indicates a -5 kJ/mol threshold of confidence, and the red segment of the solid line indicates the region within the α-syn primary sequence predicted to be the Hsp70 binding site (residues 36-41, highlighted in red).