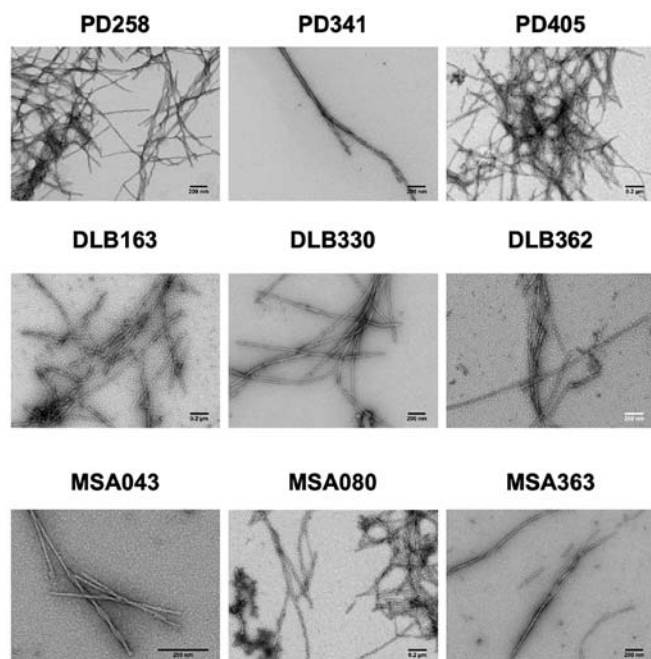


Expanded View Figures

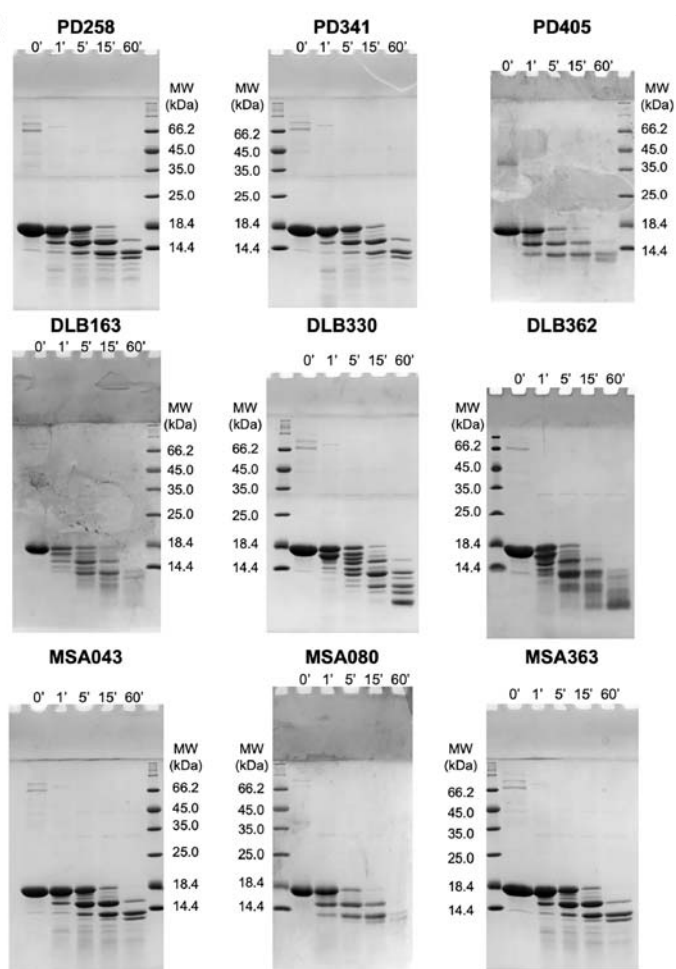
Figure EV1. Characterization of α Syn fibrils PMCA-amplified from PD, MSA, and DLB-patient brains.

Transmission electron microscopy of patient-derived α Syn fibrils (A). Scale bar = 200 nm. Limited proteolytic profiles of patient-derived α Syn fibrils (B). Digestion of α Syn samples (100 μ M monomeric concentration) in the presence of Proteinase K (3.8 μ g/ml) was monitored over time at 37 °C and stopped after 0, 1, 5, 15, 60 min digestion by addition of 100 μ M PMSF. Limited proteolysis products were dissolved by Hexafluoroisopropanol before denaturation, SDS-PAGE separation and Coomassie staining. Time (min), molecular weight markers (MW, kDa) are shown on the sides and the top of the gels. (C, D) Thioflavin T fluorescence of amplified strains (C) and of brain homogenates used as starting material for amplification. (D) The significance of differences between the fibrillar polymorphs derived from PD, DLB, and MSA was assessed using a two-tailed Welch's *t*-test and is indicated as follows: **p* val <0.05, ***p* val <0.01, ****p* val <0.001. Exact *p* values are: *p* = 0.0108 (PD vs MSA), *p* = 0.0122 (PD vs DLB), *p* = 0.0093 (DLB vs MSA) in (B), and *p* = 0.0108 (PD vs MSA), *p* = 0.0122 (PD vs DLB), *p* = 0.0093 (DLB vs MSA) and *p* = 0.0048 (PD vs MSA), *p* = 0.0008 (PD vs DLB), *p* = 0.0005 (DLB vs MSA), *p* = 0.0032 (PD vs Control), *p* = 0.0008 (DLB vs Control), and *p* = 0.0008 (MSA vs Control) in (C). Source data are available online for this figure.

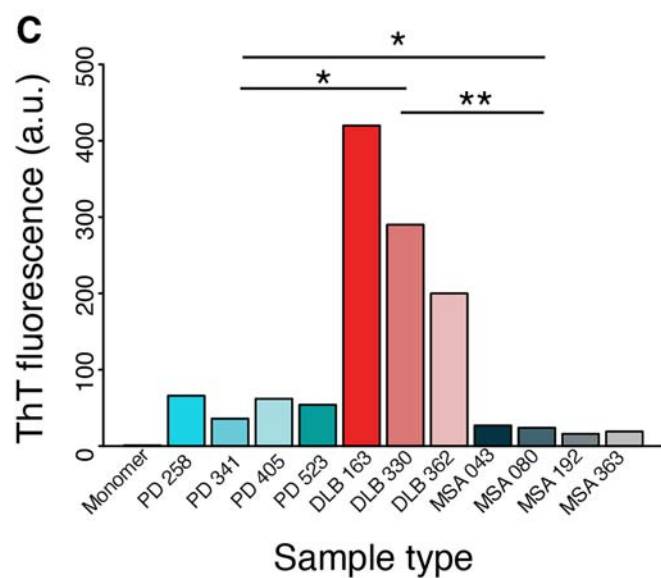
A



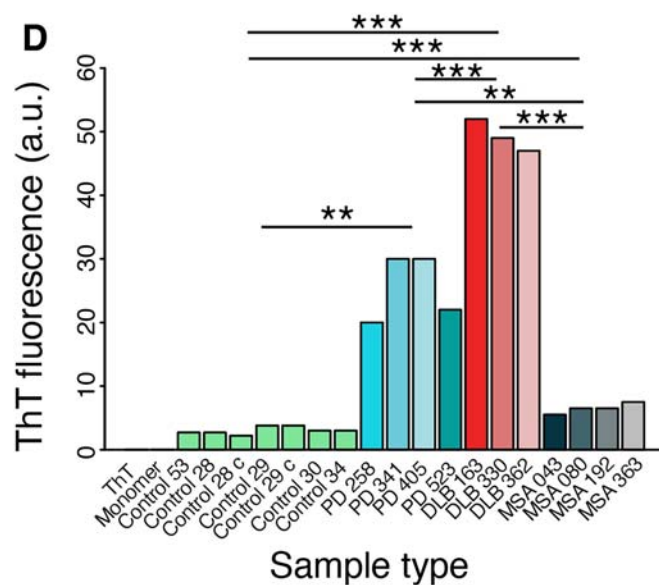
B



C



D



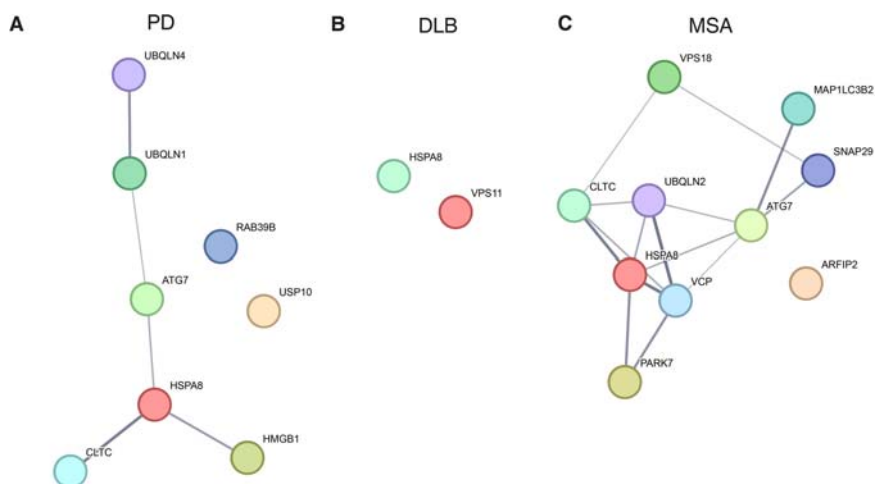


Figure EV2. Autophagy-related proteins respond differentially to α Syn fibrils of the three disease strains.

Hit proteins responding to α Syn fibril uptake ($FC > 1.5$, $q\text{ val} < 0.05$) and involved in autophagy (based on annotation in Uniprot) were analyzed in String to reveal possible protein networks. Resulting plots are shown for PD (A), DLB (B), and MSA (C) strains. Nodes indicate proteins, edges indicate physical or functional interactions based on experiments, databases, and textmining. Line thickness indicates the strength of the data support.