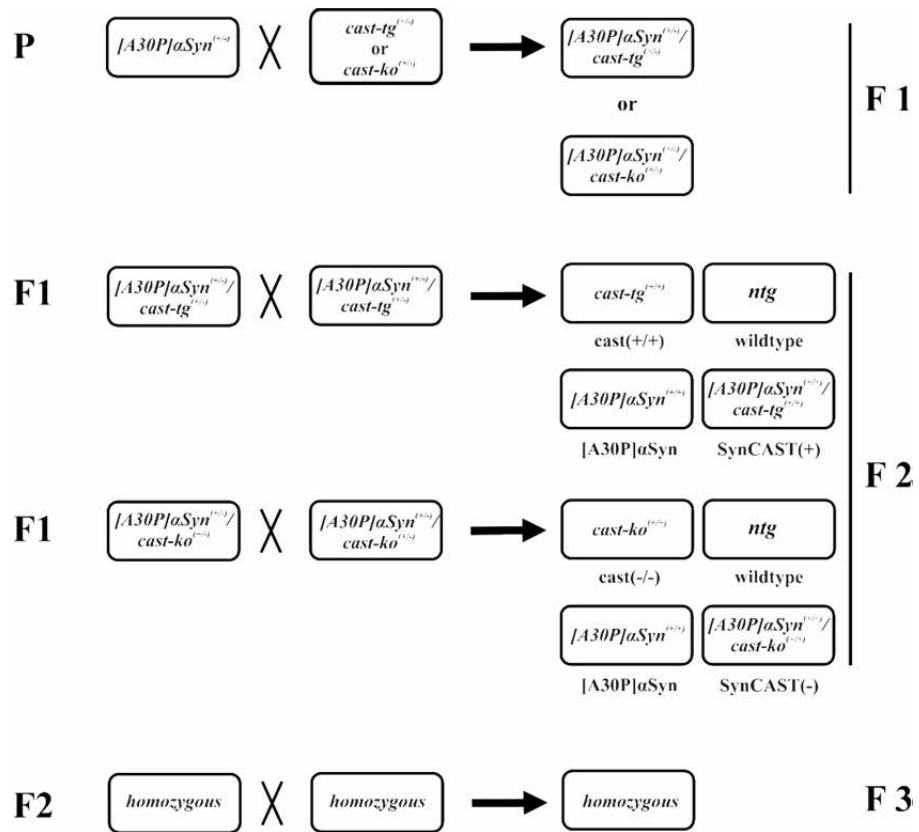
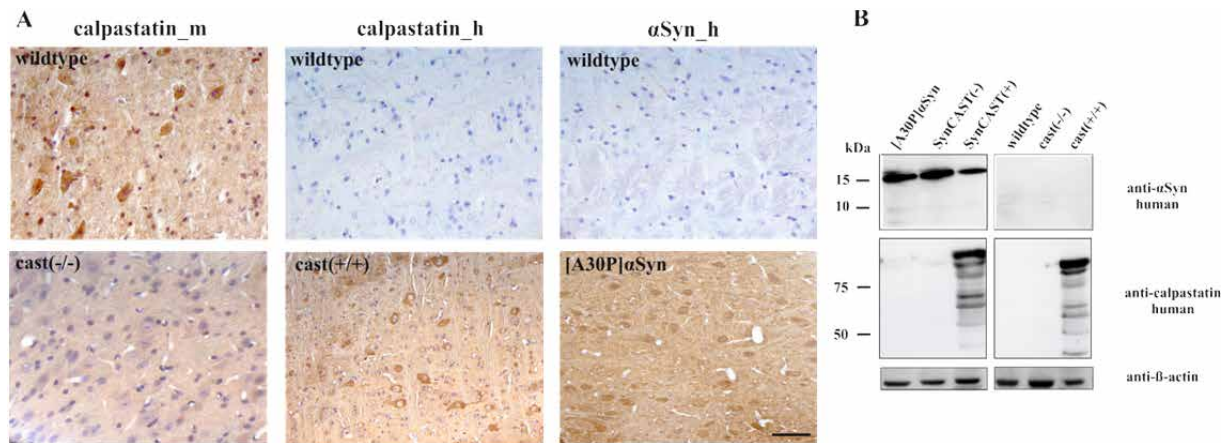


**Supplementary Figure S1 (A)** Sedimentation velocity analysis for soluble [WT] $\alpha$ Syn 300  $\mu$ M at 50000 rpm and 15  $^{\circ}$ C in assembly buffer. Shown are sedimentation boundaries obtained at intervals of 20 min. **(B)** Sedimentation coefficient continuous  $c(s)$  distribution of soluble [WT] $\alpha$ Syn calculated from the sedimentation velocity data. A blow up is shown in the inset. The major species, representing 94 % of the material has a sedimentation coefficient ( $s_{20,w}$ ) of 1.09 S, consistent with the sedimentation coefficient of monomeric  $\alpha$ Syn ( $RH = 3.15$ ;  $f/f_0 = 1.96$ ). An additional peak with  $S_{20,w} = 2.46$  consistent with the sedimentation coefficient of dimeric  $\alpha$ Syn, representing 2.2% of the material, as well as higher order oligomeric species representing 3.8 % of the material are also observed (inset). **(C)** Stability of WT or A30P  $\alpha$ Syn. Western blot analysis of recombinant wt or A30P  $\alpha$ Syn (soluble or fibrillar) incubated in assembly buffer at 37 $^{\circ}$ C for 1 h performed using monoclonal anti- $\alpha$ Syn (BD biosciences ref # 610787). No degradation is observed.



**Supplementary Figure S2** Breeding strategy to generate SynCAST(+) and SynCAST(-) mice. P, F1, F2 and F3 representing each generation of crossbreeding.



**Supplementary Figure S3** Expression of murine (m) and human (h) calpastatin as well as human (h)  $\alpha$ Syn in the brain stem. **(A)** Representative immunohistochemical staining of single transgenic mice with specific antibodies. Scale bar = 50  $\mu$ m. **(B)** Western blot analysis showing the overexpression of human calpastatin (SynCAST(+), cast(+/+)) and human  $\alpha$ Syn ([A30P] $\alpha$ Syn, SynCAST(-), SynCAST(+)).