

SUPPLEMENTARY MATERIAL

Supplementary Figures

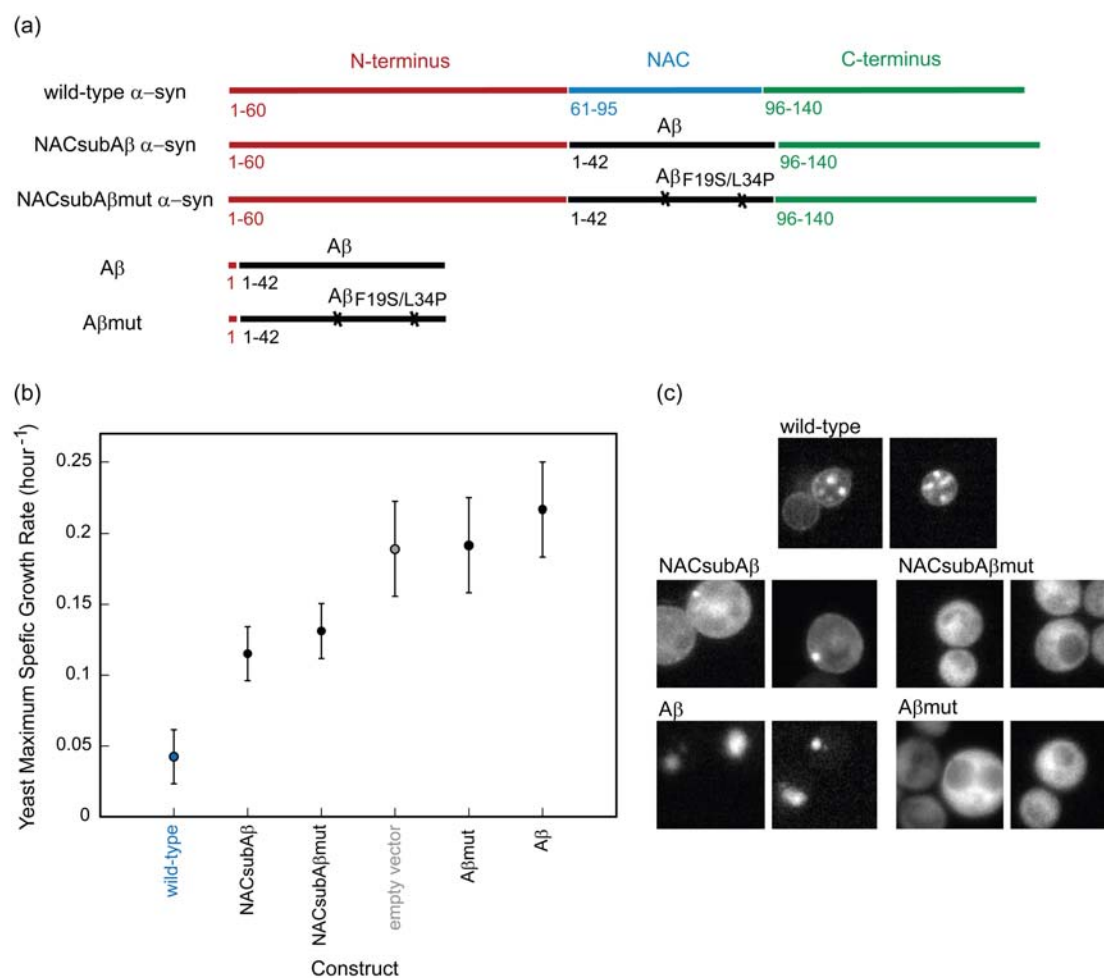


Figure 1. Properties of α -syn/A β_{42} chimeras. (a) Schematic illustration of the sequences tested in yeast. The A β_{42} F19S/L34P mutant does not aggregate, and was included as a control. (b) Both NACsubA β and NACsubA β mut variants decreased α -syn toxicity. When expressed independently, neither A β nor A β mut were toxic to yeast. (c) Microscopy of GFP-tagged proteins. NACsubA β formed fewer aggregates than wild-type; NACsubA β mut was cytosolic. A β formed intracellular inclusions in yeast, whereas A β mut remained dispersed throughout the cytoplasm.

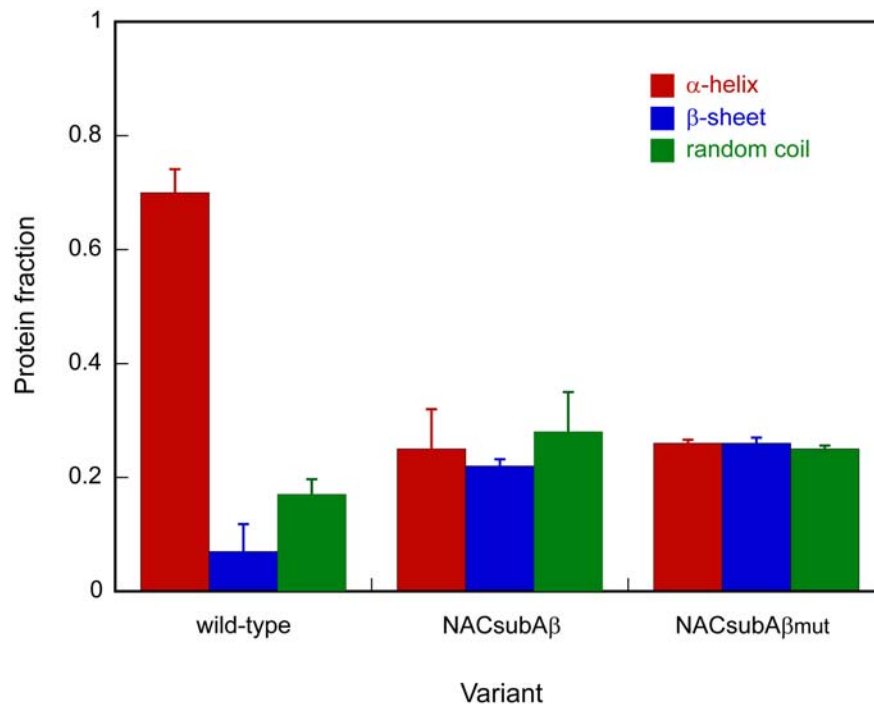


Figure 2. Structural content of wild-type α -syn, NACsubA β and NACsubA β mut in 4% HFIP, determined by CD spectroscopy.

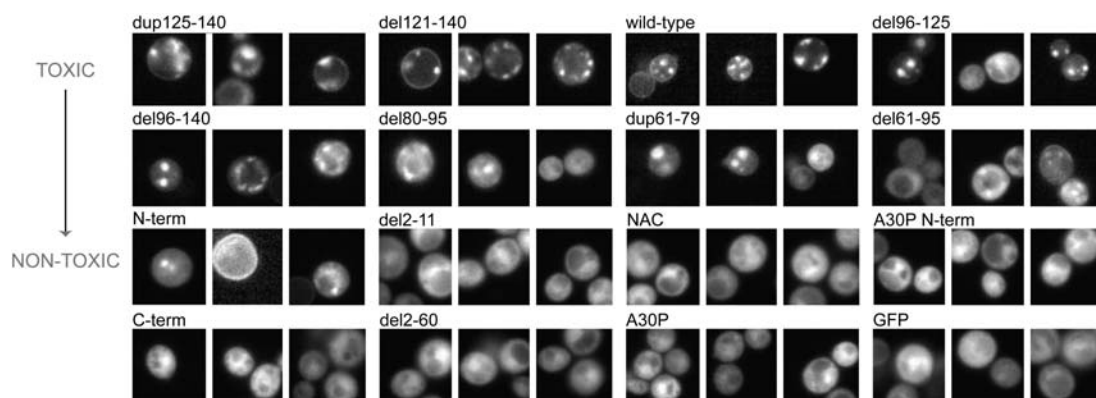


Figure 3. Microscopic images of GFP-tagged α -syn variants, arranged in order of decreasing yeast toxicity. Dup9-30 and del9-30 GFP fusions exhibited very weak fluorescence (data not shown), possibly attributable to GFP misfolding or cell lysis. The representative pictures shown were taken 48 h after induction of protein expression (growth in galactose media), using identical excitation intensity and exposure time.

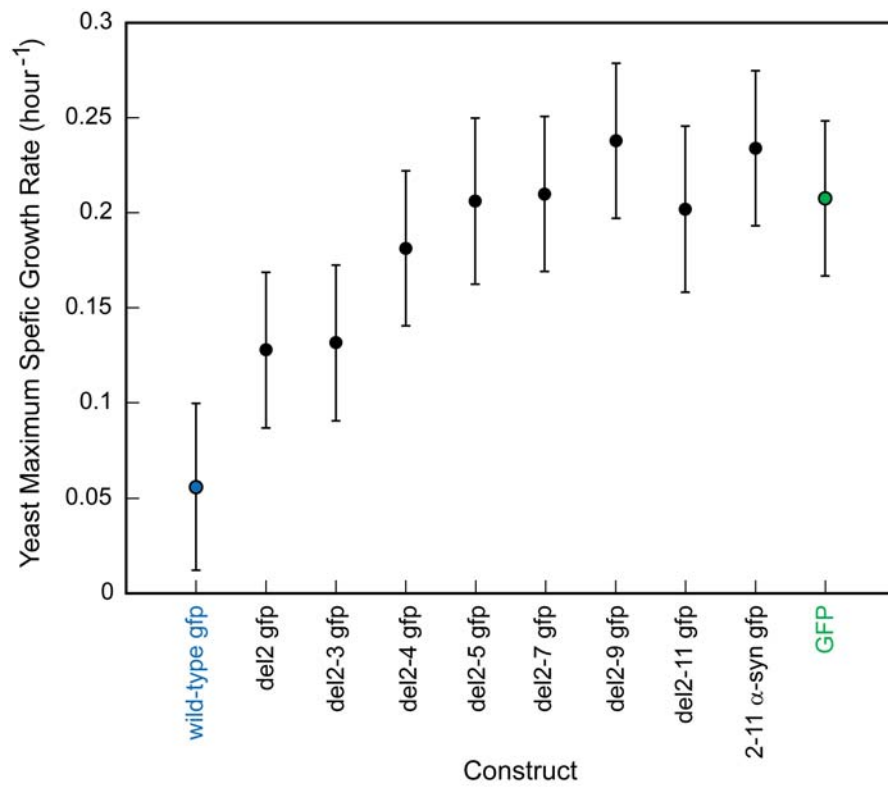


Figure 4. Yeast maximum specific growth rate of GFP-tagged α -syn variants, arranged in order of increasing deletion size. GFP was included as a control.

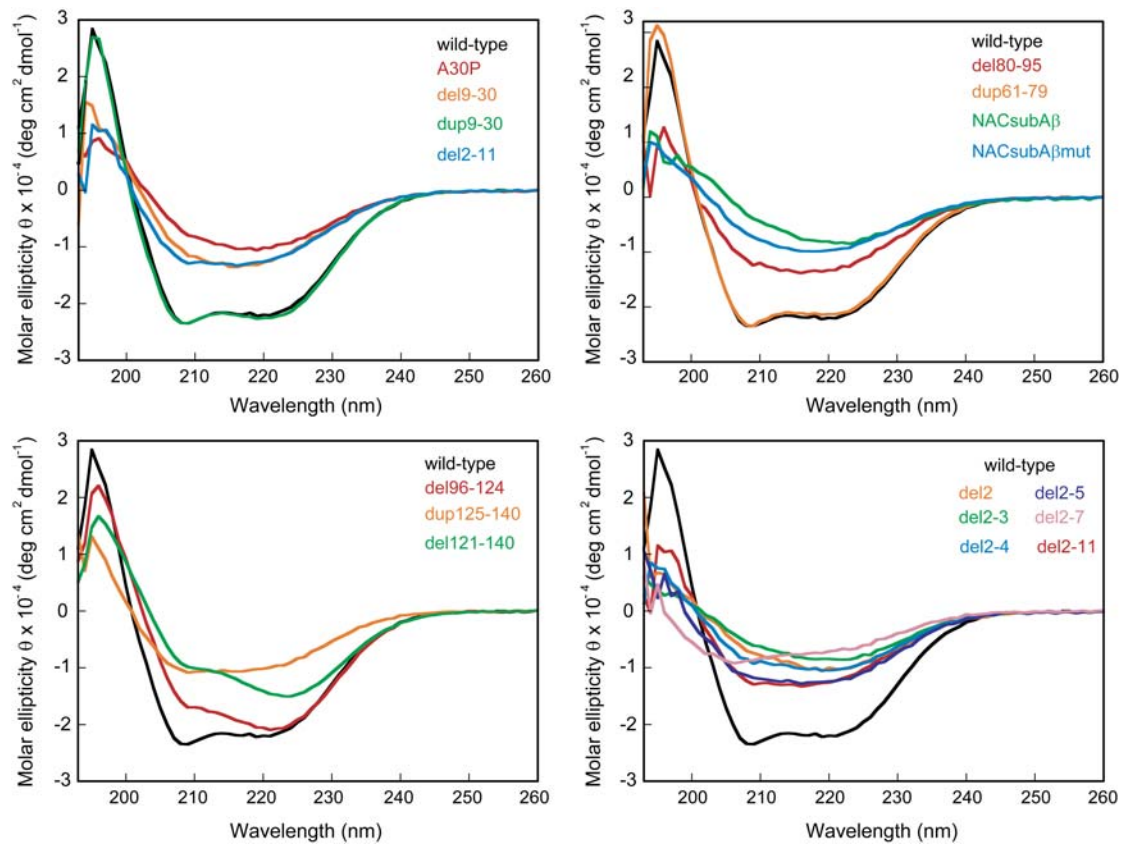


Figure 5. CD spectra of α -syn variants, in the presence of 4% HFIP.

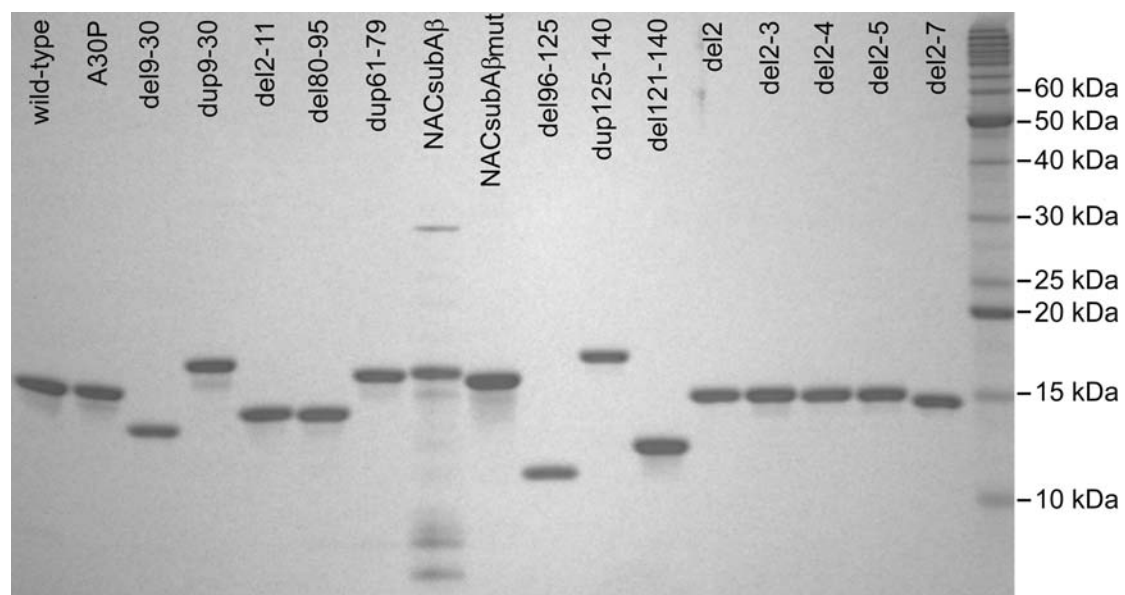


Figure 6. SDS PAGE gel of α -syn variants.

DNA sequences

wild-type α -syn, 420 bp

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AAAACCAAACAGGGTGTGGCAGAAGCAGCAGGAAAAGACAAAAGAGGGTGTTCCTATGT
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AAGAGCAAGTGACAAATGTTGGAGGAGCAGTGGTGCACGGGTGTGACAGCAGTAGCCCAG
AAGACAGTGGAGGGAGCAGGGAGCATTGCAGCAGCCACTGGCTTTGTCAAAAAGGACCA
GTTGGGCAAGAATGAAGAAGGAGCCCCACAGGAAGGAATTCTGGAAGATATGCCTGTGG
ATCCTGACAATGAGGCTTATGAAATGCCTTCTGAGGAAGGGTATCAAGACTACGAACCTG
AAGCCTAA

dup9-30 α -syn, 486bp

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GCCAGAAGACAGTGGAGGGAGCAGGGAGCATTGCAGCAGCCACTGGCTTTGTCAAAA
GGACCAGTTGGGCAAGAATGAAGAAGGAGCCCCACAGGAAGGAATTCTGGAAGATATGC
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AACCTGAAGCCTAA

del9-30 α -syn, 354bp

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AGTGACAAATGTTGGAGGAGCAGTGGTGCACGGGTGTGACAGCAGTAGCCCAGAAGACAG
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AAGAATGAAGAAGGAGCCCCACAGGAAGGAATTCTGGAAGATATGCCTGTGGATCCTGA
CAATGAGGCTTATGAAATGCCTTCTGAGGAAGGGTATCAAGACTACGAACCTGAAGCCTA
A

del2 α -syn, 417bp

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CTCCAAAACCAAGGAGGGAGTGGTGCATGGTGTGGCAACAGTGGCTGAGAAGACCAAAG
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GGGCAAGAATGAAGAAGGAGCCCCACAGGAAGGAATTCTGGAAGATATGCCTGTGGATC
CTGACAATGAGGCTTATGAAATGCCTTCTGAGGAAGGGTATCAAGACTACGAACCTGAAG
CCTAA

del2-3 α -syn, 414 bp

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CAAAACCAAGGAGGGAGTGGTGCATGGTGTGGCAACAGTGGCTGAGAAGACCAAAGAGC
AAGTGACAAATGTTGGAGGAGCAGTGGTGCACGGGTGTGACAGCAGTAGCCCAGAAGACA
GTGGAGGGAGCAGGGAGCATTGCAGCAGCCACTGGCTTTGTCAAAAAGGACCAGTTGGG
CAAGAATGAAGAAGGAGCCCCACAGGAAGGAATTCTGGAAGATATGCCTGTGGATCCTG
ACAATGAGGCTTATGAAATGCCTTCTGAGGAAGGGTATCAAGACTACGAACCTGAAGCCT
AA

del2-4 α-syn, 411bp

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AGAATGAAGAAGGAGCCCCACAGGAAGGAATTCTGGAAGATATGCCTGTGGATCCTGAC
AATGAGGCTTATGAAATGCCTTCTGAGGAAGGGTATCAAGACTACGAACCTGAAGCCTAA

del2-5 α-syn, 408bp

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del2-7 α-syn, 402bp

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del2-9 α-syn, 396bp

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CATTGCAGCAGCCACTGGCTTTGTCAAAAAGGACCAGTTGGGCAAGAATGAAGAAGGAG
CCCCACAGGAAGGAATTCTGGAAGATATGCCTGTGGATCCTGACAATGAGGCTTATGAAA
TGCCTTCTGAGGAAGGGTATCAAGACTACGAACCTGAAGCCTAA

del2-11 α-syn, 390bp

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GTGGTGACGGGTGTGACAGCAGTAGCCCAGAAGACAGTGGAGGGAGCAGGGAGCATTGC
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CTGAGGAAGGGTATCAAGACTACGAACCTGAAGCCTAA

A30P α-syn, 420bp

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AAGCCTAA

del2-60 α-syn, 243bp

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N-term, 180bp

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AATAA

A30P N-term, 180bp

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AATAA

dup61-79 α-syn, 477 bp

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CCTAA

del80-95 α-syn, 372bp

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del61-95 α-syn, 315bp

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GACTACGAACCTGAAGCCTAA
NAC, 108bp

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dup125-410 α -syn, 468bp

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del96-124 α -syn, 333bp

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del121-140 α -syn, 360 bp

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del96-140 α -syn, 285bp

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C-term, 138bp

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NACsubA β α -syn, 441bp

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VAEKTKDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIAKKDQLGKNEEGAP
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TATGAAATGCCTTCTGAGGAAGGGTATCAAGACTACGAACCTGAAGCCTAA

NACsubA β_{mut} α -syn, 441bp

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AGGCTCCAAAACCAAGGAGGGAGTGGTGCATGGTGTGGCAACAGTGGCTGAGAAGACCA
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TCAAGACTACGAACCTGAAGCCTAA

A β_{42} , 129bp

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TCGCTGAAGACGTTGGTTCTAACAAGGGTGCTATCATCGGTTTGATGGTTGGTGGTGGTGGT
TATCGCTTAA

A β_{mut} , 129bp

ATGGACGCTGAATTCAGACACGACTCTGGTTACGAAGTTCACCACCAAAAAGTTGGTTTTCT
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TATCGCTTAA

Protein sequences

wild-type α -syn

MDVFMKGLSKAKEGVVAAAETKQGVAAEAGKTKEGVLYVGSKTKEGVVHGVATVAEKT
KEQVTNVGGAVVTGVTAVAQKTVEGAGSIAAATGFVKKDQLGKNEEGAPQEGILEDMPVDP
DNEAYEMPSEEGYQDYEPEA

dup9-30 α -syn

MDVFMKGLSKAKEGVVAAAETKQGVAAEASKAKEGVVAAAETKQGVAAEAGKTKEGV
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del9-30 α -syn

MDVFMKGLGKTKEGVLYVGSKTKEGVVHGVATVAEKTKEQVTNVGGAVVTGVTAVAQKT
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del2 α -syn

MVFMKGLSKAKEGVVAAAETKQGVAAEAGKTKEGVLYVGSKTKEGVVHGVATVAEKT
EQVTNVGGAVVTGVTAVAQKTVEGAGSIAAATGFVKKDQLGKNEEGAPQEGILEDMPVDP
NEAYEMPSEEGYQDYEPEA

del2-3 α -syn

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EAYEMPSEEGYQDYEPEA

del2-4 α -syn

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VTNVGGAVVTGVTAVAQKTVEGAGSIAAATGFVKKDQLGKNEEGAPQEGILEDMPVDPDNE
AYEMPSEEGYQDYEPEA

del2-5 α -syn

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NVGGAVVTGVTAVAQKTVEGAGSIAAATGFVKKDQLGKNEEGAPQEGILEDMPVDPDNEAY
EMPSEEGYQDYEPEA

del2-7 α -syn

MLSKAKEGVVAAAETKQGVAAEAGKTKEGVLYVGSKTKEGVVHGVATVAEKTKEQVTNV
GGAVVTGVTAVAQKTVEGAGSIAAATGFVKKDQLGKNEEGAPQEGILEDMPVDPDNEAYEM
PSEEGYQDYEPEA

del2-11 α -syn

MKEGVVAAAETKQGVAAEAGKTKEGVLYVGSKTKEGVVHGVATVAEKTKEQVTNVGGA
VVTGVTAVAQKTVEGAGSIAAATGFVKKDQLGKNEEGAPQEGILEDMPVDPDNEAYEMPSEE
GYQDYEPEA

A30P α -syn

MDVFMKGLSKAKEGVVAAAETKQGVAAEAPGKTKEGVLYVGSKTKEGVVHGVATVAEKT
KEQVTNVGGAVVTGVTAVAQKTVEGAGSIAAATGFVKKDQLGKNEEGAPQEGILEDMPVDP
DNEAYEMPSEEGYQDYEPEA

dup61-79 α -syn

MDVFMKGLSKAKEGVVAAAETKQGVAAEAGKTKEGVLYVGSKTKEGVVHGVATVAEKT
KEQVTNVGGAVVTGVTAVAQEQVTNVGGAVVTGVTAVAQKTVEGAGSIAAATGFVKKDQL
GKNEEGAPQEGILEDMPVDPDNEAYEMPSEEGYQDYEPEA

del80-95 α -syn

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YEPEA

dup125-410 α -syn

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KEQVTNVGGAVVTGVTAVAQKTVEGAGSIAAATGFVKKDQLGKNEEGAPQEGILEDMPVDP
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del96-124 α -syn

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del121-140 α -syn

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NACsubA β α -syn

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DMPVDPDNEAYEMPSEEGYQDYEPEAATATGCCTGTGGATCCTGACAATGAGGCTTATGAA
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NACsubA β_{mut} α -syn

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