A newly discovered mechanism reveals how Parkinson's disease can spread between brain cells

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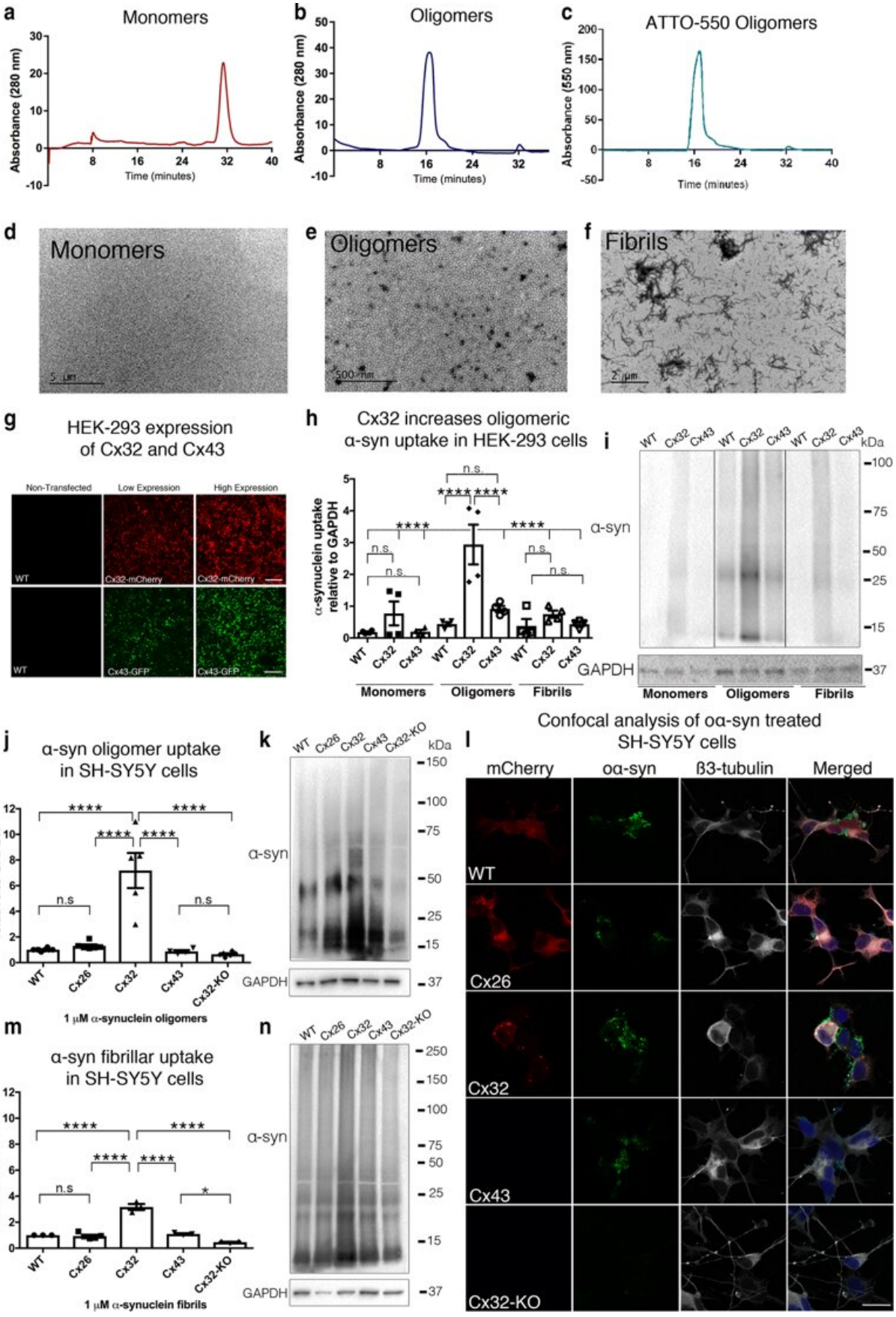
a
Monomers
Absorbance (280 nm)
Time (minutes)
b
Oligomers
Absorbance (280 nm)
Time (minutes)
c
ATTO-550 Oligomers
Absorbance (550 nm)
Time (minutes)
d
Monomers
5 μm
e
Oligomers
500 nm
f
Fibrils
2 μm
g
HEK-293 expression of Cx32 and Cx43
Non-Transfected
Low Expression
High Expression
WT
Cx32-mCherry
Cx43-GFP
h
Cx32 increases oligomeric α-syn uptake in HEK-293 cells
α-synuclein uptake relative to GAPDH
n.s.
****
α-syn
GAPDH
Monomers
Oligomers
Fibrils
i
WT
Cx32
Cx43
kDa
100
75
50
25
15
37
j
α-syn oligomer uptake in SH-SY5Y cells
α-synuclein uptake relative to GAPDH
n.s
****
WT
Cx26
Cx32
Cx43
Cx32-KO
1 μM α-synuclein oligomers
k
α-syn
GAPDH
l
Confocal analysis of oα-syn treated SH-SY5Y cells
mCherry
oα-syn
ß3-tubulin
Merged
WT
Cx26
Cx32
Cx43
Cx32-KO
m
α-syn fibrillar uptake in SH-SY5Y cells
1 μM α-synuclein fibrils
n
250
150
100
75
50
25
15
37

Fig. 1 Cx32 facilitates the uptake of oα-syn preferentially to monomers or fibrillar assemblies. a SEC analysis of α-syn monomers or b oligomeric α-syn (oα-syn) assemblies at 280 nm absorbance. c SEC confirmation of labeled ATTO-550 oα-syn assemblies at 550 nm absorbance. d TEM characterization of α-syn monomers, e oligomers, or f fibrillar assemblies; scale bars represent 5 µm, 500 nm, and 2 µm, respectively. g Confocal image analysis of non-transfected wild-type (WT) or transfected HEK-293 cells with low (15 µg) or high (50 µg) expression of Cx32-mCherry or Cx43-GFP plasmid constructs. Scale bars represent 200 µm. h Densitometric analysis of i Western blot of monomeric, oligomeric or fibrillar α-syn uptake in WT HEK-293 cells or HEK-293 cells expressing Cx32 or Cx43 (n = 4, two-way ANOVA followed by Tukey's post hoc test for multiple comparisons, n.s. = no significance, F(8, 24) = 13.1, ****p