

Supplementary Information

Naturally-occurring antibodies isolated from PD patients inhibit synuclein seeding *in vitro* and recognize Lewy pathology

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Table S1: Peptides and protein used in the study

	Peptide	Residues	Amino Acid sequence
	syn1-25	Syn 1-25	MDVFMKGLSKAKEGVVAAAETKQG
	syn18-44	Syn 18-44	AAEKTQGVAAEAGKTKEGVLYVGSKT
	syn40-65	Syn 40-65	VGSKTKEGVVHGVATVAEKTKEQVTN
	s17	Syn101-120	GKNEEGAPQEGILEDMPVDP
	s18	Syn111-130	GILEDMPVDPDNEAYEMPSE
	s19	Syn121-140	DNEAYEMPSEEGYQDYEPEA
Bait	pS129-(111-140)-LCBiot	Syn 111-140	GILEDMPVDPDNEAYEMP(pS)EEGYQDYEPEA-LCBiot
Bait	LCBiot-pS87-(73-93)	Syn 73-93	LCBiot-GVTAVAQKTVEGAG(pS)IAAATG
Bait	61-95-LCBiot	Syn 61-95	EQVTNVGGAVVTGVTAVAQKTVEGAGSIAAATGFV-K-LCBiot
Bait	LCBiot-61-95	Syn 61-95	LCBiot-EQVTNVGGAVVTGVTAVAQKTVEGAGSIAAATGFVK
Bait	α -Synuclein-Biot	Syn 1-140	Full Length-Biot
Bait	LCBiot-79-110	Syn 79-110	LCBiot- QKTVEGAGSIAAATGFVKKDQLGKNEEGAPQE
Bait	LCBiot-100-120	Syn 100-120	LCBiot-LGKNEEGAPQEGILEDMPVDP
Bait	121-140-LCBiot	Syn 121-140	DNEAYEMPSEEGYQDYEPEA-LCBiot
	NP129-(111-140)-LCBiot	Syn 111-140	GILEDMPVDPDNEAYEMPSEEGYQDYEPEA-LCBiot
	LCBiot-NP87-(73-93)	Syn 73-93	LCBiot-GVTAVAQKTVEGAGSIAAATG
	A6940	Tau 42-103	GLKESPLQPTPTEDGSEEPGSETSDAKSTPTAEDVTAPLVDEGAPGKQAA AQPHTIPEGTTA
	A7416	Tau 166-211	ANATRIPAKTPPAPKTPPSSGEPKSGDRSGYSSPGSPGTPGSRSR
	NPAT8	Tau 194-212	RSGYSSPGSPGTPGSRRT
	A6907	Tau 186-253	GEPKSGDRSGYSSPGSPGTPGSRRTPLPTPTREPKKVAVVRTPPKSP SSAKSRLQTAPVMPDL
	A6897	Tau 299-369	HVPGGGSVQIVYKPVDSLKVTSKCGSLGNIHHKPGGGQVEVKSEKLDLDF KDRVQSKIGSLDNITHVPGGGNK
	A7024	Tau 139-198	DKKAKGADGKTKIATPRGAAPPQKGQANATRIPAKTPPAPKTPPSSGE PPKSGDRSGYS

SA, Streptavidin conjugated -APC or -PE

Bait are peptides used in BSelex screening.

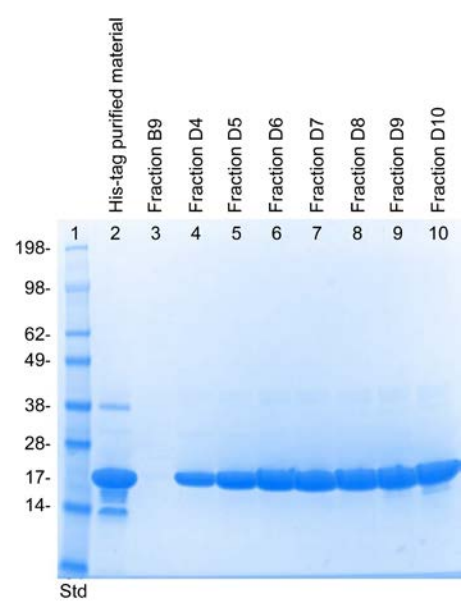
Numbering for Tau peptides corresponds to the 2N4R tau isoform.

Fig. S1 Recombinant full length α -Synuclein-Biot purification and quality analysis. **a** SDS-PAGE under non-reducing conditions of different fractions from preparative SEC. **b** Analytical SEC of final batch. **c** SEC-MALS binding experiment of biotinylated α -synuclein with streptavidin-PE. The highly pure fractions D4, 5, 6, 7, 8, 9 and 10 were pooled together as the final batch.

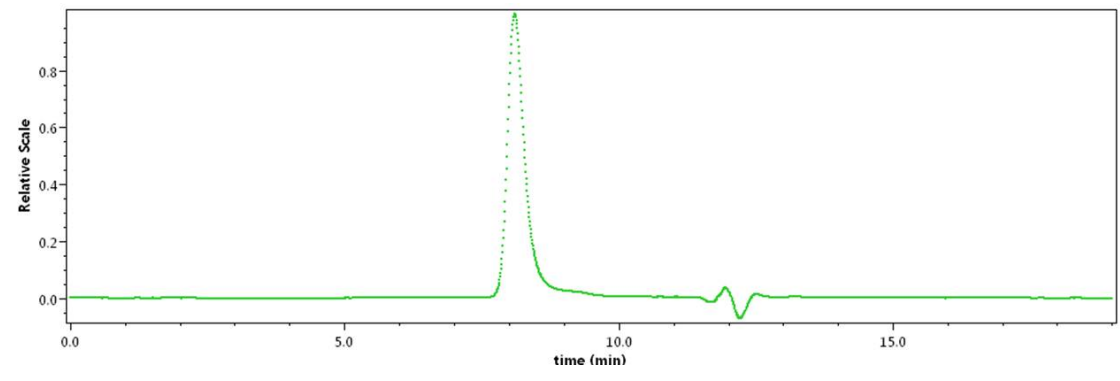
Fig. S2 Affinity of aSyn-323.1, aSyn-336.1 and aSyn-338.1 to synuclein peptides. Isothermal Titration Calorimetry (ITC) measurements for aSyn-323.1 with peptide syn19 (Syn121-140) **a**, aSyn-336.1 with peptide syn18 (Syn111-130) **b**, and aSyn-338.1 with peptide syn19 (Syn121-140)**c**. Variation in enthalpy is observed following incremental addition of mAb stock to synuclein peptide. No binding of antibodies to negative control peptide syn17 (Syn101-120) was observed. Continuous lines represent the best fit of experimental data assuming a single set of binding sites. Experiments were performed in PBS. Equilibrium dissociation constants (K_d) are shown on the individual graphs. The amino acid sequences of synuclein peptides are shown in Table S1.

Fig. S1

a



b



c

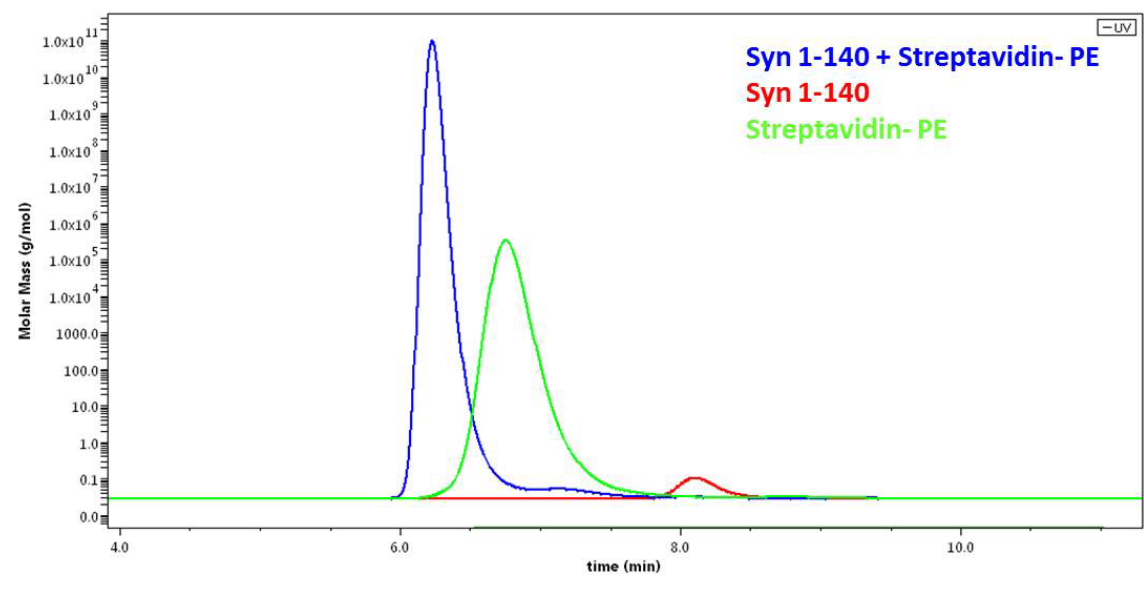
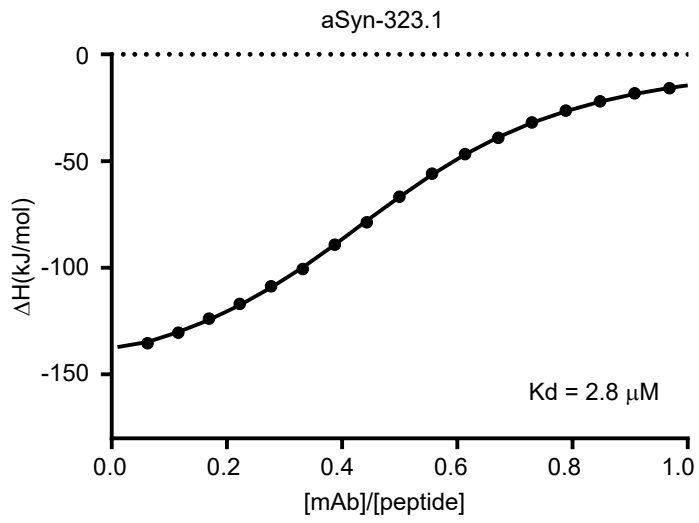
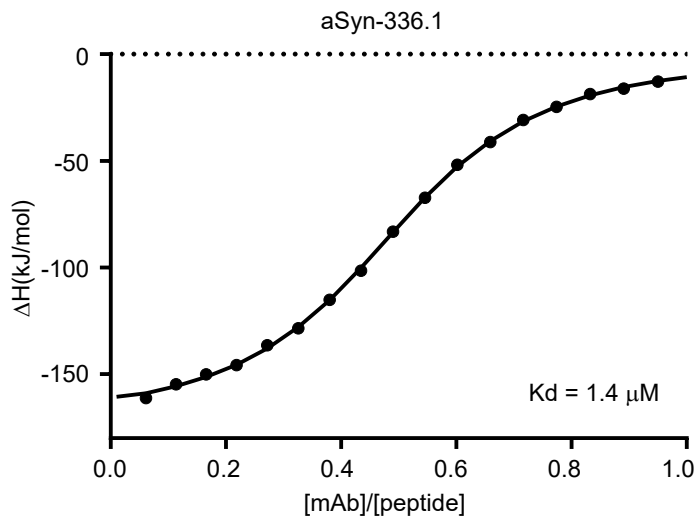


Fig. S2

a



b



c

