

Supporting information for:

Cell invasive amyloid assemblies from SARS-CoV-2 peptides can form multiple polymorphs with varying neurotoxicity

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Supplementary Materials and Methods

Circular Dichroism Spectroscopy (CD)

CD spectroscopy was performed using an AVIV 410-SF CD spectrometer. Spectra were collected between 190 and 260 nm in PBS at 1 mg mL⁻¹ using 1 mm quartz cuvettes with a step size of 0.5 nm and 2 s averaging time. Data were analysed using the BeStSel (Beta Structure Selection) method of secondary structure determination.³⁴ HT values were monitored in order to select a optimum wavelength range for secondary structure determination. HT values below 700 V are considered to produce reliable data therefore secondary structures analysis was only performed between 260-200 nm for ILLIIM and RNYIAQVD.

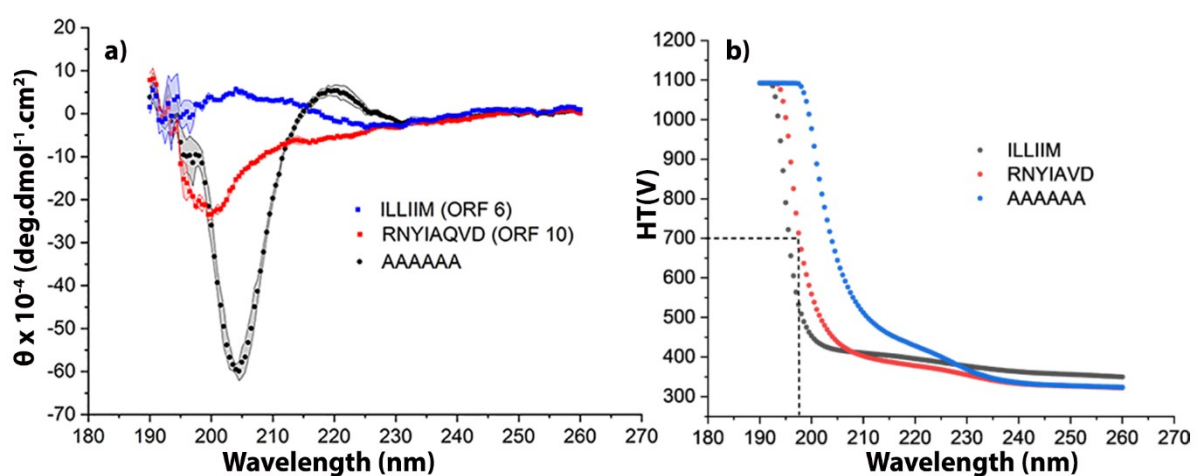


Figure S1: a) Circular dichroism of ILLIIM, RNYIAQVD and AAAAAA assemblies in PBS at 1 mgmL⁻¹, b) high tension (wavelength dependent gain) used to determine optimum region for secondary structure determination (e.g. all HT values > 700 V are considered unsuitable).

Table S1: Secondary Structure Determination from CD spectra

	Left Twisted β -Sheet	Right Twisted β -Sheet	Relaxed β -Sheet	β -turn	Total β -sheet	α -helix	unclassified	RMSD
RNYIAQVD	0	77.6	0	0	77.6	22.4	0	3.763
ILLIIM	20.8	11.9	38.7	28.6	100	0	0	1.054

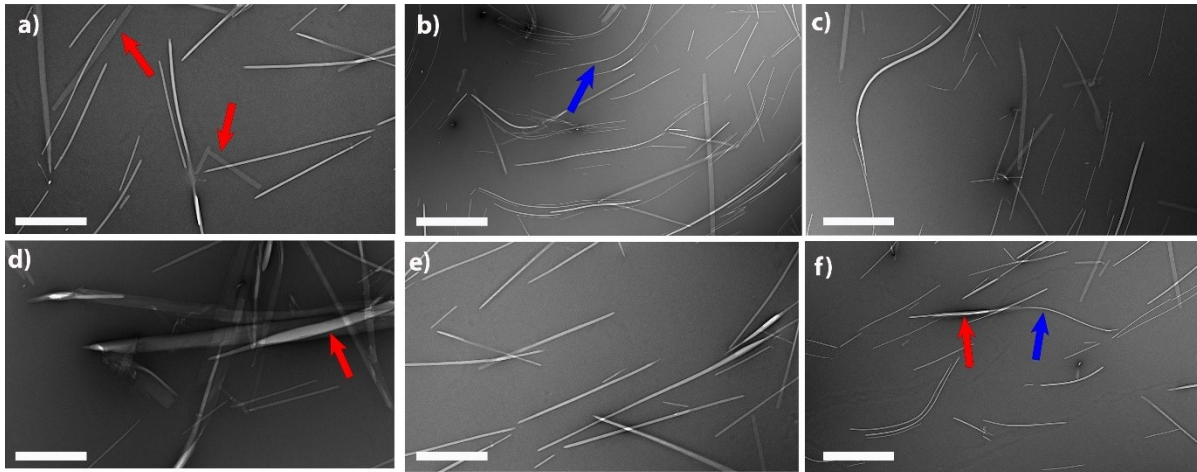


Figure S2: Additional TEM figures of ILLIIM assemblies, red arrows highlight crystalline polymorphs, blue arrows highlight crystalline polymorphs. Scale bars a) = 200 nm, b) = 600 nm, c) = 400 nm, d) = 200 nm, e) = 200 nm, f) = 400 nm

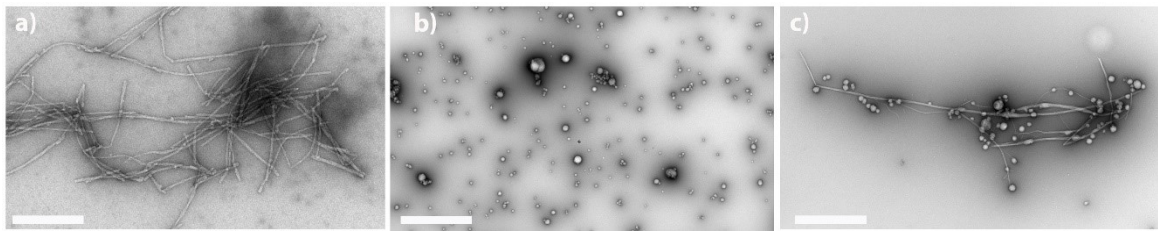


Figure S3: Additional TEM figures of RNYIAQVD assemblies, showing a) fibrillar polymorphs, b) oligomers, c) mixed populations of oligomers and fibrils. Scale bars a) = 200 nm, b) = 1000 nm, c) = 600 nm.

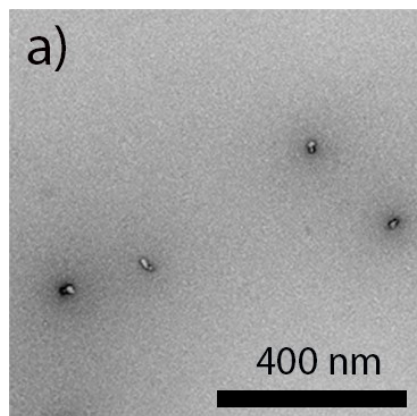


Figure S4: TEM image of small amorphous aggregates formed by the control peptide AAAAAA

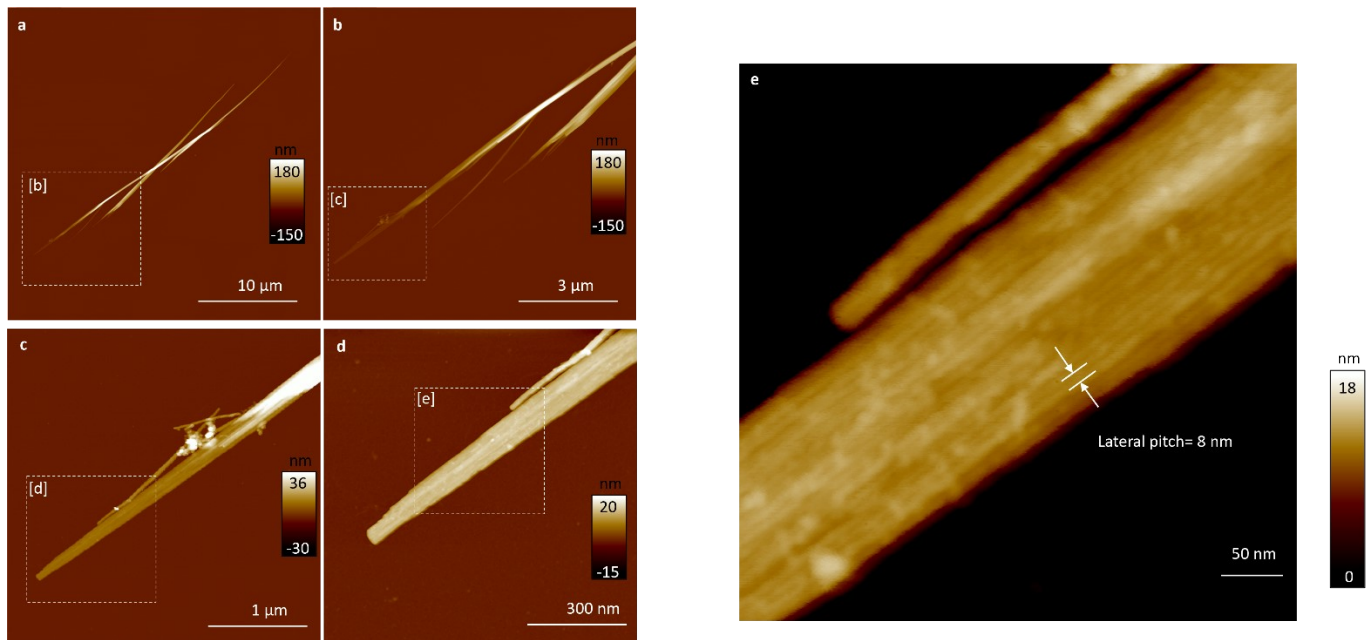


Figure S5: Additional AFM images showing that ILLIIM crystals are made from laterally associated protofilaments with a diameter of 8 nm.

Table S2: Fitting Parameters used to fit SAXS plots in figure 4 (NB. for χ^2_R a perfect fit = 1)

	Form Factor Used	Length (nm)	Width (nm)	Thickness (nm)	Reduced Chi2 (χ^2_R)
ILLIIM	Flattened bicelle	105.34	38.84	10	0.81
RNYIAQVD	Flexible cylinder	$3.17 \times 10^{32} (\infty)$	50.2	n/a	1.15
AAAAAA	Flexible cylinder	149.6	21.9	n/a	0.35 bad fit