Electronic Supplementary Material (ESI) for RSC Advances.

Electronic Supplementary Information

Cholesterol-sensing role of phenylalanine in the interaction of human islet amyloid polypeptide with lipid bilayers

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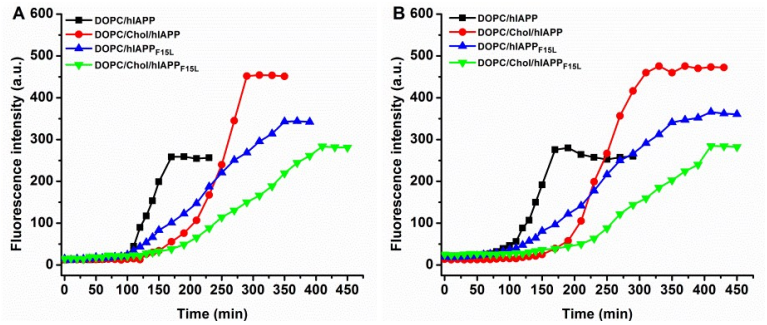

Fig. S1. Comparison between the kinetics of fibrillar assembly of hIAPP and hIAPP$_{F15L}$ in 10 mM Tris-HCl buffer with 100 mM NaCl at pH 7.4 (A) and in 25 mM phosphate buffer with 50 mM NaCl at pH 7.4 (B) in the presence of DOPC and DOPC/20%Chol LUVs monitored by ThT fluorescence.

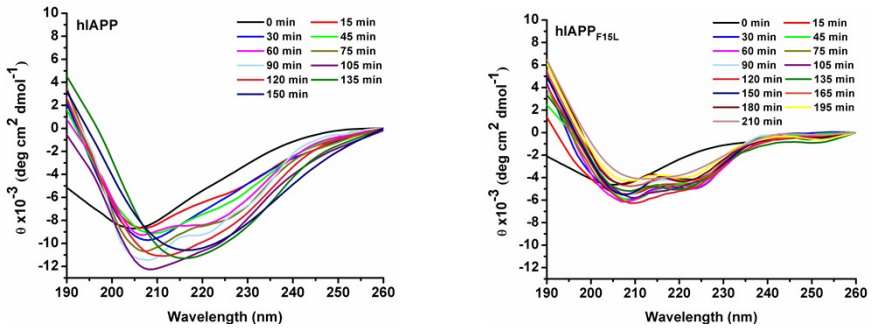

Fig. S2. CD spectra of hIAPP and hIAPP$_{F15L}$ (15 μM) at various incubation time recorded in phosphate buffer at pH 7.4, room temperature.

Table S1 Secondary structure data of hIAPP and hIAPP$_{F15L}$ in phosphate buffer at various time.

Peptide	Time (min)	Secondary structure (%)			
		Helix	Strand	Turn	Unordere
hIAPP	0	16.7	26.9	25.6	30.8
	60	20.3	25.2	24.7	29.7
	150	5.7	31.7	26.4	36.2
hIAPP$_{F15L}$	0	10.1	32.7	23.2	34.1
	60	14.3	31.4	21.0	33.0
	210	7.4	38.3	21.0	33.2

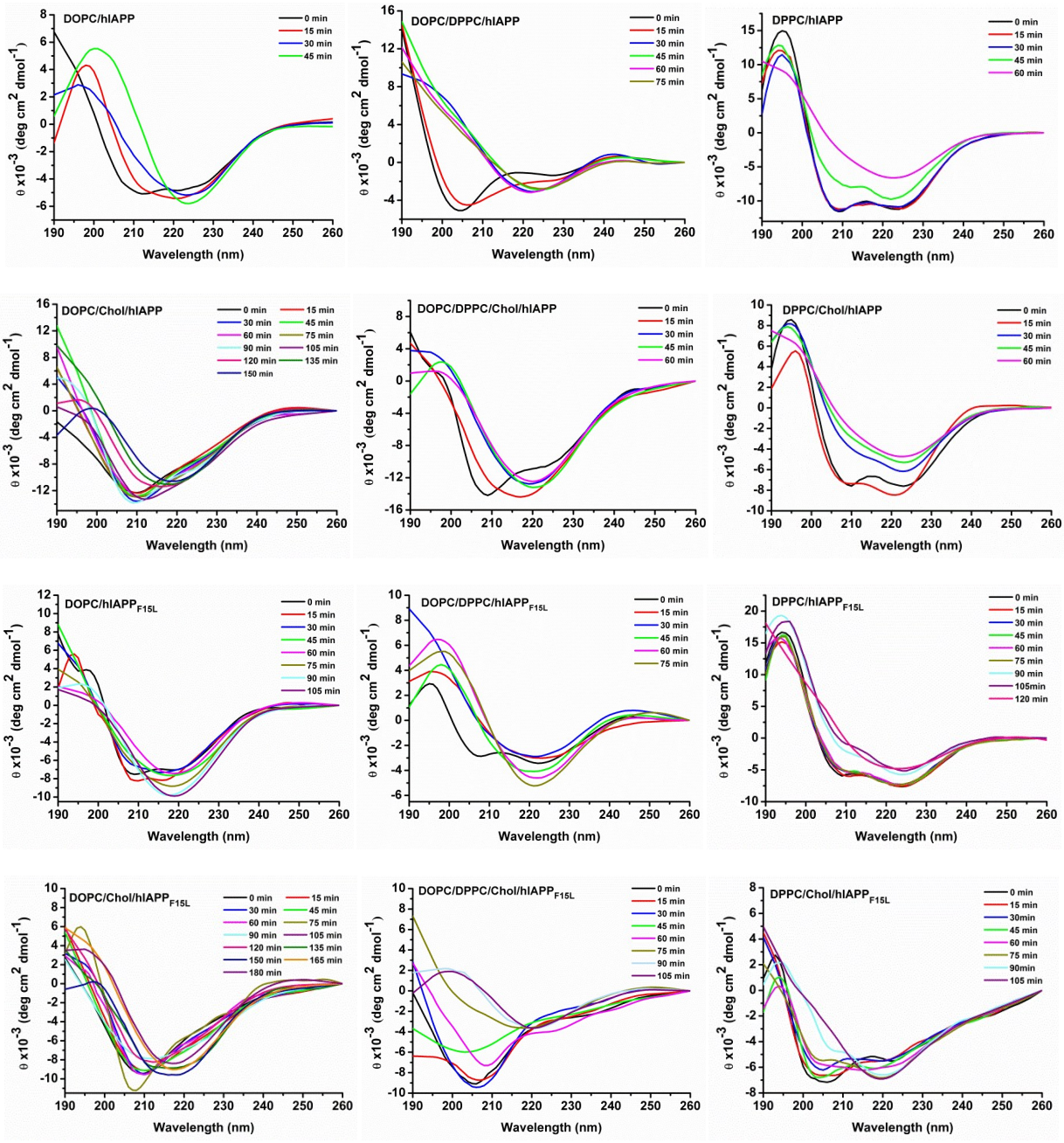

Fig. S3. CD spectra of hIAPP and $hIAPP_{F15L}$ in phosphate buffer in the presence of DOPC, DOPC/20%Chol, DOPC/DPPC 1:2, DOPC/DPPC/Chol 1:2:1, DPPC and DPPC/20%Chol LUVs at various incubation time.

Table S2 Secondary structure data of hIAPP and $hIAPP_{F15L}$ in phosphate buffer in the presence of DOPC, DOPC/20%Chol, DOPC/DPPC 1:2, DOPC/DPPC/Chol 1:2:1, DPPC and DPPC/20%Chol LUVs at various incubation time.

Peptide	Lipid	Time (min)	Secondary structure (%)			
			Helix	Strand	Turn	Unordered
hIAPP	DOPC	0	16.1	31.7	21.8	30.4
		15	7.8	33.8	26.5	31.9
		30	6.8	37.5	34.2	31.6
	DOPC/20%Chol	0	21.2	19.8	26.1	32.9
		60	23.2	22.9	21.8	32.2
		120	17.4	29.9	21.0	31.7
$hIAPP_{F15L}$	DOPC	0	19.2	26.4	21.8	32.6
		15	14.5	32.6	21.1	31.8
		45	8.9	35.7	21.9	33.5
	DOPC/20%Chol	0	18.9	26.6	22.4	32.1
		90	15.3	24.5	24.3	35.8
		135	7.8	33.2	29.2	29.9
hIAPP	DOPC/DPPC 1:2	0	17.2	30.3	17.5	34.9
		15	17.5	26.5	19.4	36.7
		30	2.9	44.9	21.0	31.1
	DOPC/DPPC/Chol 1:2:1	0	37.7	11.1	22.1	29.1
		15	20.0	23.9	22.2	33.9
		30	7.1	38.4	23.9	30.8
$hIAPP_{F15L}$	DOPC/DPPC 1:2	0	7.3	36.7	22.0	34.2
		15	4.8	41.4	21.9	31.9
		45	4.5	40.2	21.4	33.9
	DOPC/DPPC/Chol 1:2:1	0	7.6	33.3	24.9	34.3
		45	7.1	30.3	24.9	37.6
		90	4.1	41.4	21.5	33.0
hIAPP	DPPC	0	46.5	9.8	22.0	21.5
		45	29.5	21.2	22.2	27.2
		60	14.2	34.7	22.3	28.9
	DPPC/20%Chol	0	28.5	20.3	21.2	30.0
		30	17.2	31.1	21.0	30.6
		60	14.2	34.7	22.3	28.9
$hIAPP_{F15L}$	DPPC	0	29.5	23.5	21.1	25.9
		90	24.9	31.5	18.6	25.1
		120	5.3	42.5	22.4	29.9
	DPPC/20%Chol	0	23.8	17.3	25.8	33.1
		90	11.3	28.8	23.4	36.5
		105	8.6	36.9	25.5	29.1

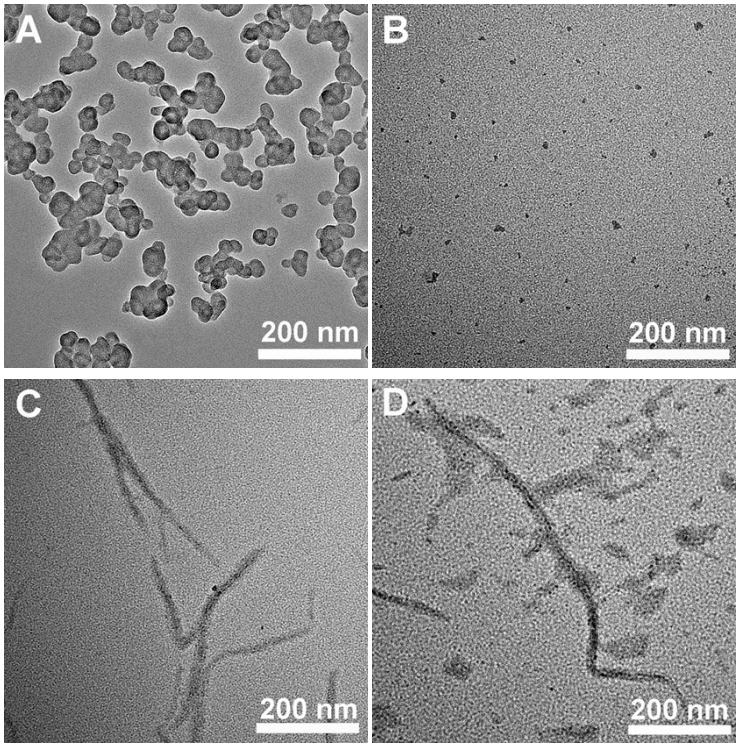

Fig. S4. TEM images of hIAPP and $hIAPP_{1-19/F15L}$ measured after incubation in phosphate buffer for 30 min (A and B, respectively) and 5 h (C and D, respectively).

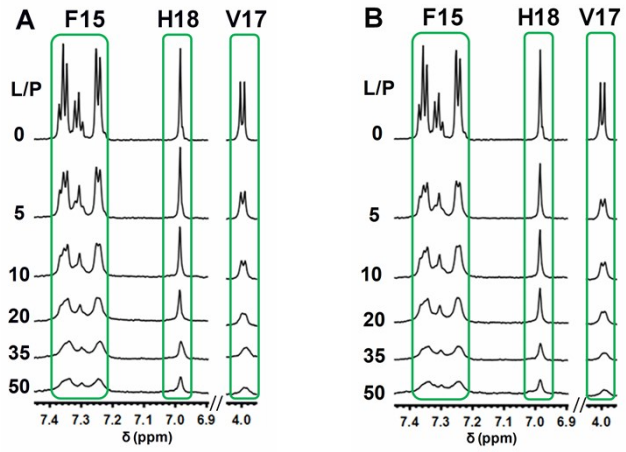

Fig. S5. ^{1}H-NMR signals in the regions of 6.95-7.40 ppm (aromatic protons of F15 and H18-H_δ) and 3.96-4.03 ppm (V17-H_α) used for calculation of dissociation constants of $hIAPP_{1-19}$ binding with DOPC (A) and DOPC/20%Chol (B) LUVs. The ^{1}H-NMR spectra were recorded in phosphate buffer at 25°C at various lipid-to-peptide ratios (L/P).

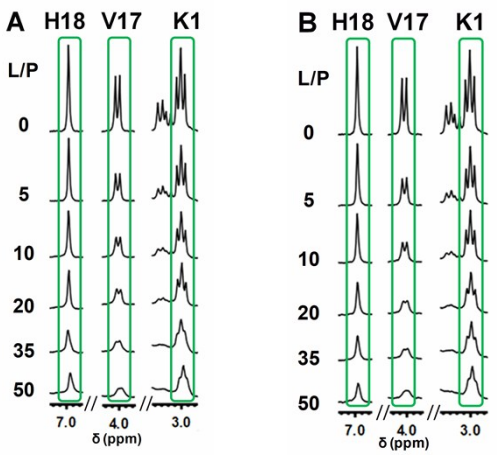

Fig. S6. ^{1}H-NMR signals in the regions of 6.95-7.03 ppm (H18-H_{δ}), 3.96-4.03 ppm (V17-H_{α}) and 2.97-3.02 ppm (K1-H_{ε}) used for calculation of dissociation constants of $hIAPP_{1\text{-}19/F15L}$ binding with DOPC (A) and DOPC/20%Chol (B) LUVs. The ^{1}H-NMR spectra were recorded in phosphate buffer at 25°C at various lipid-to-peptide ratios (L/P).

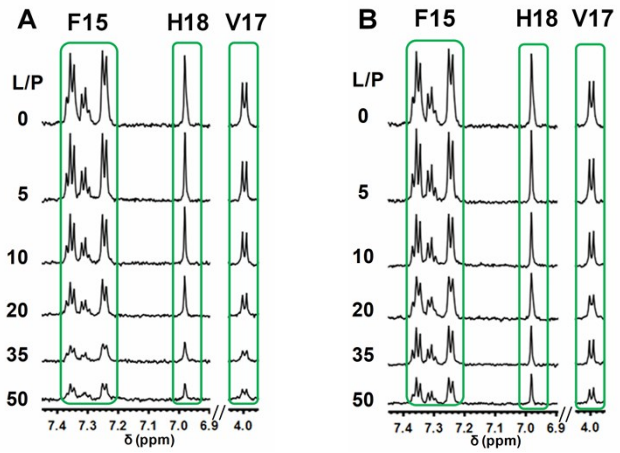

Fig. S7. ^{1}H-NMR signals in the regions of 6.95-7.40 ppm (aromatic protons of F15 and H18-H_{δ}) and 3.96-4.03 ppm (V17-H_{α}) used for calculation of dissociation constants of $hIAPP_{1\text{-}19}$ binding with DPPC (A) and DPPC/20%Chol (B) LUVs. The ^{1}H-NMR spectra were recorded in phosphate buffer at 25°C at various lipid-to-peptide ratios (L/P).

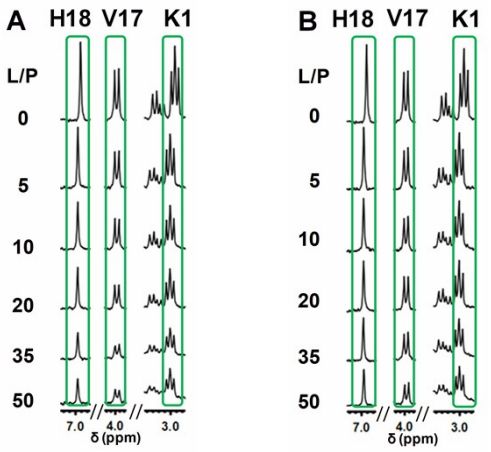

Fig. S8. ^{1}H-NMR signals in the regions of 6.95-7.03 ppm (H18-H_{δ}), 3.96-4.03 ppm (V17-H_{α}) and 2.97-3.02 ppm (K1-H_{ε}) used for calculation of dissociation constants of $hIAPP_{1\text{-}19/F15L}$ binding with DPPC (A) and DPPC/20%Chol (B) LUVs. The ^{1}H-NMR spectra were recorded in phosphate buffer at 25°C at various lipid-to-peptide ratios (L/P).