

## Supplementary Information

### **Mechanistic Insight into Functionally Different Human Islet Polypeptide (hIAPP) amyloid: The Intrinsic Role of the C-terminal Structural Motifs**

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**Table S1.** Fitting parameters of ThT fluorescence kinetics at 37 °C, under shaking conditions (250 rpm).

Peptide	hIAPP	VY21
$T_{\text{half}}$	$8.45 \pm 1.07$ min	$50.85 \pm 1.77$ min
$t_{\text{lag}}$	Not determined	$18.4 \pm 1.6$ min

**Table S2.** Fitting parameters of ThT fluorescence kinetics at 25 °C, under shaking conditions (250rpm).

Peptide	hIAPP	VY21
$T_{\text{half}}$	$31.73 \pm 2.14$ min	$109.72 \pm 18.94$ min
$t_{\text{lag}}$	$8.41 \pm 2.10$ min	$61.78 \pm 18.54$ min

**Table S3.** Fitting parameters of time-resolve fluorescence lifetime magic angle (54.7°) decay of 20  $\mu\text{M}$  ThT with 80  $\mu\text{M}$  hIAPP at 25 °C, under non-shaking condition.

Time/min	$a_1$	$\tau_1/\text{ps}$	$a_2$	$\tau_2/\text{ps}$	$a_3$	$\tau_3/\text{ps}$	$\langle\tau_{\text{life}}\rangle/\text{ps}$
0	0.99	5	0.005	498	0.005	1851	17
10	0.99	5	0.005	512	0.005	1907	17
20	0.99	5	0.005	551	0.005	1973	18
30	0.99	5	0.005	540	0.005	1970	18
40	0.99	5	0.005	537	0.005	1968	18
50	0.99	5	0.005	510	0.005	1973	17
60	0.99	5	0.005	592	0.005	2058	18
70	0.99	5	0.005	559	0.005	2044	18
80	0.99	5	0.005	585	0.005	2055	18
90	0.99	5	0.005	529	0.005	2034	18
100	0.98	5	0.01	572	0.01	2050	31
110	0.98	6	0.01	577	0.01	2072	32
120	0.98	6	0.01	557	0.01	2042	32
130	0.98	6	0.01	579	0.01	2068	32
140	0.98	6	0.01	595	0.01	2080	33
150	0.98	6	0.01	566	0.01	2077	32
160	0.98	6	0.01	594	0.01	2077	33
170	0.98	6	0.01	574	0.01	2063	32
180	0.98	6	0.01	571	0.01	2042	32
190	0.98	7	0.01	557	0.01	2017	33
200	0.90	14	0.06	511	0.04	1951	121

210	0.88	14	0.07	503	0.05	1921	144
220	0.86	15	0.08	528	0.06	1929	171
230	0.85	14	0.09	515	0.06	1896	172
240	0.81	16	0.12	522	0.07	1889	208
250	0.70	24	0.19	527	0.11	1872	323
260	0.55	53	0.30	614	0.15	1925	502
270	0.50	60	0.34	612	0.16	1908	543
280	0.45	97	0.38	685	0.17	1961	637
290	0.42	108	0.40	697	0.18	1951	675
300	0.40	100	0.40	648	0.20	1887	677
310	0.40	109	0.41	673	0.19	1912	683
320	0.40	148	0.41	737	0.19	1972	736
330	0.41	188	0.42	810	0.17	2028	762
340	0.41	183	0.42	790	0.17	2007	742
350	0.44	224	0.42	907	0.14	2185	785
360	0.46	241	0.42	951	0.12	2217	776

**Table S4.** Fitting parameters of time-resolve fluorescence lifetime magic angle (54.7°) decay of 20  $\mu$ M ThT with 80  $\mu$ M VY21 at 25 °C, under non-shaking condition.

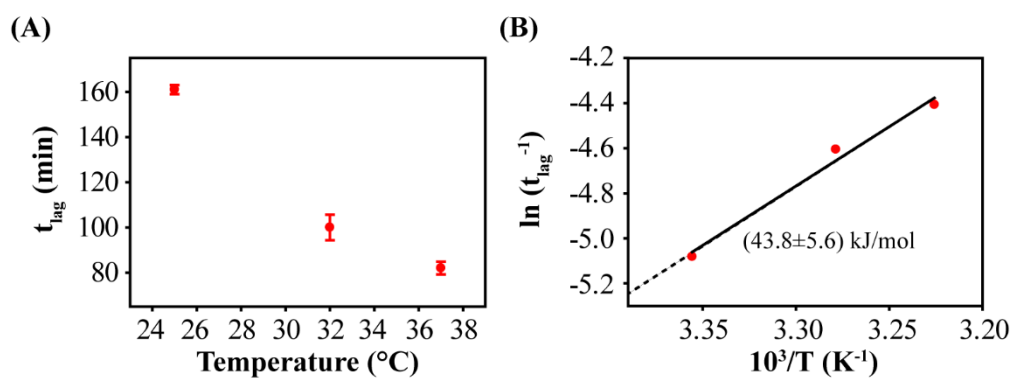
Time/min	a <sub>1</sub>	$\tau_1$ /ps	a <sub>2</sub>	$\tau_2$ /ps	a <sub>3</sub>	$\tau_3$ /ps	$\langle\tau_{life}\rangle$ /ps
0	0.61	42	0.31	398	0.08	1278	251
10	0.57	49	0.35	408	0.08	1210	268
20	0.54	57	0.37	410	0.09	1175	288
30	0.52	59	0.39	402	0.09	1163	292
40	0.52	53	0.39	389	0.09	1156	283
50	0.51	53	0.39	381	0.10	1131	289
60	0.49	55	0.41	387	0.10	1147	300
70	0.49	58	0.41	376	0.10	1105	293
80	0.51	75	0.39	420	0.10	1118	313
90	0.54	78	0.36	417	0.10	1127	305
100	0.47	79	0.43	432	0.10	1221	345
110	0.46	75	0.43	410	0.11	1182	341
120	0.46	82	0.43	414	0.11	1187	346
140	0.46	81	0.43	404	0.11	1160	339

160	0.46	77	0.43	412	0.11	1164	341
180	0.45	77	0.44	397	0.11	1155	337
210	0.46	78	0.43	411	0.11	1167	341
240	0.45	72	0.44	389	0.11	1132	328
270	0.45	86	0.44	407	0.11	1147	344
300	0.45	84	0.44	397	0.11	1140	338
330	0.45	85	0.44	405	0.11	1153	343
360	0.45	83	0.44	402	0.11	1138	339

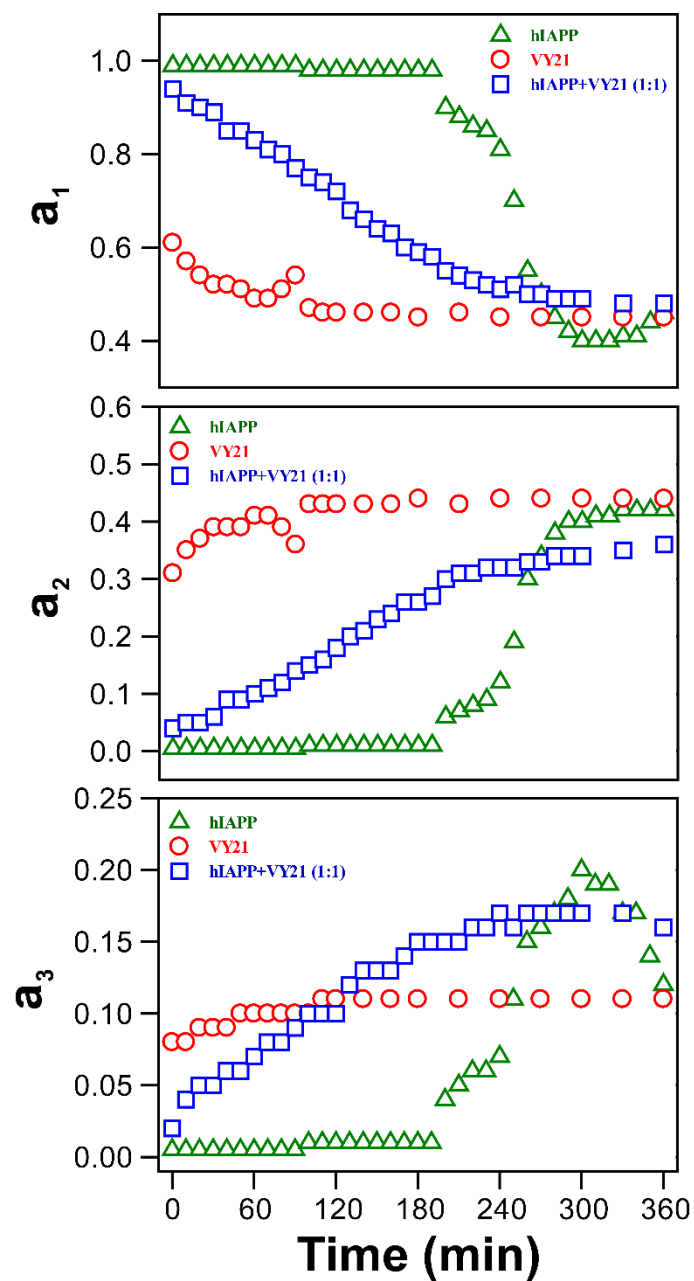
**Table S5.** Fitting parameters of time-resolve fluorescence lifetime magic angle (54.7°) decay of 20  $\mu$ M ThT with 80  $\mu$ M of both hIAPP and VY21 (1:1 molar ratio) at 25 °C, under non-shaking condition.

Time/min	a <sub>1</sub>	$\tau_1$ /ps	a <sub>2</sub>	$\tau_2$ /ps	a <sub>3</sub>	$\tau_3$ /ps	$\langle\tau_{life}\rangle$ /ps
0	0.94	10	0.04	565	0.02	2038	73
10	0.91	13	0.05	581	0.04	1995	121
20	0.90	15	0.05	582	0.05	1975	141
30	0.89	16	0.06	625	0.05	2005	152
40	0.85	17	0.09	574	0.06	1958	184
50	0.85	18	0.09	608	0.06	1989	189
60	0.83	20	0.10	591	0.07	1956	213
70	0.81	21	0.11	612	0.08	1982	243
80	0.80	23	0.12	615	0.08	1968	250
90	0.77	26	0.14	616	0.09	1974	284
100	0.75	27	0.15	624	0.10	1979	312
110	0.74	28	0.16	606	0.10	1954	313
120	0.72	30	0.18	620	0.10	1963	329
130	0.68	35	0.20	694	0.12	1969	399
140	0.66	36	0.21	634	0.13	1917	406
150	0.64	37	0.23	613	0.13	1894	411
160	0.63	38	0.24	607	0.13	1890	415
170	0.60	46	0.26	643	0.14	1905	461
180	0.59	45	0.26	628	0.15	1890	473
190	0.58	48	0.27	639	0.15	1909	487
200	0.55	50	0.30	644	0.15	1911	507
210	0.54	58	0.31	659	0.15	1909	522

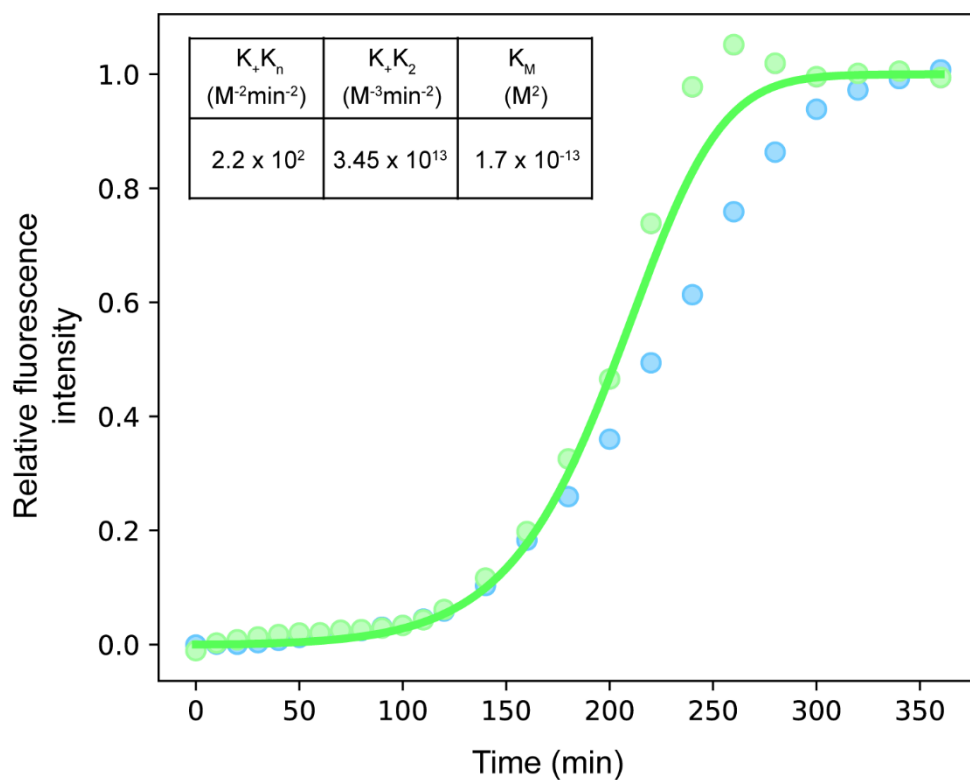
220	0.53	60	0.31	670	0.16	1924	547
230	0.52	63	0.32	673	0.16	1925	556
240	0.51	60	0.32	649	0.17	1895	560
250	0.52	65	0.32	691	0.16	1935	564
260	0.50	68	0.33	669	0.17	1900	577
270	0.50	68	0.33	669	0.17	1898	577
280	0.49	70	0.34	695	0.17	1926	598
290	0.49	68	0.34	674	0.17	1898	585
300	0.49	67	0.34	673	0.17	1903	585
330	0.48	70	0.35	672	0.17	1887	590
360	0.48	72	0.36	706	0.16	1924	597



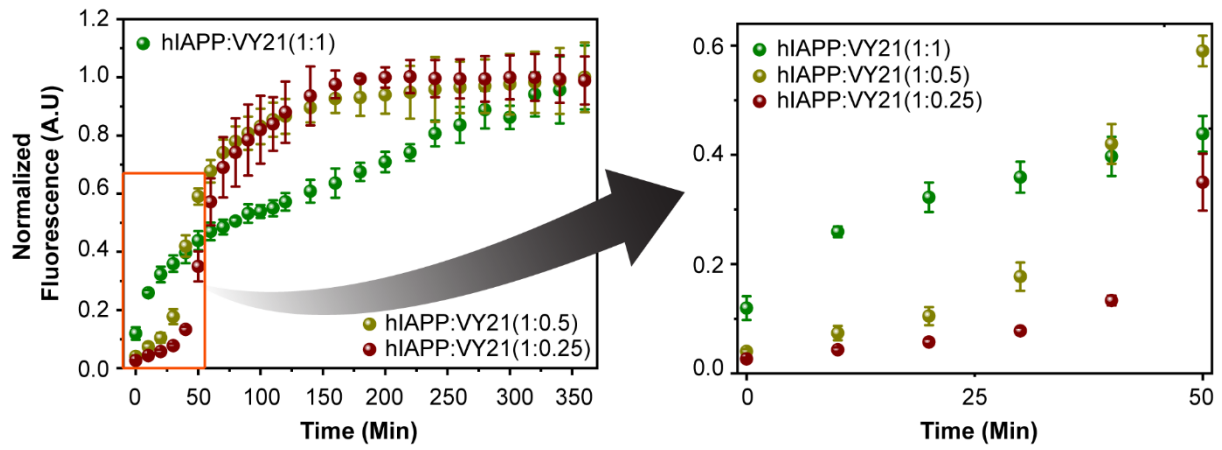
**Figure S1.** (A) Aggregation lag time ( $t_{lag}$ ) of hIAPP under non-shaking conditions plotted as a function of aggregation reaction temperature. (B) Arrhenius plot of initial elongation rate vs. inverse temperature for 80  $\mu$ M hIAPP samples. The activation energy calculated from the well fitted ( $R = 0.99$ ) data was  $43.8 \pm 5.6$  kJ/mol.



**Figure S2.** Stoichiometry of respective time scale in time-resolved fluorescence average lifetime of ThT with hIAPP, VY21, 1:1 mixture of hIAPP and VY21 (80  $\mu$ M) in phosphate buffer (20  $\mu$ M) solution up to 360 min at 25°C, under non-shaking conditions. All representations are color-coded.

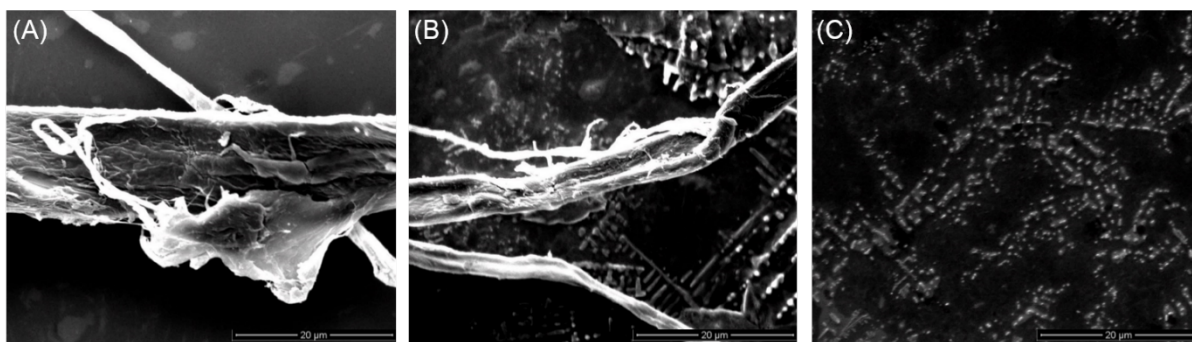


**Figure S3.** Fitting of ThT fluorescence curve of hIAPP at 25 °C under non-shaking conditions using the online platform Amylofit. Inset table shows the combined rate constant for secondary nucleation,  $k_+k_2$ , the combined rate constant for primary nucleation,  $k_+k_n$ , and the Michaelis constant,  $K_M$ , calculated from the fitting.



**Figure S4.** ThT fluorescence assay of hIAPP co-incubated with different ratios of VY21. Inset shows the aggregation kinetics of individual samples at the initial phase. With decreasing concentration of VY21, an increase in the lag-time was apparent.





**Figure S5.** SEM images of (A) hIAPP, (B) hIAPP co-incubated with VY21 at a 1:1 molar ratio, and (C) VY21 aggregates at 25 °C, under non-shaking conditions.