Supporting Information

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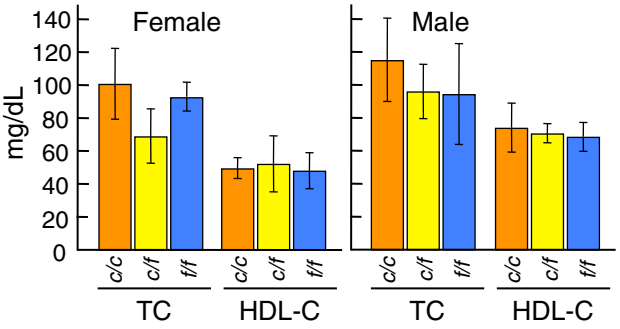

Fig. S1. Concentrations of plasma cholesterols in 2-mo-old R1.SPRET-*Apoa2*^{f} mice. Concentrations of plasma total and HDL cholesterols (TC and HDL-C, respectively) were assessed by enzymatic procedures. Each column and bar represents the mean ± SD (n = 3 females and 4 males). There were no significant differences in various pair-wise comparisons (Tukey–Kramer method for a multiple comparison).

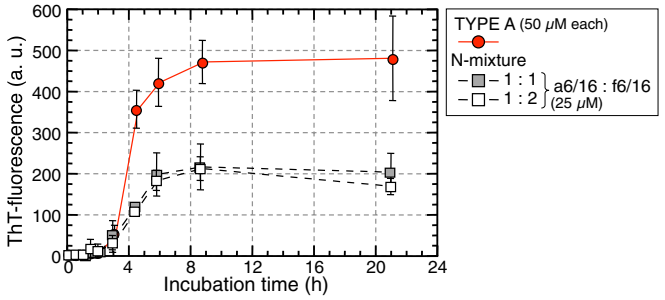

Fig. S2. Amyloid fibril formation by type A apolipoprotein (apo) A-II (APOA2A) peptides mixed with N-terminal peptide of type F apoA-II (APOA2F) at various concentrations. Reaction mixtures contained synthetic peptides in the reaction solution that consisted of 50 mM sodium citrate buffer (pH 2.5), 100 mM NaCl, and 5% (vol/vol) dimethyl sulfoxide (DMSO). Mixtures were agitated at 300 rpm at 37 °C, and aliquots were removed for Thioflavin T (ThT) binding assays at arbitrary intervals. ThT-fluorescence intensities of the mixture of amyloidogenic APOA2A peptides (a6/16 + a48/65, TYPE A) (50 μM each) were stable for ∼2 h of incubation (the nucleation phase), after which they increased linearly until reaching a plateau phase after ∼8 h (the extension phase). ThT intensities increased in a fashion similar to that of the N-mixture at equal concentrations (25 μM a6/16 + 25 μM f6/16 + 50 μM a48/65, N-mixture 1:1). In an N-mixture with f6/16 at a twofold concentration excess of a6/16 (N-mixture 1:2), the ThT-plot was similar to that of N-mixture 1:1. Each symbol and bar represents the mean ± SD (n = 3). a.u., arbitrary units.

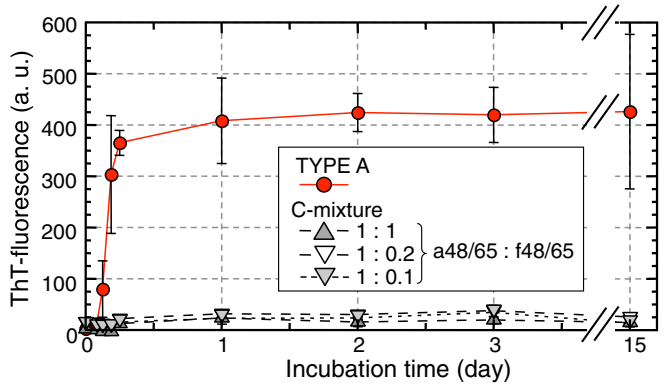

Fig. S3. Amyloid fibril formation of APOA2A peptides mixed with C-terminal peptide of APOA2F at various concentrations for reference to Fig. 5*E*. Concentration of the a48/65 was 25 μM in the reaction mixture. When APOA2A peptides were mixed with f48/65 at one-tenth concentration (C-mixture 1:0.1), ThT intensities did not increase even when incubation was continued for 15 d. Each symbol and bar represents the mean ± SD (n = 3). a.u., arbitrary units.

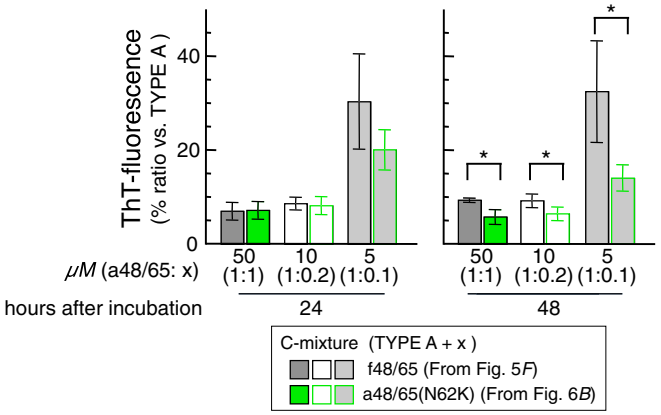

Fig. S4. Comparison of the inhibitory abilities of f48/65 and a48/65(N62K) peptides. Using ThT plots of Figs. 5*F* and 6*B*, we compared the inhibitory properties of the f48/65 and a48/65(N62K). ThT intensities are expressed as a percentage of each ThT level of type A observed after 24 and 48 h of incubation. Each bar and line represents the mean ± SD ($n = 4$). *$P < 0.05$ (Student's t test).

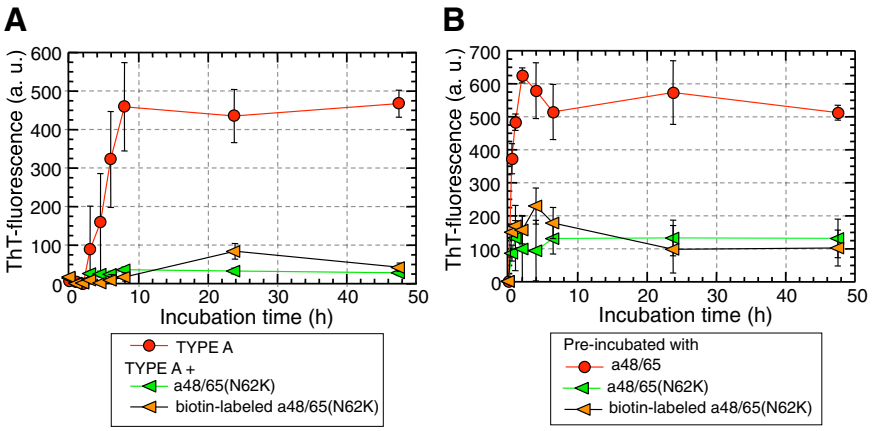

Fig. S5. Inhibitory effects of biotin-labeled a48/65(N62K) peptide on the polymerization and extension of TYPE A peptides. Similar to the experiments shown in Figs. 6*B* and 7*B*, we evaluated the inhibitory effects of biotin-labeled a48/65(N62K) on the polymerization of the amyloidogenic APOA2A peptides (*A*) and the extension of APOA2A peptides in the presence of preincubated seeds with C-terminal peptides (*B*). Both ThT plots in the mixtures using the biotin-labeled a48/65(N62K) were quite similar to those using the a48/65(N62K) over a 48-h incubation period. Each symbol and bar represents the mean ± SD (*A*, $n = 4$; *B*, $n = 3$). a.u., arbitrary units.

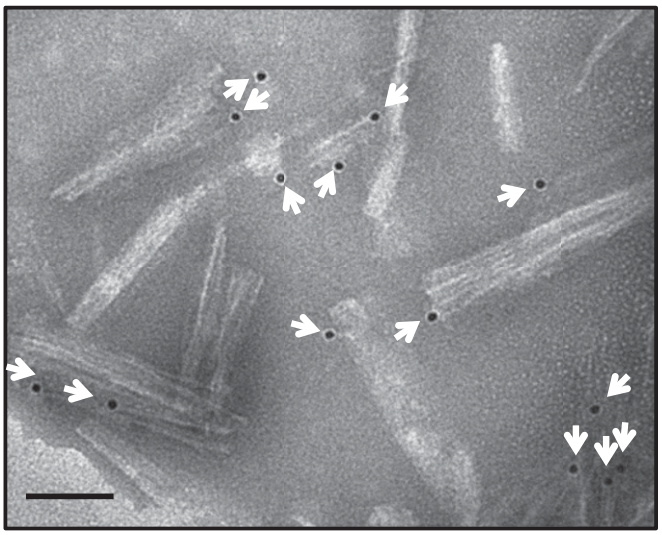

Fig. S6. TEM image of preincubated seeds with biotin-labeled a48/65(N62K) for reference to Fig. 7*D*. The preincubated seeds with biotin-labeled a48/65(N62K) were immersed in 1:4 streptavidin-conjugated 10 nm colloidal gold. There were many gold beads with streptavidin close to the heads of amyloid fibrils preincubated with biotin-labeled a48/65(N62K) (arrows). (Scale bar: 100 nm.)

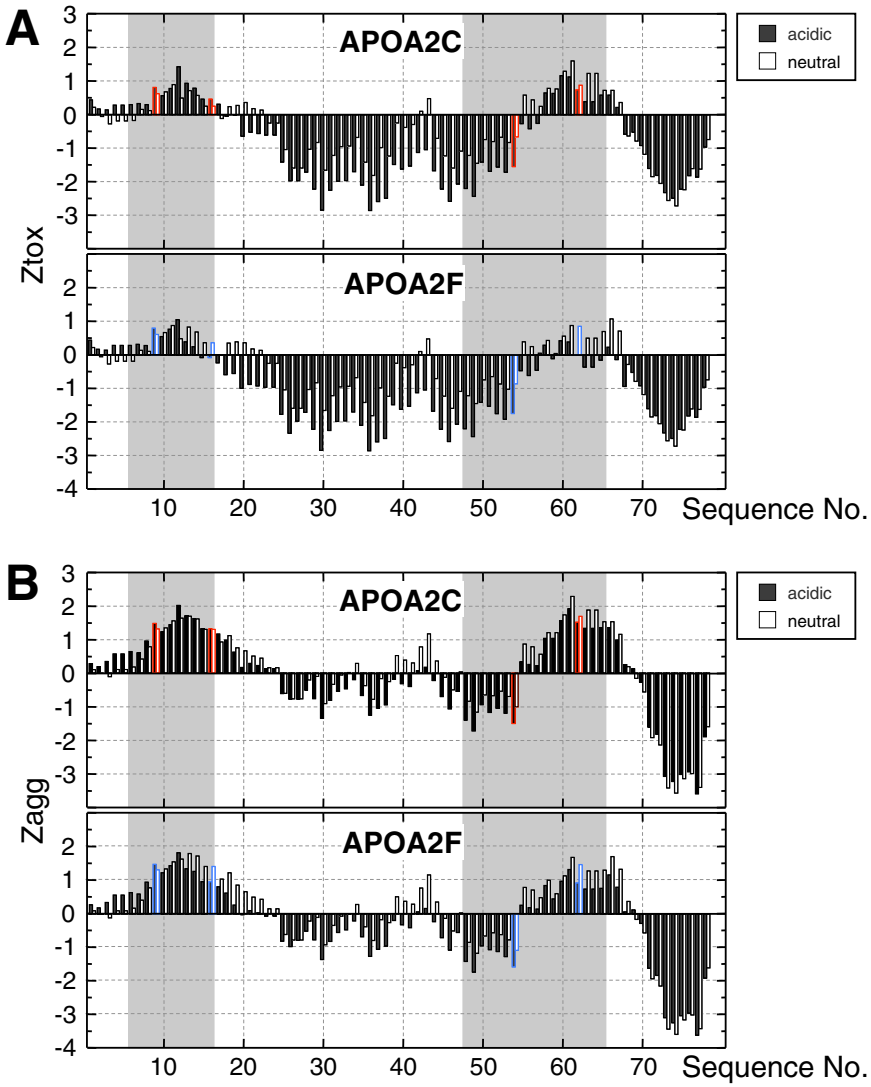

Fig. S7. Predicted amyloidogenic properties of APOA2C and APOA2F proteins. Images indicate the propensities of oligomeric (Ztox, *A*) and amyloid (Zagg, *B*) states of APOA2C and APOA2F proteins under neutral (native) and acidic (experimental) conditions using the Zyggregator Web Software (University of Cambridge). Gray zones indicate the critical sequences for polymerization into amyloid fibrils from our in vitro experiments. Orange and blue bars represent the predicted values at substitutions between APOA2C and APOA2F.

Table S1. Raw data of amyloid deposits in mice injected with AApoAII amyloid fibrils as shown in Fig. 2*A*

After induction, mo	*Apoa2* type	No.	Amyloid grade, average									
			Tongue	Stomach	Small intestine	Lung	Heart	Liver	Spleen	Skin	Kidney	AI
			Strain B6.SPRET-*Apoa2*^{f}									
3	*a/a*	5	2.30	1.60	0.80	1.60	0	0.20	0.20	0.20	0	0.76
3	*a/f*	8	1.21	0.57	0.14	0	0	0.14	0.14	0	0	0.31
3	*f/f*	4	0	0	0	0	0	0	0	0	0	0
6	*a/a*	7	3.29	2.43	1.64	2.79	0	1.86	0.14	1.07	2.00	1.49
6	*a/f*	11	1.27	0.82	0.73	0.55	0.09	0.09	0	0	0	0.43
6	*f/f*	4	0	0	0	0	0	0	0	0	0	0
9	*a/a*	4	3.50	3.75	2.75	3.75	1.00	2.50	1.75	2.25	2.25	2.65
9	*a/f*	6	1.58	1.08	0.67	0.50	0	0.33	0	0	0.17	0.52
9	*f/f*	4	0	0	0	0	0	0	0	0	0	0
			Strain R1.SPRET-*Apoa2*^{f}									
2	*c/c*	6	3.17	2.50	2.33	2.83	1.50	1.83	2.33	1.50	0.83	2.17
2	*c/f*	6	1.83	1.33	1.17	1.50	0.83	0.83	1.00	0	0.83	1.00
2	*f/f*	4	0	0	0	0	0	0	0	0	0	0
6	*c/c*	9	3.94	3.00	3.11	3.11	2.83	3.72	4.00	2.56	3.56	3.31
6	*c/f*	9	2.94	2.28	2.44	3.22	0.56	0.44	0.22	1.50	0	1.48
6	*f/f*	4	0	0	0	0	0	0	0	0	0	0

AI, the average of amyloid deposit grades in the tongue, stomach, small intestine, heart, liver, spleen, and skin.

Table S2. Spontaneous amyloid deposits in R1.SPRET-*Apoa2*^{f} mice without injection of AApoAII fibrils

Apoa2 type	Age, mo	Case/at risk	Amyloid grade, average									
			Tongue	Stomach	Small intestine	Lung	Heart	Liver	Spleen	Skin	Kidney	AI
c/c	10	6/6	2.67	1.83	1.83	2.33	1.33	1.33	2.33	0	1.17	1.62
c/f	13	2/5	0.40	0	0.80	0.40	0.20	0	0	0	0	0.20
f/f	13	0/8	0	0	0	0	0	0	0	0	0	0

AI, the average of amyloid deposit grades in the tongue, stomach, small intestine, heart, liver, spleen, and skin.

Table S3. Raw data of amyloid deposits in amyloidosis-susceptible mice injected with AApoAII fibrils as shown in Fig. 8*A*

Treatment	Case/at risk	Amyloid grade, average									
		Tongue	Stomach	Small intestine	Lung	Heart	Liver	Spleen	Skin	Kidney	AI
Vehicle	5/5	3.00	2.00	2.20	2.20	1.40	1.60	1.20	1.00	1.20	1.77
a48/65	4/4	2.50	2.00	3.25	2.50	0.75	2.00	1.75	0.75	0.25	1.86
a48/65(N62K)	6/6	2.17	0.83	1.67	2.00	0.33	0.17	0.17	0.33	0	0.81

AI, the average of amyloid deposit grades in the tongue, stomach, small intestine, heart, liver, spleen, and skin.

Table S4. The specific primers for *Apoa2*^{f} congenic mice

Gene	Primer sequences (5′–3′)	
	Forward	Reverse
Apoa2^a	GCCTGTTCACTCAATACTTTCAG	CAGACTAGTTCCTGCTGACC
Apoa2^c	GCCTGTTCACTCAGTACTTTCAG	CAGACTAGTTCCTGCTGACC
Apoa2^f	ACCTGTTCACTCAGTACTTTCAT	CAGACTAGTTCCTGCTGACT

Bold and colored letters indicate the variant nucleotides among *Apoa2*^{a}, *Apoa2*^{c}, and *ApoA2*^{f} genes. Red letters represent polymorphisms in nucleotide positions of *Apoa2*^{f} gene (blue letters).