Supplementary Information

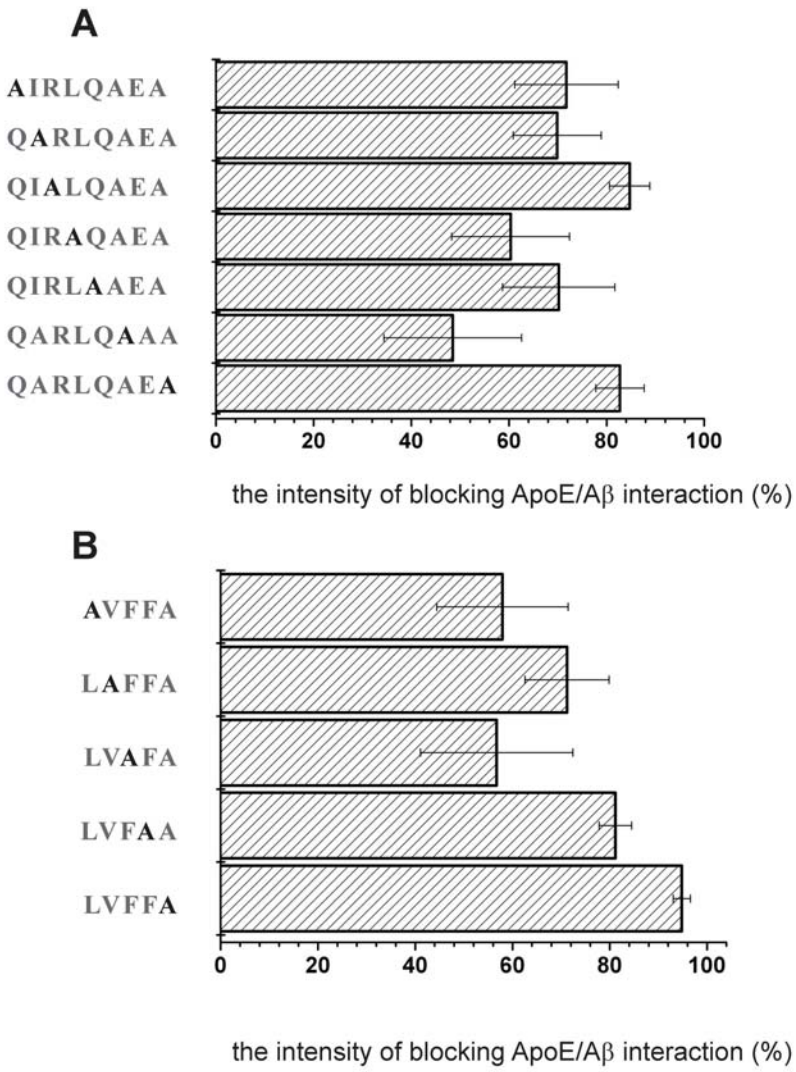

Figure S1. Alanine scanning mutagens of ApoE249-256 and Aβ17-21. (A) Alanine scanning of ApoE249-256,; (B) Alanine scanning of Aβ17-21. Peptides (Left) corresponding to the sequences of ApoE 249-256 or Aβ17-21 were synthesized. The sites for alanine mutagens are denoted in bold. The concentration of each peptide was 300 μM. The values are means ± SD, n = 3 replicate wells.

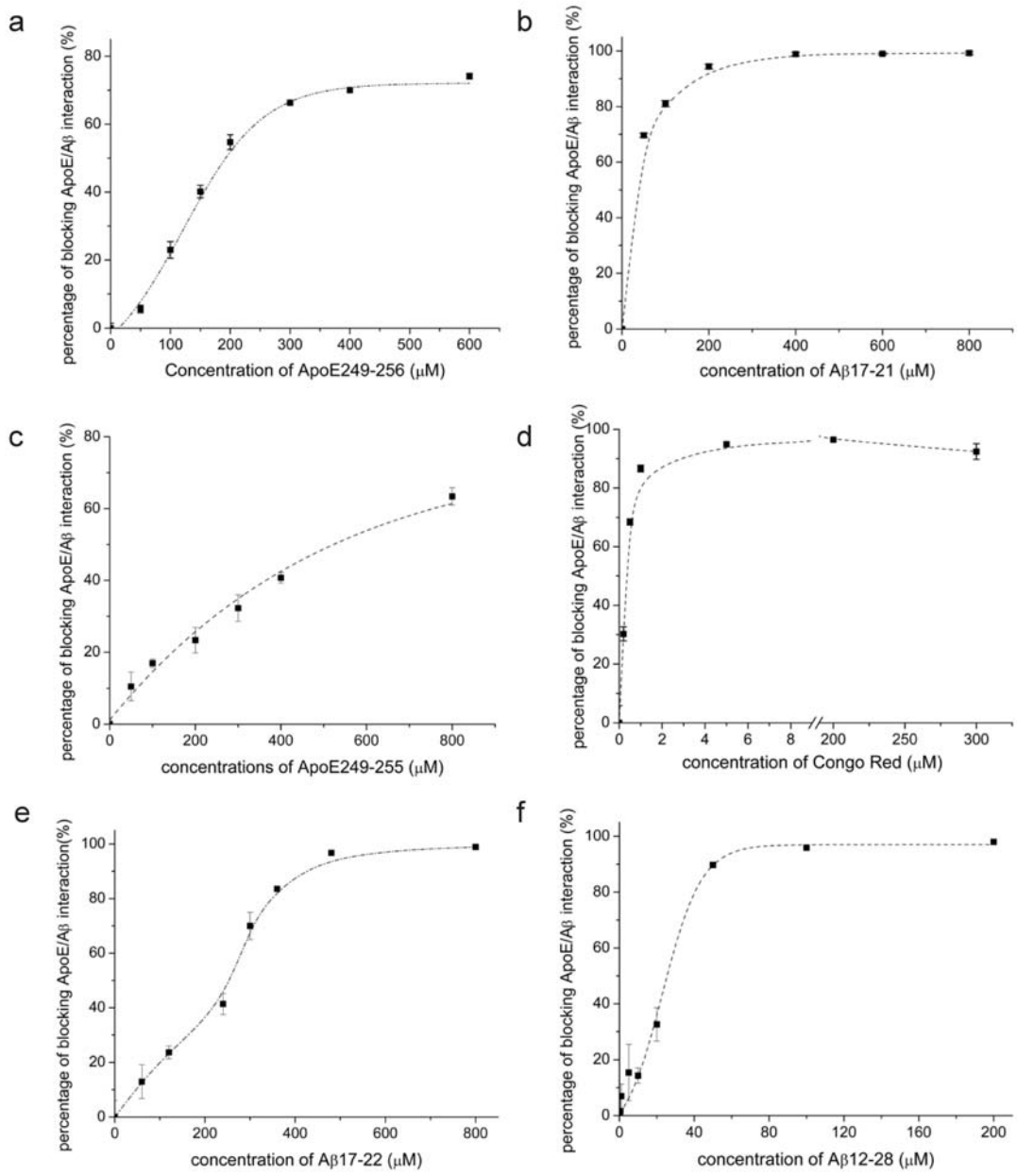

Figure S2. The compounds (a) QIRLQAEA (ApoE249-256), (b) LVFFA (Aβ17-21), (c) QIRLQAE (ApoE249-255), (d) Congo Red, (e) LVFFAE (Aβ17-22) and (f) Aβ12-28 show their dose-dependent inhibition of ApoE4/Aβ binding at increasing compound concentrations. The values are means ± SD, n = 3 replicate wells.

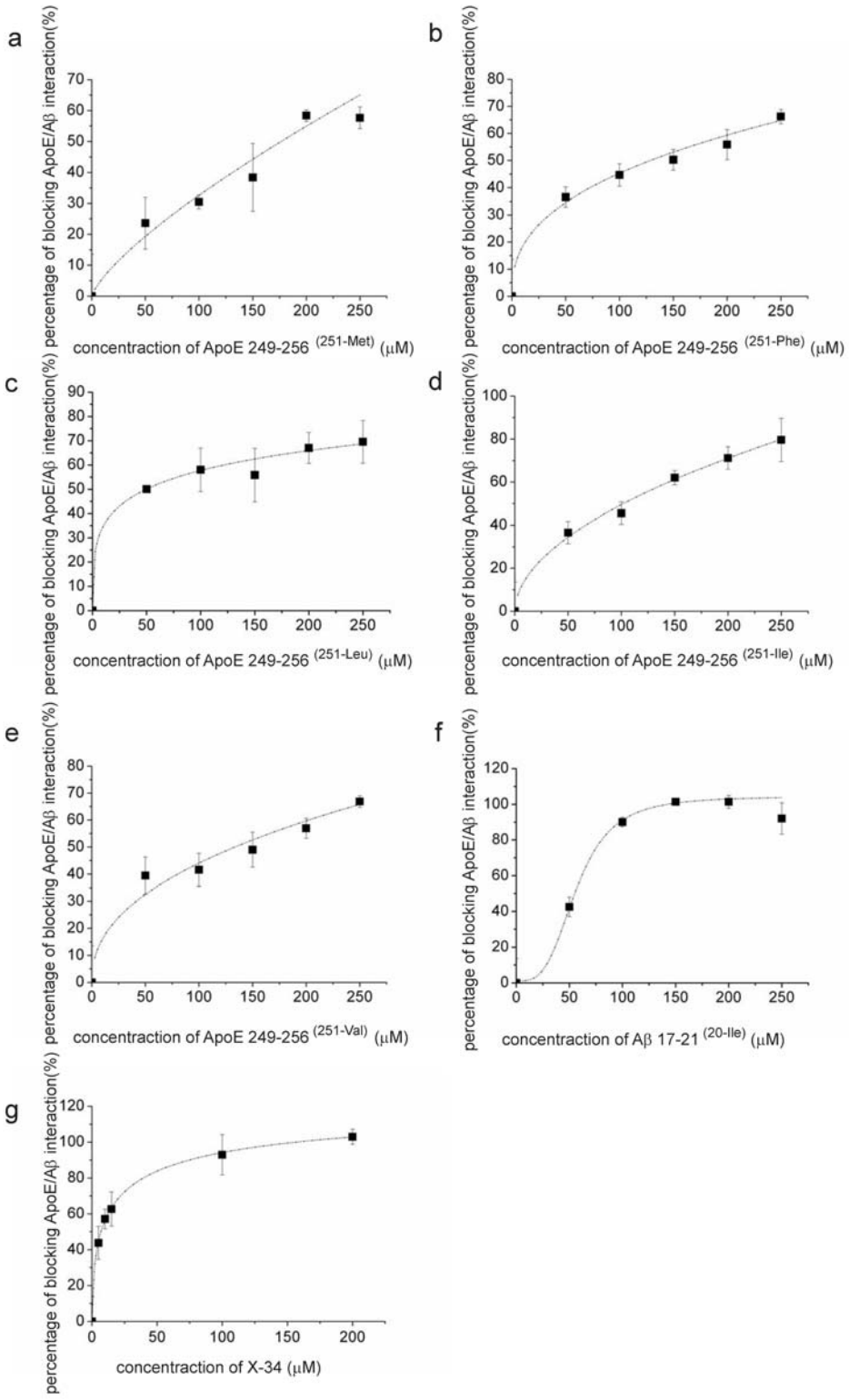

Figure S3. The compounds (a) QIMLQAEA (ApoE249-256$^{251\text{-Met}}$), (b) QILLQAEA (ApoE249-256$^{251\text{-Phe}}$), (c) QIVLQAEA (ApoE249-256$^{251\text{-Leu}}$), (d) QIFLQAEA (ApoE249-256$^{251\text{-Ile}}$), (e) QIILQAEA (ApoE249-256$^{251\text{-Val}}$), (f) LVFIA (Aβ17-21$^{20\text{-Ile}}$), (g) X-34 show their dose-dependent inhibition of ApoE4/Aβ binding at increasing compound concentrations. The values are means ± SD, n = 3 replicate wells.

K_d calculation:

There are two dependent heterogeneous equilibria in the competitive assay, shown as follows,

$$K_{d,x} = \frac{[A\beta]_I[x]}{[A\beta - x]_I} \quad (1)$$

$$K_{d,ApoE} = \frac{[A\beta]_I[ApoE]}{[A\beta - ApoE]_I} \quad (2)$$

where $K_{d,x}$ is the dissociation constant between immobilized Aβ1-40 and small compound (x), subscript I means immobilized, and Aβ-x means the complex of Aβ1-40 and small compound.

The denotation in formula (2) is similar to that in formula (1).

Concentration (IC_{50}) of such inhibitory compounds at which half inhibitory ability compared to that of well containing no ApoE can be read directly from Figure 3. At this specific concentration, the amounts of Aβ1-40-ApoE complex and Aβ1-40-x complex will be the same and by combining two equilibrium formulas (1, 2) together, the following formula for $K_{d,x}$ can be obtained,

$$K_{d,x} = \frac{[x] * K_{d,ApoE}}{[ApoE]} \quad (3)$$

According to Adam's work [S1], the stoichiometry of Aβ1-40 to ApoE binding is 1:1. Therefore it is reasonable to assume the same stoichiometry for x to ApoE4 binding. Taking the fact that [ApoE] is half of the total concentration into account $[ApoE]_0$ as well, formula (3) can be converted to:

$$K_{d,x} = \frac{(IC_{50} - [ApoE]_0/2) * K_{d,ApoE}}{[ApoE]_0/2} \quad (4)$$

from which $K_{d,x}$ can be easily calculated ($K_{d,ApoE}$=20 nM, according to the report S1).