Design and synthesis of curcumin analogues for in vivo fluorescence imaging and inhibiting copper-induced crosslinking of amyloid beta species in Alzheimer's disease

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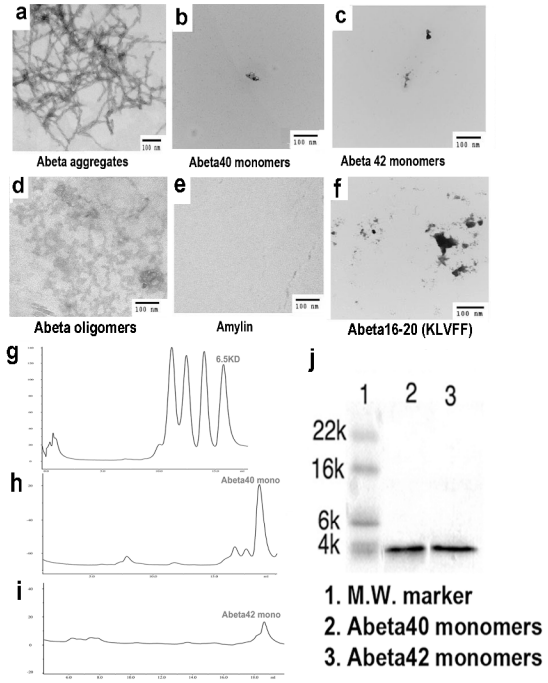
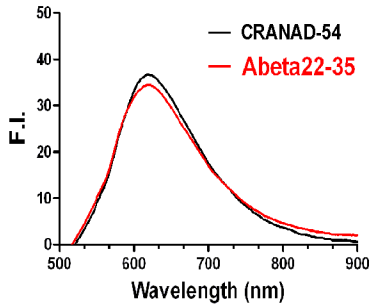
Supplemental Information

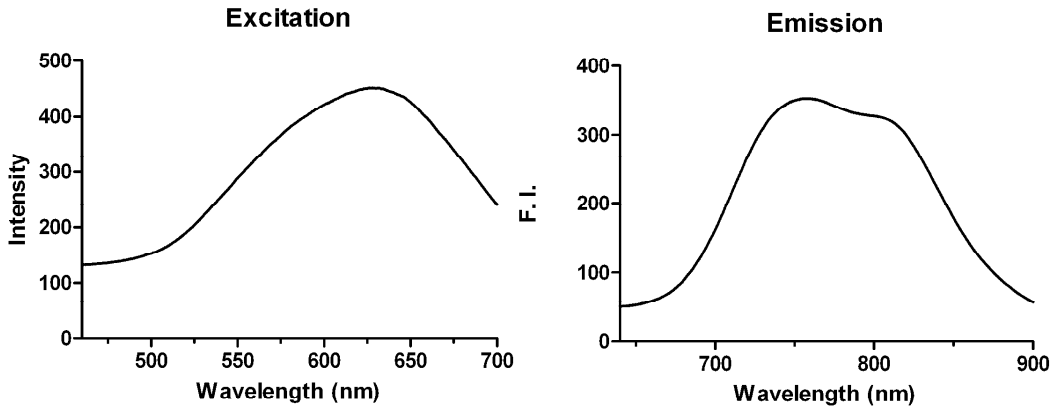
SI Figure legends



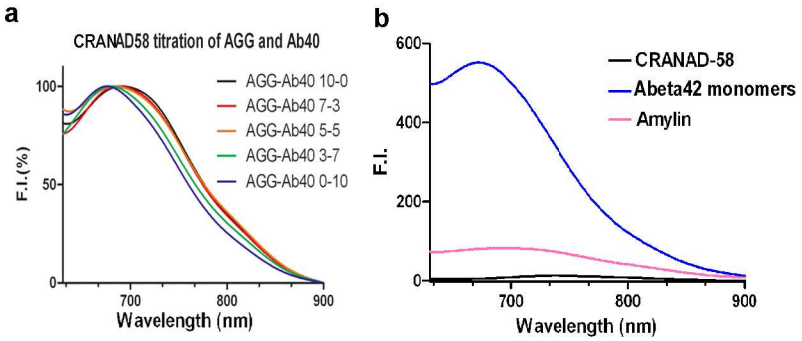
SI Fig.1 TEM (negative staining with PTA) of Aβ40 aggregates (a), Aβ40 monomers (b), Aβ42 monomers (c), Aβ42 oligomers (d), Amylin (e), and Aβ16-20 (f), scale bar: 100nm. (g-i) Size exclusion chromatography (SEC) of standard protein (g), Aβ40 monomers (h) and Aβ42 monomers (i). (j) SDS-PAGE gel of Aβ40 and Aβ42 monomers.



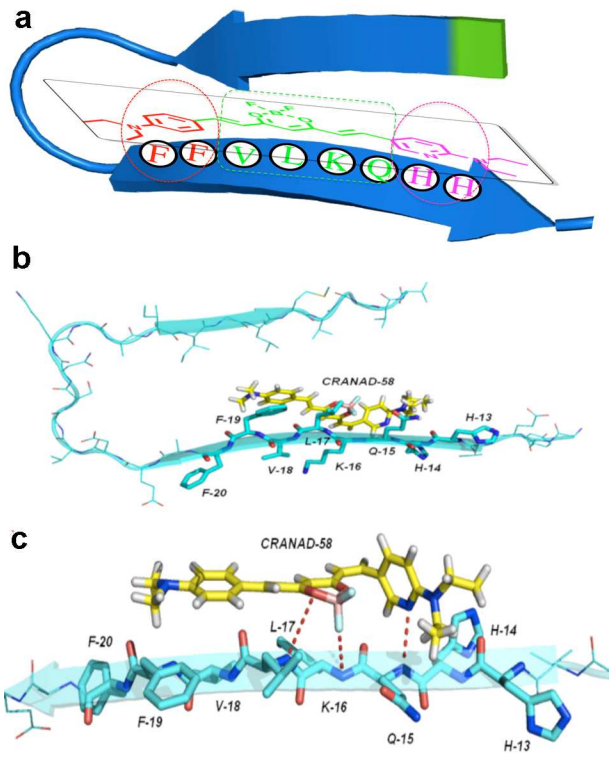
SI Fig.2 Fluorescence emission spectra of CRANAD-54 alone (black), and with Aβ22-35 (red).



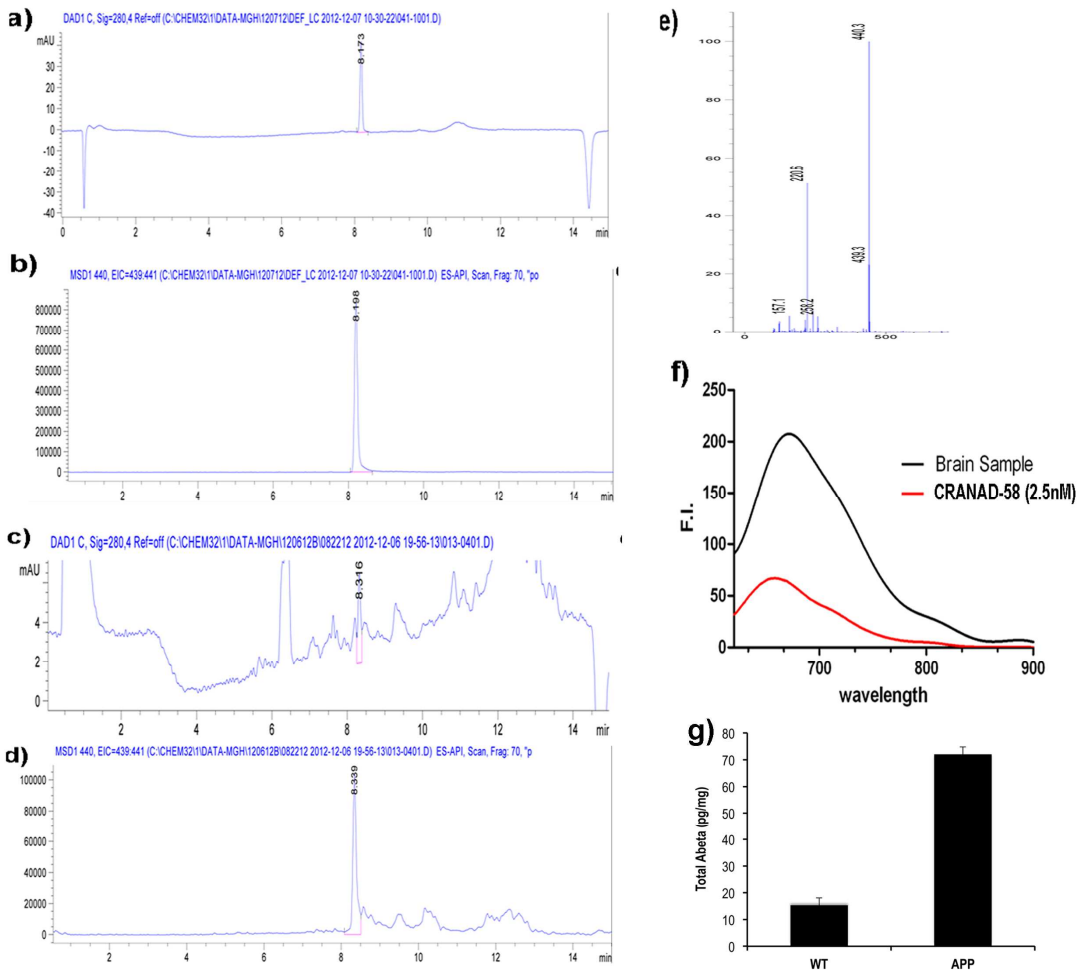
SI Fig.3 The excitation and emission spectra of CRANAD-58 (2.5μM in PBS, pH 7.4).



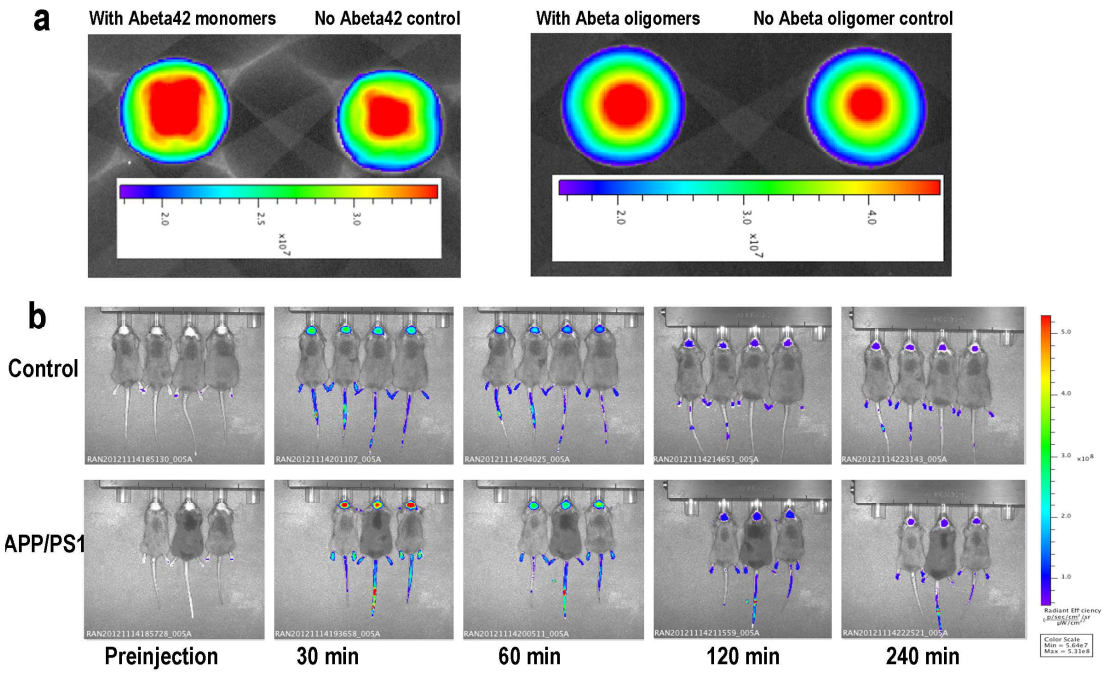
SI Fig.4 (a) Fluorescence spectra of CRANAD-58 titration with Aβ monomers and aggregates. (b) Fluorescence emission spectra of CRANAD-58 alone (black), with amylin (pink) and Aβ42 monomers (blue).



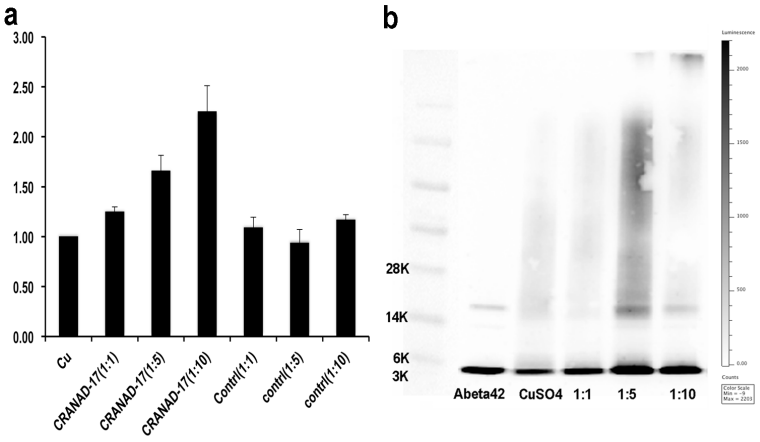
SI Fig.5 (a) The proposed interaction model of CRANAD-58 with Aβ40/42, in which the three interacting pockets are highlighted with circles or rectangle. (b) Docking results of CRANAD-58 with Aβs, and (c) a zoomed in image of (b).



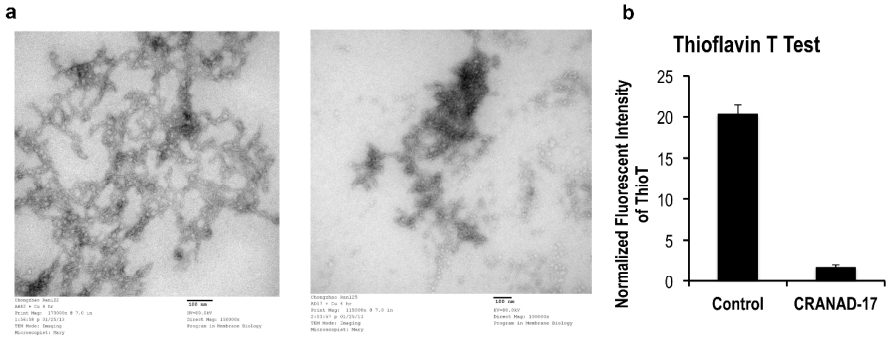
SI Fig.6 LC-MS and fluorescence spectra measurements of brain extracts (in 80% acetonitrile) 60 min after CRANAD-58 injection. (a) LC spectrum of CRANAD-58 (UV = 280nm); (b) LC-MS of ion extraction with m/z = 439-411 (M.W. of CRANAD-58: 440.3). (c) LC spectrum of CRANAD-58 from the brain extracts (UV = 280nm); (d) LC-MS of ion extraction with m/z = 439-411; the peak corresponds to the M.W. of CRANAD-58. (e) MS spectra of CRANAD-58. (f) Fluorescence spectra of standard CRANAD-58 (red line, in 80% acetonitrile), and brain extractions (black). (g) ELISA of Aβ levels in brain homogenates of APP/PS1 mice and control mice.



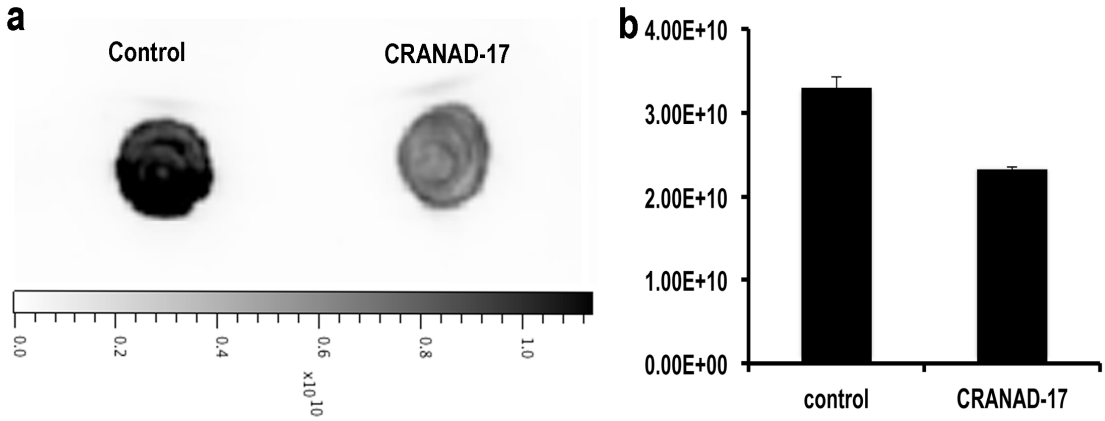
SI Fig.7 (a) Brain phantom imaging with Aβ monomers (left) and oligomers (right). (b) Images of all mice used for in vivo imaging.



SI Fig.8 Quantitative analysis of monomeric bands in Fig.8c. (b) Western blot of Aβ42 (without copper, lane 1), treated with $CuSO_4$ (lane 2), and $CuSO_4$ + CRANAD-17 (lanes 3-5) (Aβ42/CRANAD-17 = 1:1, 1:5, and 1:10).



SI Fig.9 (a) TEM imaging of Aβ42 treated with $CuSO_4$ (left), and with $CuSO_4$+CRANAD-17 (right). (b) Fluorescence intensity of Thioflavin T obtained from Aβ42 solutions treated with $CuSO_4$ and $CuSO_4$+CRANAD-17.



SI Fig.10 (a) Dot-blotting of Aβ42 treated with $CuSO_4$ (left) and with $CuSO_4$+CRANAD-17 (right) using Aβ antibody 2H4, which has better recognizing capability for Aβ fibrils. (b) Quantitative analysis of (a) (n =2).