Supplementary Material (ESI) for Molecular BioSystems

Clarifying the Influence of Core Amino Acid Hydrophobicity, Secondary Structure Propensity, and Molecular Volume on Amyloid-β 16–22 Self-Assembly †

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ELECTRONIC SUPPORTING INFORMATION

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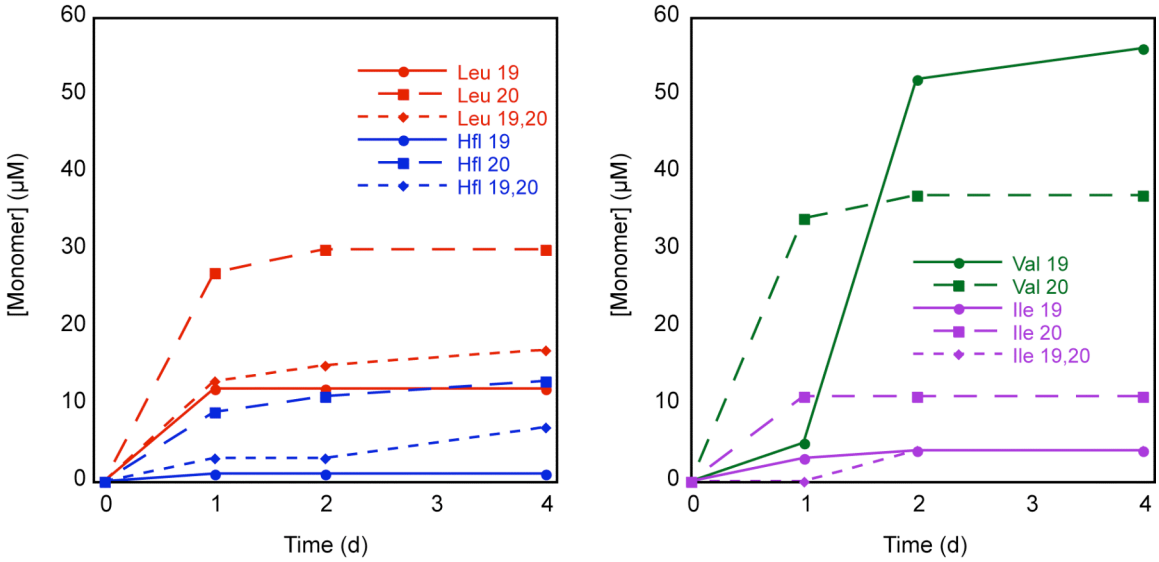

Figure S2. HPLC trace (215 nm) of Aβ(16–22) Val 19.

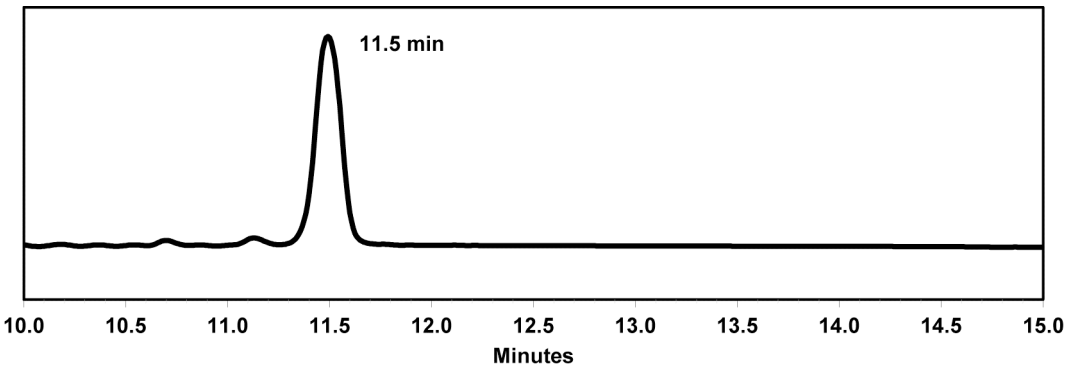

Figure S3. HPLC trace (215 nm) of Aβ(16–22) Val 20.

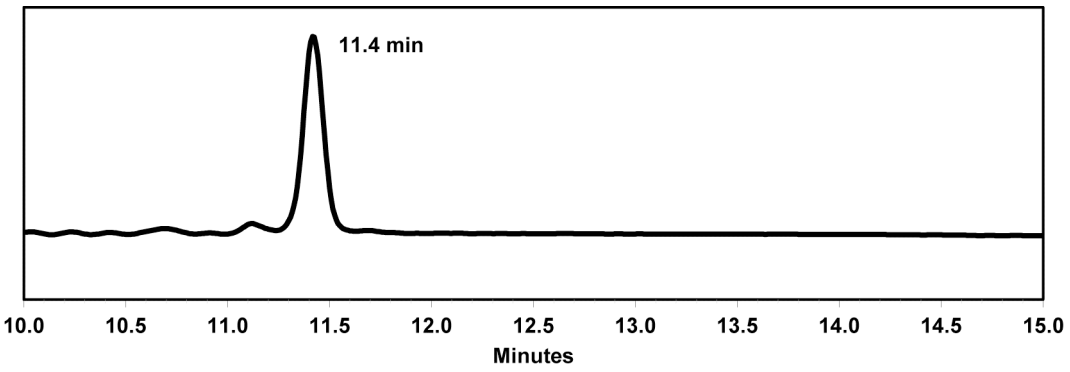

Figure S4. HPLC trace (215 nm) of Aβ(16–22) Val 19,20.

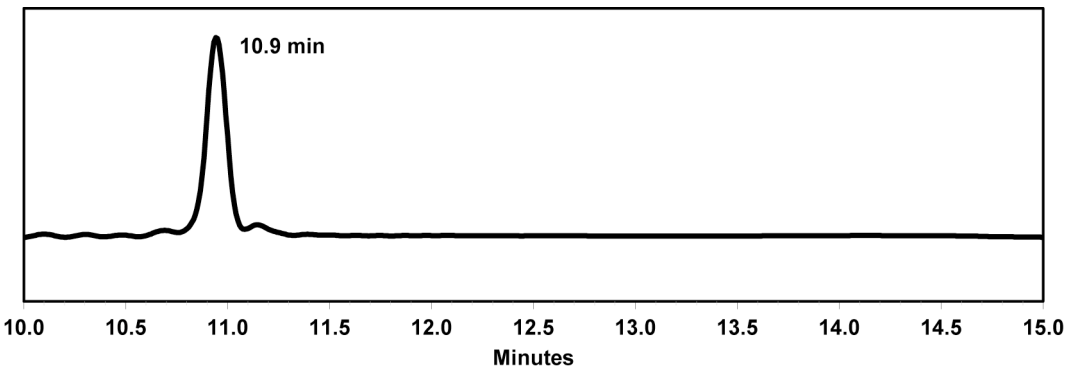

Figure S5. HPLC trace (215 nm) of Aβ(16–22) Leu 19.

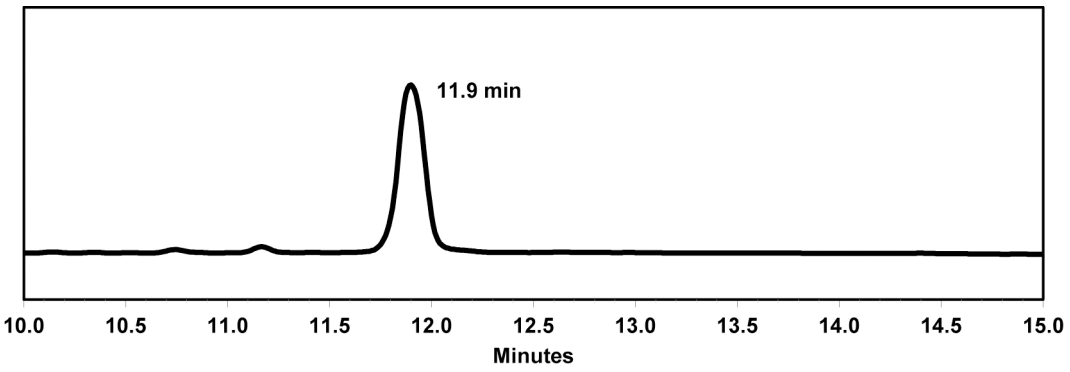

Figure S6. HPLC trace (215 nm) of Aβ(16–22) Leu 20.

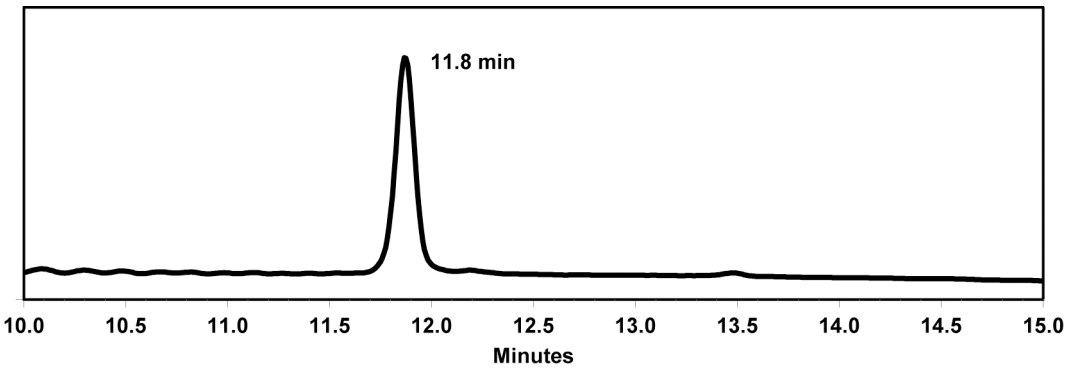

Figure S7. HPLC trace (215 nm) of Aβ(16–22) Leu 19,20.

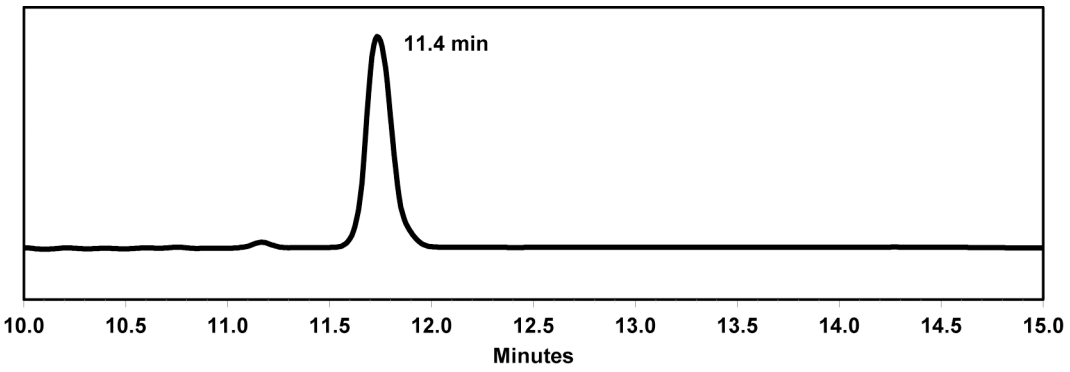

Figure S8. HPLC trace (215 nm) of Aβ(16–22) Ile 19.

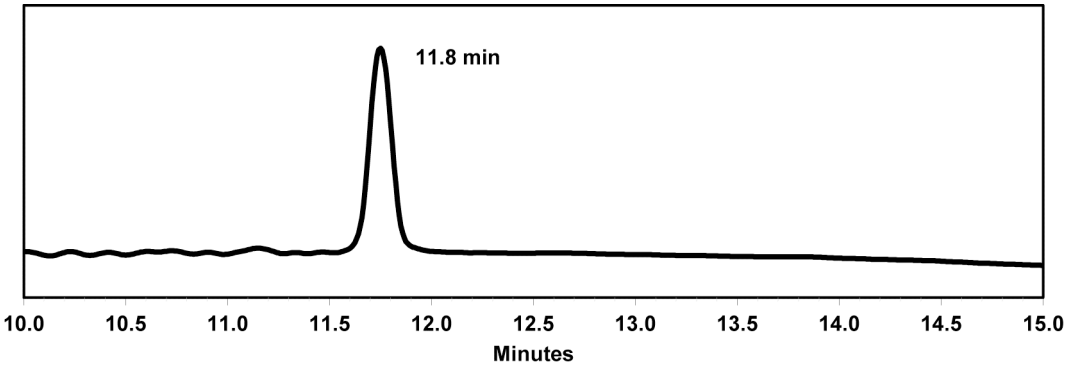

Figure S9. HPLC trace (215 nm) of Aβ(16–22) Ile 20.

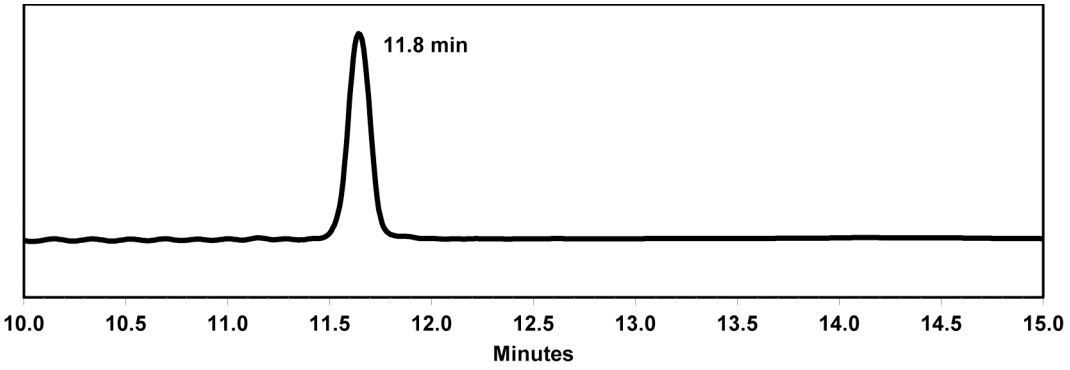

Figure S10. HPLC trace (215 nm) of Aβ(16–22) Ile 19,20.

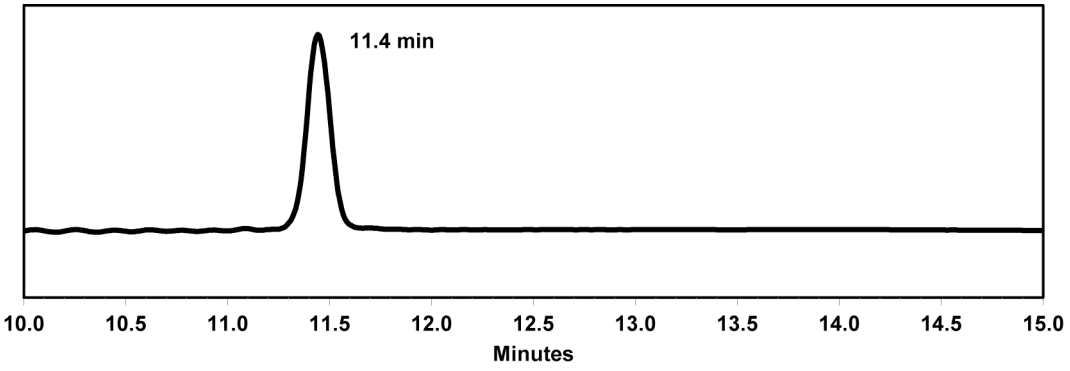

Figure S11. HPLC trace (215 nm) of Aβ(16–22) Hfl 19.

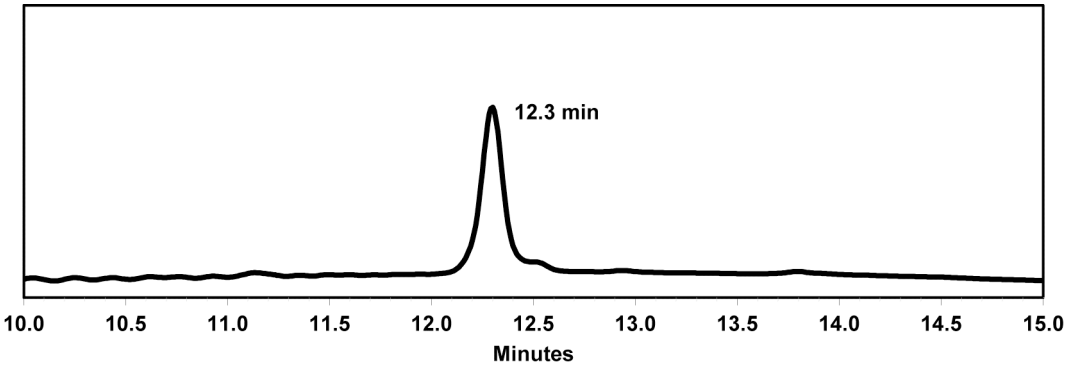

Figure S12. HPLC trace (215 nm) of Aβ(16–22) Hfl 20.

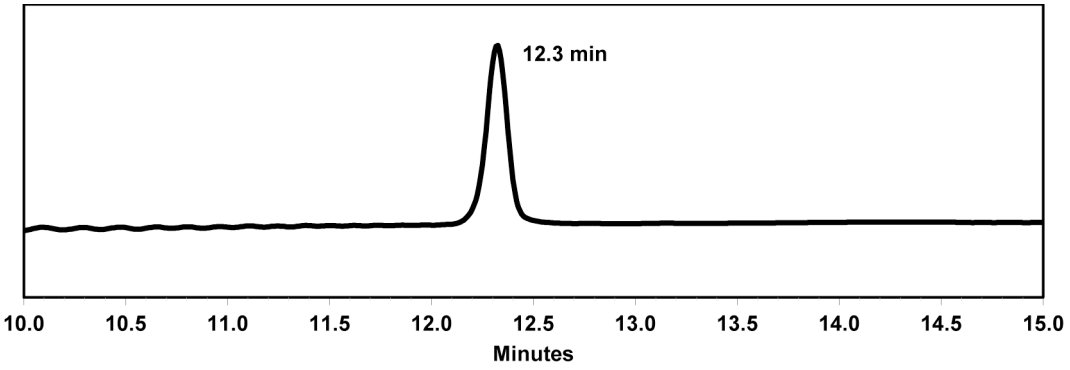

Figure S13. HPLC trace (215 nm) of Aβ(16–22) Hfl 19,20.

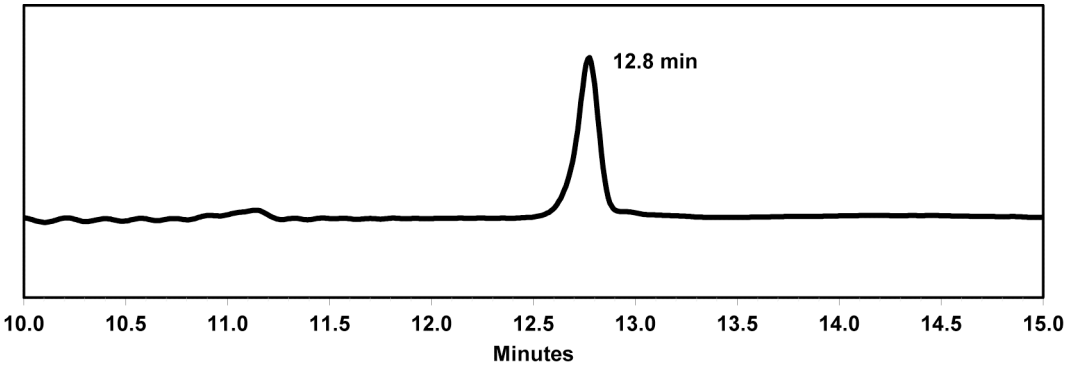

Table S1. Analytical HPLC conditions for peptides **1–12**.

Peptide	**Sequence**	**Retention time** (min)	**Gradient** (solution A: water/0.5% TFA; solution B: acetonitrile/0.5% TFA)
1	Ac-KLVVFAE-NH_2	11.5	Isocratic 5% **B** over 5 minutes, increase 5-95% **B** over 10 minutes, maintain at 95% **B** over 5 minutes
2	Ac-KLVFVAE-NH_2	11.4	Isocratic 5% **B** over 5 minutes, increase 5-95% **B** over 10 minutes, maintain at 95% **B** over 5 minutes
3	Ac-KLVVVAE-NH_2	10.9	Isocratic 5% **B** over 5 minutes, increase 5-95% **B** over 10 minutes, maintain at 95% **B** over 5 minutes
4	Ac-KLVLFAE-NH_2	11.9	Isocratic 5% **B** over 5 minutes, increase 5-95% **B** over 10 minutes, maintain at 95% **B** over 5 minutes
5	Ac-KLVFLAE-NH_2	11.8	Isocratic 5% **B** over 5 minutes, increase 5-95% **B** over 10 minutes, maintain at 95% **B** over 5 minutes
6	Ac-KLVLLAE-NH_2	11.7	Isocratic 5% **B** over 5 minutes, increase 5-95% **B** over 10 minutes, maintain at 95% **B** over 5 minutes
7	Ac-KLVIFAE-NH_2	11.8	Isocratic 5% **B** over 5 minutes, increase 5-95% **B** over 10 minutes, maintain at 95% **B** over 5 minutes
8	Ac-KLVFIAE-NH_2	11.8	Isocratic 5% **B** over 5 minutes, increase 5-95% **B** over 10 minutes, maintain at 95% **B** over 5 minutes
9	Ac-KLVIIAE-NH_2	11.4	Isocratic 5% **B** over 5 minutes, increase 5-95% **B** over 10 minutes, maintain at 95% **B** over 5 minutes
10	Ac-KLV(Hfl)FAE-NH_2	12.3	Isocratic 5% **B** over 5 minutes, increase 5-95% **B** over 10 minutes, maintain at 95% **B** over 5 minutes
11	Ac-KLVF(Hfl)AE-NH_2	12.3	Isocratic 5% **B** over 5 minutes, increase 5-95% **B** over 10 minutes, maintain at 95% **B** over 5 minutes
12	Ac-KLV(Hfl)(Hfl)AE-NH_2	12.8	Isocratic 5% **B** over 5 minutes, increase 5-95% **B** over 10 minutes, maintain at 95% **B** over 5 minutes

Figure S14. HPLC co-injection of Aβ(16–22) variants.

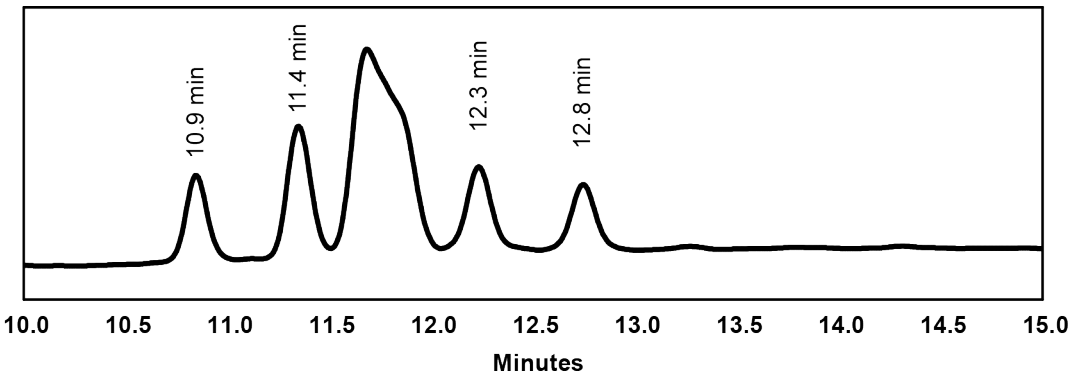

Table S2. HPLC co-injection results.

Peak #	Retention time	Peptide Identity by MS
1	10.9 min	Val 19,20
2	11.4 min	Val 20, Ile 19,20
3	11.5-12.0 min	Leu 20, Ile 20, Leu 19,20, WT
4	12.3 min	Hfl 19
5	12.8 min	Hfl 19,20

Figure S15. MALDI mass spectrum of A*β*(16–22) Val 19.

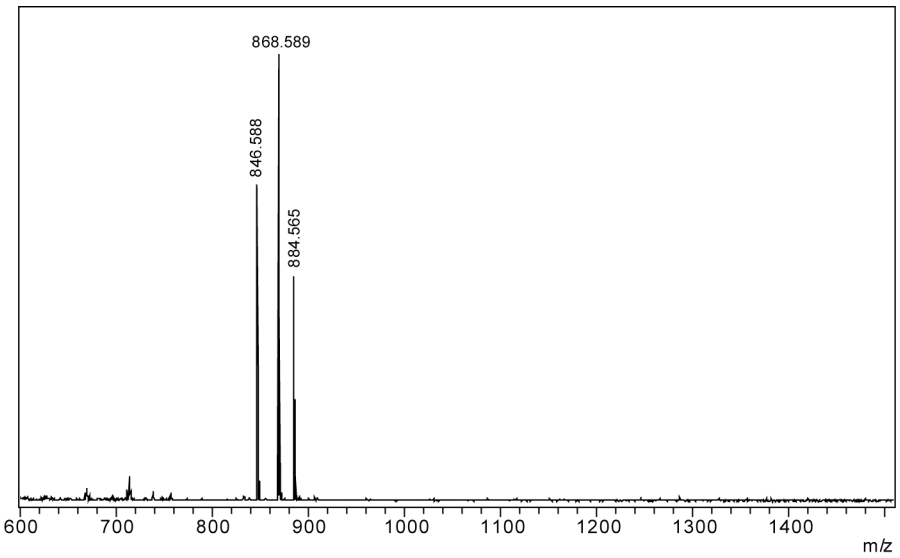

Figure S16. MALDI mass spectrum of A*β*(16–22) Val 20.

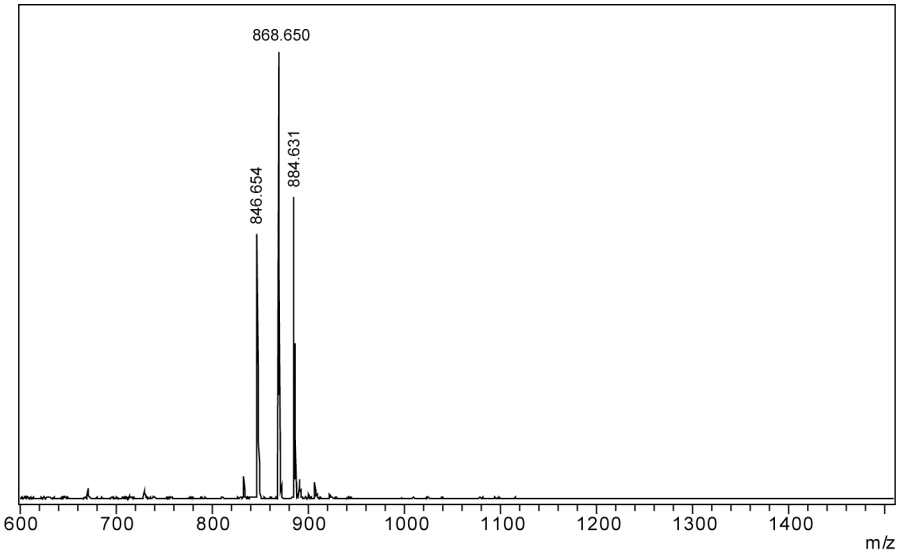

Figure S17. MALDI mass spectrum of Aβ(16–22) Val 19,20.

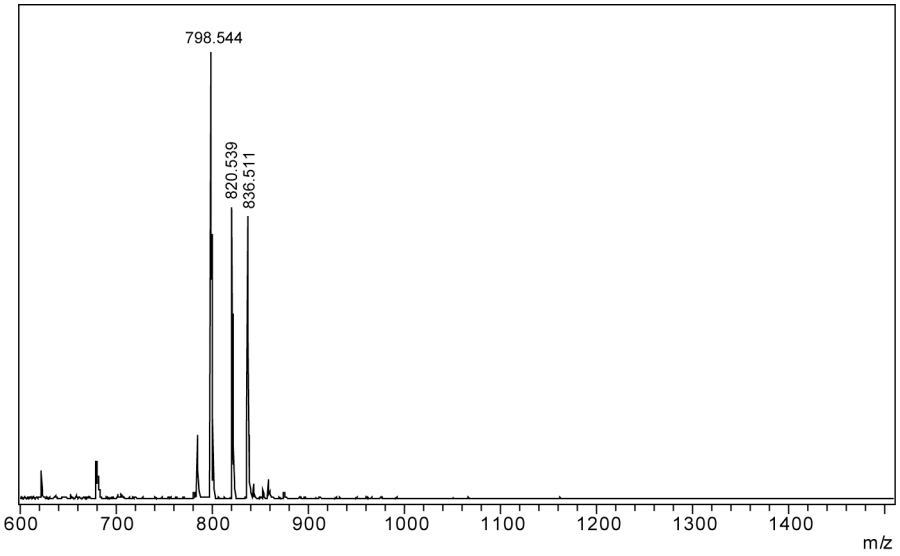

Figure S18. ESI mass spectrum of Aβ(16–22) Leu 19.

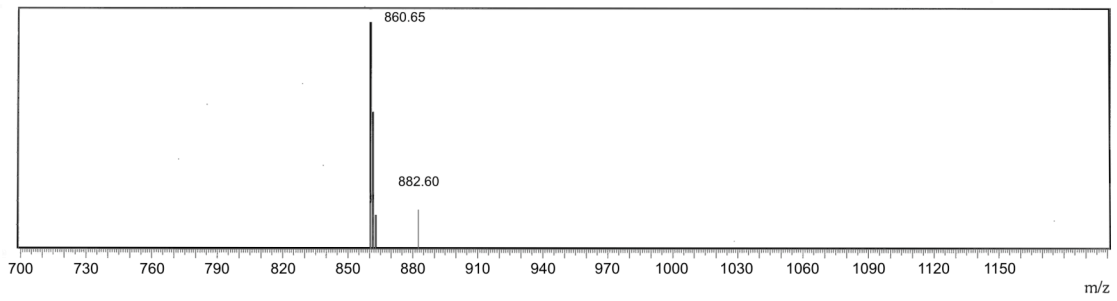

Figure S19. ESI mass spectrum of Aβ(16–22) Leu 20.

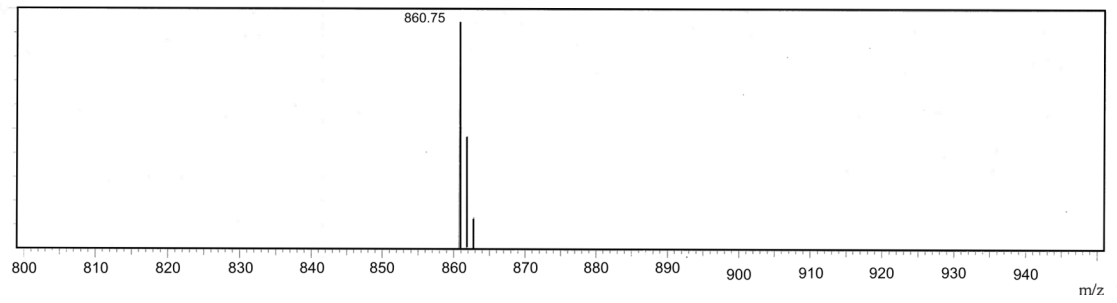

Figure S20. ESI mass spectrum of Aβ(16–22) Leu 19,20.

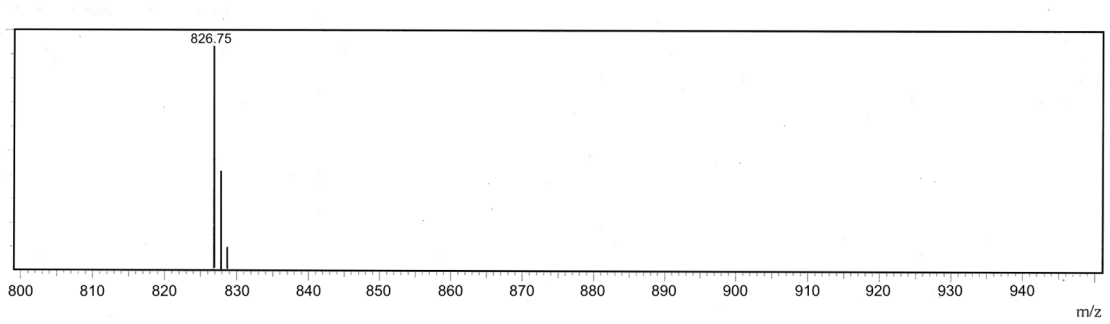

Figure S21. MALDI mass spectrum of Aβ(16–22) Ile 19.

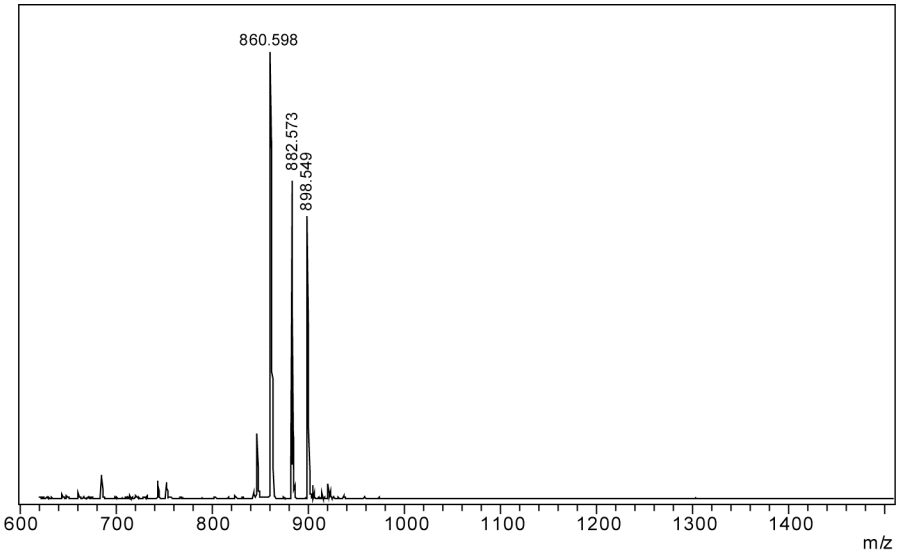

Figure S22. MALDI mass spectrum of Aβ(16–22) Ile 20.

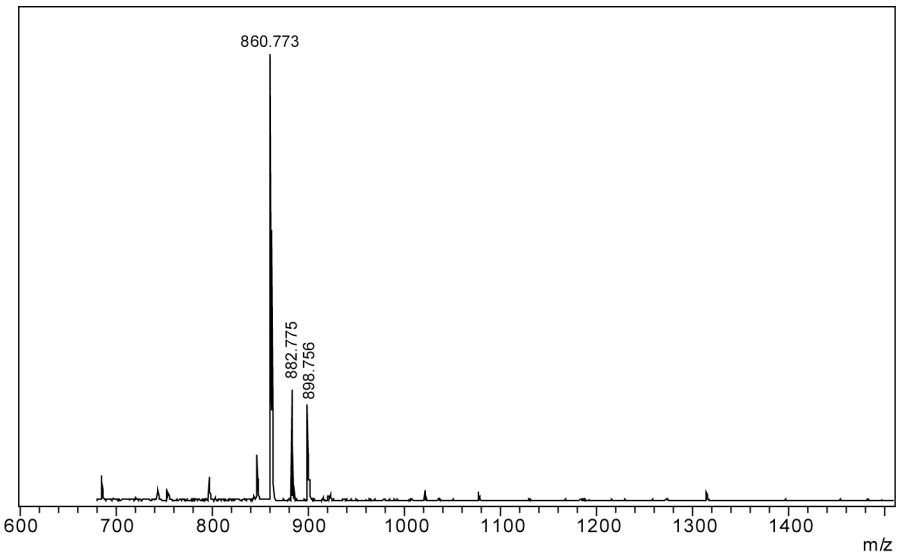

Figure S23. MALDI mass spectrum of Aβ(16–22) Ile 19,20.

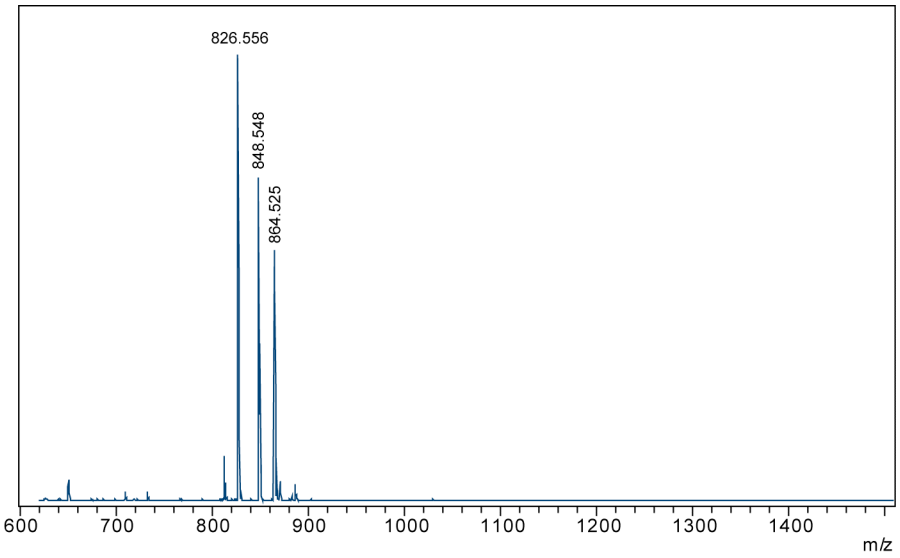

Figure S24. ESI mass spectrum of Aβ(16–22) Hfl 19.

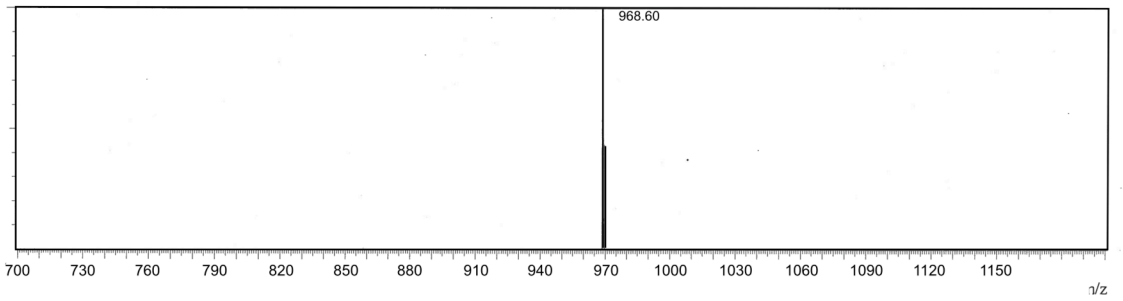

Figure S25. MALDI mass spectrum of Aβ(16–22) Hfl 20.

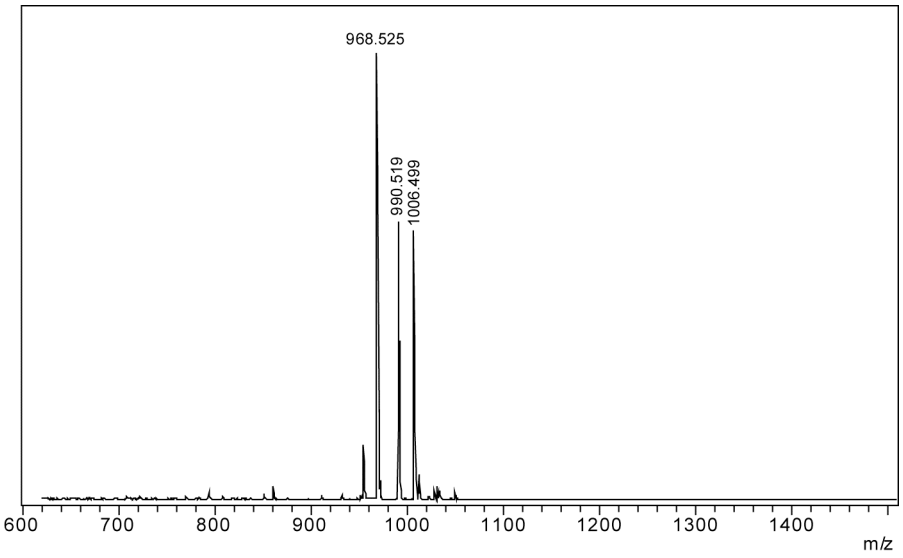

Figure S26. MALDI mass spectrum of Aβ(16–22) Hfl 19,20.

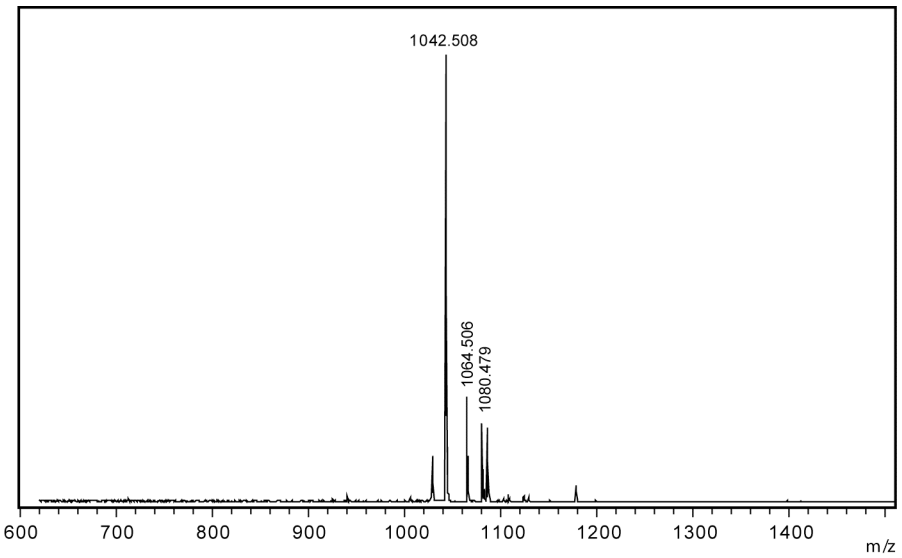

Figure S27. MALDI mass spectrum of Aβ(16–22) Val 19 ([1-^{13}C] Leu 17, Phe 20).

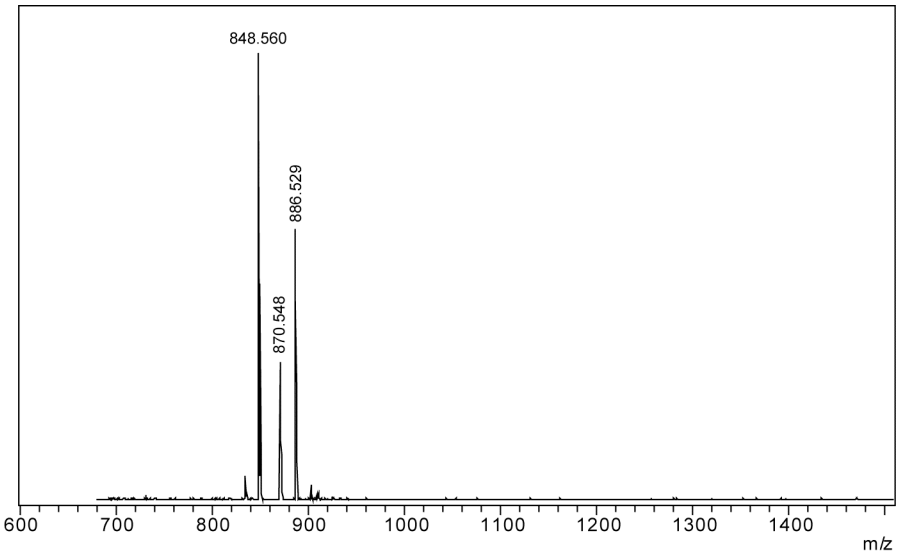

Figure S28. MALDI mass spectrum of Aβ(16–22) Val 20 ([1-^{13}C] Leu 17, Val 20).

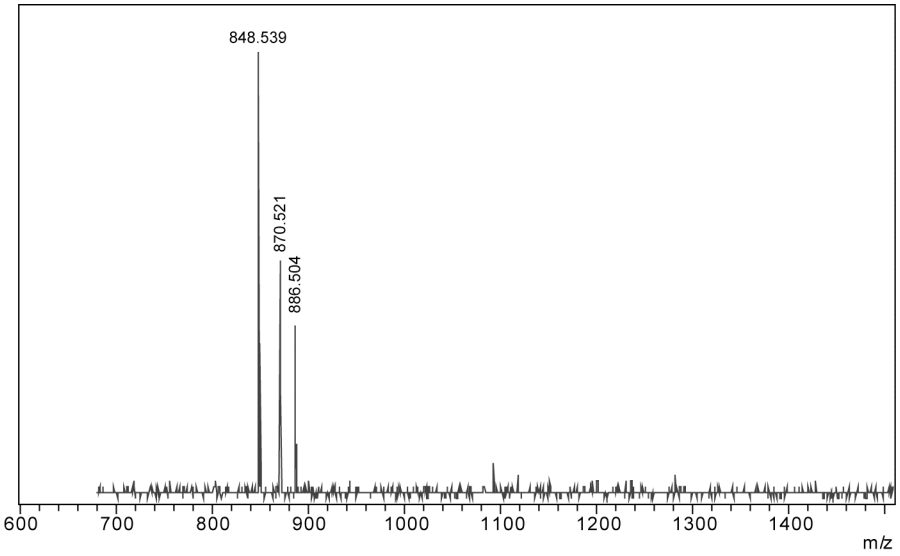

Figure S29. MALDI mass spectrum of Aβ(16–22) Val 19,20 ([1-^{13}C] Leu 17, Val 20).

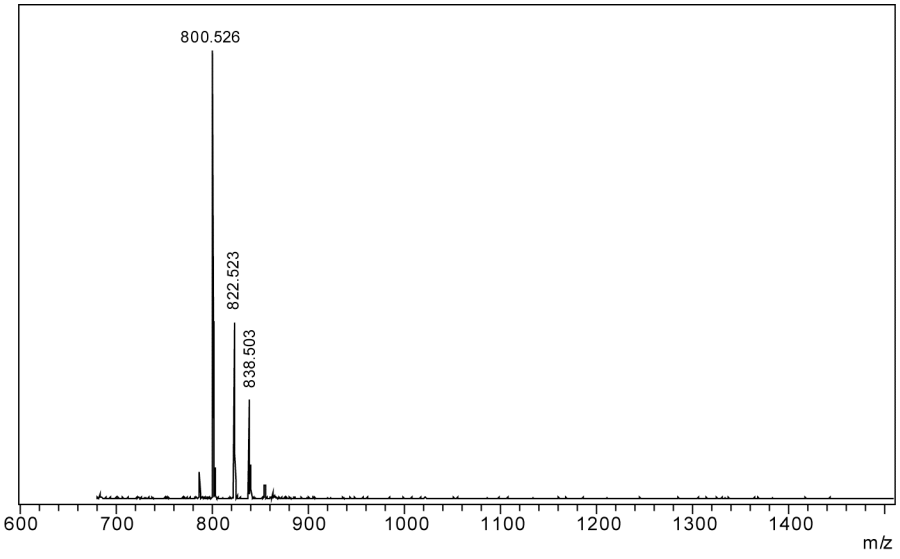

Figure S30. MALDI mass spectrum of Aβ(16–22) Leu 19 ([1-^{13}C] Leu 17, Phe 20).

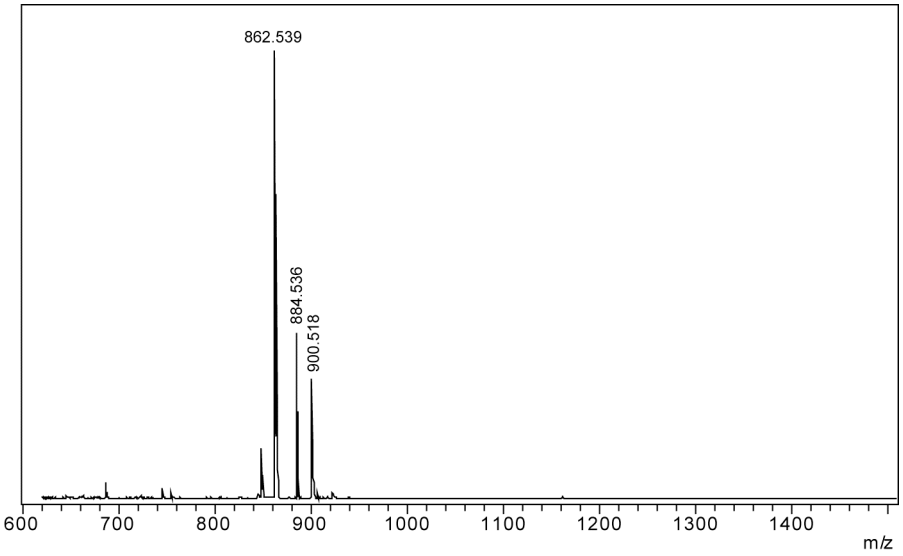

Figure S31. MALDI mass spectrum of Aβ(16–22) Leu 20 ([1-^{13}C] Leu 17, Leu 20).

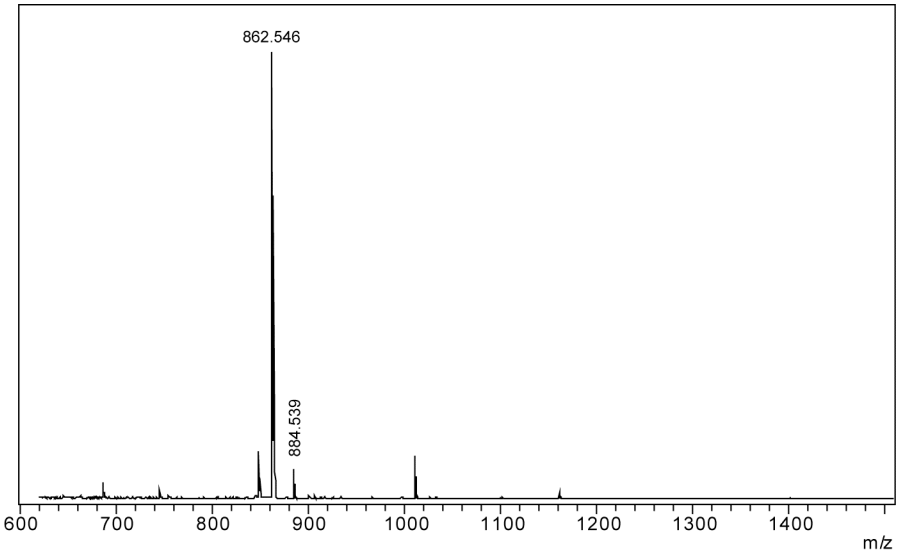

Figure S32. MALDI mass spectrum of Aβ(16–22) Leu 19,20 ([1-^{13}C] Leu 17, Leu 20).

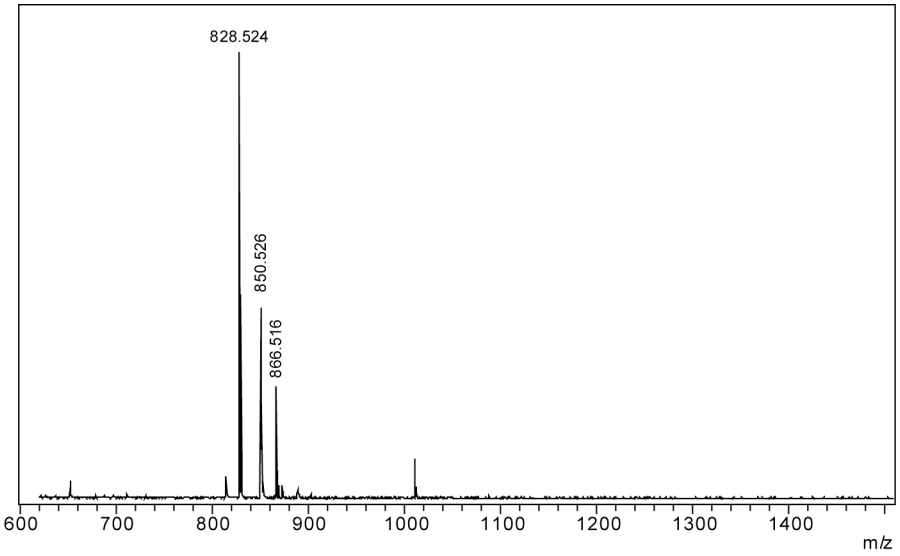

Figure S33. MALDI mass spectrum of Aβ(16–22) Ile 19 ([1-^{13}C] Leu 17, Phe 20).

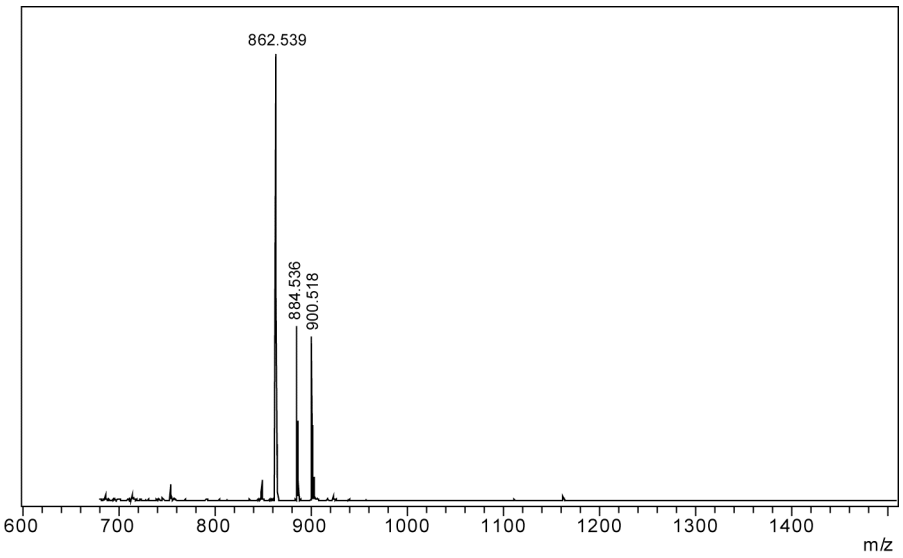

Figure S34. MALDI mass spectrum of Aβ(16–22) Ile 20 ([1-^{13}C] Lys 16, Ala 21).

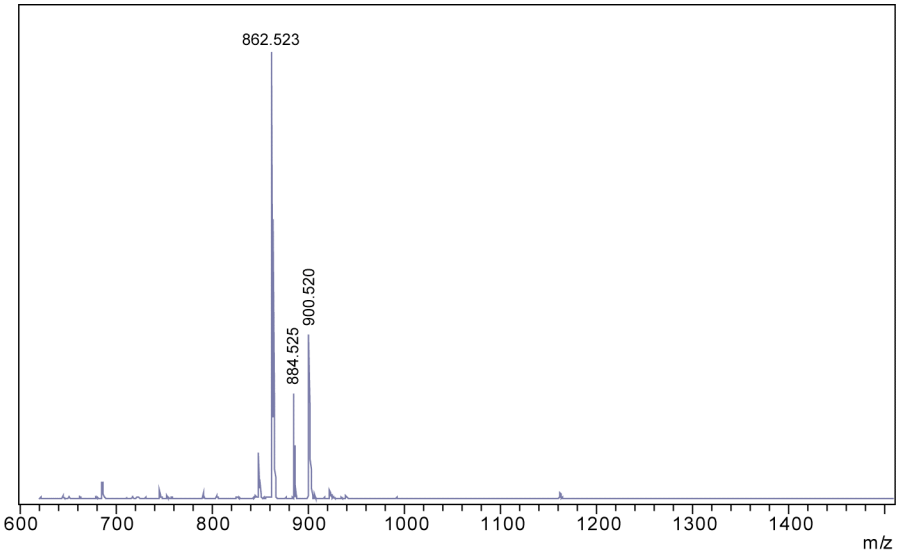

Figure S35. MALDI mass spectrum of Aβ(16–22) Ile 19,20 ([1-^{13}C] Lys 16, Ala 21).

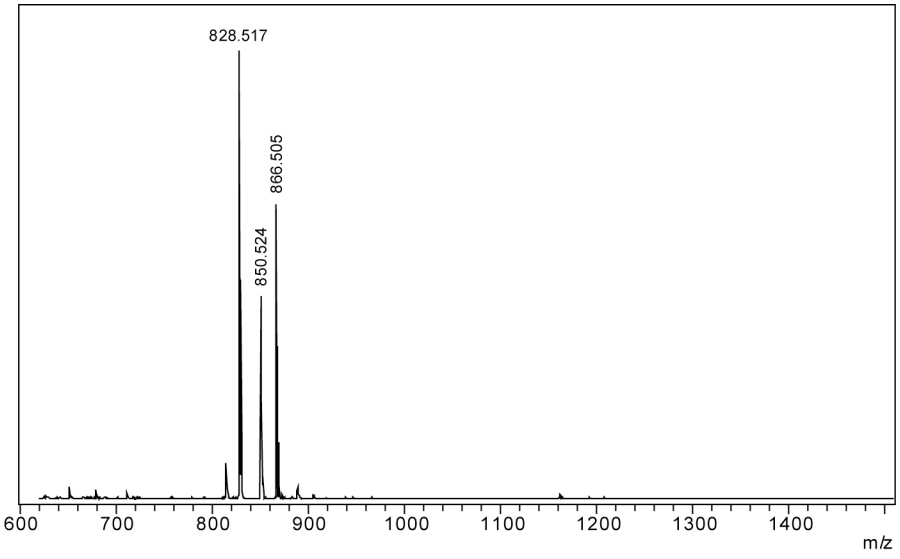

Figure S36. MALDI mass spectrum of Aβ(16–22) Hfl 19 ([1-^{13}C] Leu 17, Phe 20).

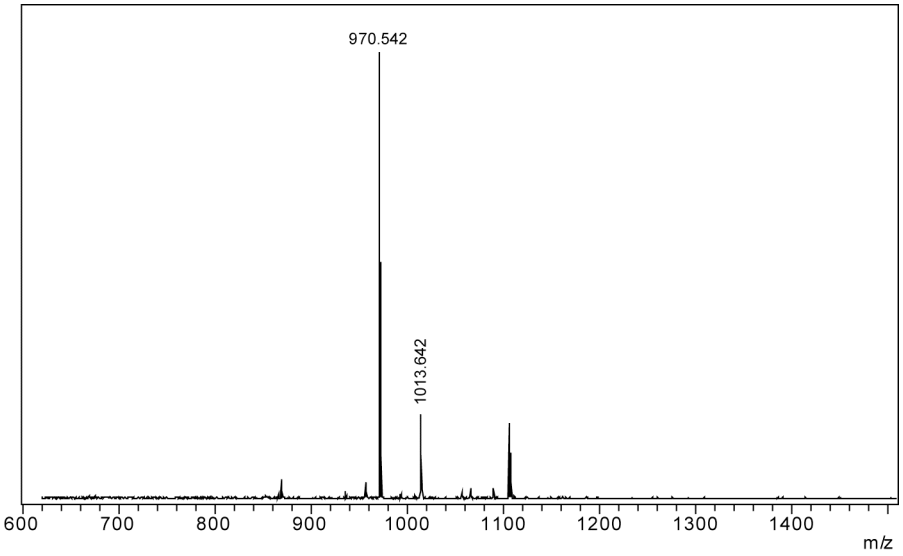

Figure S37. MALDI mass spectrum of Aβ(16–22) Hfl 20 ([1-^{13}C] Lys 16, Ala 21).

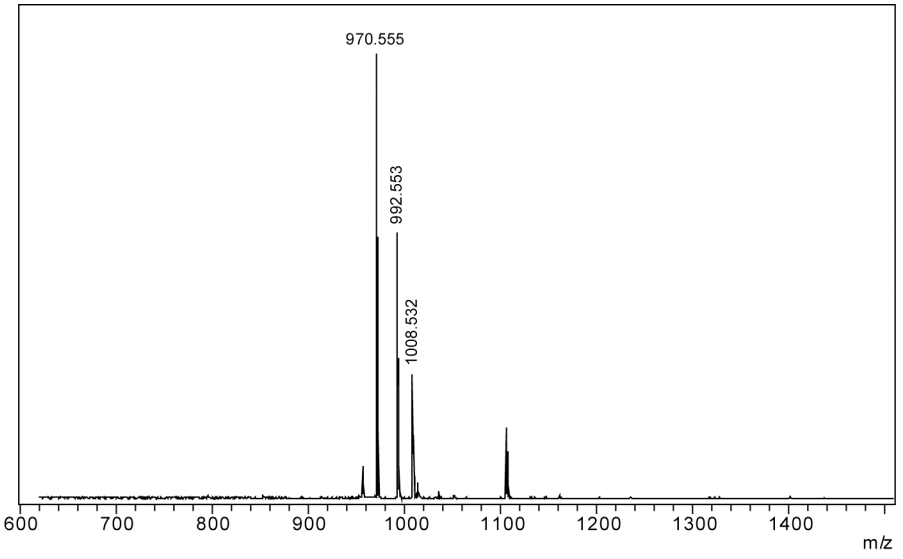

Figure S38. MALDI mass spectrum of Aβ(16–22) Hfl 19,20 ([1-^{13}C] Lys 16, Ala 21).

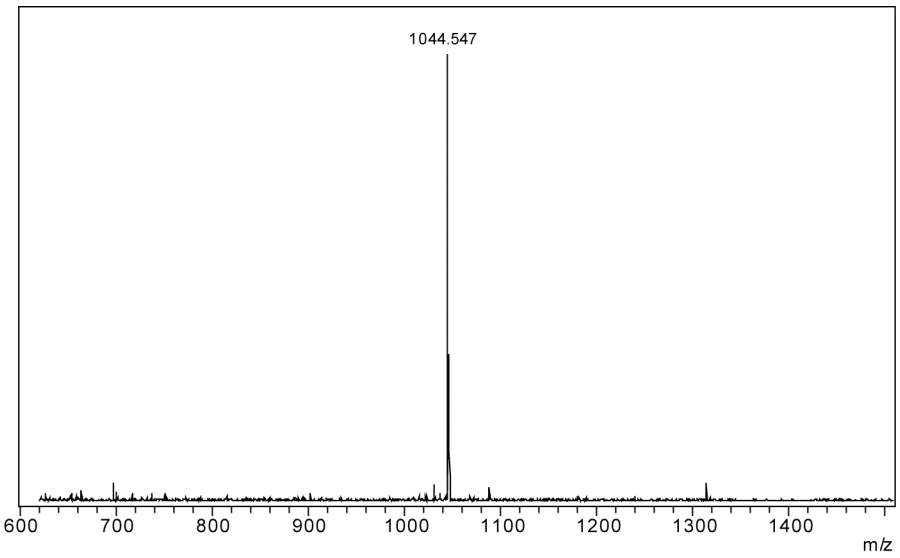

Figure S39. ESI mass spectrum of Aβ(16–22) Ile 19 ([1-^{13}C] Leu 17, Ala 21).

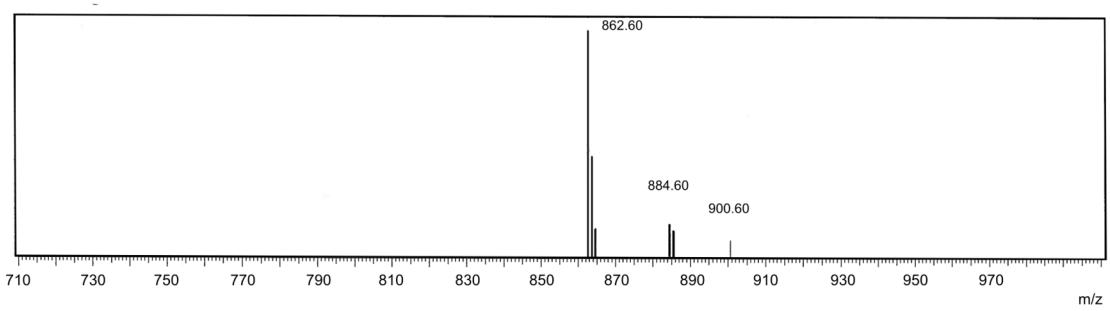

Figure S40. ESI mass spectrum of Aβ(16–22) Ile 19,20 ([1-^{13}C] Leu 17, Ala 21).

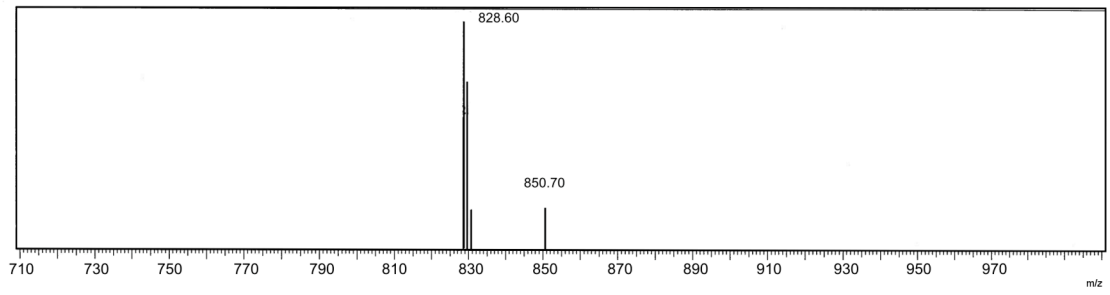

Table S3. Calculated and observed *m/z* for peptides **1–27**.

Peptide	Sequence	Calculated m/z	Observed m/z
1	Ac-KLVVFAE-NH_2	846.502 (M^+H)	846.588
2	Ac-KLVFVAE-NH_2	846.502 (M^+H)	846.654
3	Ac-KLVVVAE-NH_2	798.503 (M^+H)	798.544
4	Ac-KLVLFAE-NH_2	860.518 (M^+H)	860.65
5	Ac-KLVFLAE-NH_2	860.518 (M^+H)	860.75
6	Ac-KLVLLAE-NH_2	826.528 (M^+H)	826.75
7	Ac-KLVIFAE-NH_2	860.518 (M^+H)	860.598
8	Ac-KLVFIAE-NH_2	860.518 (M^+H)	860.773
9	Ac-KLVIIAE-NH_2	826.534 (M^+H)	826.556
10	Ac-KLV(Hfl)FAE-NH_2	968.554 (M^+H)	968.50
11	Ac-KLVF(Hfl)AE-NH_2	968.554 (M^+H)	968.525
12	Ac-KLV(Hfl)(Hfl)AE-NH_2	1042.605 (M^+H)	1042.508
13	Ac-K*LVV*FAE-NH_2	848.502 (M^+H)	848.560
14	Ac-K*LVF*VAE-NH_2	848.502 (M^+H)	848.539
15	Ac-K*LVV*VAE-NH_2	800.503 (M^+H)	800.526
16	Ac-K*LVL*FAE-NH_2	862.518 (M^+H)	862.539
17	Ac-K*LVF*LAE-NH_2	862.518 (M^+H)	862.546
18	Ac-K*LVL*LAE-NH_2	828.528 (M^+H)	828.524
19	Ac-K*LVI*FAE-NH_2	862.518 (M^+H)	862.559
20	Ac-*KLVFI*AE-NH_2	862.518 (M^+H)	862.523
21	Ac-*KLVII*AE-NH_2	828.528 (M^+H)	828.517
22	Ac-K*LV(Hfl)*FAE-NH_2	970.554 (M^+H)	970.542
23	Ac-*KLVF(Hfl)*AE-NH_2	970.554 (M^+H)	970.555
24	Ac-*KLV(Hfl)(Hfl)*AE-NH_2	1044.605 (M^+H)	1044.547
25	Ac-K*LVIF*AE-NH_2	862.518 (M^+H)	862.60
26	Ac-K*LVII*AE-NH_2	828.528 (M^+H)	828.60
27	Ac-K*LV(Hfl)F*AE-NH_2	970.554 (M^+H)	970.65

Figure S41. HPLC calibration curve of Aβ(16–22) Val 19.

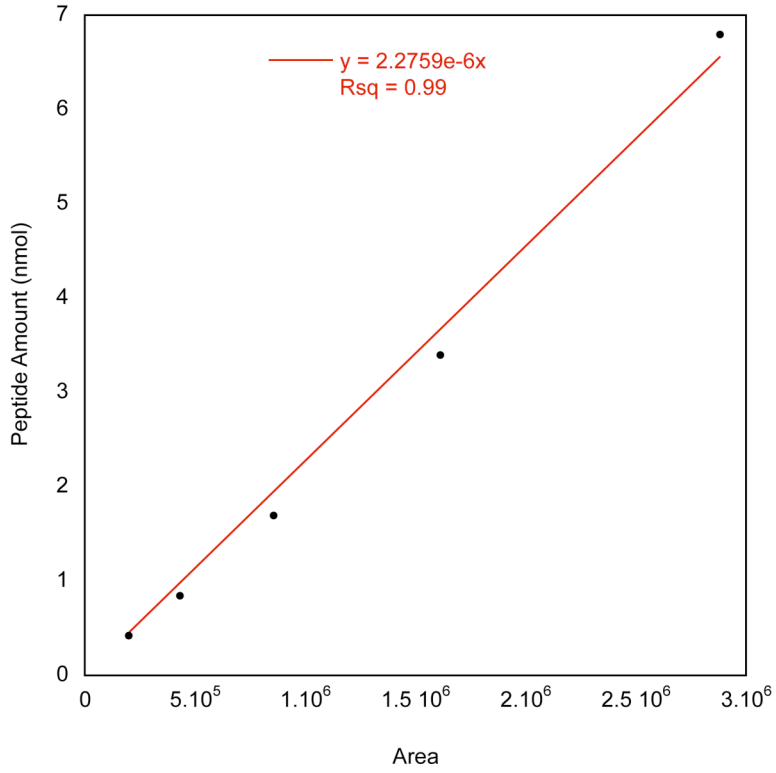

Figure S42. HPLC calibration curve of Aβ(16–22) Val 19,20.

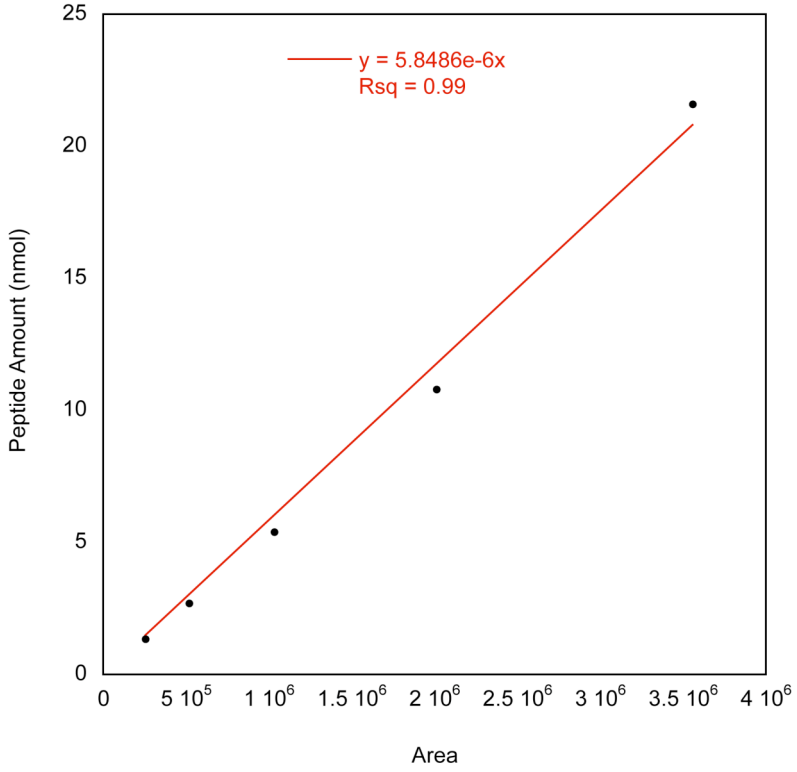

Figure S43. HPLC calibration curve of Aβ(16–22) Leu 19.

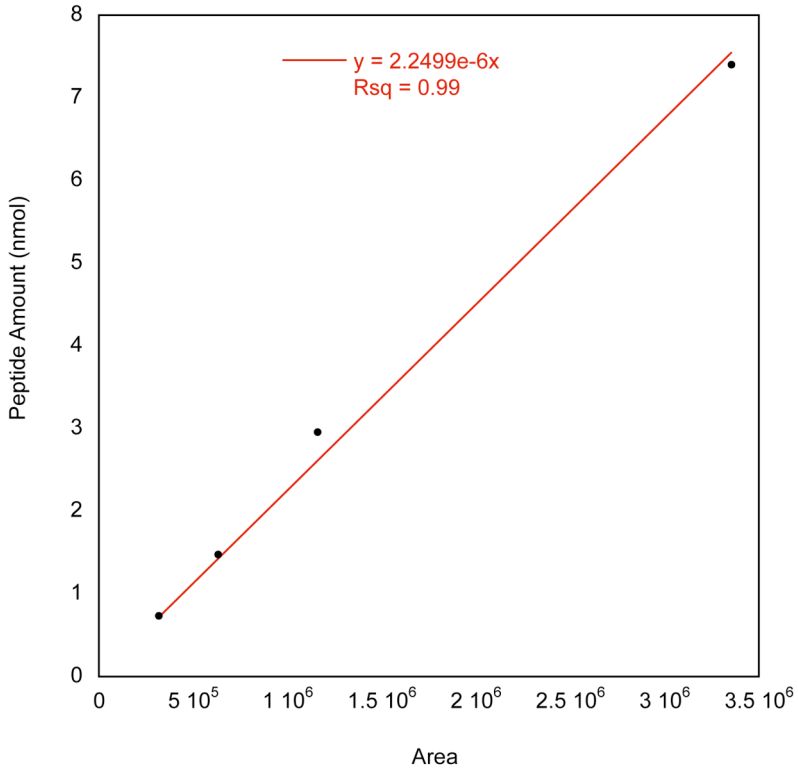

Figure S44. HPLC calibration curve of Aβ(16–22) Leu 19,20.

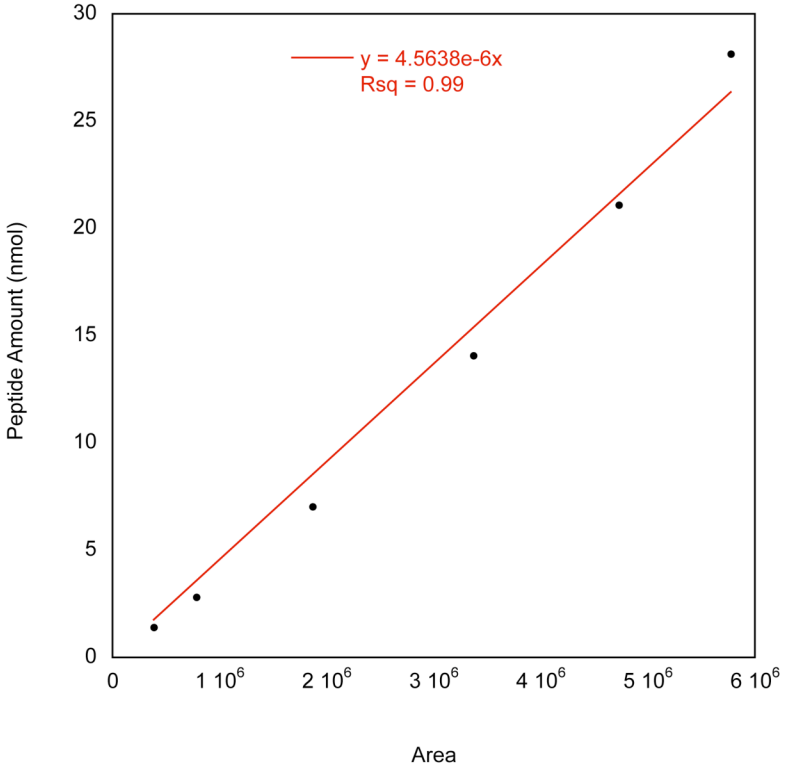

Figure S45. HPLC calibration curve of Aβ(16–22) Ile 19.

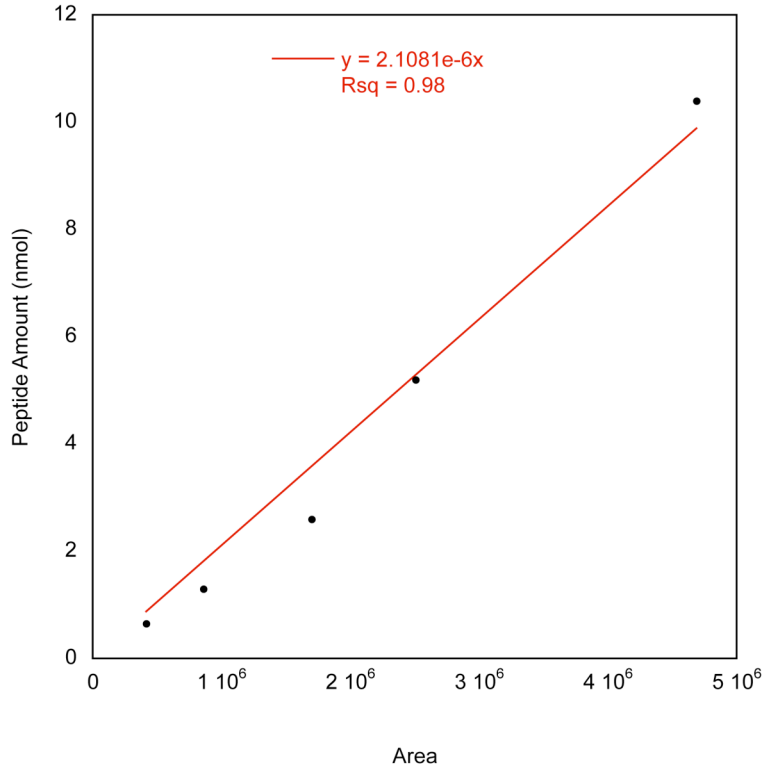

Figure S46. HPLC calibration curve of Aβ(16–22) Ile 19,20.

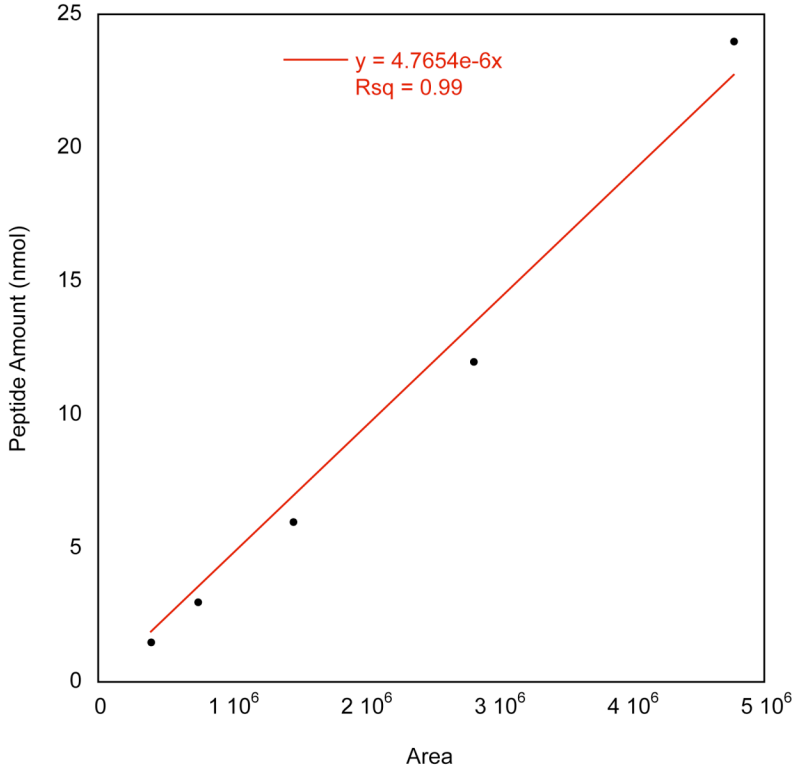

Figure S47. HPLC calibration curve of Aβ(16–22) Hfl 19.

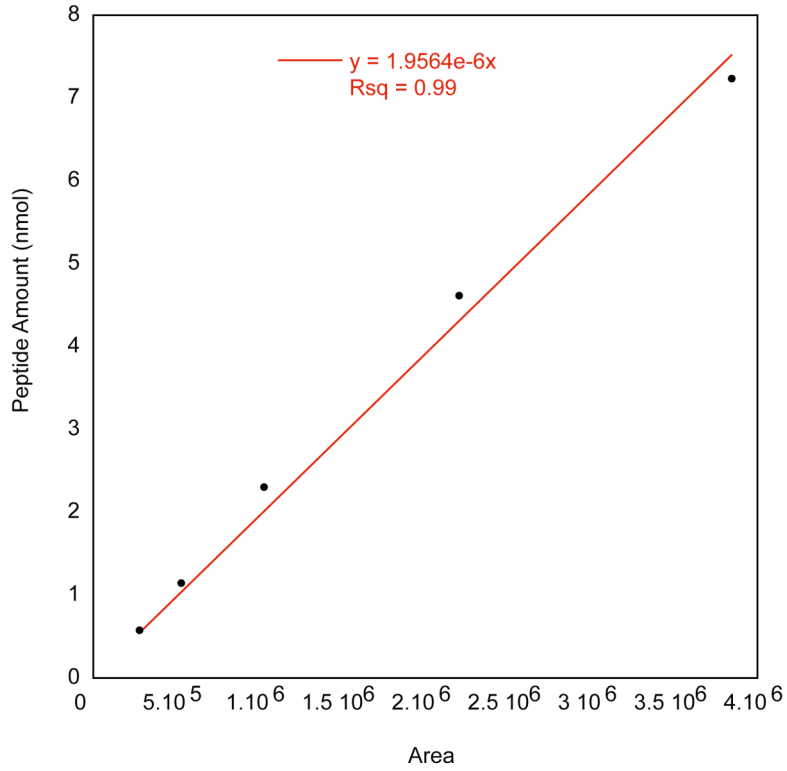

Figure S48. HPLC calibration curve of Aβ(16–22) Hfl 19,20.

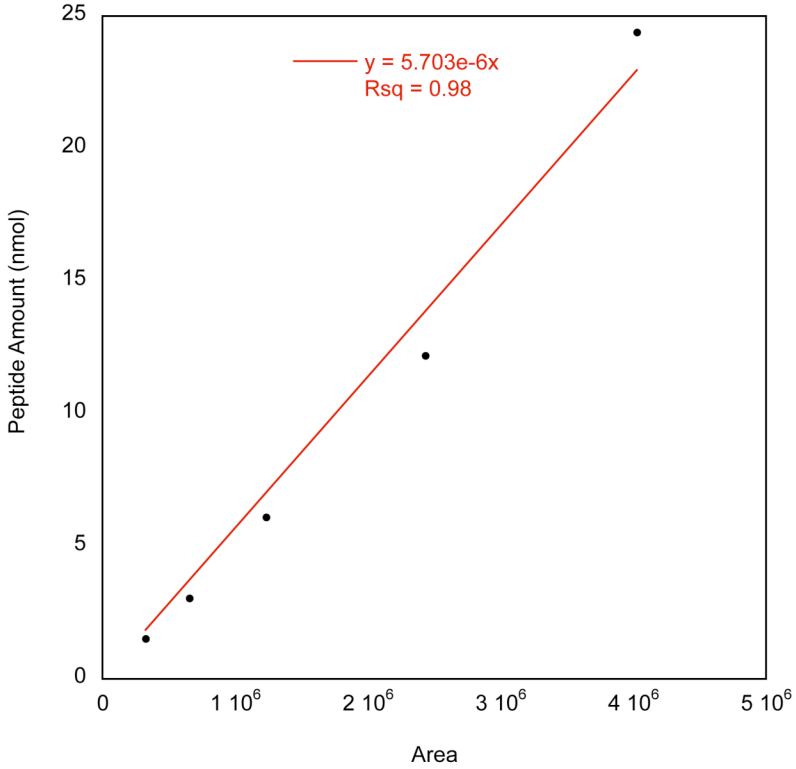

Figure S49. Electron diffraction image of Aβ(16–22) Val 19 fibrils.

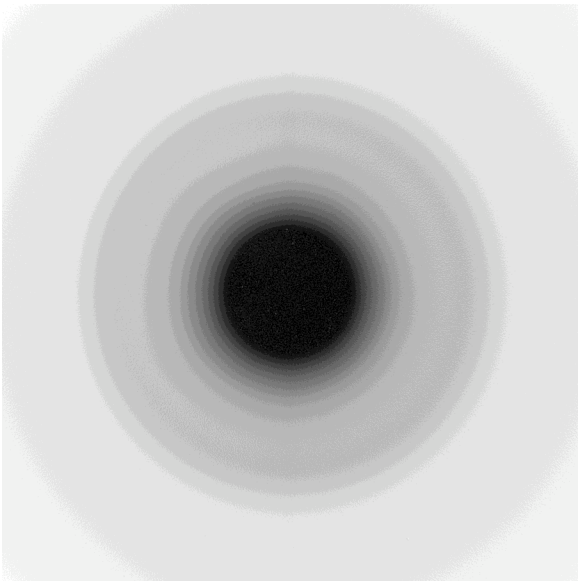

Figure S50. Electron diffraction image of Aβ(16–22) Val 20 fibrils.

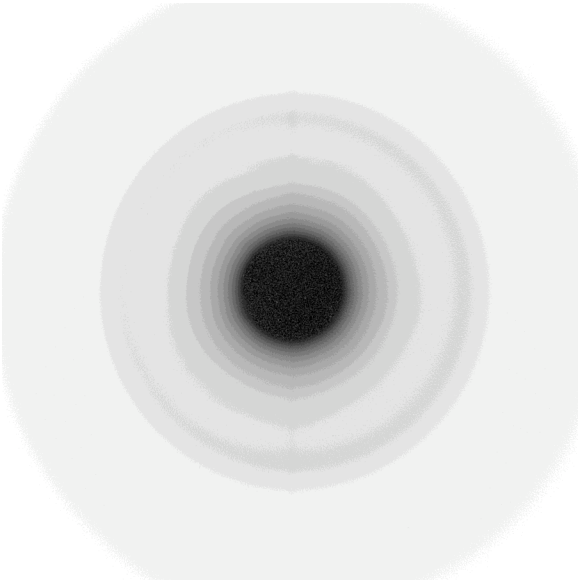

Figure S51. Electron diffraction image of Aβ(16–22) Leu 19 fibrils.

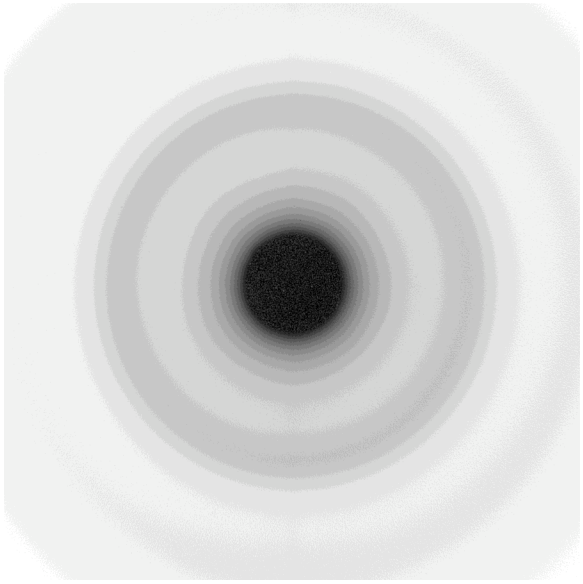

Figure S52. Electron diffraction image of Aβ(16–22) Leu 20 fibrils.

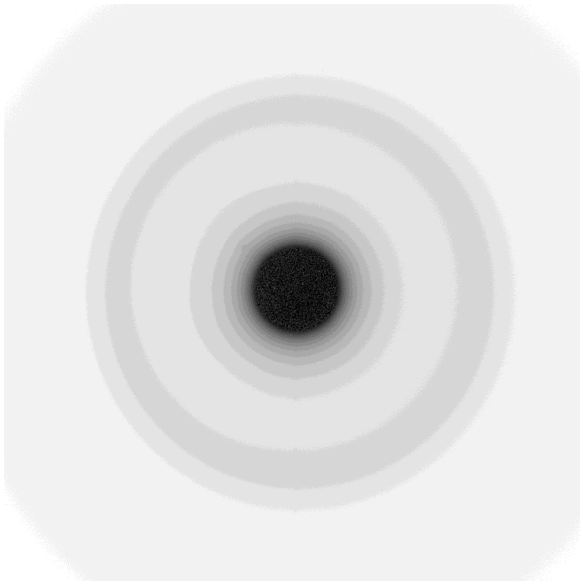

Figure S53. Electron diffraction image of Aβ(16–22) Leu 19,20 fibrils.

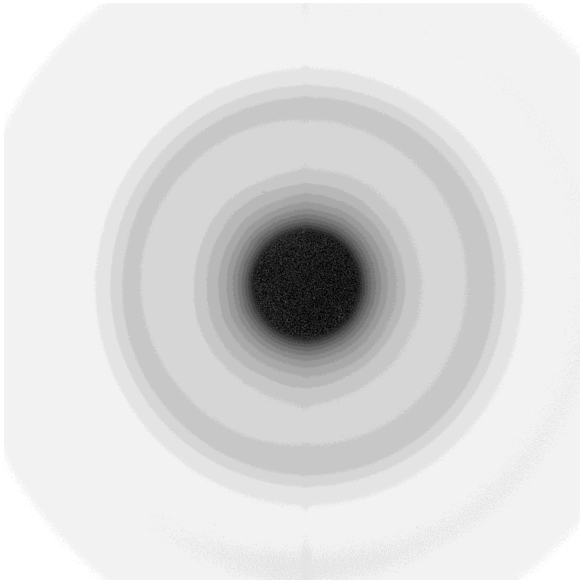

Figure S54. Electron diffraction image of Aβ(16–22) Ile 19 fibrils.

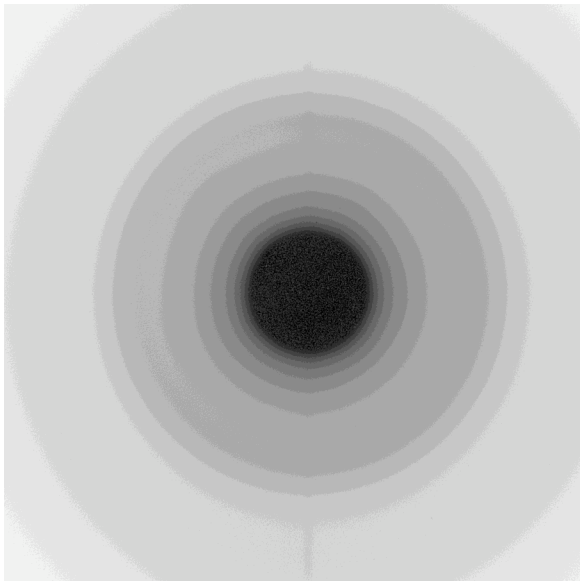

Figure S55. Electron diffraction image of Aβ(16–22) Ile 20 fibrils.

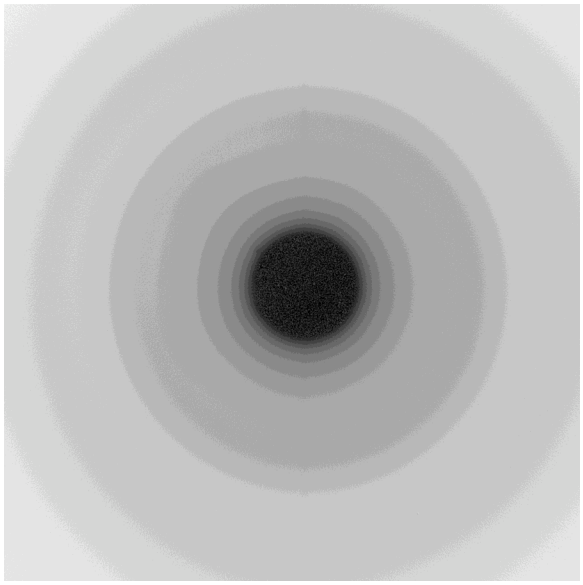

Figure S56. Electron diffraction image of Aβ(16–22) Ile 19,20 fibrils.

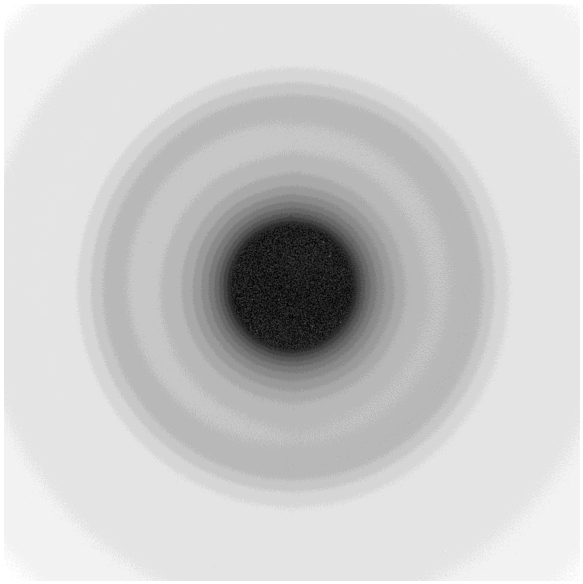

Figure S57. Electron diffraction image of Aβ(16–22) Hfl 19 fibrils.

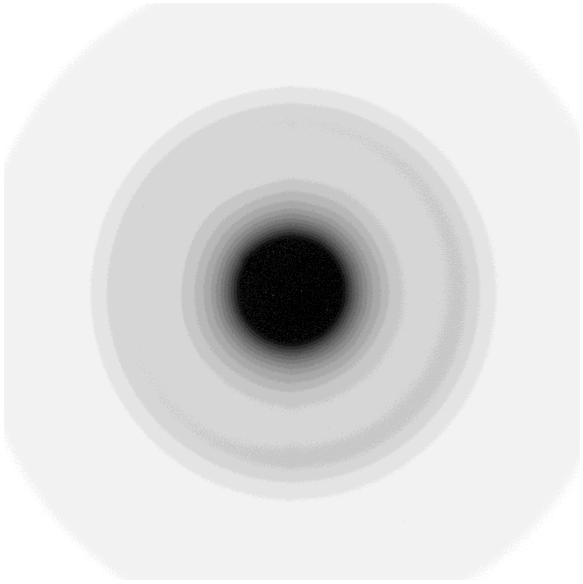

Figure S58. Electron diffraction image of Aβ(16–22) Hfl 20 fibrils.

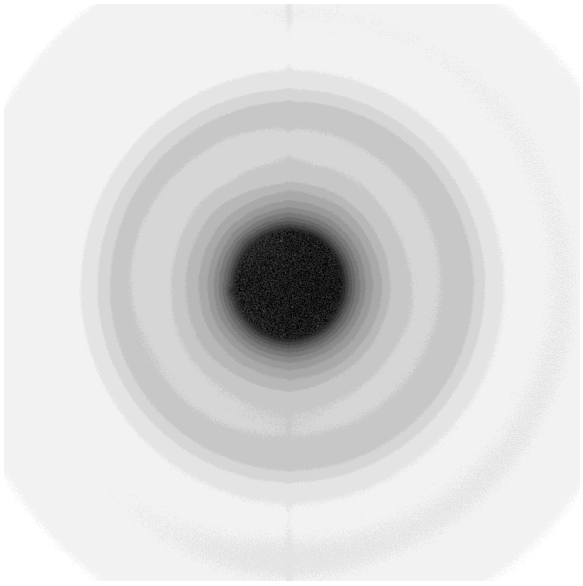

Figure S59. Electron diffraction image of Aβ(16–22) Hfl 19,20 fibrils.

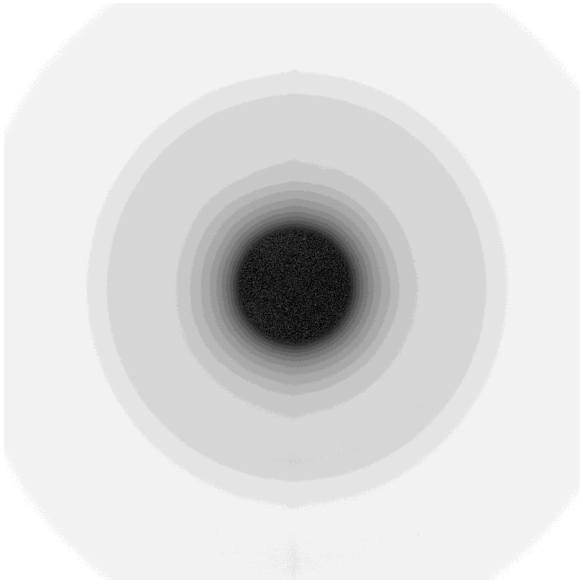

Table S4. Observed amide I infrared bands of peptides **1–27**.

Peptide	Sequence	IR Shifts (cm^{-1})
Wild-type	Ac-KLVFFAE-NH_2	1624, 1691
1	Ac-KLVVFAE-NH_2	1626, 1693
2	Ac-KLVFVAE-NH_2	1629, 1685
3	Ac-KLVVVAE-NH_2	N/A
4	Ac-KLVLFAE-NH_2	1626, 1687
5	Ac-KLVFLAE-NH_2	1626, 1688
6	Ac-KLVLLAE-NH_2	1626, 1690
7	Ac-KLVIFAE-NH_2	1629, 1688
8	Ac-KLVFIAE-NH_2	1628, 1688
9	Ac-KLVIIAE-NH_2	1629, 1688
10	Ac-KLV(Hfl)FAE-NH_2	1629, 1686
11	Ac-KLVF(Hfl)AE-NH_2	1628, 1689
12	Ac-KLV(Hfl)(Hfl)AE-NH_2	1629, 1691
13	Ac-K*LVV*FAE-NH_2	1599, 1641, 1684
14	Ac-K*LVF*VAE-NH_2	1599, 1641, 1684
15	Ac-K*LVV*VAE-NH_2	N/A
16	Ac-K*LVL*FAE-NH_2	1597, 1643, 1686
17	Ac-K*LVF*LAE-NH_2	1597, 1643, 1684
18	Ac-K*LVL*LAE-NH_2	1597, 1643, 1684
19	Ac-K*LVI*FAE-NH_2	1602, 1634, 1688
20	Ac-*KLVFI*AE-NH_2	1597, 1632, 1688
21	Ac-*KLVII*AE-NH_2	1601, 1632, 1685
22	Ac-K*LV(Hfl)*FAE-NH_2	1597, 1645, 1690
23	Ac-*KLVF(Hfl)*AE-NH_2	1597, 1634, 1683
24	Ac-*KLV(Hfl)(Hfl)*AE-NH_2	1595, 1632, 1688
25	Ac-K*LVIF*AE-NH_2	1606, 1641, 1686
26	Ac-K*LVII*AE-NH_2	1606, 1640, 1688
27	Ac-K*LV(Hfl)F*AE-NH_2	1606, 1643, 1689

* Indicates [1-^{13}C]-labeled amino acid.

Figure S60. Isotope-edited IR spectra for fibrils derived from the Ile 19 and Ile 19,20 variants (Leu 17/Ala 21 [1-^{13}C]-labeled) and the Hfl 19 variant (Leu 17/Ala 21 [1-^{13}C]-labeled). All spectra are consistent with an uncoupled relationship between the labeled amino acids.