Interface Determination and Dynamics of Apolipoprotein E Oligomerization by Hydrogen Deuterium Exchange and Electron-Transfer Dissociation Mass Spectrometry

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Supporting information

SUPPLEMENTAL FIGURES

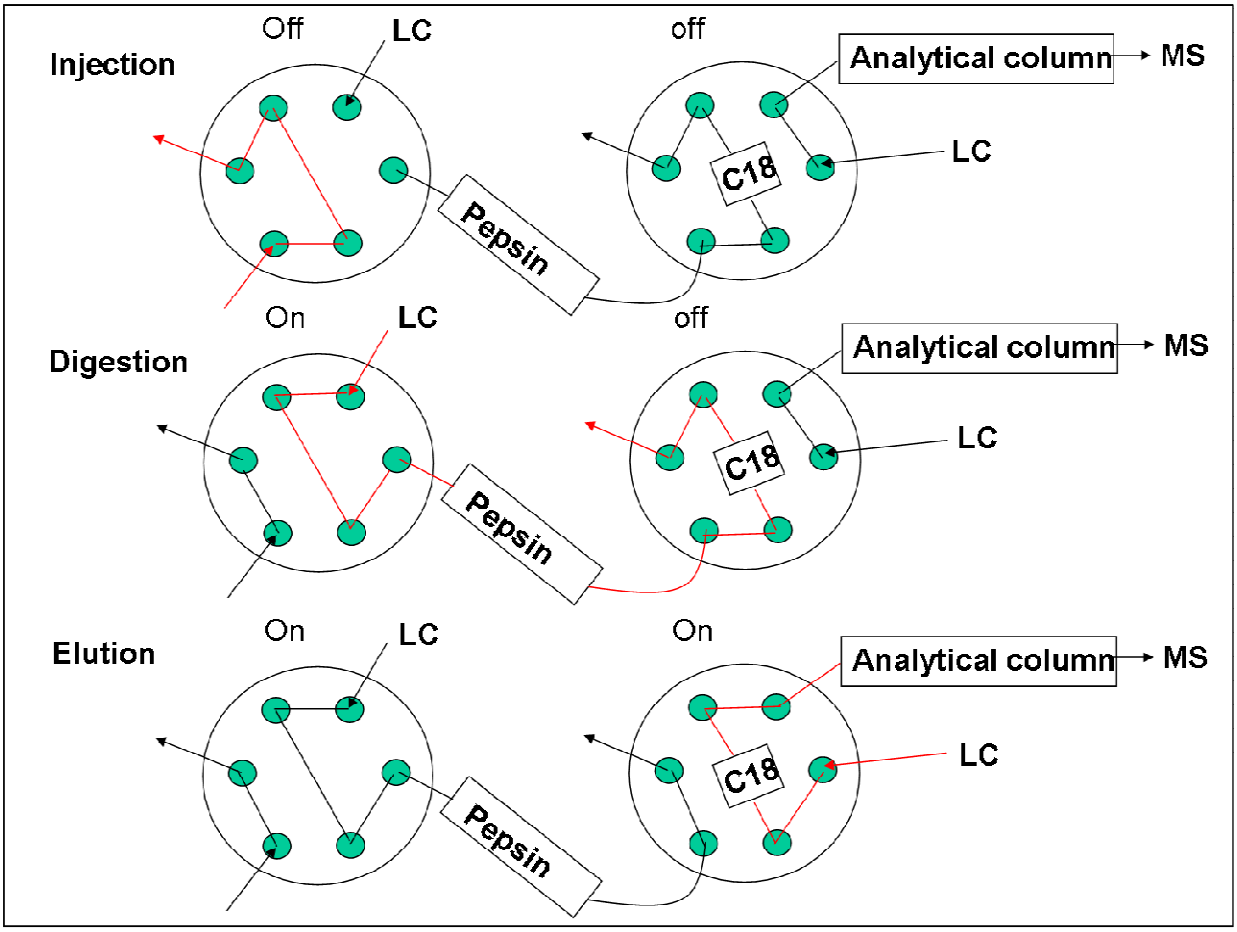


Figure S1. Diagram for on-line pepsin digestion device.

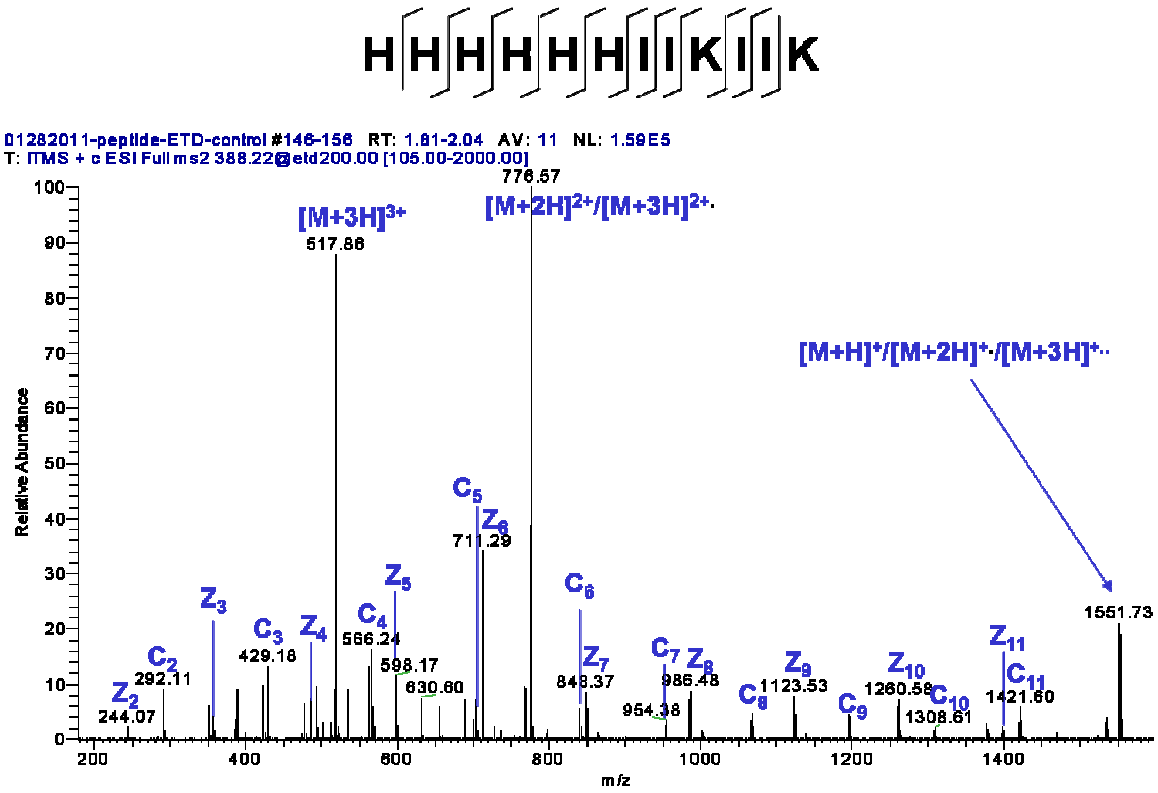
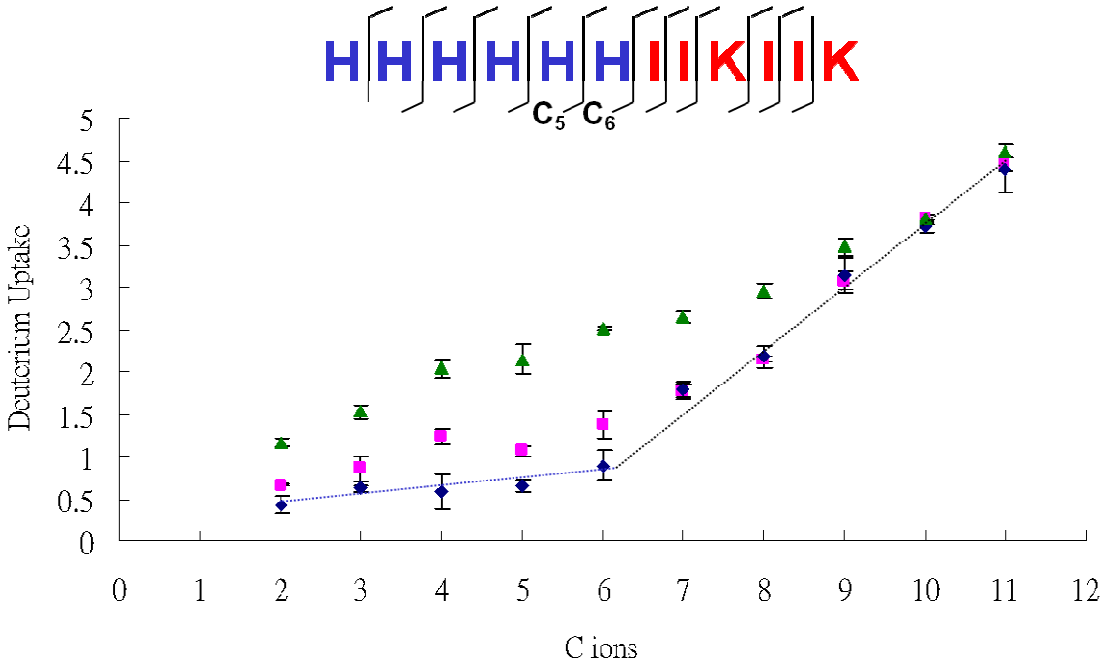


Figure S2. ETD product ion spectrum of standard peptide HHHHHHIIKIIK.



	Capillary Temperature	Capillary Voltage	Tube lens
☆	50 ◦ C	20 V	50 V
	100 ◦ C	50 V	50 V
	200 ◦ C	100 V	100 V

Figure S3. The deuterium uptake of C ions of the standard peptide HHHHHHIIKIIK after performing the H/DX-ETD. Three different ESI conditions were marked in different colors (blue, pink, and green).

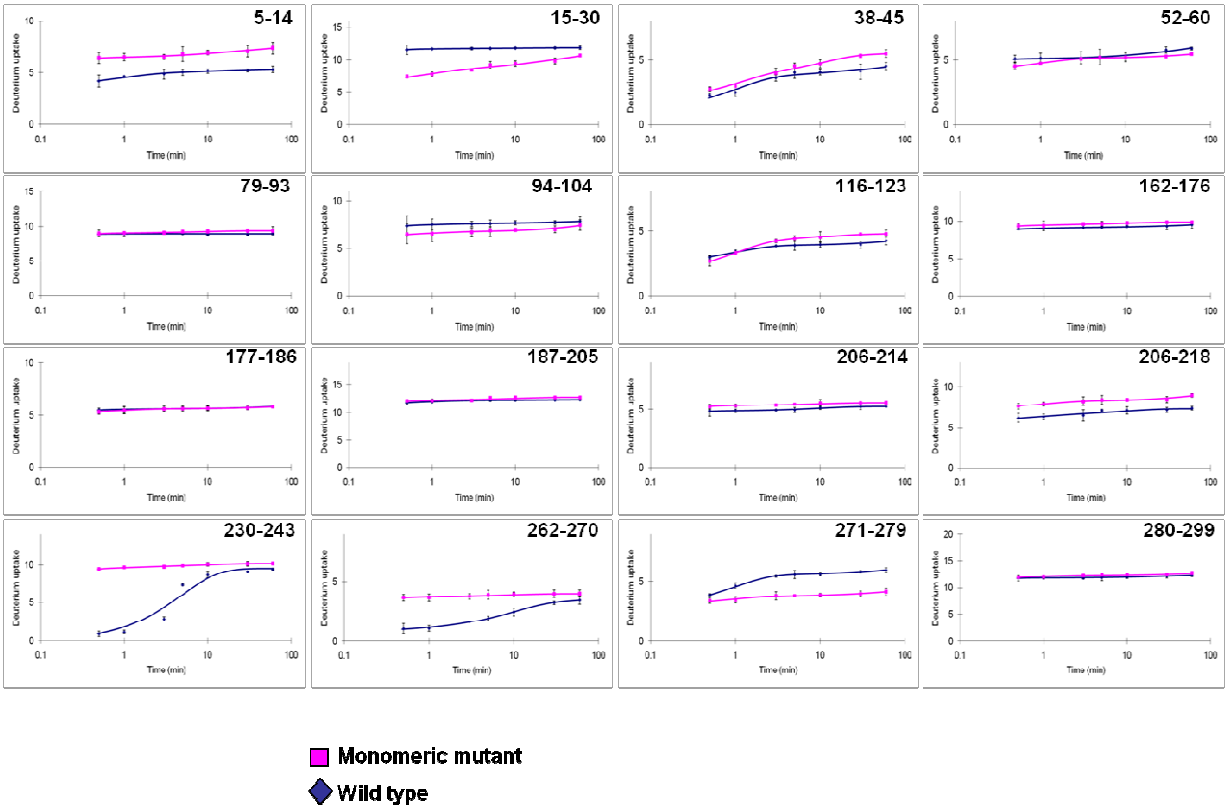


Figure S4. Peptide-level H/DX kinetics of ApoE2. The extent of deuterium uptake is plotted as a function of exchange time. Wild type is marked in blue and monomeric mutant is marked in pink.

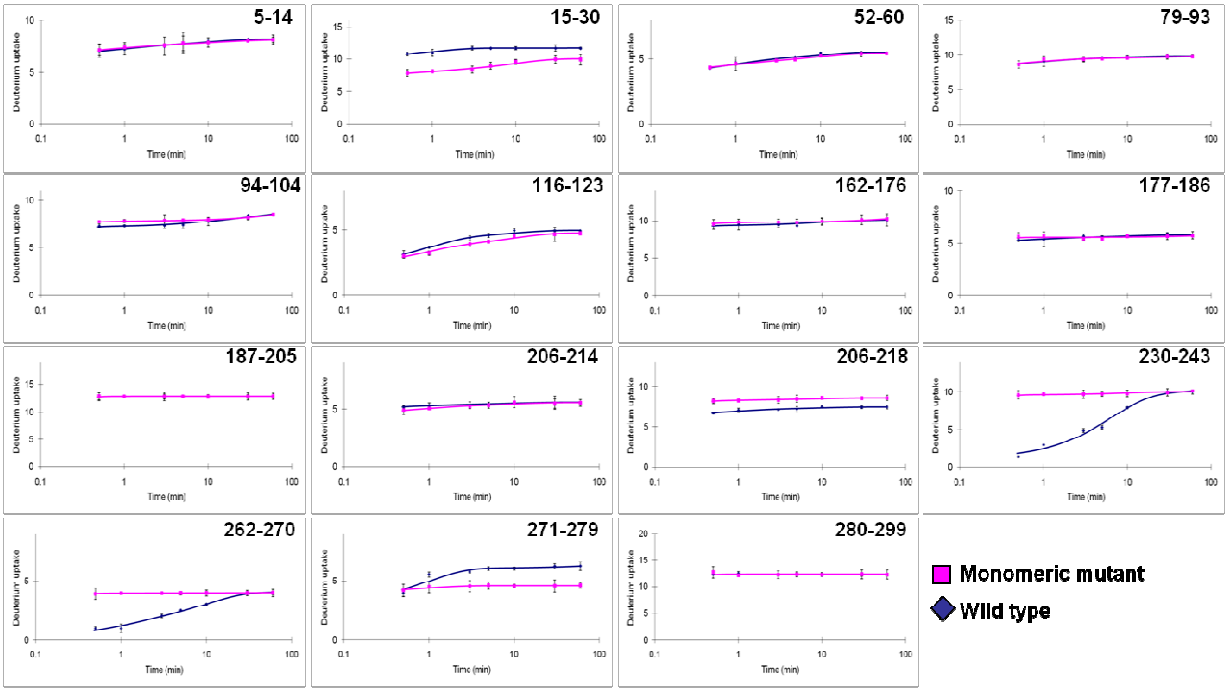


Figure S5. Peptide-level H/DX kinetics of ApoE3. The extent of deuterium uptake is plotted as a function of exchange time. Wild type is marked in blue and monomeric mutant is marked in pink.

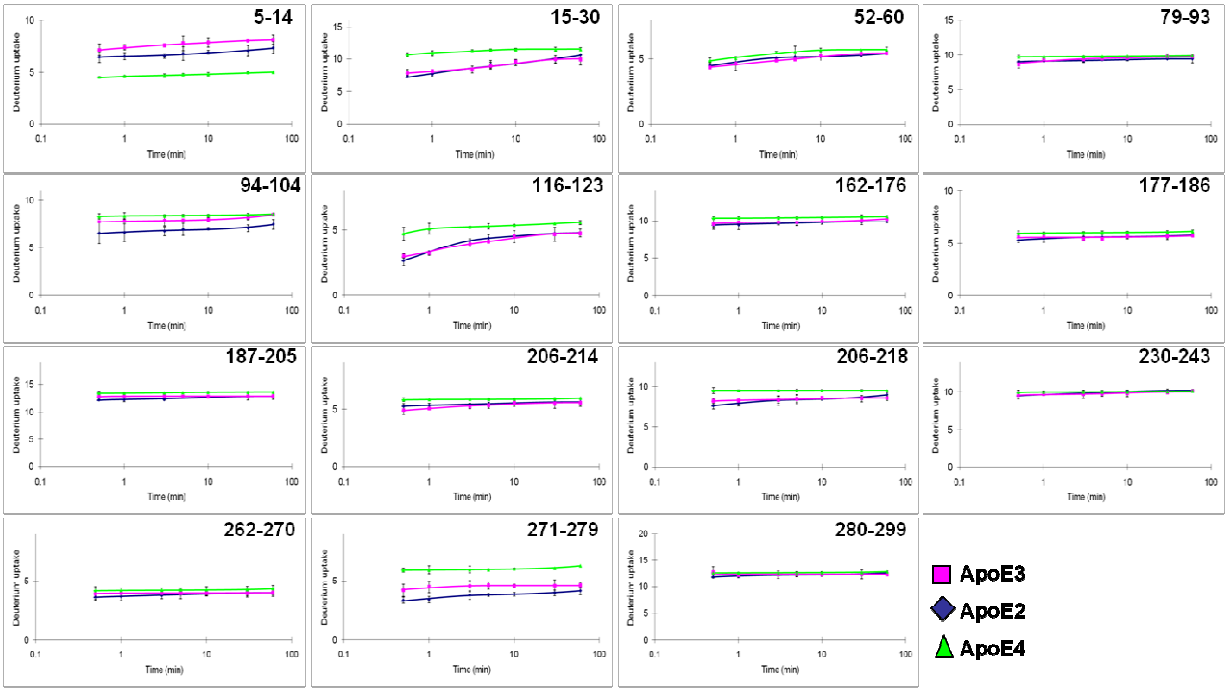


Figure S6. Peptide-level H/DX kinetics of ApoE2, ApoE3 and ApoE4 monomeric mutant. The extent of deuterium uptake is plotted as a function of exchange time. ApoE2 is marked in blue, ApoE3 is marked in pink, and ApoE4 is marked in green.

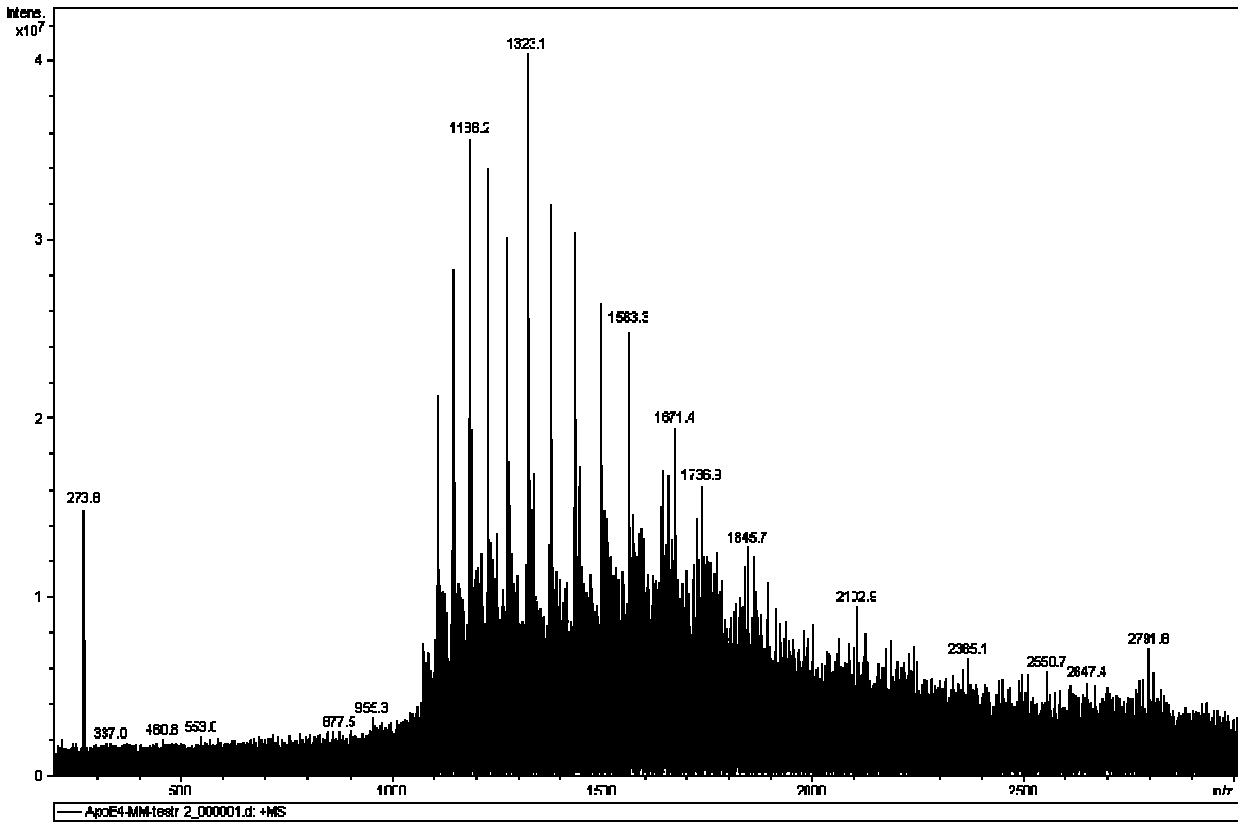


Figure S7. The ESI spectrum of ApoE4 monomeric mutant. The presence of multiple peaks with lower relative abundance in between the major protein charge state distribution indicates that sample solution contains mixture of proteins with multiple modifications.

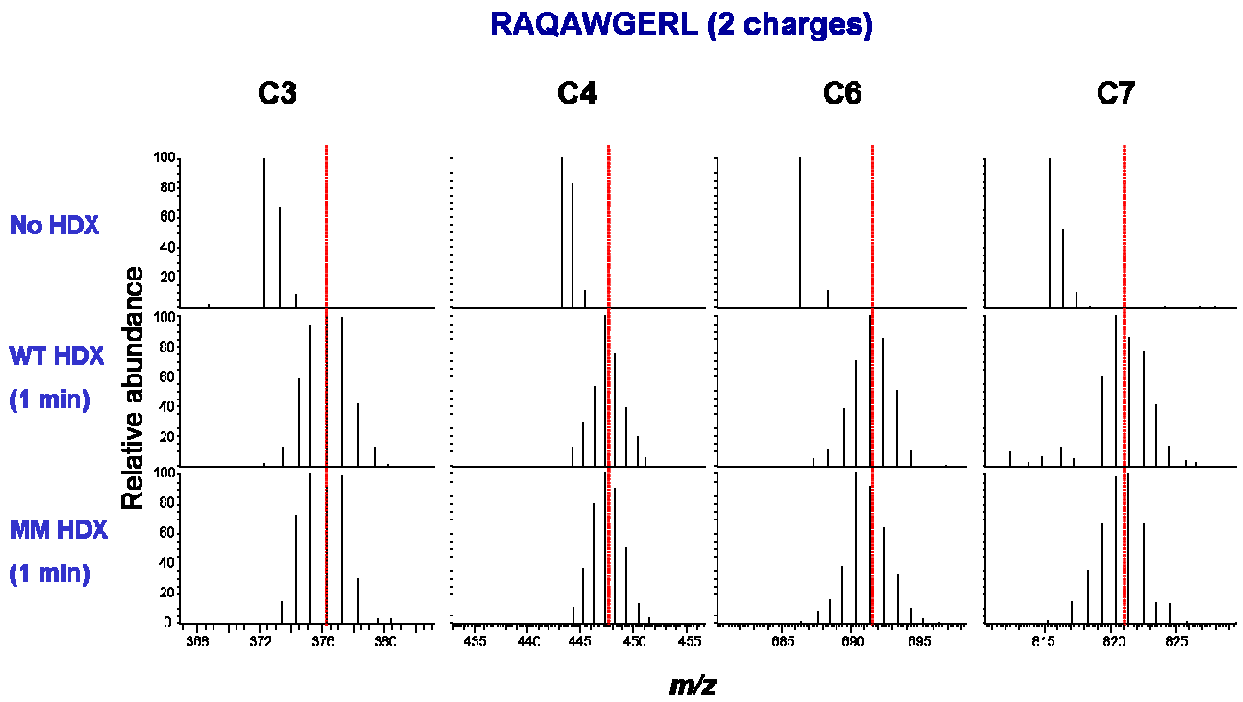


Figure S8. ETD product-ion spectra of peptides 206-214 of ApoE4 after H/DX. The centroid of the distribution of C ions from MM is shown as red dotted line, showing there are no significant differences in H/DX between WT and MM.

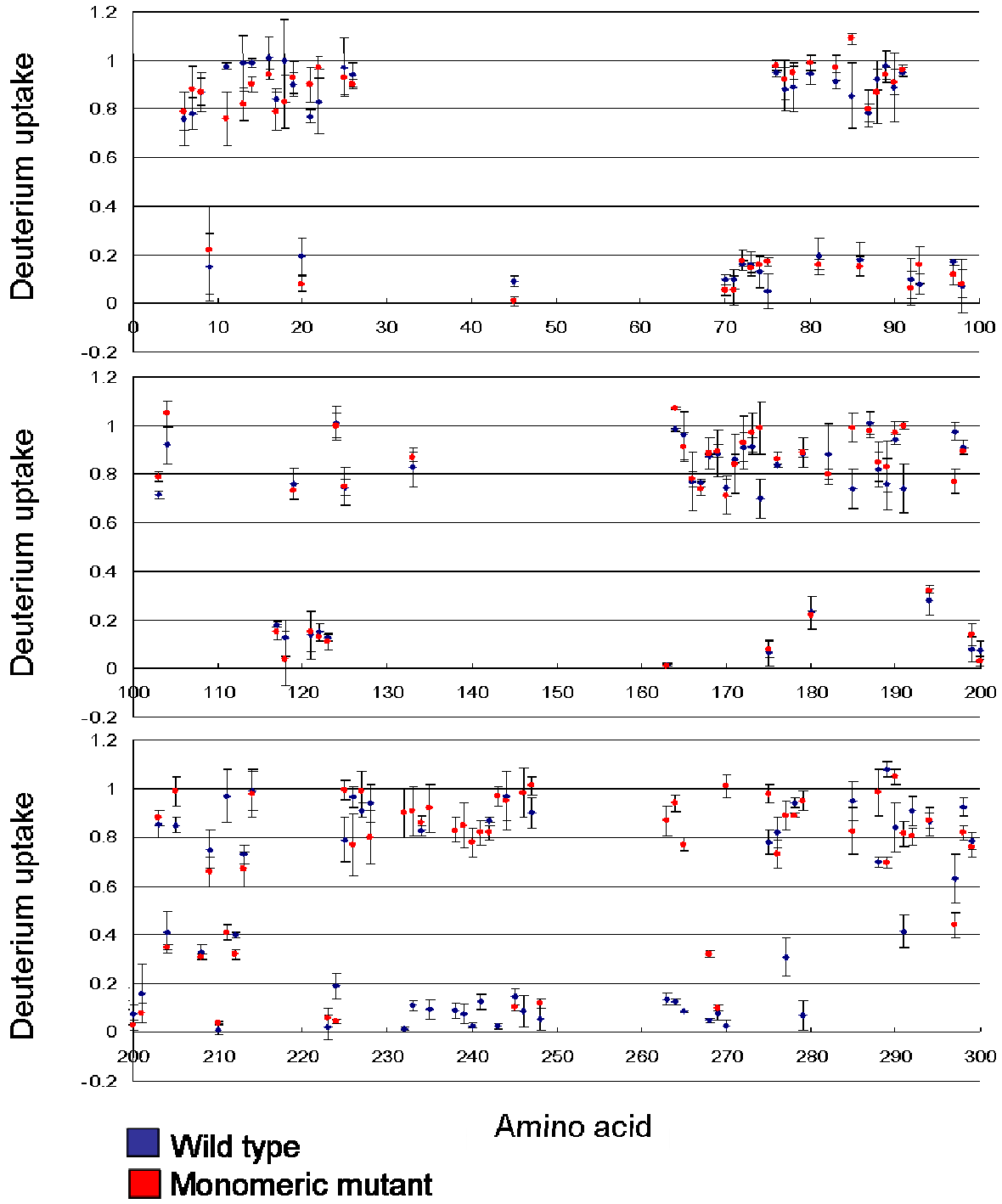
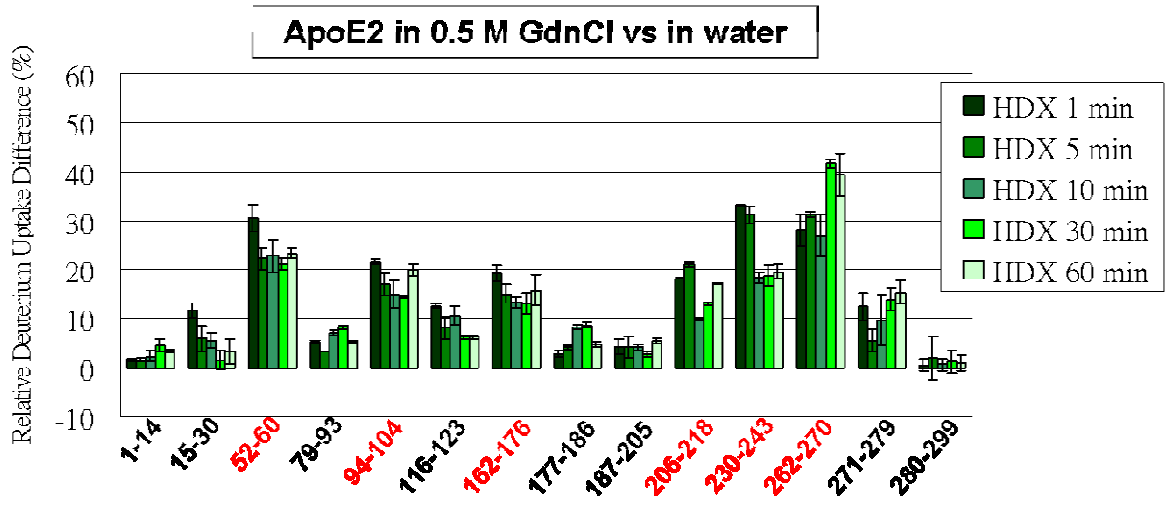
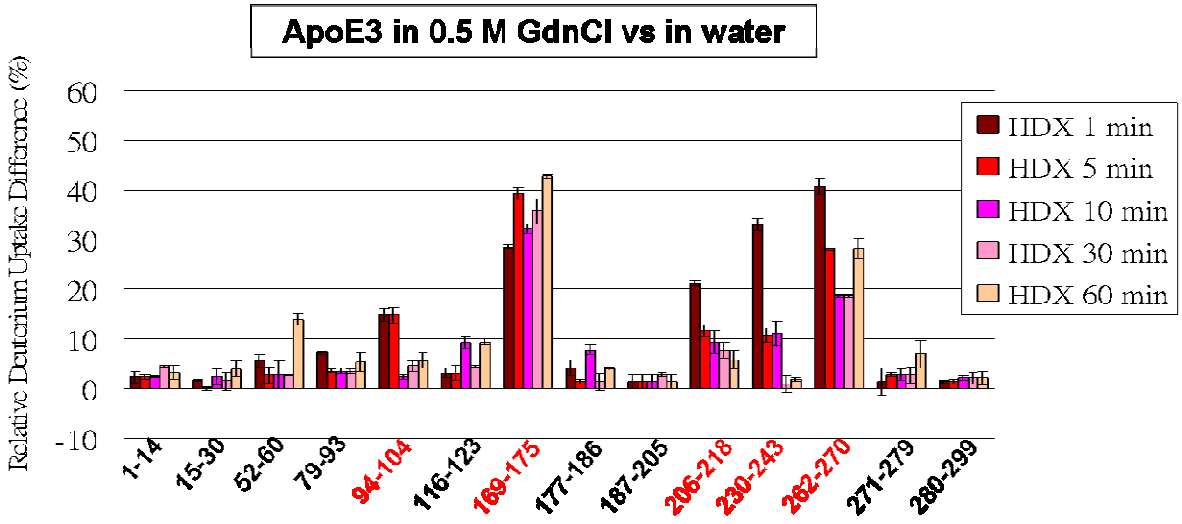


Figure S9. The extent of deuterium uptake of each residue of ApoE4. Several residues in C-terminus of wild type (blue) have lower level (<0.3D) of deuterium uptake compared to monomeric mutant (red).


ApoE2 in 0.5 M GdnCl vs in water
Relative Deuterium Uptake Difference (%)
60
50
40
30
20
10
0
-10
HDX 1 min
HDX 5 min
HDX 10 min
HDX 30 min
HDX 60 min
1-14
15-30
52-60
79-93
94-104
116-123
162-176
177-186
187-205
206-218
230-243
262-270
271-279
280-299


ApoE3 in 0.5 M GdnCl vs in water
Relative Deuterium Uptake Difference (%)
60
50
40
30
20
10
0
-10
HDX 1 min
HDX 5 min
HDX 10 min
HDX 30 min
HDX 60 min
1-14
15-30
52-60
79-93
94-104
116-123
169-175
177-186
187-205
206-218
230-243
262-270
271-279
280-299

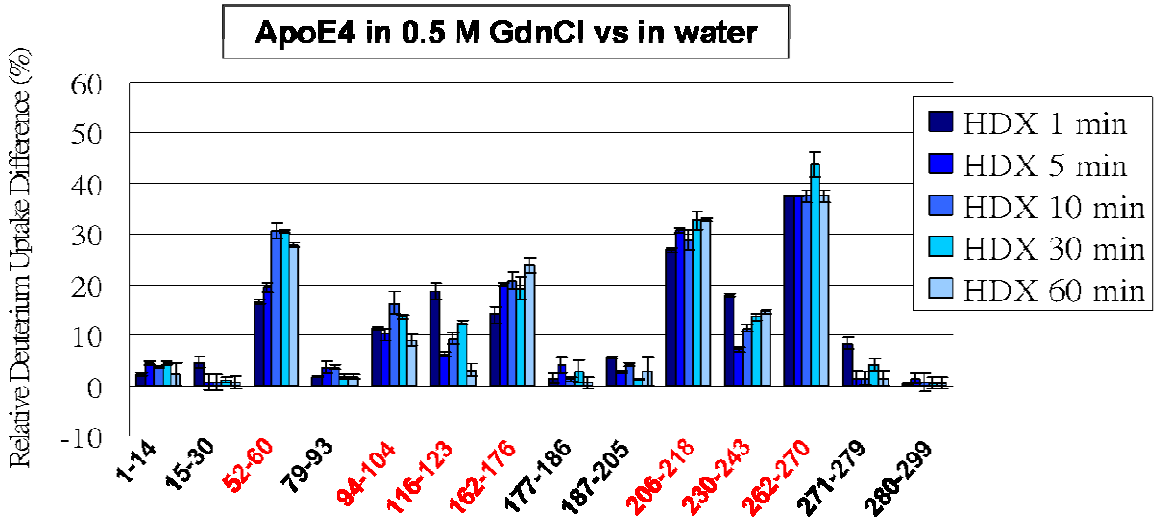

ApoE4 in 0.5 M GdnCl vs in water
Relative Deuterium Uptake Difference (%)
60
50
40
30
20
10
0
-10
HDX 1 min
HDX 5 min
HDX 10 min
HDX 30 min
HDX 60 min
1-14
15-30
52-60
79-93
94-104
116-123
162-176
177-186
187-205
206-218
230-243
262-270
271-279
280-299

Figure S10. Peptide-level H/DX of ApoE2, ApoE3, and ApoE4 with or without the presence of 0.5 M GdnCl. The relative deuterium uptake difference is plotted as different peptide regions. The large difference indicates the regions (red) having less stable H-bonding or more relative solvent accessibilities in the presence of denaturant.

Supplemental tables

Amino acid	WT	STD	MM	STD	D 100%	Normalized MM	STD
V6	0.76	0.11	0.79	0.08	0.78	1.01	0.10
E7	0.78	0.07	0.88	0.10	0.93	0.95	0.11
T8	0.87	0.06	0.87	0.08	0.82	1.06	0.10
E9	0.15	0.14	0.22	0.18	0.31	0.71	0.11
E11	0.98	0.02	0.76	0.11	1.01	0.75	0.11
E13	0.99	0.12	0.82	0.07	0.98	0.84	0.07
L14	0.99	0.02	0.90	0.03	1.00	0.90	0.03
Q16	1.01	0.09	0.94	0.02	0.99	0.95	0.02
Q17	0.84	0.04	0.79	0.08	0.80	0.99	0.10
T18	1.00	0.17	0.83	0.11	0.88	0.94	0.13
E19	0.90	0.05	0.93	0.07	0.95	0.98	0.07
W20	0.20	0.08	0.08	0.03	0.11	0.73	0.02
Q21	0.77	0.03	0.90	0.07	0.93	0.97	0.08
S22	0.83	0.13	0.97	0.04	0.98	0.99	0.04
R25	0.97	0.12	0.93	0.07	1.00	0.93	0.07
W26	0.94	0.05	0.90	0.02	0.98	0.92	0.02
E45	0.09	0.02	0.01	0.02	0.98	0.01	0.02
E70	0.10	0.02	0.06	0.02	0.94	0.06	0.02
L71	0.10	0.04	0.06	0.06	1.08	0.05	0.06
K72	0.17	0.01	0.18	0.04	0.89	0.20	0.05
A73	0.16	0.05	0.15	0.02	1.00	0.15	0.02
Y74	0.13	0.07	0.16	0.03	1.02	0.16	0.03
K75	0.05	0.07	0.17	0.02	1.00	0.17	0.02
S76	0.95	0.02	0.98	0.02	0.97	1.01	0.02
E77	0.88	0.09	0.92	0.08	0.99	0.93	0.08
L78	0.89	0.10	0.95	0.03	0.98	0.97	0.03
E80	0.95	0.05	0.99	0.03	0.99	1.00	0.03
Q81	0.20	0.08	0.16	0.02	1.00	0.16	0.02
T83	0.92	0.04	0.97	0.05	0.98	0.99	0.05
V85	0.86	0.14	1.09	0.02	0.99	1.10	0.02
A86	0.18	0.07	0.15	0.04	1.02	0.15	0.04

E87	0.79	0.04	0.80	0.08	0.95	0.84	0.08
E88	0.92	0.04	0.87	0.13	0.85	1.02	0.15
T89	0.98	0.06	0.94	0.03	0.95	0.99	0.03
R90	0.89	0.14	0.91	0.05	0.92	0.99	0.05
A91	0.95	0.02	0.96	0.02	0.93	1.03	0.02
R92	0.10	0.08	0.06	0.07	1.02	0.06	0.07
L93	0.08	0.04	0.16	0.08	1.03	0.16	0.07
L97	0.17	0.01	0.12	0.04	0.99	0.12	0.04
Q98	0.07	0.11	0.08	0.06	0.98	0.08	0.06
R103	0.72	0.02	0.79	0.02	1.00	0.79	0.02
L104	0.92	0.08	1.05	0.05	0.99	1.06	0.05
Q117	0.18	0.01	0.15	0.03	0.98	0.15	0.03
Y118	0.13	0.08	0.04	0.11	0.78	0.05	0.14
R119	0.76	0.07	0.73	0.03	1.04	0.71	0.03
E121	0.14	0.10	0.15	0.08	0.89	0.17	0.09
V122	0.15	0.04	0.13	0.02	0.88	0.15	0.02
Q123	0.13	0.02	0.11	0.03	0.66	0.17	0.05
A124	1.01	0.07	1.00	0.05	0.99	1.02	0.05
M125	0.75	0.04	0.75	0.08	0.72	1.05	0.11
L133	0.83	0.08	0.87	0.02	0.89	0.98	0.02
Q163	0.02	0.01	0.01	0.01	0.77	0.01	0.01
A164	0.99	0.01	1.07	0.00	0.99	1.08	0.00
G165	0.96	0.10	0.91	0.06	1.00	0.91	0.06
A166	0.77	0.12	0.78	0.03	0.81	0.96	0.04
R167	0.77	0.02	0.74	0.03	0.70	1.06	0.04
E168	0.88	0.01	0.89	0.07	1.01	0.88	0.06
G169	0.89	0.10	0.90	0.03	1.00	0.90	0.03
A170	0.74	0.04	0.71	0.08	0.74	0.96	0.11
E171	0.86	0.02	0.84	0.12	0.93	0.91	0.13
R172	0.91	0.06	0.93	0.11	0.97	0.96	0.11
G173	0.92	0.04	0.97	0.08	0.99	0.98	0.08
L174	0.70	0.08	0.99	0.11	1.00	0.99	0.11
S175	0.07	0.06	0.08	0.03	0.33	0.24	0.10
A176	0.84	0.01	0.86	0.03	0.88	0.98	0.04
E179	0.89	0.02	0.89	0.06	0.99	0.90	0.06

R180	0.23	0.07	0.22	0.02	0.31	0.71	0.06
G182	0.88	0.13	0.80	0.02	0.84	0.95	0.02
V185	0.74	0.08	0.99	0.06	0.97	1.02	0.06
Q187	1.01	0.05	0.98	0.03	0.93	1.05	0.03
G188	0.82	0.07	0.85	0.08	0.99	0.86	0.08
R189	0.76	0.11	0.83	0.11	0.88	0.94	0.12
V190	0.94	0.02	0.97	0.05	0.98	0.99	0.05
R191	0.74	0.10	1.00	0.02	1.02	0.99	0.01
T194	0.28	0.06	0.32	0.01	0.47	0.69	0.02
S197	0.98	0.04	0.77	0.05	0.98	0.79	0.05
L198	0.91	0.03	0.90	0.02	0.96	0.93	0.02
A199	0.08	0.05	0.14	0.04	0.91	0.15	0.05
G200	0.08	0.04	0.03	0.02	0.76	0.04	0.03
Q201	0.16	0.12	0.08	0.04	0.98	0.08	0.04
L203	0.86	0.06	0.88	0.03	1.02	0.87	0.03
Q204	0.41	0.09	0.35	0.01	0.35	1.00	0.03
E205	0.85	0.03	0.99	0.06	1.01	0.98	0.06
Q208	0.33	0.03	0.31	0.01	0.33	0.94	0.03
A209	0.75	0.08	0.66	0.06	0.94	0.70	0.06
W210	0.01	0.02	0.04	0.01	0.05	0.80	0.10
G211	0.97	0.11	0.41	0.03	0.58	0.71	0.05
E212	0.40	0.01	0.32	0.02	0.32	1.00	0.06
R213	0.73	0.04	0.67	0.07	0.88	0.76	0.08
L214	0.99	0.08	0.98	0.10	1.01	0.97	0.10
S223	0.02	0.05	0.06	0.04	0.93	0.06	0.04
R224	0.19	0.05	0.05	0.01	0.89	0.05	0.01
T225	0.79	0.09	1.00	0.04	1.00	1.00	0.04
R226	0.97	0.05	0.77	0.13	0.95	0.81	0.13
D227	0.91	0.03	0.99	0.08	1.02	0.97	0.08
L228	0.94	0.08	0.80	0.11	0.98	0.82	0.11
V232	0.02	0.01	0.90	0.10	1.02	0.88	0.10
K233	0.11	0.02	0.91	0.10	0.96	0.95	0.10
E234	0.83	0.02	0.86	0.03	0.96	0.90	0.03
Q235	0.10	0.04	0.92	0.10	1.01	0.91	0.10
E238	0.09	0.03	0.83	0.05	0.95	0.88	0.05

V239	0.08	0.04	0.85	0.09	0.85	1.01	0.11
R240	0.03	0.01	0.78	0.06	0.92	0.85	0.07
A241	0.13	0.03	0.82	0.05	1.00	0.82	0.05
K242	0.87	0.01	0.82	0.03	0.93	0.88	0.03
L243	0.03	0.01	0.97	0.04	1.02	0.95	0.04
E244	0.97	0.10	0.95	0.12	1.00	0.95	0.12
E245	0.15	0.04	0.10	0.01	0.16	0.64	0.06
Q246	0.09	0.07	0.98	0.10	0.99	1.00	0.10
A247	0.90	0.06	1.01	0.04	0.95	1.07	0.04
Q248	0.06	0.05	0.12	0.02	0.31	0.39	0.07
S263	0.14	0.03	0.87	0.06	0.92	0.95	0.07
W264R	0.13	0.02	0.94	0.03	0.99	0.95	0.03
F265	0.09	0.01	0.77	0.03	0.89	0.87	0.03
L268	0.05	0.01	0.32	0.01	0.45	0.71	0.03
V269	0.08	0.03	0.10	0.01	0.10	1.00	0.10
E270	0.03	0.03	1.01	0.05	0.99	1.02	0.05
Q275	0.78	0.05	0.98	0.04	0.99	0.99	0.04
W276	0.82	0.06	0.73	0.06	0.81	0.90	0.07
A277	0.31	0.08	0.89	0.06	0.93	0.96	0.06
G278	0.94	0.02	0.89	0.01	0.92	0.97	0.01
L279Q	0.07	0.06	0.95	0.04	1.02	0.93	0.04
A285	0.95	0.08	0.83	0.10	0.89	0.93	0.11
G288	0.70	0.02	0.99	0.10	0.93	1.06	0.10
T289	1.08	0.03	0.70	0.03	0.71	0.98	0.04
S290	0.84	0.10	1.05	0.03	1.01	1.04	0.03
A291	0.42	0.07	0.82	0.05	0.81	1.01	0.06
A292	0.91	0.06	0.81	0.04	0.89	0.90	0.04
V294	0.87	0.06	0.87	0.03	0.92	0.95	0.03
D297	0.63	0.10	0.44	0.05	0.58	0.76	0.09
N298	0.93	0.04	0.82	0.03	0.89	0.92	0.03
H299	0.79	0.04	0.76	0.04	0.99	0.77	0.04

Table S1. A complete list of deuterium uptake for 132 residues in ApoE4.