Supporting Information

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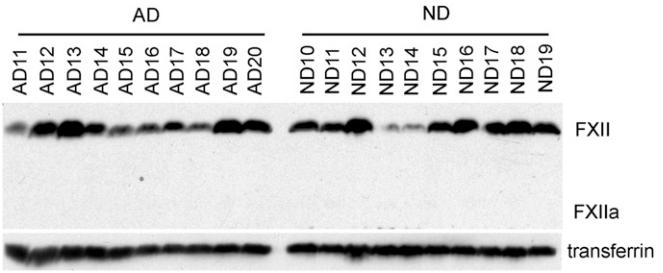

Fig. S1. Western blot analysis of FXII in AD patient plasma. Western blot of plasma samples from group 2 analyzed with an antibody against FXII and against transferrin as a loading control. No FXIIa heavy chain was detected.

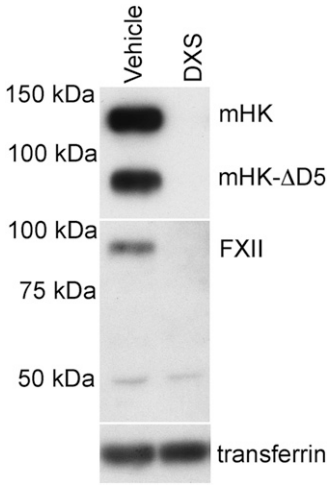

Fig. S2. FXII cleavage in mouse plasma cannot be detected via Western blot. Reducing Western blot with transferrin as a loading control. Plasma from mice injected with DXS has complete cleavage of mHK and mHK-ΔD5, whereas plasma from mice injected with vehicle does not (*Top*). Although FXII zymogen is completely cleaved, there are no specific bands corresponding to FXIIa fragments (*Middle*). Thus, it is not possible to detect increased FXIIa in mouse plasma even after complete FXII activation.

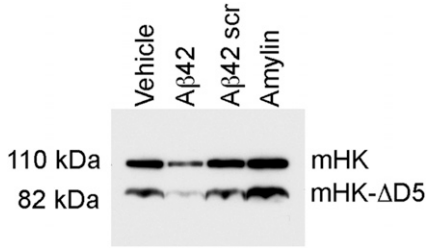

Fig. S3. In vitro activation of WT mouse plasma by Aβ42 and control peptides. C57BL/6 (WT) mouse plasma incubated with Aβ42 but not vehicle, Aβ42 scr, or amylin results in HK cleavage.

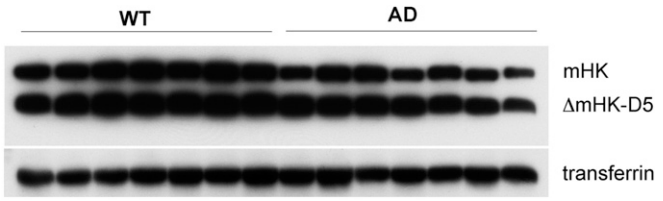

Fig. S4. Full Western blot analysis of HK in AD and WT mouse plasma. Plasma from AD mice (n = 7) and littermate controls (WT; n = 7) was analyzed by Western blot with an antibody against mHK light chain and transferrin as a loading control.

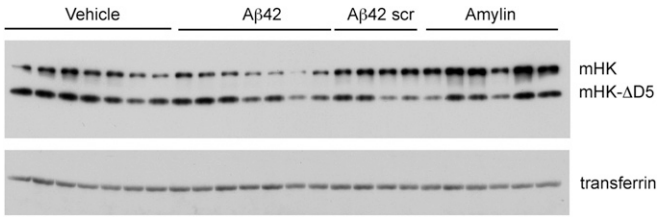

Fig. S5. Full Western blot analysis of HK in WT mouse plasma injected with vehicle, Aβ42, Aβ42 scr, or amylin. Plasma from C57BL/6 (WT) mice injected with vehicle (n = 7), Aβ42 (n = 7), Aβ42 scr (n = 4), or amylin (n = 6) was analyzed by Western blot with an antibody against mHK light chain and transferrin.

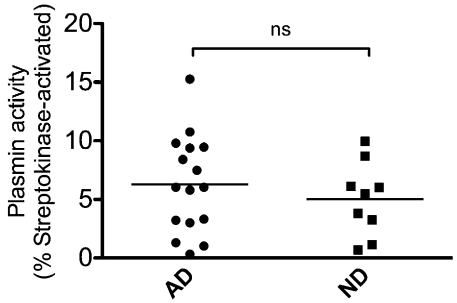

Fig. S6. Plasmin activity does not differ between AD and ND plasma. Plasmin activity in samples from group 1 was measured by chromogenic substrate Pefa-5329 for plasmin (Pentapharm). Plasma samples diluted 1:30 were mixed with 0.67 mM Pefa-5329 (final concentration), and absorbance read at 405 nm for 30 min. The rate of substrate conversion over time was calculated for each sample and expressed as percentage plasmin activity measured in plasma activated with 1 μM streptokinase (Sigma).

Table S1. Characteristics of AD and ND cases from group 1

Characteristic	AD (n = 18)	ND (n = 11)
Sex, % male	61	64
Mean age at blood draw, y (SD)	82.4 (9.1)	82.5 (6.3)
Mean CDR at blood draw, score (SD)	1.56 (1.28)	0 (0.2)
Mean MMSE at blood draw, score (SD)	16.5 (9.6)	28.5 (1.5)
CERAD, %		
None	0	100
B	27.8	0
C	72.2	0
Braak stage, %		
0–2	16.7	100
3–4	5.6	0
5–6	77.8	0
History, %		
Hypertension	50	63.6
Atrial fibrillation	5.6	18.2
Stroke	27.8	0
Diabetes	5.6	18.2
Hypercholesterolemia	38.5*	45.5
Myocardial infarction	11.1	27.3

*History of hypercholesterolemia data were available for only 13 AD cases.

Table S2. Characteristics of AD and ND cases from group 2

Characteristic	AD (n = 10)	ND (n = 10)
Sex, % male	30	50
Mean age at blood draw, y (SD)	73.6 (5.8)	70.5 (3.9)
Mean CDR at blood draw, score (SD)	1.0 (0.6)	0 (0)
CDR, %		
0	0	100
0.5	40	0
1	40	0
2	20	0