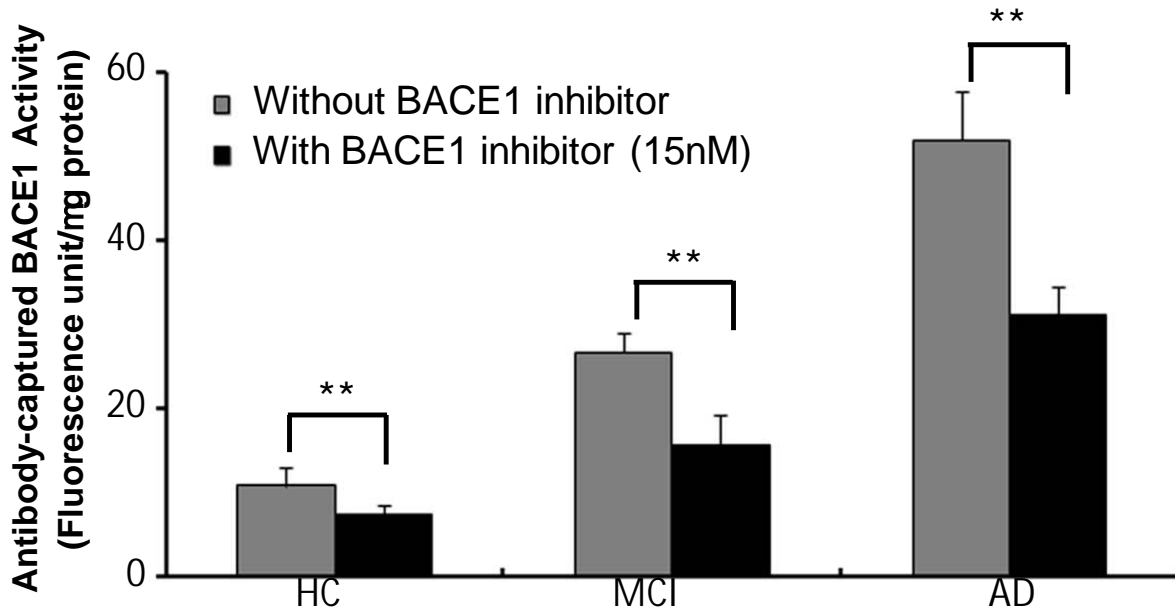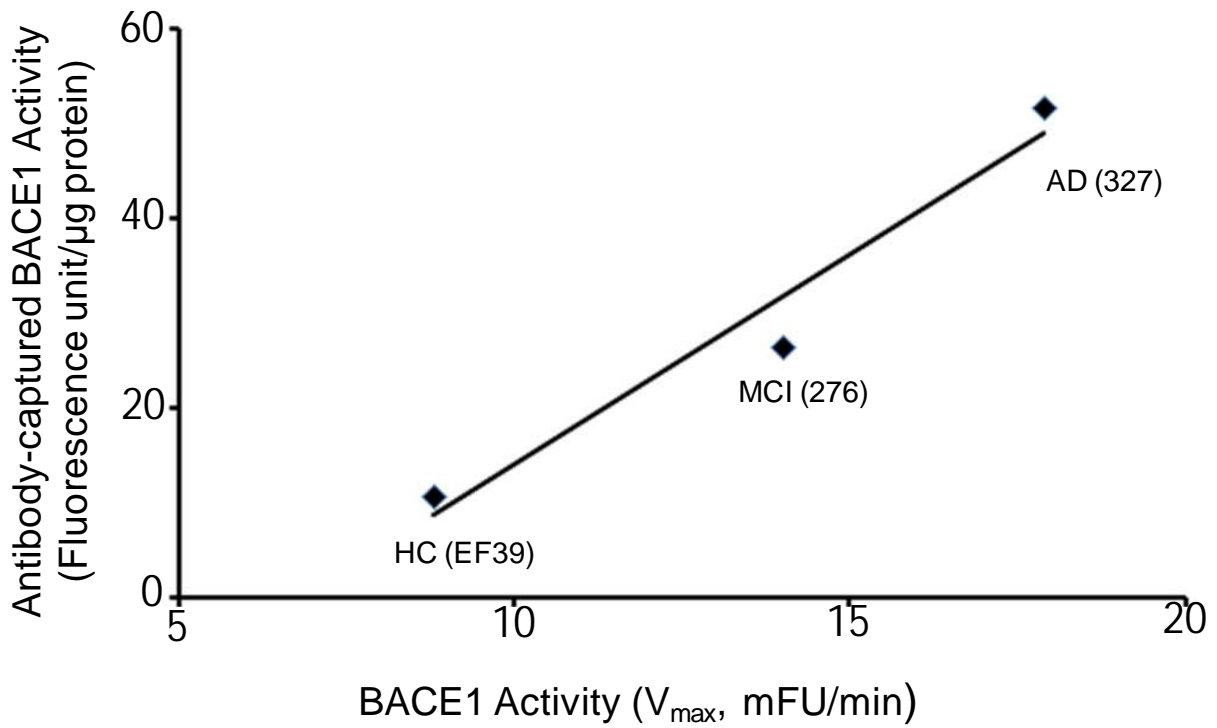# Increased Plasma BACE1 May Predict Conversion to Alzheimer's Disease Dementia in Individuals With Mild Cognitive Impairment
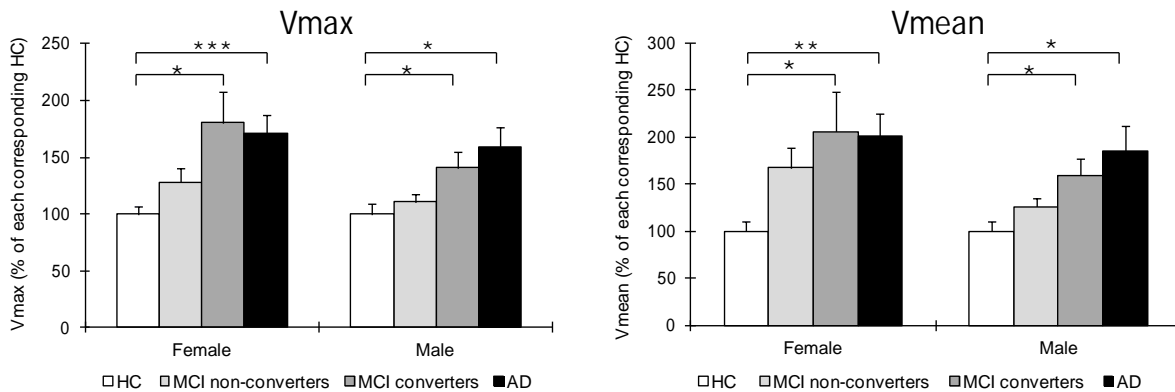
Supplemental Information

Supplementary Figure S1. Specific BACE1 activity was detected using the BACE1 antibody and was specifically inhibited by the BACE1 inhibitor. The antibody-captured BACE1 activity was measured in HC, MCI and AD. Plasma BACE1 was precipitated using the anti-BACE antibody (MAB5308) and measured as previously described (1). The antibody-captured BACE1 activity is expressed as adjusted fluorescence intensity per microgram of total protein. The BACE1 enzymatic activity was inhibited by BACE inhibitor at 15nM (IC50). ** $P < 0.01$.

Supplementary Figure S2. Association between the activity of BACE1 in HC (#EF 39), MCI (#276), and AD (#327) plasma samples measured as previously described (1) and as we reported (2) with modifications.

BACE1 activity comparisons of Female and Male in plasma samples

BACE1 activity Group	V_{max}(mean± S.E.) mFu/min/μg		P^a	V_{mean}(mean± S.E.) mFu/min/μg		P^b
	female	male	V_{max}	female	male	V_{mean}
HC	6.5± 0.4	6.2± 0.5	0.4	4.2± 0.4	4.1± 0.4	0.8
MCI	10.7± 1.4	8.6± 0.7	0.2	8.2± 1.4	3.6± 0.5	0.1
AD	11.1± 1.0	9.93± 1.1	0.4	8.5± 1.0	5.0± 1.0	0.5

P^a: Difference between Female and Male in Vmax
P^b: Difference between Female and Male in Vmean

Supplementary Figure S3. Plasma BACE1 activity comparison between female and male participants. All error bars represent S.E. (**A**) BACE1 activity comparisons between females and males in V_{max}. BACE1 activity is expressed as percentage of each age-and sex-matched HC group. Plasma samples from female and male participants include HC (53 cases, F=28, M=25), MCI non-converters (25 cases, F=13, M=12), MCI converters (71 cases, F=39, M=32) and AD (75 cases, F=52, M=23), overall 224 cases. *P< 0.05, **P<0.01, ***P<0.001. (**B**) BACE1 activity comparisons between females and males in V_{mean}. BACE1 activity is expressed as percentage of each HC group. The numbers of participants are the same as those in listed in (**A**), above. *P< 0.05, **P<0.01. (**C**) BACE1 activity comparisons between females and males in V_{max} and V_{mean}. BACE1 activity is expressed as testing values (mean ± S.E.) in the spectrometer (units are indicated as mFU/min/μg). There were no significant sex-related differences in BACE1 activity between the four study groups (cognitively HC, MCI non converters, MCI converters, AD patients), therefore BACE1 activity seems to be mainly driven by the diagnosis (AD vs. MCI vs. cognitively HC) rather than by sex.

Supplemental References

1. Hampel H, Shen Y. Beta-site amyloid precursor protein cleaving enzyme 1 (BACE1) as a biological candidate marker of Alzheimer's disease. Arch Neurol. 2002;59:1381-1389

2. Yang L-B, Lindholm K, Yan R, Citron M, Xia W, Konishi Y, Yang XL, Beach T, Sue L, Wang P, Price D, Li R, Shen Y. Elevated b-secrtase expression and enzymatic activity detected in Sporadic Alzheimer's brains. Nature Medicine 2003;9:3-4.