

## SUPPORTING INFORMATION

**TABLE S1. Inclusion and exclusion criteria of the study sample**

| Criteria | Inclusion  | Exclusion   |
|----------|--|---|
|          | <ul style="list-style-type: none"> <li>▪ Age &gt; 65 years</li> <li>▪ Non-smoker</li> </ul>  | <ul style="list-style-type: none"> <li>▪ History of cardiovascular disease (stroke or myocardial infarction)</li> <li>▪ History of diabetes mellitus</li> <li>▪ Hypertension (defined as supine blood pressure &gt;160 mm Hg systolic or 95 mm Hg diastolic, or a physician's diagnosis of hypertension)</li> <li>▪ History of psychiatric illness such as depression</li> <li>▪ Regular alcohol consumption</li> </ul> |
|          | <ul style="list-style-type: none"> <li>▪ Clinical evaluation of cognitive function at CSHA-2:<br/><i>For cases:</i> with diagnosis of CIND<br/><i>For controls:</i> with diagnosis of no cognitive impairment</li> <li>▪ Clinical evaluation of cognitive function at CSHA-3:<br/><i>For cases:</i> CIND at CSHA-2 with a diagnosis of AD at CSHA-3<br/><i>For controls:</i> controls at CSHA-2 with diagnosis of no cognitive impairment at CSHA-3</li> </ul> |   |

**TABLE S2. APOE genotype of the study participants**

|                 | E2/E2 | E2/E3 | E3/E3 | E2/E4 | E3/E4 | E4/E4 |
|-----------------|-------|-------|-------|-------|-------|-------|
| <b>Controls</b> | 0     | 4     | 17    | 0     | 0     | 0     |
| <b>CIND-AD</b>  | 0     | 0     | 5     | 0     | 8     | 2     |

**TABLE S3. Univariate correlation of the studied factors with BMI and sex**

|            |          | Plasma TAC      | cEVs PCs | cEVs apoD | Plasma apoD | cEVs apoJ/D |
|------------|----------|-----------------|----------|-----------|-------------|-------------|
| <b>BMI</b> | <u>r</u> | .203            | -.022    | -.169     | -.180       | .154        |
|            | <u>p</u> | .243            | .901     | .331      | .301        | .378        |
|            | <u>N</u> | 35 <sup>a</sup> | 35       | 35        | 35          | 35          |
| <b>Sex</b> | <u>r</u> | -.122           | .073     | -.054     | .046        | .094        |
|            | <u>p</u> | .478            | .678     | .754      | .790        | .587        |
|            | <u>N</u> | 36              | 35       | 36        | 36          | 36          |

**TABLE S4. Raw Data for Figure 5**

| <b>Groups</b>   | <b>N°</b>                                | <b>Plasma TAC</b> | <b>ApoD</b> | <b>ApoJ/D</b> | <b>cEVs PC</b>    |       |
|-----------------|--|-------------------|-------------|---------------|-------------------|-------|
| <b>Controls</b> | 1  | 0.30*             | 0.77        | 0.49          | 0.161             |       |
|                 | 2  | 0.87              | 0.64        | 0.69          | 0.182             |       |
|                 | 3  | 0.34              | 0.30        | 1.57          | 0.165             |       |
|                 | 4  | 0.34              | 0.50        | 1.22          | 0.166             |       |
|                 | 5  | 0.18              | 0.61        | 1.28          | 0.170             |       |
|                 | 6  | 1.12              | 0.20        | 2.9           | N.D. <sup>a</sup> |       |
|                 | 7  | 0.85              | 0.357       | 0.905         | 0.22              |       |
|                 | 8  | 0.80              | 0.368       | 0.509         | 0.233             |       |
|                 | 9  | 1.43              | 0.386       | 0.928         | 0.244             |       |
|                 | 10                                       | 0.95              | 0.674       | 0.69          | 0.224             |       |
|                 | 11                                       | 0.94              | 0.742       | 0.706         | 0.241             |       |
|                 | 12                                       | 0.44              | 0.173       | 1.027         | 0.122             |       |
|                 | 13                                       | 0.80              | 0.227       | 1.11          | 0.197             |       |
|                 | 14                                       | 0.86              | 0.204       | 1.184         | 0.135             |       |
|                 | 15                                       | 0.79              | 0.267       | 0.979         | 0.144             |       |
|                 | 16                                       | 0.63              | 0.155       | 1.667         | 0.117             |       |
|                 | 17                                       | 0.36              | 0.404       | 1.132         | 0.235             |       |
|                 | 18                                       | 0.37              | 0.135       | 1.697         | 0.131             |       |
|                 | 19                                       | 1.39              | 0.078       | 0.99          | 0.155             |       |
|                 | 20                                       | 0.60              | 1.298       | 0.559         | 0.25              |       |
|                 | 21                                       | 0.82              | 0.081       | 2.19          | 0.105             |       |
| <b>CIND-AD</b>  | <b>CIND-AD<br/>APOE ε4<sup>(+)</sup></b> | 1                 | 0.64        | 1.619         | 0.23              | 0.148 |
|                 |  | 2                 | 0.38        | 1.236         | 0.44              | 0.175 |
|                 |  | 3                 | 0.21        | 0.780         | 0.68              | 0.215 |
|                 |  | 4                 | 0.76        | 1.499         | 0.55              | 0.209 |
|                 |  | 5                 | 0.24        | 0.711         | 0.72              | 0.268 |
|                 |  | 6                 | 0.48        | 0.552         | 0.781             | 0.251 |
|                 |  | 7                 | 0.31        | 0.56          | 0.762             | 0.316 |
|                 |  | 8                 | 0.30        | 0.853         | 0.71              | 0.267 |
|                 | <b>CIND-AD<br/>APOE ε4<sup>(-)</sup></b> | 9                 | 0.27        | 0.439         | 0.738             | 0.182 |
|                 |  | 10                | 0.10        | 0.289         | 1.34              | 0.233 |
|                 |  | 11                | 0.32        | 0.376         | 0.641             | 0.229 |
|                 |  | 12                | 0.62        | 0.373         | 0.749             | 0.22  |
|                 |  | 13                | 0.42        | 0.386         | 0.668             | 0.225 |
|                 |  | 14                | 0.51        | 0.378         | 0.782             | 0.275 |
|                 |  | 15                | 0.44        | 0.216         | 1.150             | 0.241 |

**TABLE S1.** Inclusion and exclusion criteria of the study population

**TABLE S2.** *APOE* genotype of the study participants

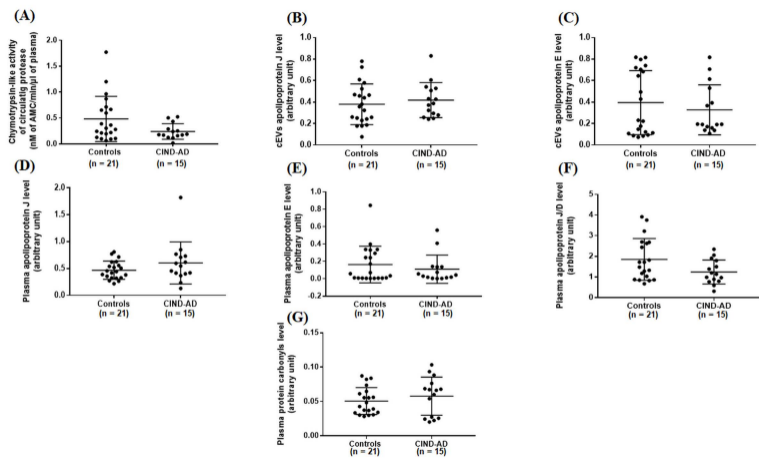
Abbreviations: CIND, cognitively impaired, no dementia; AD, Alzheimer's Disease; *APOE*, apolipoprotein E.

**TABLE S3.** Univariate correlation of the studied factors with BMI and sex

Abbreviations: BMI, body mass index; TAC, total antioxidant capacity; cEVs, circulating extracellular vesicles; PCs, protein carbonyls; apoD, apolipoprotein D; apoJ/D, apolipoprotein J / apolipoprotein D; r, pearson correlation coefficient; *p*, significance (2-tailed); N, number of participants; <sup>a</sup>, BMI data from one participant is missing.

**TABLE S4.** Raw Data for Figure 5

Abbreviations: TAC, total antioxidant capacity; cEVs, circulating extracellular vesicles; apoD, apolipoprotein D; apoJ/D, apolipoprotein J / apolipoprotein D; PCs, protein carbonyls; CIND, cognitively impaired, no dementia; AD, Alzheimer's Disease; *APOE*, apolipoprotein E; (-), ε4 non-carriers; (+), ε4 carriers; \*, Each value represents the ratio of each marker band intensity and the corresponding total proteins intensity stained with the Coomassie Blue; N.D., non-determined; <sup>a</sup> PCs data from one participant is missing.



**FIGURE S1** Regulation of oxidative factors in plasma and in cEVs from the study participants. (A) circulating proteasome activity, (B) cEVs apolipoprotein J, (C) cEVs apolipoprotein E, (D) plasma apolipoprotein J, (E) plasma apolipoprotein E, (F) plasma apoJ/D levels, (J) plasma protein carbonyls (N = 36, including 21 controls and 15 CIND-AD). Each point represents the ratio of marker band intensity and the corresponding total protein intensity stained with the Coomassie Blue. Abbreviations: CIND, cognitively impaired, no dementia; AD, Alzheimer's Disease; cEVs, circulating extracellular vesicles. Statistical analysis was performed using Student-*t* test.