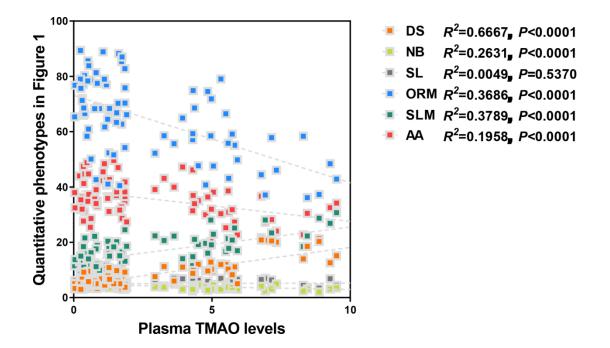
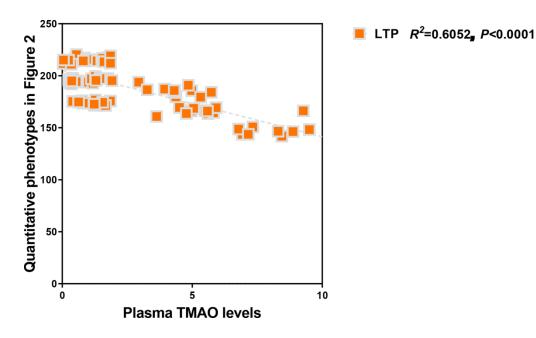
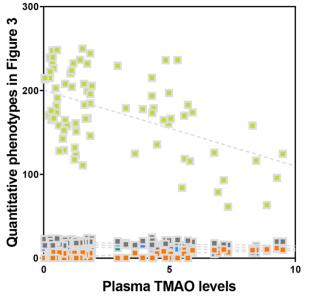
## **SUPPLEMENTARY FIGURES**



Supplementary Figure 1. Spearman correlation between the plasma TMAO concentrations and senescence / cognitive impairments in WT and APP/PS1 mice. DS means degree of senescence, NB means nest building, SL means spontaneous locomotor activity, ORM means object recognition memory, SLM means spatial learning and memory, AA means active avoidance. n=80.

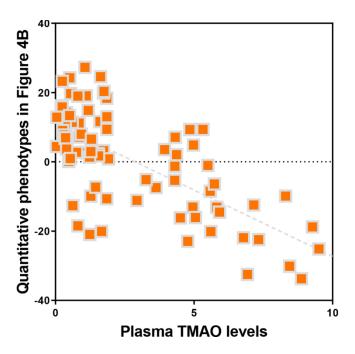


Supplementary Figure 2. Spearman correlation between the plasma TMAO concentrations and long-term potentiation in WT and APP/PS1 mice. LTP means long-term potentiation. n=80.



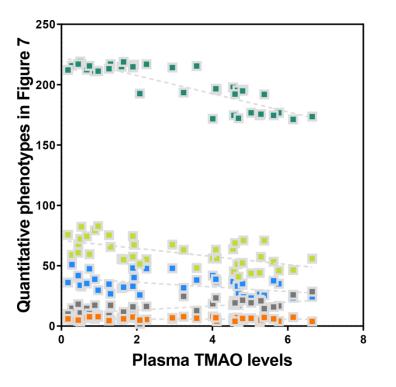
💻 Aβ deposit		R <sup>2</sup> =0.3869	<i>P</i> <0.0001
🔳 Nissl body in	n hippocampus	R <sup>2</sup> =0.2783	<i>P</i> <0.0001
Nissl body in	n CA1	R <sup>2</sup> =0.1243	<i>P</i> =0.0013
Nissl body in	n CA3	R <sup>2</sup> =0.1379	<i>P</i> =0.0007
Nissl body in	n DG	R <sup>2</sup> =0.1359	<i>P</i> =0.0008

Supplementary Figure 3. Spearman correlation between the plasma TMAO concentrations and pathological deterioration in the hippocampus of WT and APP/PS1 mice. n=80.



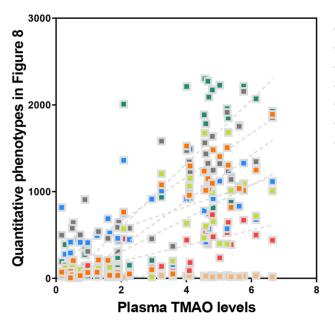
AD-related index *R*<sup>2</sup>=0.4959, *P*<0.0001

Supplementary Figure 4. Spearman correlation between the plasma TMAO concentrations and global index of AD-like behavioral and pathological profile of WT and APP/PS1 mice. n=80.



SL R<sup>2</sup>=0.0048, P=0.6687
 ORM R<sup>2</sup>=0.3526, P<0.0001</li>
 SLM R<sup>2</sup>=0.2935, P=0.0003
 AA R<sup>2</sup>=0.2303, P=0.0017
 LTP R<sup>2</sup>=0.7498, P<0.0001</li>

Supplementary Figure 5. Spearman correlation between the plasma TMAO concentrations and cognitive impairments in WT and APP/PS1 mice. SL means spontaneous locomotor activity, ORM means object recognition memory, SLM means spatial learning and memory, AA means active avoidance, LTP means long-term potentiation. n=40.

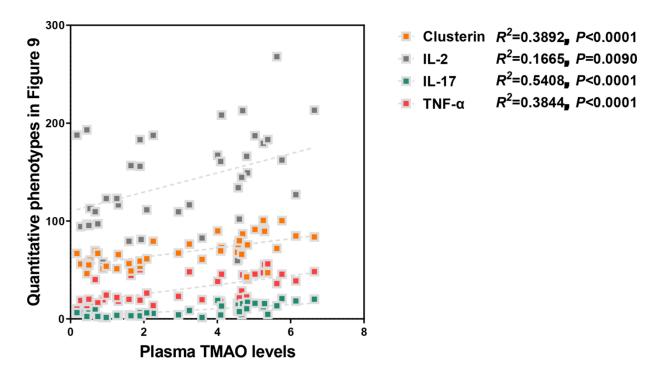


- Aβ<sub>1-42</sub> in hippocampus R<sup>2</sup>=0.7797, P<0.0001</p>
- Aβ<sub>1-40</sub> in hippocampus *R*<sup>2</sup>=0.5946 *P*<0.0001
- $A\beta_{1.42}$  in plasma  $R^2 = 0.7419$ , P<0.0001
- Aβ<sub>1-40</sub> in plasma
  - β-secretase
- R<sup>2</sup>=0.6020, P<0.0001
- APP βCTF
  γ-secretase
- R<sup>2</sup>=0.0183, P=0.4059

R<sup>2</sup>=0.4177, P<0.0001

R<sup>2</sup>=0.6789 P<0.0001

Supplementary Figure 6. Spearman correlation between the plasma TMAO concentrations and the levels of amyloid- $\beta$  (A $\beta$ ) in WT and APP/PS1 mice. n=40.



Supplementary Figure 7. Spearman correlation between the plasma TMAO concentrations and the levels of clusterin in plasma and inflammatory status in the hippocampus of WT and APP/PS1 mice. IL means interleukin, TNF- $\alpha$  means tumor necrosis factor  $\alpha$ . n=40.