## Supplementary Data

## Deletion of the Cathepsin B Gene Improves Memory Deficits in a Transgenic Alzheimer's Disease Mouse Model Expressing AβPP Containing the Wild-Type β-Secretase Site Sequence

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Supplementary Figure 1. AβPPWT/Lon mice with knockout of the CatB or BACE1 genes lack the respective protease activities. CatB and BACE1 protease activities were measured in brain extracts of control AβPPWT/Lon mice, AβPPWT/Lon × CatB knockout (CatB KO), and AβPPWT/Lon × BACE1 KO (BACE1 KO), as described in the methods. CatB protease activity (A) and BACE1 activity (B) are expressed as the  $x \pm$  s.e.m. (n = 6 per group, \*\*\* p < 0.05). Knockout of each these protease genes resulted in elimination of the respective protease activity.



Supplementary Figure 2. AβPPSwe/Lon mice with knockout of the CatB or BACE1 genes lack the respective protease activities. CatB and BACE1 protease activities were measured in brain extracts of control AβPPSwe/Lon mice, AβPPSwe/Lon × CatB knockout (CatB KO), and AβPPSwe/Lon × BACE1 KO (BACE1 KO), as described in the methods. CatB protease activity (A) and BACE1 activity (B) are expressed as the mean,  $x \pm s.e.m.$  (n=6 per group, \*\*\* p < 0.05). Knockout of each these protease genes resulted in elimination of the respective protease activity.



Supplementary Figure 3. Normal memory of non-transgenic mice is not affected by knockout of CatB or BACE1 genes. Normal nontransgenic mice with knockout of CatB or BACE1 (age and strain matched to the transgenic mice of this study) were assessed for memory function by the Morris water maze test, achieved by measuring the latency period for mice to swim to a submerged hidden platform in a pool of water, after training, as described in the methods. The latency period measurements (secs) are expressed as the mean  $\pm$  s.e.m. (n = 10).

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