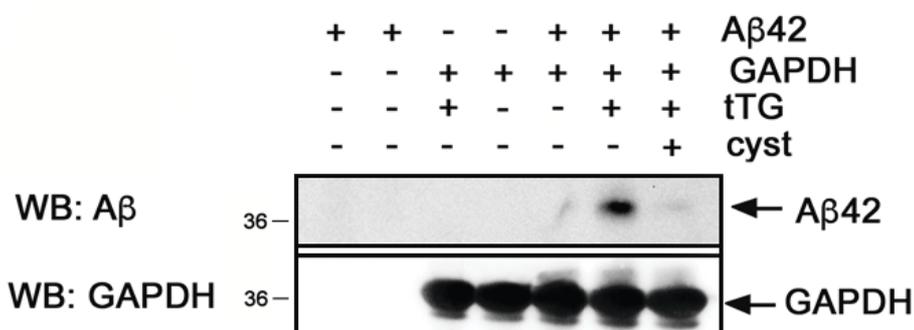
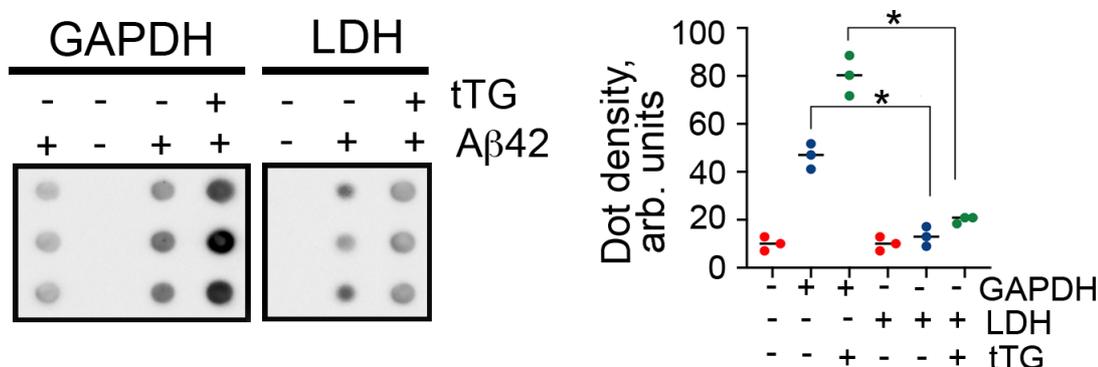


**Extracellular GAPDH promotes Alzheimer disease progression by enhancing amyloid- $\beta$  aggregation and cytotoxicity**

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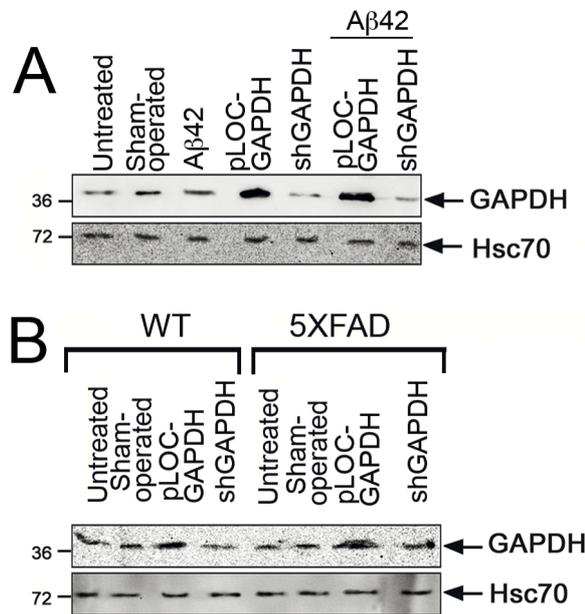


**Fig. S1. GAPDH and A $\beta$ 42 form SDS insoluble complex in the presence of tTG.** Western blotting of protein complexes between GAPDH and A $\beta$ 42 formed during a 12-h incubation in the presence of tTG or tTG and cystamine. The filter was probed with an antibody against A $\beta$  (upper panel), and GAPDH (lower panel).



**Fig. S2. An arbitrary cytosolic protein (LDH) released from dying cells does not form insoluble aggregates with A $\beta$ .** A $\beta$ 42 (10  $\mu$ M) was mixed with GAPDH (50  $\mu$ g) alone or with GAPDH and tTG (1  $\mu$ g) and with LDH (50  $\mu$ g) alone or with LDH and tTG for 48 hours and

then subjected to ultrafiltration. The filter was probed with antibody against A $\beta$  (left panel). Dot density of (A) was measured with TotalLab software (right panel). \*  $p < 0.05$ .



**Fig. S3. Accumulation of GAPDH in hippocampus of experimental animals.** (A) Representative Western blots of hippocampal samples from rats injected with vehicle ( $n = 3$ , sham-operated), with lentiviral pLOC-GAPDH plasmid ( $n = 3$ ), or with lentiviral shGAPDH RNA ( $n = 3$ ), with or without A $\beta$ 42 introduced at the same time. An antibody to Hsc70 was used as the loading control. (B) Western blots of hippocampal samples from wt and 5XFAD mice injected with vehicle ( $n = 3$ , sham-operated), with lentiviruses bearing the pLOC-GAPDH plasmid ( $n = 3$ ), or with lentiviruses bearing shGAPDH RNA ( $n = 3$ ).

**Table S1. Cohort of MCI and AD patients used for GAPDH detection in CSF**

#	Stage of Disease	Number of patients in group	Average age	MMSE, range
1	MCI	n=22; 12 males, 10 females	69,4 $\pm$ 2,5	26-30
2	Mild AD	n=41; 22 males, 19 females	75,5 $\pm$ 1,1	21-25
3	Moderate AD	n=49; 26 males, 23 females	75,6 $\pm$ 0,9	12-20
4	Severe AD	n=51; 31 males; 20 females	74,8 $\pm$ 3,5	0-11

**Table S2. Cohort of MCI and AD disease patients used for detecting A $\beta$ -GAPDH aggregates in CSF.**

#	Stage of Disease	Number of patients in group	Average age	MMSE, range
1	MCI	n=6; 4 males, 2 females	71,5 $\pm$ 2,5	26-28
2	Mild AD	n=8; 6 males, 2 females	76 $\pm$ 2,2	21-25
3	Moderate AD	n=7; 3 males, 4 females	78,3 $\pm$ 2,4	12-20
4	Severe AD	n=6; 3males; 3 females	74,8 $\pm$ 3,5	0-11