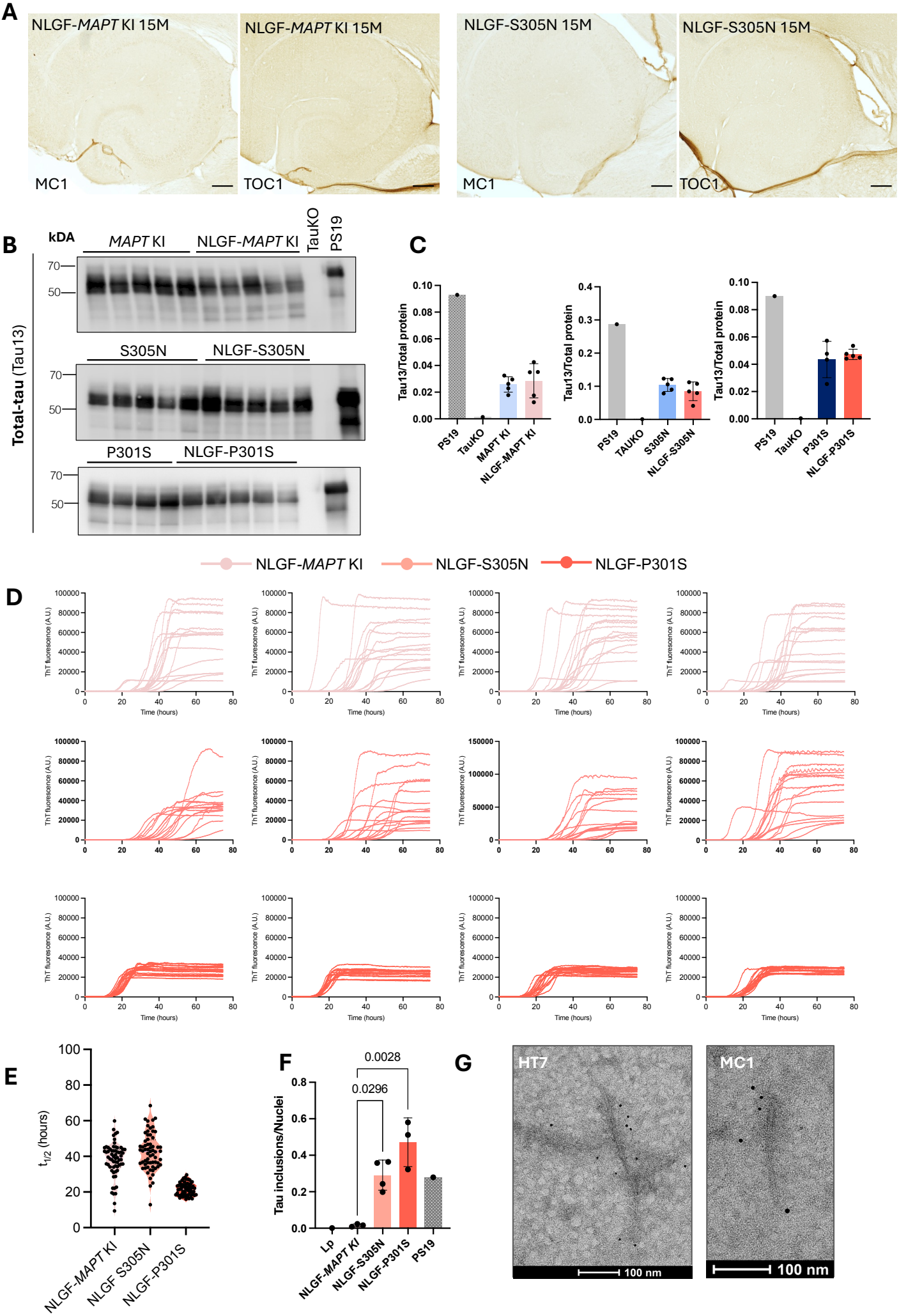
A
NLGF-MAPT KI 15M
MC1
NLGF-MAPT KI 15M
TOC1
NLGF-S305N 15M
MC1
NLGF-S305N 15M
TOC1
B
kDA
MAPT KI
NLGF-MAPT KI
TauKO
PS19
Total-tau (Tau13)
70
50
S305N
NLGF-S305N
P301S
NLGF-P301S
C
Tau13/Total protein
PS19
TauKO
MAPT KI
NLGF-MAPT KI
TAUKO
S305N
NLGF-S305N
P301S
NLGF-P301S
NLGF-MAPT KI
NLGF-S305N
NLGF-P301S
D
ThT fluorescence (A.U.)
Time (hours)
E
t1/2 (hours)
NLGF-MAPT KI
NLGF S305N
NLGF-P301S
F
Tau inclusions/Nuclei
0.0028
0.0296
Lp
NLGF-MAPT KI
NLGF-S305N
NLGF-P301S
PS19
G
HT7
MC1
100 nm
100 nm

**Fig. S6.** (**A**) Tau immunostaining detected by TOC1 (oligomeric tau) and MC1 (conformationally abnormal tau) antibodies in the hippocampus of NLGF-*MAPT* KI, NLGF-S305N at 15M. Scale bar represents 200µm. (**B**) Immunoblotting of total tau detected by Tau13 antibodies in the RIPA fraction of hippocampi brain lysates from NLGF-*MAPT* KI, NLGF-S305N and NLGF-P301S KI mice at 15M of age (N=5 for each group, expect for P301S with N=4; N=2-3 female and N=2 males), along with *Mapt* knock-out (KO) at 9M and positive control PS19 mice at 9M and (**C**) quantification to total protein. Data represents mean±S.D. (**D**) Raw RT-QuIC ThT reactions from posterior cortex of mice at 15M, NLGF-*MAPT* KI (N=4), NLGF-S305N (N=3) and NLGF-P301S (N=4; all sex-matched). (**E**) RT-QuIC aggregates half-way curve ($t_{1/2}$) from the combination of 16 replicates per biological sample from 15M posterior cortex from NLGF-*MAPT* KI (N=4), NLGF-S305N (N=3) and NLGF-P301S (N=4; all sex-matched). (**F**) Tau seeding activity from posterior cortex NLGF-*MAPT* KI, NLGF-S305N and NLGF-P301S (N=3 per group, N=2 female and N=1 male) using S305N biosensor cells nuclear inclusions in S305N biosensor at 30M, compared to PS19 mouse at 9M and lipofectamine negative control ("Lp"). Data represents mean±S.D. (**G**) Immunogold labelling (tau antibodies HT7 and MC1 on 6nm gold beads) of sarkosyl-insoluble extracted fibrils from whole-brain of 24M NLGF-P301S mice