Supplementary Material

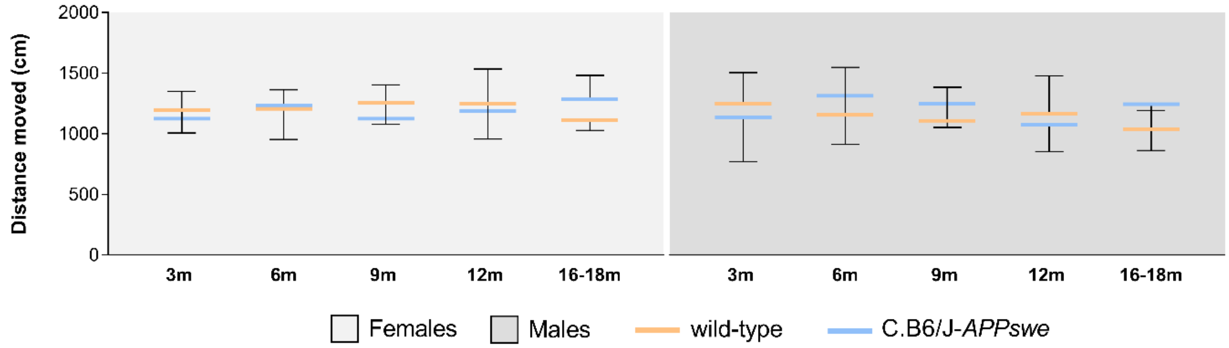
Generation and Characterization of the First Murine Model of Alzheimer's Disease with Mutated AβPP Inserted in a BALB/c Background (C.B6/J-APP_{swe})

Supplementary Table 1. Detailed outcomes of significant statistical analyses performed by ANOVA

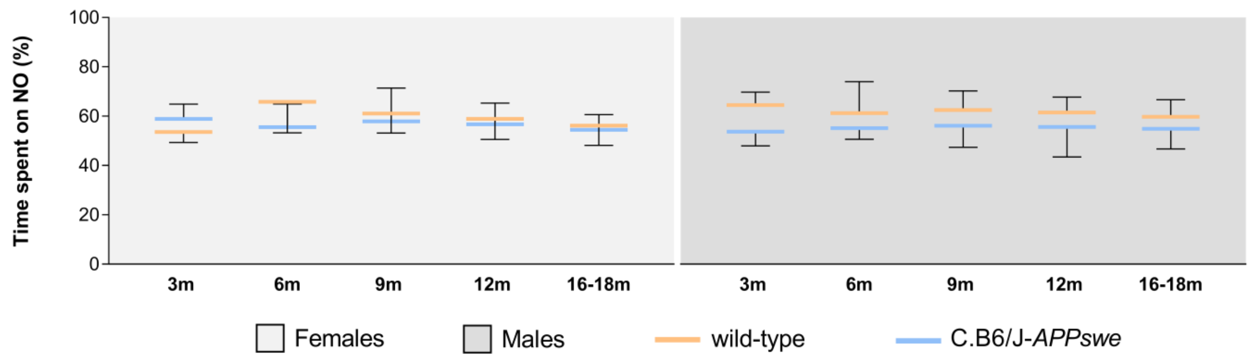
Figure 4C	*6E10 antibody*: hippocampus, $F_{4,55}$=7.28 and *p*<0.0001; cortex, $F_{4,55}$=5.28 and *p*=0.0011. One-way ANOVA.
Figure 4D	*22C11 antibody*: hippocampus, genotype ($F_{1,110}$=355.70 and *p*<0.0001) and interaction between genotype and age ($F_{4,105}$=6.94 and *p*<0.0001); cortex, genotype ($F_{1,110}$=414.50 and *p*<0.0001), age ($F_{4,110}$=2.74 and *p*=0.0323) and interaction between genotype and age ($F_{4,110}$=9.08 and *p*<0.0001). Two-way ANOVA.
Figure 5	*Soluble $A\beta_{42}$*: hippocampus, F=11.71 and *p*<0.0001; cortex, F=9.56 and *p*<0.0001. *Insoluble $A\beta_{40}$*: hippocampus, F=104.50 and *p*<0.0001; cortex, F=47.75 and *p*<0.0001. *Insoluble $A\beta_{42}$*: hippocampus, F=64.83 and *p*<0.0001; cortex, F=66.94 and *p*<0.0001. One-way ANOVA.
Figure 6D	*6E10 antibody*: CA1, $F_{4,35}$=8.75 and *p*<0.0001; CA3, $F_{4,35}$=9.50 and *p*<0.0001; DG, $F_{4,35}$=31.97 and *p*<0.0001; PCtx, $F_{4,35}$=7.33 and *p*=0.0002. *4G8 antibody*: CA1, $F_{4,35}$=7.94 and *p*=0.0001; CA3, $F_{4,3}$ =10.29 and *p*<0.0001; DG, $F_{4,35}$=7.75 and *p*<0.0001; PCtx, $F_{4,35}$=11.42 and *p*<0.0001. One-way ANOVA.
Figure 6E	*Anti-Ptau antibody*: CA1, genotype ($F_{1,70}$=124.00 and *p*<0.0001); CA3, genotype ($F_{1,70}$=117.30 and *p*<0.0001) and age ($F_{4,54}$=3.00 and *p*=0.0240); DG, genotype ($F_{1,70}$=233.90 and *p*<0.0001); PCtx, genotype ($F_{1,70}$=216.00 and *p*<0.0001) and age ($F_{4,70}$=3.29 and *p*=0.0158). Two-way ANOVA.
Figure 7C	*Anti-SYP antibody*: CA1, genotype ($F_{1,70}$=137.40 and *p*<0.0001) and age ($F_{4,70}$=3.05 and *p*=0.0224); CA3, genotype ($F_{1,70}$=194.50 and *p*<0.0001) and age ($F_{4,70}$=5.96 and *p*=0.0003); PCtx, genotype ($F_{1,70}$=301.70 and *p*<0.0001), age ($F_{4,70}$=3.44 and *p*=0.00125), and interaction between genotype and age ($F_{4,70}$=3.18 and *p*=0.0185). Two-way ANOVA.
Figure 7D	*Anti-NeuN antibody*: CA1, age ($F_{4,70}$=4.73 and *p*=0.0019) and interaction between genotype and age ($F_{4,70}$=4.05 and *p*=0.0052); PCtx, genotype ($F_{1,70}$=16.36 and *p*=0.0001), age ($F_{4,70}$=20.89 and *p*<0.0001), and interaction between genotype and age ($F_{4,70}$=8.74 and *p*<0.0001). Two-way ANOVA.
Figure 7E	*Anti-CASP3 antibody*: CA1, genotype ($F_{1,42}$=57.86 and *p*<0.0001), age ($F_{2,42}$=10.24 and *p*=0.0002) and interaction between genotype and age ($F_{2,42}$=9.16 and *p*=0.0005); PCtx, genotype ($F_{1,42}$=161.10 and *p*<0.0001), age ($F_{2,42}$=13.62 and *p*<0.0001) and interaction between genotype and age ($F_{2,42}$=4.10 and *p*=0.0236). *Anti-RIP3 antibody*: CA1, genotype ($F_{1,42}$=108.30 and *p*<0.0001) and age ($F_{2,42}$=3.62 and *p*=0.0355); PCtx, genotype ($F_{1,42}$=58.44 and *p*<0.0001) and age ($F_{2,42}$=3.87 and *p*=0.0288). Two-way ANOVA.
Figure 8C	*Anti-GFAP antibody*: CA1, genotype ($F_{1,70}$=38.36 and *p*<0.0001), age ($F_{4,70}$=9.41 and *p*<0.0001), and interaction between genotype and age ($F_{4,70}$=5.27 and

	p=0.0009); DG, genotype ($F_{1,70}$=137.70 and p<0.0001) and age ($F_{4,70}$=6.98 and p<0.0001); PCtx, genotype ($F_{1,70}$=955.80 and p<0.0001), age ($F_{4,70}$=14.53 and p<0.0001), and interaction between genotype and age ($F_{4,70}$=24.57 and p<0.0001). Two-way ANOVA.
Figure 8D	*Anti-Iba1 antibody*: CA1, genotype ($F_{1,70}$=37.37 and p<0.0001), age ($F_{4,70}$=9.68 and p<0.0001), and interaction between genotype and age ($F_{4,70}$=13.96 and p<0.0001); CA3, genotype ($F_{1,70}$=54.53 and p<0.0001), age ($F_{4,70}$=8.39 and p<0.0001), and interaction between genotype and age ($F_{4,70}$=10.05 and p<0.0001); DG, genotype ($F_{1,70}$=10.50 and p=0.0018) and age ($F_{4,70}$=7.14 and p<0.0001). Two-way ANOVA.
Figure 9	*fEPSP slopes*: stim strength ($F_{9,279}$=105.54 and p<0.001), genotype ($F_{1,31}$=12.40 and p=0.001), interaction between stim strength and genotype ($F_{9,279}$=7.32 and p<0.001). Two-way ANOVA and Bonferroni *post hoc* test.
Figure 10A	*Females*: total distance moved, genotype ($F_{1,70}$=61.87 and p<0.0001), age ($F_{4,70}$=12.72 and p<0.0001), and interaction between genotype and age ($F_{4,70}$=15.24 and p<0.0001); number of rearings, genotype ($F_{1,70}$=91.01 and p<0.0001), age ($F_{4,70}$=28.37 and p<0.0001), and interaction between genotype and age ($F_{4,70}$= 4.30 and p<0.0001); number of line crossings, genotype ($F_{1,70}$=48.85 and p<0.0001), age ($F_{4,70}$=12.12 and p<0.0001), and interaction between genotype and age ($F_{4,70}$=12.09 and p<0.0001); percent time spent in the center, genotype ($F_{1,70}$=26.81 and p<0.0001), age ($F_{4,70}$=8.07 and p<0.0001), and interaction between genotype and age ($F_{4,70}$=8.27 and p<0.0001). *Males*: total distance moved, genotype ($F_{1,70}$=115.60 and p<0.0001), age ($F_{4,70}$=5.71 and p=0.0005), and interaction between genotype and age ($F_{4,70}$=2.92 and p<0.0274); number of rearings, genotype ($F_{1,70}$=158.10 and p<0.0001); number of line crossings, genotype ($F_{1,70}$=97.51 and p<0.0001) and age ($F_{4,70}$=6.38 and p=0.0002); percent time spent in the center, genotype ($F_{1,70}$=137.20 and p<0.0001). Two-way ANOVA.
Figure 10B	*Females*: percent time spent in the open arms, genotype ($F_{1,70}$=31.00 and p<0.0001), age ($F_{4,70}$=16.70 and p<0.0001), and interaction between genotype and age ($F_{4,70}$=8.99 and p<0.0001); number of entries into the open arms, genotype ($F_{1,70}$=21.00 and p<0.0001), age ($F_{4,70}$=3.65 and p=0.0093), and interaction between genotype and age ($F_{4,70}$=6.17 and p=0.0003); number of head dipping, genotype ($F_{1,70}$=16.53 and p=0.0001), age ($F_{4,70}$=5.28 and p=0.0009), and interaction between genotype and age ($F_{4,70}$=7.53 and p<0.0001). *Males*: percent time spent in the open arms, genotype ($F_{1,70}$=112.70 and p<0.0001); number of entries into the open arms, genotype ($F_{1,70}$=103.70 and p<0.0001); number of head dipping, genotype ($F_{1,70}$=79.64 and p<0.0001). Two-way ANOVA.
Figure 11	*Latency*. Wild-type females aged 3 months (F=29.74 and p<0.0001), 6 months (F=6.60 and p=0.0046), 9 months (F=7.29 and p=0.0024), 12 months (F=12.03 and p=0.0006) and 16-18 months (F=37.46 and p<0.0001); wild-type males aged 3 months (F=39.66 and p<0.0001), 6 months (F=6.60 and p=0.0046), 9 months (F=29.31 and p<0.0001), 12 months (F=15.67 and p=0.0002) and 16-18 months (F=5.80 and p=0.0003); C.B6/J-APP_{swe} females aged 3 months (F=33.02 and p<0.0001), 6 months (F=4.31 and p=0.0155), 9 months (F=10.52 and p=0.0005),

	12 months (F=14.93 and p<0.0001) and 16-18 months (F=33.24 and p<0.0001); C.B6/J-*APP$_{swe}$* males aged 3 months (F=17.51 and p=0.0001), 6 months (F=20.05 and p<0.0001), 9 months (F=5.02 and p=0.0097), 12 months (F=25.37 and p<0.0001) and 16-18 months (F=9.47 and p=0.0009). One-way ANOVA for repeated measures. *Proximity*. Females: genotype ($F_{1,70}$=47.36 and p<0.0001), age ($F_{4,70}$=9.33 and p<0.0001), and interaction between genotype and age ($F_{4,70}$=4.14 and p=0.0045); males: genotype ($F_{1,40}$ 61.46 and p<0.0001), age ($F_{4,70}$=9.70 and p<0.0001), and interaction between genotype and age ($F_{1,70}$=4.38 and p=0.0032). Two-way ANOVA.
Figure 12	*Females*: 9 months of age (DAY1), genotype ($F_{1,14}$=20.80 and p=0.0004) and time ($F_{2.988,41.83}$=56.43 and p<0.0001); 9 months of age (DAY2), genotype ($F_{1,14}$=17.89 and p=0.0008) and time ($F_{2.951,41.32}$=21.53 and p<0.0001); 12 months of age (DAY1), genotype ($F_{1,14}$=11.56 and p=0.0043) and time ($F_{2.524,35.35}$=37.54 and p<0.0001); 12 months of age (DAY2), genotype ($F_{1,14}$=5.39 and p=0.0358), time ($F_{3.035,42.49}$=14.62 and p<0.0001), and interaction between genotype and time ($F_{4,56}$=5.10 and p=0.0014); 16-18 months of age (DAY1), genotype ($F_{1,14}$=14.04 and p=0.0022), time ($F_{3.190,44.60}$=61.51 and p<0.0001), and interaction between genotype and time ($F_{4,56}$=2.55 and p=0.0492); 16-18 months of age (DAY2), genotype ($F_{1,14}$=41.28 and p<0.0001) and time ($F_{2.774,38.83}$=31.54 and p<0.0001). *Males*: 3 months of age (DAY2), genotype ($F_{1,14}$=13.16 and p=0.0027) and time ($F_{2.781,38.94}$=6.16 and p=0.0020); 6 months of age (DAY1), genotype ($F_{1,14}$=21.18 and p=0.0004) and time ($F_{2.625,36.75}$=20.41 and p<0.0001); 6 months of age (DAY2), time ($F_{3.265,45.71}$=15.94 and p<0.0001) and interaction between genotype and time ($F_{4,56}$=3.76 and p=0.0089); 9 months of age (DAY1), time ($F_{3.156,44.18}$=39.13 and p<0.0001) and interaction between genotype and time ($F_{4,56}$=4.26 and p=0.0045); 9 months of age (DAY2), genotype ($F_{1,14}$=22.84 and p=0.0003), time ($F_{2.125,29.75}$=35.17 and p<0.0001), and interaction between genotype and time ($F_{4,56}$=3.20 and p=0.0198); 12 months of age (DAY1), genotype ($F_{1,14}$=12.23 and p=0.0036), time ($F_{3.212,44.97}$=50.50 and p<0.0001), and interaction between genotype and time ($F_{4,56}$=3.65 and p=0.0103); 12 months of age (DAY2), genotype ($F_{1,14}$=10.89 and p=0.0053) and time ($F_{2.612,35.57}$=14.40 and p<0.0001); 16-18 months of age (DAY1), genotype ($F_{1,14}$=14.00 and p=0.0022) and time ($F_{2.952,41.32}$=61.61 and p<0.0001); 16-18months of age (DAY2), genotype ($F_{1,14}$=26.59 and p=0.0001) and time ($F_{2.355,32.97}$=5.95 and p=0.0043). Two-way ANOVA for repeated measures.



Supplementary Figure 1. Wild-type and C.B6/J-*APP*$_{swe}$ mice move similar distances during the Elevated Plus Maze test, thus excluding the influence of different explorative behavior on anxiety-like behavior assessment. Mice of both genotypes and sexes and all age groups showed no significant differences in the distance moved to explore the arena. Eight male and eight female animals of each genotype were analyzed per age point. Two-way ANOVA and Tukey's test.



Supplementary Figure 2. C.B6/J-*APP$_{swe}$* mice do not have deficit in recognition memory. In the Novel Object Recognition test, mice of both genotypes, sexes, and all age groups spent a similar time exploring the novel object. Eight male and eight female animals of each genotype were analyzed per age point. Two-way ANOVA and Tukey's test.