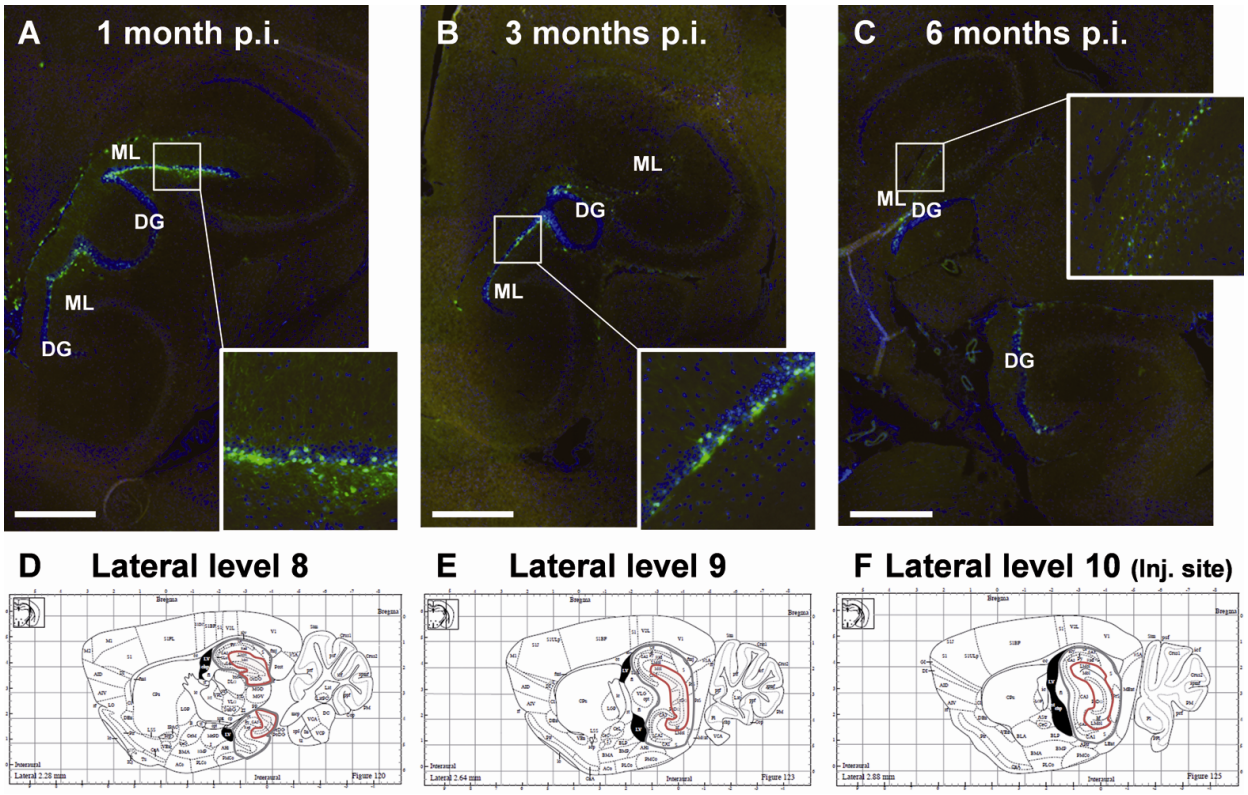

Figure S1: Distribution of GFP expressing lentiviral particles in the murine hippocampus. Lentiviral distribution was analyzed around the injection site histologically after 1 (age 7 months; **A**), 3 (age 9 months; **B**) and 6 months (age 12 months; **C**). Representative pictures of cryo-fixed brain slices from intrathecally injected APP_{SL} tg animals overexpressing GFP (Titer $7*10^8$ IU/ml). Injections were placed directly in the hippocampus (coordinates: +/- 3 mm lateral; -3.0 mm posterior; 1,8-2.0 mm ventral). Green: GFP; Blue: DAPI. Scale bars = 500 µm. Histological analyses comprised three lateral brain levels: Level 8 (2.3-2.34 mm lateral; **D**), level 9 (2.6-2.64 mm lateral; **E**) and level 10 (2.9-3.2 mm lateral, injection site; **F**). According to the lentiviral expression pattern (**A-C**) immunohistochemical evaluations were performed region specifically for the DG and ML (**D-F**, red marked region). Schemes in (**D-F**) show the annotated region scheme with nomenclature and manual definition of the AOI (red marked region). Anatomical figures were taken from Paxinos & Franklin "The Mouse Brain Atlas". *Abbreviations: GFP: green fluorescent protein, IU/ml: international units per milliliter, tg: transgenic, DAPI: 4',6-diamidino-2-phenylindole, p.i.: post injection, AOI: area of interest, DG: dentate gyrus, ML: molecular layer.*

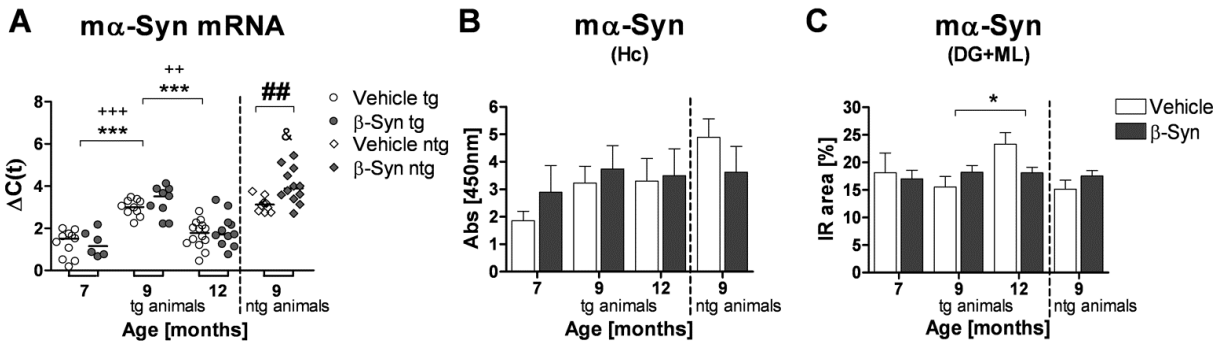

Figure S2: α-Synuclein expression in the hippocampus of APP_{SL} and ntg mice injected with human β-Syn expressing lentiviral particles. Murine α-Syn mRNA expression (**A**) was evaluated with qRT-PCR in the hippocampus (Hc) over age. mRNA levels are shown as difference in cycle numbers (ΔC(t)) between the GOI and the HKG (HPRT1). Vehicle (white dots): n=11-14; β-Syn (grey dots): n=6-12. Scatter dot blot + median. Statistical analysis: 2-way ANOVA with Bonferroni post-test. $^{++/\&\&}p< 0.01$; $***/^{+++}p<0.001$; * Vehicle vs. Vehicle; + β-Syn vs. β-Syn; # Vehicle vs. β-Syn ; & β-Syn ntg vs. β-Syn tg. Hippocampal murine α-Syn protein levels were evaluated by ELISA (**B**) in the left hemispheres. Histological analysis of the right hemispheres was evaluated region specifically as IR area in percent for ML and DG (**C**). Vehicle (white bars): n=11-14; β-Syn (grey bars): n=6-12. Bars represent group means + SEM. Statistical analysis: 2-way ANOVA with Bonferroni post-test. *p< 0.05; * Vehicle vs. Vehicle. *Abbreviations: tg: transgenic, ntg: non-transgenic, C(t): cycle treshold, GOI: gene of interest, HKG: housekeeping gene, HPRT1: hypoxanthine-guanine phosphoribosyltransferase 1, Hc: hippocampus, ML: molecular layer, DG: dentate gyrus, IR: immunoreactive.*

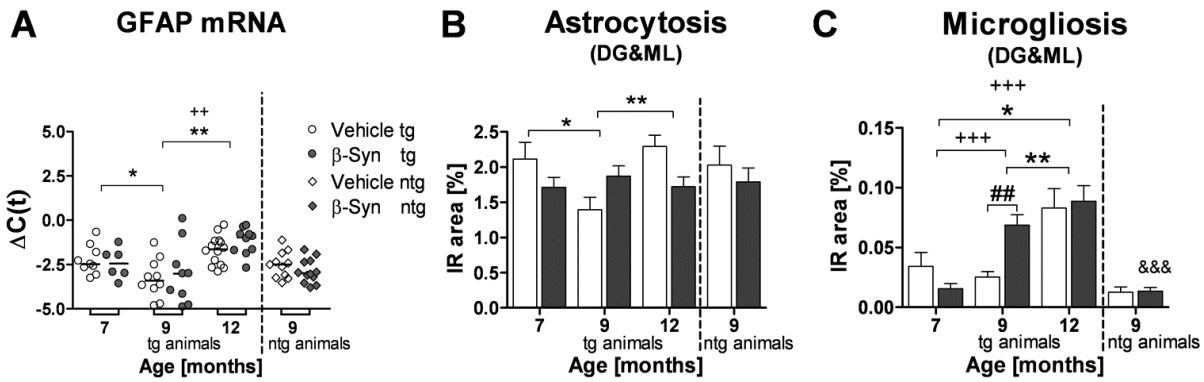

Figure S3: Hippocampal neuroinflammation in APP_{SL} and ntg mice injected with β-Syn expressing lentiviral particles. Neuroinflammation marker were analyzed on mRNA level in the whole hippocampus (**A**) as well as on protein level in DG and ML (**B,C**). mRNA expression is illustrated as difference in cycle numbers (ΔC(t)) between the GOI and the HKG (HPRT1, **A**). Vehicle (white dots): n=11-14; β-Syn (grey dots): n=6-12. Scatter dot blot + median. Statistical analysis: 2-way ANOVA with Bonferroni post-test. *p< 0.05; $**^{/++}$p<0.01; * Vehicle vs. Vehicle; + β-Syn vs. β-Syn. Immunohistochemically, astrocytosis was evaluated as IR area in percent with an anti-GFAP (**B**), and microgliosis with an anti-Iba-1 antibody (**C**) over age (7, 9, 12 months). Vehicle (white bars) n=4-6/group; β-Syn (grey bars) n=10/group. Bars represent mean + SEM. Statistical analysis: 2-way ANOVA with Bonferroni post-test. *p< 0.05; $**^{/++/\#\#/\&\&}$p<0.01; * Vehicle vs. Vehicle; + β-Syn vs. β-Syn; # Vehicle vs. β-Syn; & Vehicle/β-Syn ntg vs. Vehicle/β-Syn tg. *Abbreviations: tg: transgenic, ntg: non-transgenic, C(t): cycle threshold, GOI: gene of interest, HKG: housekeeping gene, HPRT1: hypoxanthine-guanine phosphoribosyltransferase 1, Hc: hippocampus, ML: molecular layer, DG: dentate gyrus, GFAP: glial fibrillary acidic protein, Iba1: ionized calcium binding adaptor molecule 1,IR: immunoreactive.*

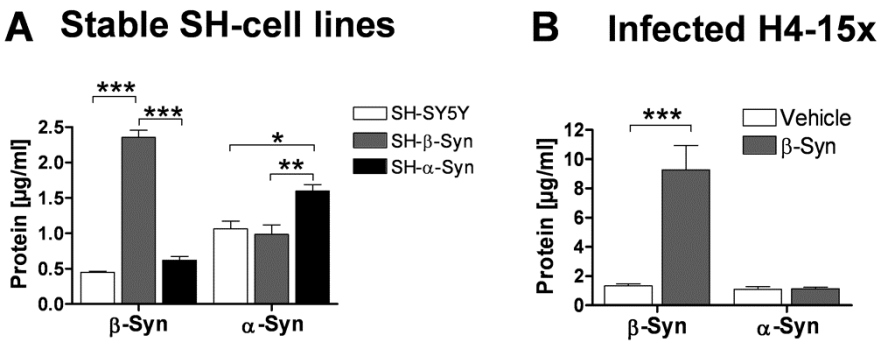

Figure S4: Synuclein protein expression in stable SH-cell lines and infected hAPP overexpressing cells. α- and β-Synuclein protein expression was measured in 2 different cell types *in vitro*: i) Stable human neuroblastoma cell lines overexpressing α-Syn (SH-α-Syn, black bars) or β-Syn (SH-β-Syn, grey bars) or ntg SH (SH-SY5Y, white bars); ii) Human neuroglioma cells overexpressing APP-695 (H4-15x) infected with empty lentiviral particles (Vehicle, white bars) or particles overexpressing β-Syn (grey bars). Synuclein protein concentrations were detected with an ELISA (**A,B**). n=6/group; Bars represent mean + SEM. Statistical analysis: 1-way ANOVA with Bonferroni post-test (**A**) or T-test (**B**). *Abbreviations: SH: SH-SY5Y, hAPP: human amyloid precursor protein.*