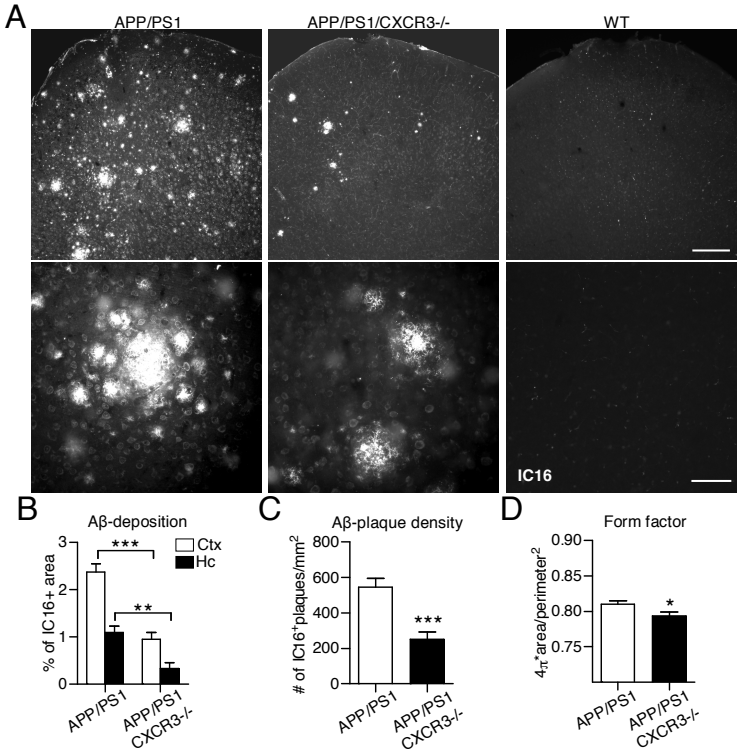
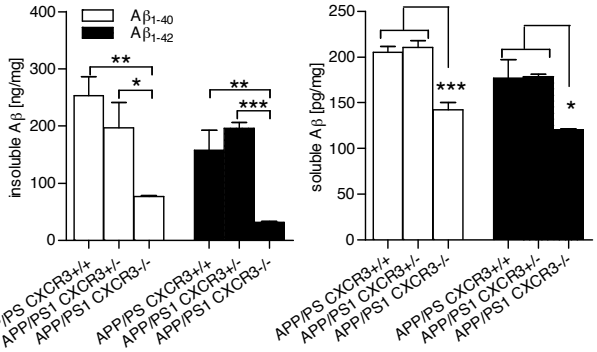
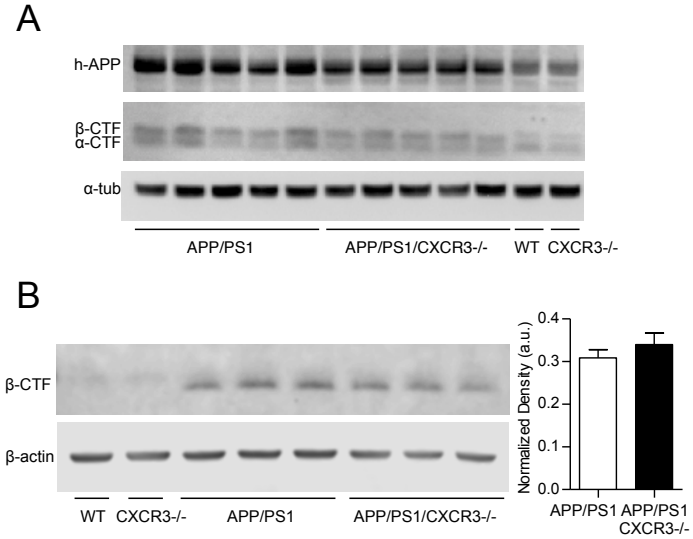


Supplemental Figure 1.
Immunfluorescent detection and analysis of plaque deposition in APP/PS1 and APP/PS1/CXCR3-/- mice. Staining for human Aβ1-16 (IC16) displays a strong reduction of Aβ-deposition in the cortex (Ctx) and hippocampus (Hc) of CXCR3-deficient APP/PS1 mice at 8 months (A-B; upper panel scale bar=200 μm, lower panel scale bar=50 μm). Quantification of IC16-positive plaques confirms the strong reduction of Aβ-deposition in the cortex of APP/PS1/CXCR3-/- animals (C). Form factor analysis of Aβ-plaques reveals morphological differences in APP/PS1/CXCR3-/- brains (D). Data are mean±SEM, 14-19 sections were assessed from each group of four mice, *p<0.05, **p<0.005, ***p<0.001).

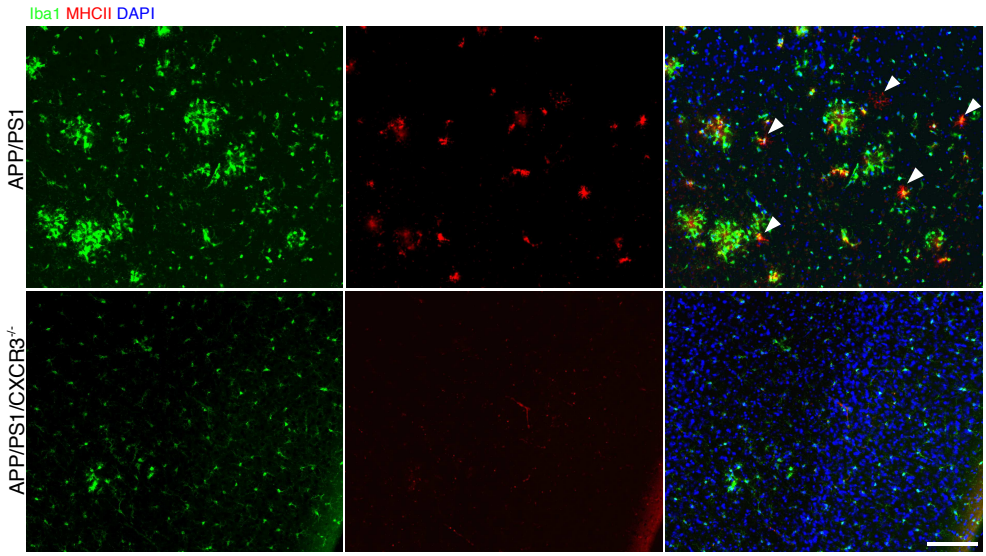


Supplemental Figure 2.
APP/PS1/CXCR3+/- mice reveal no gene dosage effect of CXCR3 on Aβ levels. Comparism of the Aβ1-40 and Aβ1-42 levels from 8 months old APP/PS1/CXCR3+/+, APP/PS1/CXCR3+/- and APP/PS1/CXCR3-/- female mice of insoluble and soluble brain fraction. No significant differences of Aβ peptide levels were found in APP/PS1/CXCR3+/- compared to APP/PS1/CXCR3+/+ mice. A strong reduction of both peptides was found in the female APP/PS1/CXCR3-/- group compared to APP/PS1/CXCR3+/+ and APP/PS1/CXCR3+/- mice. Data are mean±SEM, n=3-4 mice per group, *p<0.05, **p<0.005, ***p<0.001.

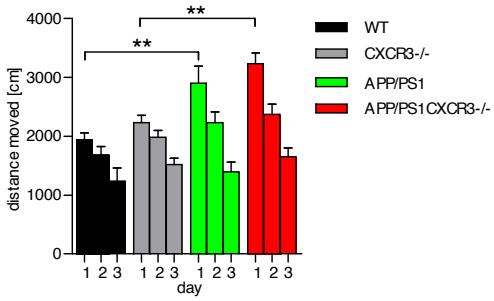


Supplemental Figure 3.
Immuno blot detection of the CTFs in APP/PS1 and APP/PS1/CXCR3-/- animals using different antibodies

A: Immunoblot analysis using a holo-APP antibody (CT15) indicates no effect of CXCR3 deficiency on APP-processing in APP/PS1 mice at 5 months. The corresponding densitometric analysis is included in Fig.1. B: Detection of β-CTFs using the 82E1 antibody and the correspondig densitometric analysis reveals no significant difference between both genotypes (a.u., density values normalized to β-actin, mean±SEM).



Supplemental Figure 4.
Reduction of MHCII$^+$ cells in APP/PS1/CXCR3-/- mice. Double immunofluorescence staining for the microglial marker Iba1 and MHCII. Numerous MHCII$^+$ cells were detected (arrowheads) in close proximity to cluster of Iba1$^+$ microglia in CXCR3 competent APP/PS1 animals, but were diminished in CXCR3-deficient APP/PS1/CXCR3$^{-/-}$ mice (scale bar = 125 μm).



Supplemental Figure 5.
Open field analysis of APP/PS1 and APP/PS1/CXCR3-/- mice over three consecutive days. At 8 month of age no significant differences in vertical locomotor activity (distance moved) were measured between APP/PS1 and APP/PS1/CXCR3-/- animals. Habituation was documented in all tested groups. APP/PS1 and APP/PS1/CXCR3-/- mice started with significant higher locomotor activity compared to the respective control animals. Data are mean±SEM, **p<0.005.

Supplemental Table 1:

Gene (alias)	**APP/PS1** (fold of change, mean ± SEM)	**APP/PS1/CXCR 3-/-**(fold of change, mean ± SEM, p-value summary)	**Primer 1** (Forward sequence)	**Primer 2** (Reverse sequence)
ARG1	1.15 ± 0.08	0.71 ± 0.08	TTTTTCCAGCAGACCAGCTT	AGAGATTATCGGAGCGCCTT
BDNF	**1.48 ± 0.07**	**4.74 ± 0.20*****	GCCTTCATGCAACCGAAGTA	TGAGTCTCCAGGACAGCAAA
CCL19	2.58 ± 0.30	1.78 ± 0.42	ATGCGGAAGACTGCTGCC	CGGAAGGCTTTCACGATGTT
CCL2	1.25 ± 0.16	1.16 ± 0.36	TGGCTCAGCCAGATGCAGT	TTGGGATCATCTTGCTGGTG
CCL3	**15.01 ± 2.53**	**2.23 ± 0.63*****	GTGGAATCTTCCGGCTGTAG	ACCATGACACTCTGCAACCA
CCL4	**0.93 ± 0.08**	**0.52 ± 0.05***	GAAACAGCAGGAAGTGGGAG	CATGAAGCTCTGCGTGTCTG
CCL5	2.60 ± 0.76	2.62 ± 1.32	CAAGTGCTCCAATCTTGCAGTC	TTCTCTGGGTTGGCACACAC
CCL7	**1.25 ± 0.11**	**0.66 ± 0.04****	TGGGAAGCTGTTATCTTCAAGACA	CTCGACCCACTTCTGATGGG
CCR2	3.00 ± 0.39	1.21 ± 0.25*	TCA ACTTGGCCATCTCTGACC	AGACCCACTCATTTGCAGCAT
CCR5	0.82 ± 0.06	0.79 ± 0.01	GGCCATGCAGGCAACAG	TCTCCAACAAAGGCATAGATGACA
CD68	**3.78 ± 0.67**	**1.18 ± 0.12****	ATCCCCACCTGTCTCTCTCA	ACCGCCATGTAGTCCAGGTA
CSF1	1.01 ± 0.12	0.74 ± 0.05	GTGGTCTACAGCCTCTCAGCA	GCATGTCATCCAGGAGGTTC
CSF2	1.93 ± 0.52	1.29 ± 0.39	GGTAGTGGTGGATGTTCCCA	CCAGGATGAGGACAGACAGG
CX3CL1	**2.62 ± 0.12**	**0.94 ± 0.13*****	TGGGATTCGTGAGGTCATCT	CGCGTTCTTCCATTTGTGTA
CXCL10	**36.70 ± 10.45**	**3.18 ± 1.20****	GACGGTCCGCTGCAACTG	GCTTCCCTATGGCCCTCATT
CXCL12	1.40 ± 0.18	0.70 ± 0.11*	AAACCAGTCAGCCTGAGCTACC	GGCTCTGGCGATGTGGC
CXCL5	**1.66 ± 0.28**	**0.73 ± 0.07***	5GGTCCACACAGTGCCCTACG'	GCGAGTGCATTCCGCTTA
CXCL9	8.05 ± 4.03	3.38 ± 1.68	5'-GCCATGAAGTCCGCTGTTCT	GGGTTCCTCGAACTCCACACT
CXCR3	6.14 ± 2.53	n.d. [+]	AATGCCACCCATTGCCAGTAC	AGCAGTAGGCCATGACCAGAAG
CXCR4	3.88 ± 0.58	1.90 ± 0.45	TCCAACAAGGAACCCTGCTTC	TTGCCGACTATGCCAGTCAAG
FASLG	**7.20 ± 1.10**	**2.33 ± 0.71***	TTAAATGGGCCACACTCCTC	ACTCCGTGAGTTCACCAACC
RETNLB	1.09 ± 0.20	1.67 ± 0.23	TGCAGGAGATCGTCTTAGGC	TTCCCACTGATAGTCCCAGG
GAPDH	n.a.	n.a.	TCACCAGGGCTGCCATTTGC	GACTCCACGACATACTCAGC
ICAM1	1.19 ± 0.23	0.88 ± 0.11	AGATCACATTCACGGTGCTA	CTTCAGAGGCAGGAAACAGG
IFNG	2.88 ± 1.09	2.71 ± 0.83	CAGCAACAGCAAGGCGAAA	GCTGGATTCCGGCAACAG
IL6	0.74 ± 0.07	0.85 ± 0.22	ACCAGAGGAAATTTTCAATAGGC	TGATGCACTTGCAGAAAACA
IL13	1.62 ± 0.28	1.20 ± 0.11	CACACTCCATACCATGCTGC	TGTGTCTCTCCCTCTGACCC
Il1B	**4.23 ± 1.21**	**1.30 ± 0.46***	GGTCAAAGGTTTGGAAGCAG	TGTGAAATGCCACCTTTTGA
IL21	1.13 ± 0.15	0.49 ± 0.09	AAAACAGGCAAAAGCTGCAT	TGACATTGTTGAACAGCTGAAA
Il4	0.81 ± 0.18	0.73 ± 0.07	CGAGCTCACTCTCTGTGGTG	TGAACGAGGTCACAGGAGAA
ITGAM	**1.70 ± 0.18**	**1.10 ± 0.03****	5'-GTTTGTTGAAGGCATTTCCC-3'	ATTCGGTGATCCCTTGGATT
MIF	1.68 ± 0.23	1.25 ± 0.21	AGAGGGGTTTCTGTCGGAG	AAAAGTCATGAGCTGGTCCG
MRC1	1.53 ± 0.10	1.84 ± 0.16	CAGGTGTGGGCTCAGGTAGT	TGGCATGTCCTGGAATGAT
NOS2	1.29 ± 0.20	0.77 ± 0.24	AAGCCCCGCTACTACTCCAT	GCTTCAGGTTCCTGATCCAA
NTF3	1.88 ± 0.15	1.20 ± 0.06	GCCACGGAGATAAGCAAGAA	ACGGATGCCATGGTTACTTC
NTF5	1.24 ± 0.05	1.58 ± 0.15	GGCCCCTTTGTAGGATACAG	AGCCGGGGAGCAGAGAAG
TNF	**4.08 ± 0.50**	**1.56 ± 0.32****	AGGGTCTGGGCCATAGAACT	CCACCACGCTCTTCTGTCTAC
TGFB1	2.48 ± 0.32	2.52 ± 0.22	CAATTCCTGGCGTTACCTTG	GCTGAATCGAAAGCCCTGTA
VCAM1	1.27 ± 0.25	1.29 ± 0.12	GCACAAAGAAGGCTTTGAAGCA	GATTTGAGCAATCGTTTTGTATTCAG

Supplemental Table 1:

Summary of quantified immune response associated transcripts, alternative activation marker and neurotrophic factors in APP/PS1 and APP/PS1/CXCR3-/- mice at 8 months of age using qRT-PCR. RNA transcripts were normalized to GAPDH and expressed relative to that of age matched WT controls (*$p < 0.05$, **$p < 0.01$, ***$p < 0.0001$, unpaired t-test, n=4-8, mean±SEM; $^{+}$ CXCR3 was neither detectable in CXCR3-/- nor in APP/PS1/CXCR3-/- mice by qRT-PCR, therefore no fold of change could be determined). Results were further statistically analysed using a False Discovery Rate Approach (Q=0.05). Groups, which were statistically revealed as "Discoveries" are written in bold letters.