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Supplementary Data

PPARγ Co-Activator-1α (PGC-1α) Reduces Amyloid-β Generation Through a PPARγ-Dependent Mechanism

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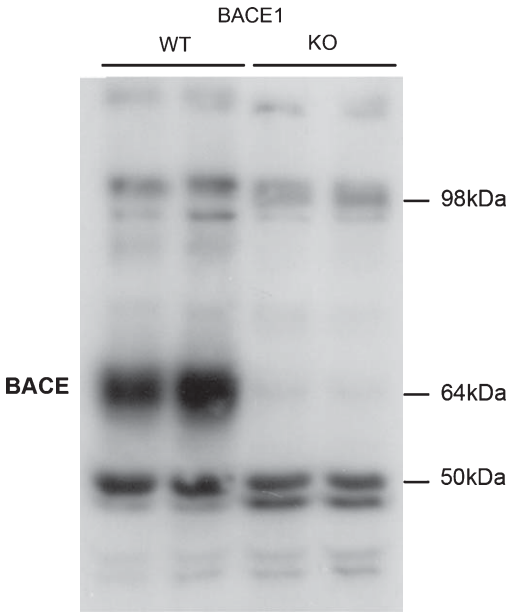

Supplementary Figure 1. BACE1 KO reveals specificity of the antibody Ab5940 for BACE1 detection. BACE1 KO mice B6.129-Bace1tm1Pcw/J were obtained from Jackson ordered via Charles River, Germany. Representative Western blot is showing the BACE1 protein level in the mouse brain homogenates of 10 day old C57Bl6 mice or BACE1 −/− mice in the same background. On the left two normal mouse brains show specific BACE1 signals (65 kDa) whereas in the two Knock-out samples on the right no signal is detected with the anti-BACE1 antibody Ab5940. Unspecific signal is detected by Ab5940 in the range below 50 kDa and above 100 kDa.

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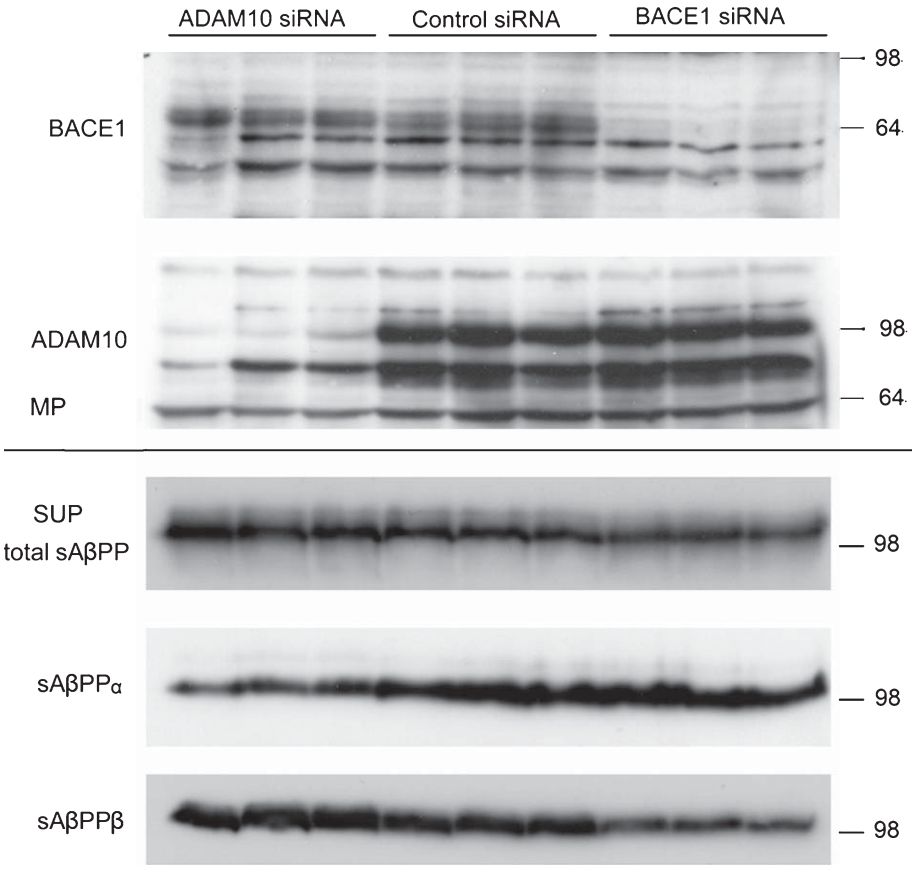
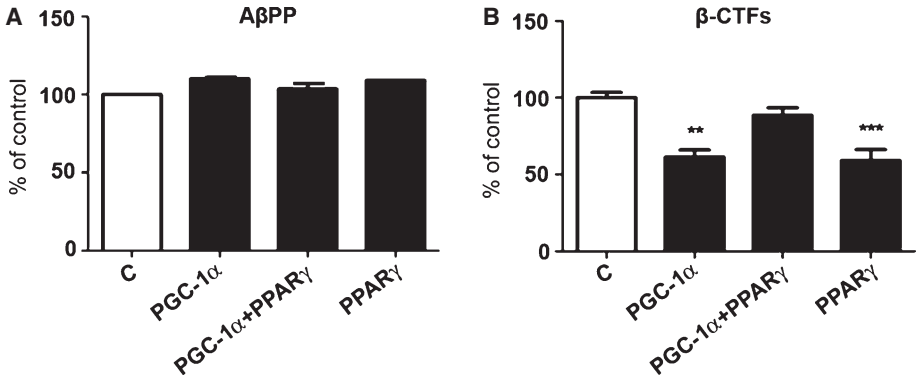


Supplementary Figure 2. Knock-down of ADAM10 and BACE1 in N2asw cells demonstrate clear ADAM10 and BACE1 signals. Representative Western blots for ADAM10 and BACE1 after 48 h of transient siRNA knock down in N2asw cells. Cells were transfected with 300 pmol siRNA against ADAM10 (Dharmacon-004503-01-50) or BACE1 (Dharmacon-003747-01-50). Controls were transfected with nonspecific siRNA (Dharmacon-001206-13-20). Upper part: Membrane-Preparations allow for detection of a robust knock-down of BACE1 (on the right) compared to the control samples in the middle. With ADAM10 siRNA transfections the immature and mature levels of ADAM10 get strongly reduced (on the left). AβPP levels are unchanged under either condition. Calnexin levels were determined as loading control for the membrane-proteins. In lower part: Supernatants (SUP) were evaluated for changes in AβPP processing by ADAM10 and BACE1. Total levels of sAβPP (22C11; Chemicon) were unchanged. In ADAM10 siRNA treated cells sAβPPα (2D8) levels were reduced as compared to controls. In BACE1 siRNA treated cells sAβPPβ levels (192swe, ELAN) were reduced. These consequences confirm the specific knock-down of the indicated α-secretase (ADAM10) and β-secretase (BACE1).



Supplementary Figure 3. PGC-1α decreases β-CTFs but does not affect total AβPP levels. A) Quantification of AβPP of total full length AβPP detected with antibody 140 in N2asw cells transfected with transfected with PGC-1α, PGC-1α siRNA, or PPARγ. B) Quantification of β-CTFs in membrane preparations of N2asw cells transfected with empty vector PGC-1α, PGC-1α + PPARγ, or PPARγ. 1α ($n = 4$). Bars represent means ± SEM. Asterisks represent significant differences between Mock control and transfected cells (One-way ANOVA, Dunnett's test). $^{**}p \leq 0.01$; $^{***}p \leq 0.001$.