Figure 7. Membrane fluidity and cleavage of APP in neuronal cells. SH-SY5Y-APP695 cells were treated as described in Materials and Methods; **A)** Membrane fluidity of living cells was correlated to endogenous $A\beta_{(1-40)}$ levels [pg/mg protein]; cells were treated for 24 h with Lovastatin (1, 2 & 4 μM), Benzyl alcohol (5 & 10 mM) and Pluronic F68 (4.5 & 7.5 μM); **B-D)** Representative fluorescence microscopy images of the SH-SY5Y-AβPP695 cells; **B)** Fluoro-oligo$A\beta_{(1-40)}$ was added to the medium and cells were incubated for 24h; **C)** Cells were stained for GM-1 ganglioside using Alexa 555-conjugated cholera toxin subunit B; **D)** Co-localization of Fluoro-oligo$A\beta_{(1-40)}$ and Alexa 555-conjugated cholera toxin sub-unit B. Data are means ± SD; n=6-12.

Supplementary Figure 1. Characterization of $A\beta_{(1-40)}$ species. $A\beta_{(1-40)}$ peptides were prepared as described in Materials and Methods. Native SDS-PAGE gel electrophoresis followed by silver staining reveals **A)** monomeric $A\beta_{(1-40)}$ (Mono; MW 4 kDa) in the disaggregated (monomer, Mono) preparation and **B)** predominantly $A\beta_{(1-40)}$ polymers (MW 50 - 75 kDa) in the oligomeric (Oligo) and Fibrillar (Fibril) preparation. The oligomeric preparation also contains dimers (MW 11 kDa). Electron micrographs of negatively stained $A\beta_{(1-40)}$ **C)** oligomers and **D)** fibrils reveal predominantly spherical aggregates and proto-fibrils or mature amyloid fibrils, respectively (magnification: 7.000; scale bar: μm).

Supplementary Figure 2. Effects of $A\beta_{(1-40)}$ species on membrane properties the and production of $A\beta_{(1-42)}$; HEK293-APP695 cells were incubated for 24h in the presence or absence of 2μM **A)** monomeric (mono), **C)** oligomeric (oligo) or **E)** fibrillar (fibril) $A\beta_{(1-40)}$; **B), D), F)** Changes in the membrane fluidity, which is inversely correlated to the anisotropy of the fluorescence probe TMA-DPH, were determined using fluorescence polarization spectroscopy in living cells; Levels of endogenous $A\beta_{(1-42)}$ were determined by ELISA [pg/mg protein]. Data are means ± SD n=3-6 (n.s. not significant; p*< 0.05; p***<0.001).

Supplementary Figure 3. Levels of sAPPα; Secreted levels of sAPPα (ng/ml) were determined by ELISA [ng/ml] in collected conditioned media of HEK293 and HEK293-APP695 cells, respectively. Data are means ± SD n=4 (p***<0.001).