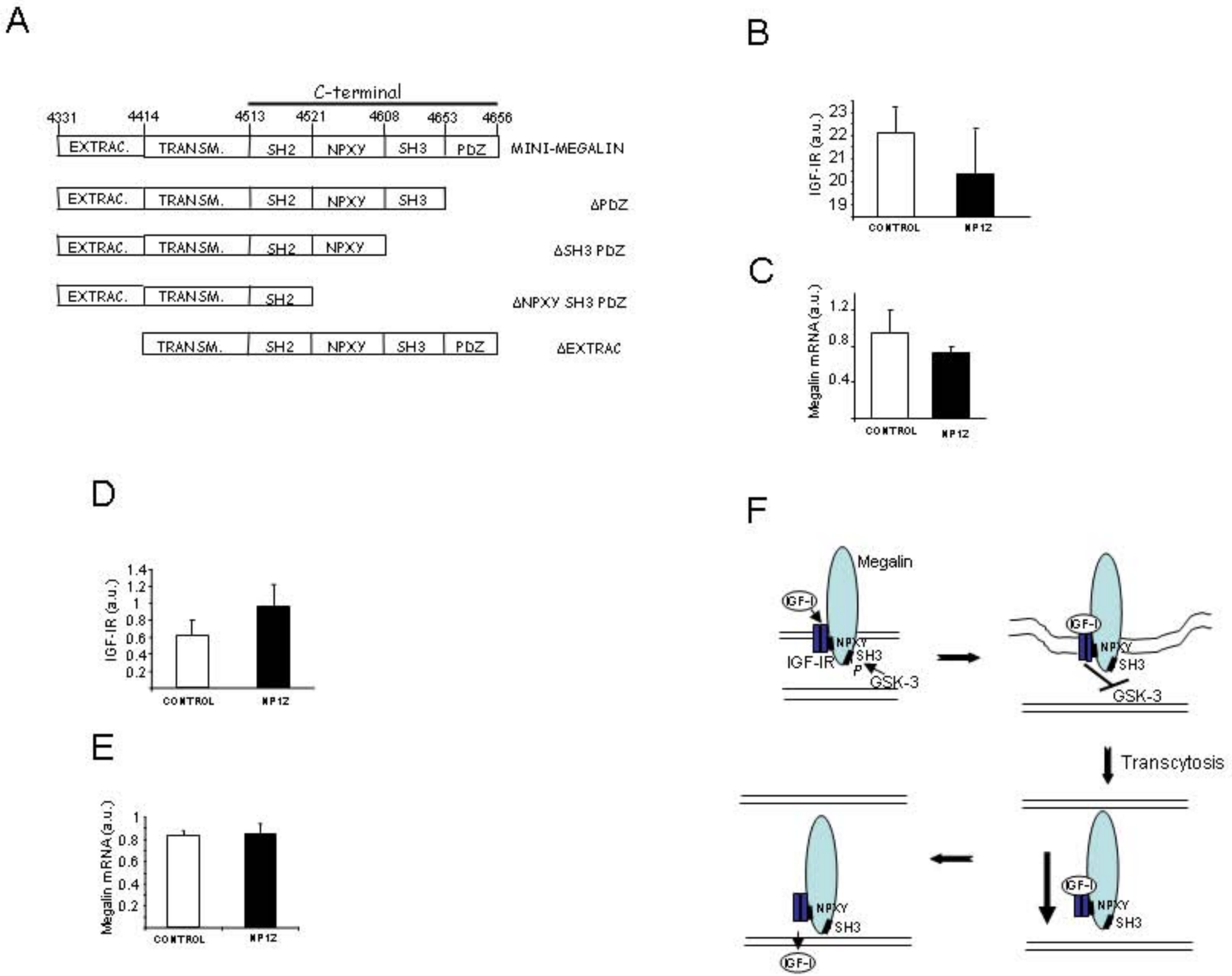
Supplementary materials

Supplemmental Fig.: **A,** Schematic representation of the mutants generated from mini-Megalin. **B**, Brain levels of IGF-I receptor were not modified after treatment with NP12, as determined by WB (n=4). **C**, Similarly, NP12 did not affect megalin mRNA levels in the choroid plexus, as determined by qPCR (n=4). **D,** Treatment with NP12 did not change brain IGF-IR in APP/PS1 mice (n=4). **E,** No changes were observed in megalin mRNA in choroid plexus of APP7PS1 mice after NP12 (n=4). **F,** Interactions between the IGF-I receptor and megalin in transcytosis of IGF-I. In a first step IGF-I binds to its receptor that is constitutively associated (either directly or through an as yet undetermined docking protein(s)) to megalin. Upon binding to its receptor the IGF-I/IGF-IR complex internalizes and the PI3K/Akt/GSK3 pathway is activated. Once GSK activity is inhibited by Akt, megalin activity is enhanced and IGF-I transcytosis proceeds.



Suppl Figure 1