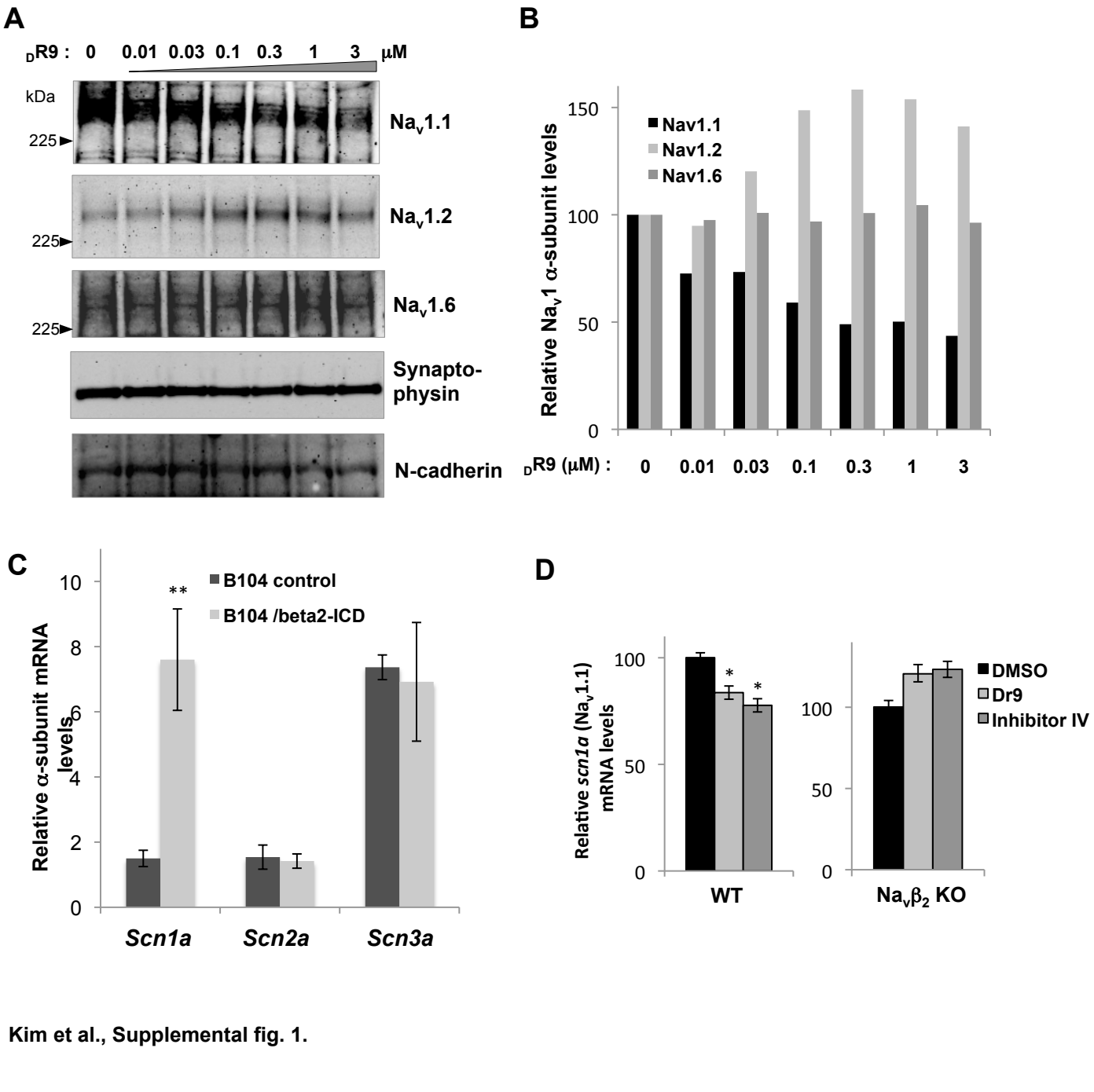
Supplemental fig 1., The BACE inhibitor $_{D}$R9 alters Na_v1 α-subunit levels in a dose-dependent manner. **(A)** Western blot analysis of $Na_v1.1$, $Na_v1.2$, and $Na_v1.6$ in rat primary neurons (DIV14) treated with various concentrations of $_{D}$R9 and control vehicle DMSO for 72 hrs. Same samples were used to show $Na_v1.1$ level changes in Fig. 1A. **(B)** Graph showing quantitative analysis of $Na_v1.1$ protein levels in rat primary neurons (DIV14) treated with various concentrations of $_{D}$R9 and control vehicle DMSO. **(C)** TaqMan real-time RT PCR analysis of *Scn1a* ($Na_v1.1$), *Scn2a* ($Na_v1.2$), and *Scn3a* ($Na_v1.3$) mRNA levels in B104 rat neuroblastoma cells with or without stably expressing recombinant β2 -ICD, the intracellular domain of $Na_v\beta_2$ (Student t-test; **, $p<0.01$; n=3 for B104 control, 4 for B104/β2 -ICD. **(D)** TaqMan real-time RT PCR analysis of *scn1a* ($Na_v1.1$) mRNA levels in WT and $Na_v\beta_2$ KO neurons (DIV 14) treated with DMSO, $_{D}$R9, or DAPT for 24 hrs.

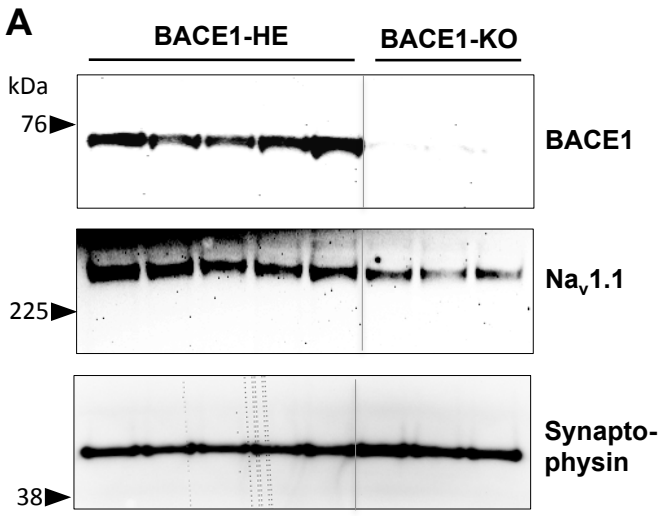
Supplemental fig 2. Decreased $Na_v1.1$ protein and mRNA levels in homozygous BACE1 knockout (BACE1-KO) as compared to heterozygous knockout mice (BACE1-HE) in the same litter. **(A)** Representative Western blot showing $Na_v1.1$ levels in total brain extracts from 1-month old BACE1-HE and BACE1-KO. BACE1-KO and –HE shown here belong to the same littermate group. **(B)** Quantitative analysis of $Na_v1.1$ protein levels in total brain extracts from BACE1-HE and BACE1-KO (Student t-test; *, $p<0.05$; n=5 for BACE1-HE and 3 for BACE1-KO). Synaptophysin levels were used to normalize $Na_v1.1$ levels.

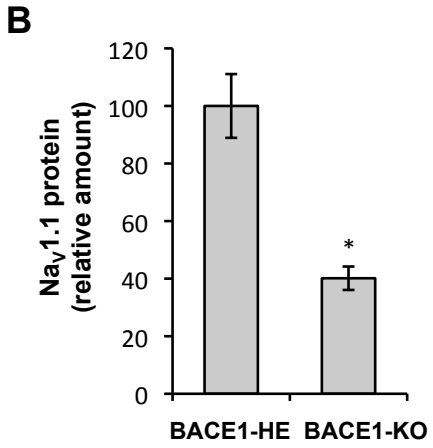
Supplemental fig 3. Confocal immunofluorescence analysis of $Na_v1.1$ (green) in hippocampal dentate gyrus and CA3 regions of 1-month-old wild type control (A) and BACE1-null (BACE1-KO, B).

Supplemental fig 4. Taqman real-time RT-PCR analysis of *scn2a* ($Na_v1.2$) and *scn8a* ($Na_v1.2$) mRNA levels in 1-month-old WT, BACE1-HE, and BACE1-KO (ANOVA followed by a *post-hoc* Tukey's test ; n=5 for WT, 8 for BACE1-HE, and 6 for BACE1 KO). GAPDH levels were used to normalize *Scn2a* ($Na_v1.2$) and *Scn8a* ($Na_v1.2$) mRNA levels.

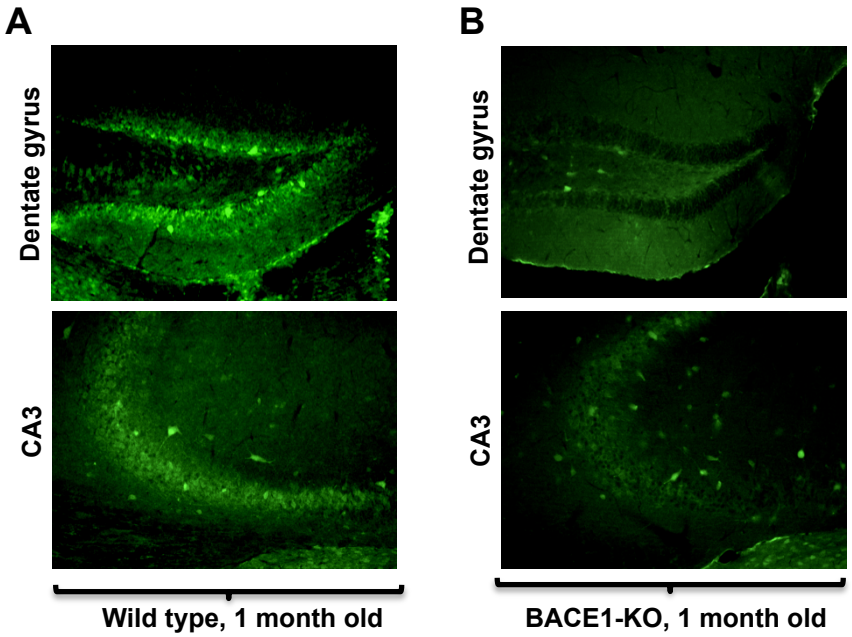


Kim et al., Supplemental fig. 1.

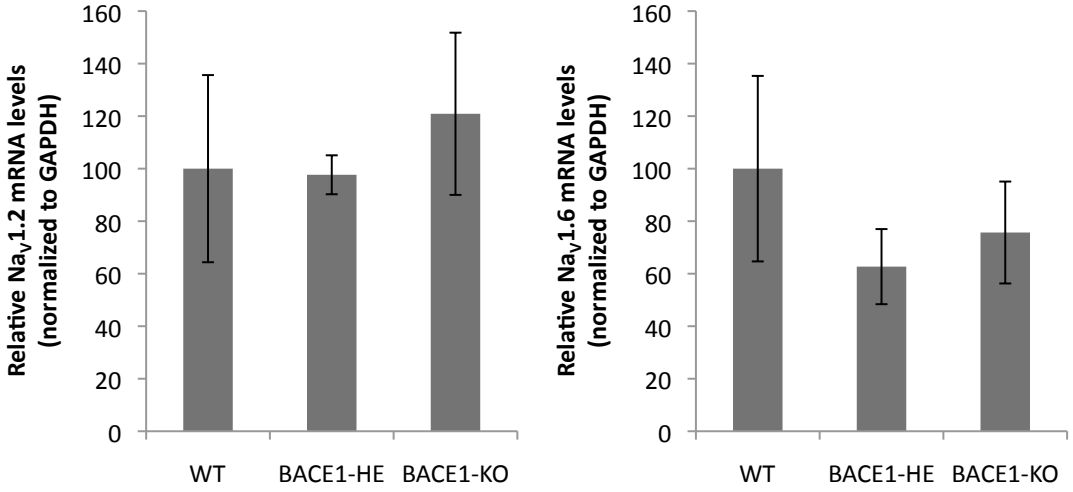




Kim et al., Supplemental fig.2



Kim et al., Supplemental fig. 3



Kim et al., Supplemental fig. 4