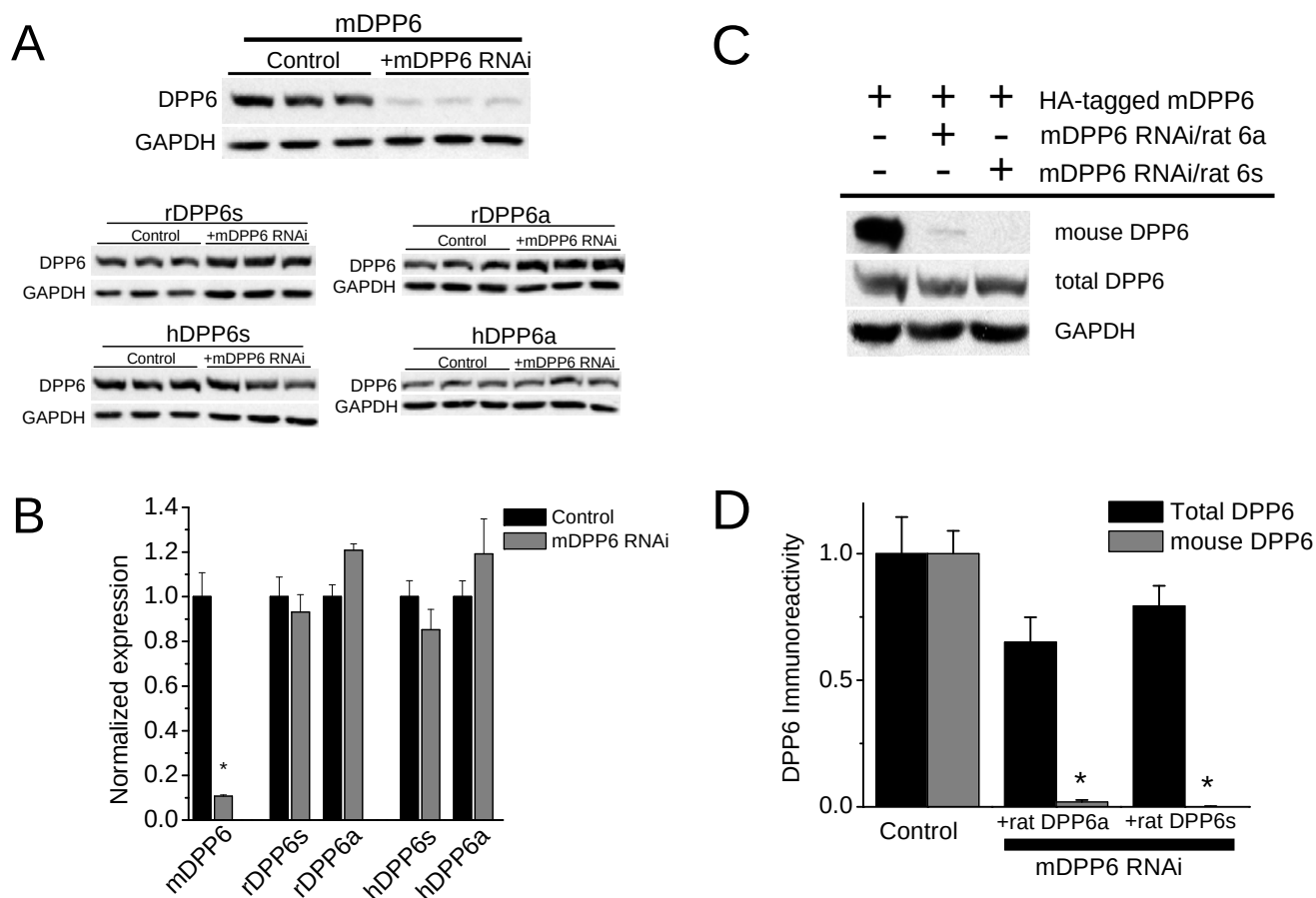
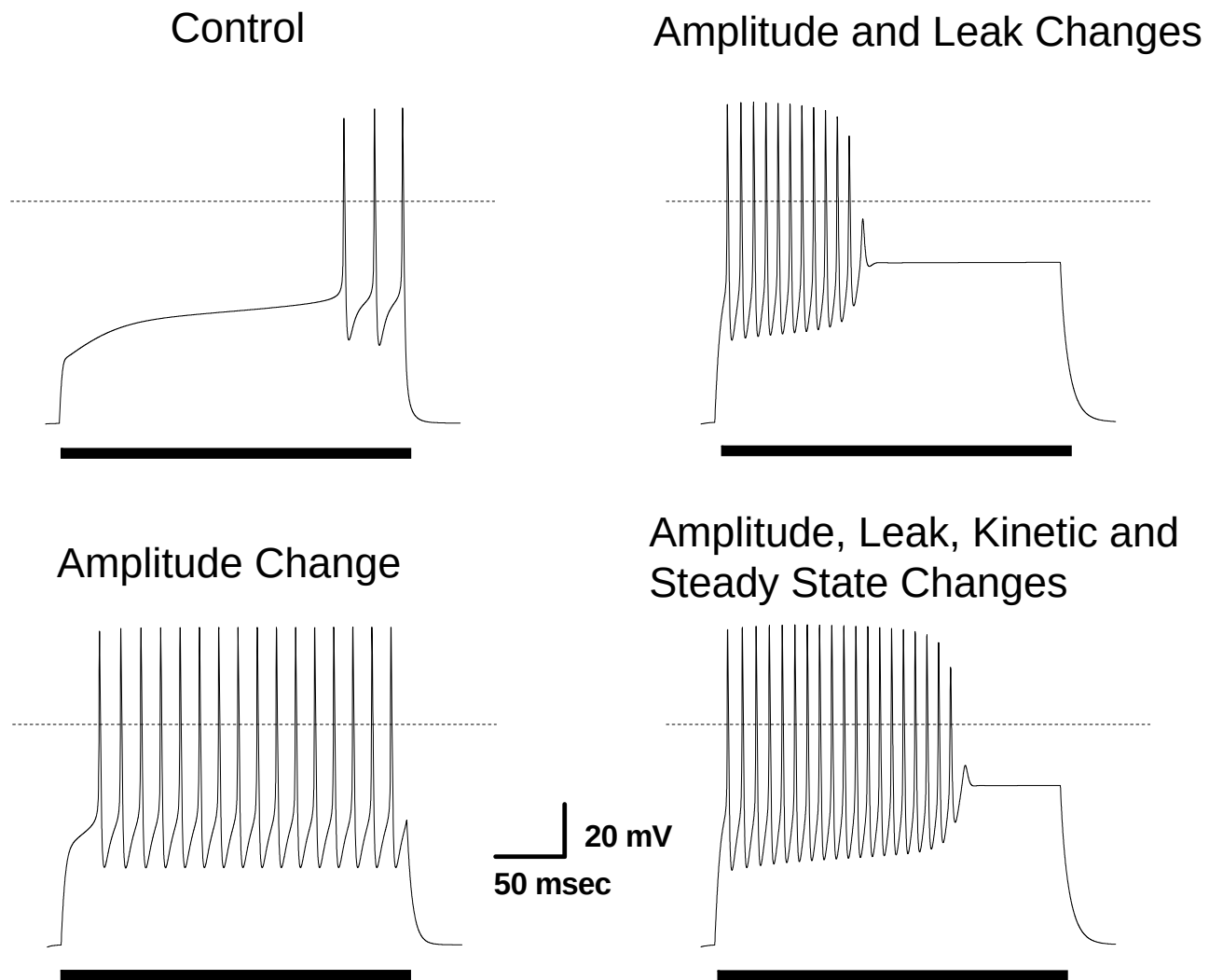
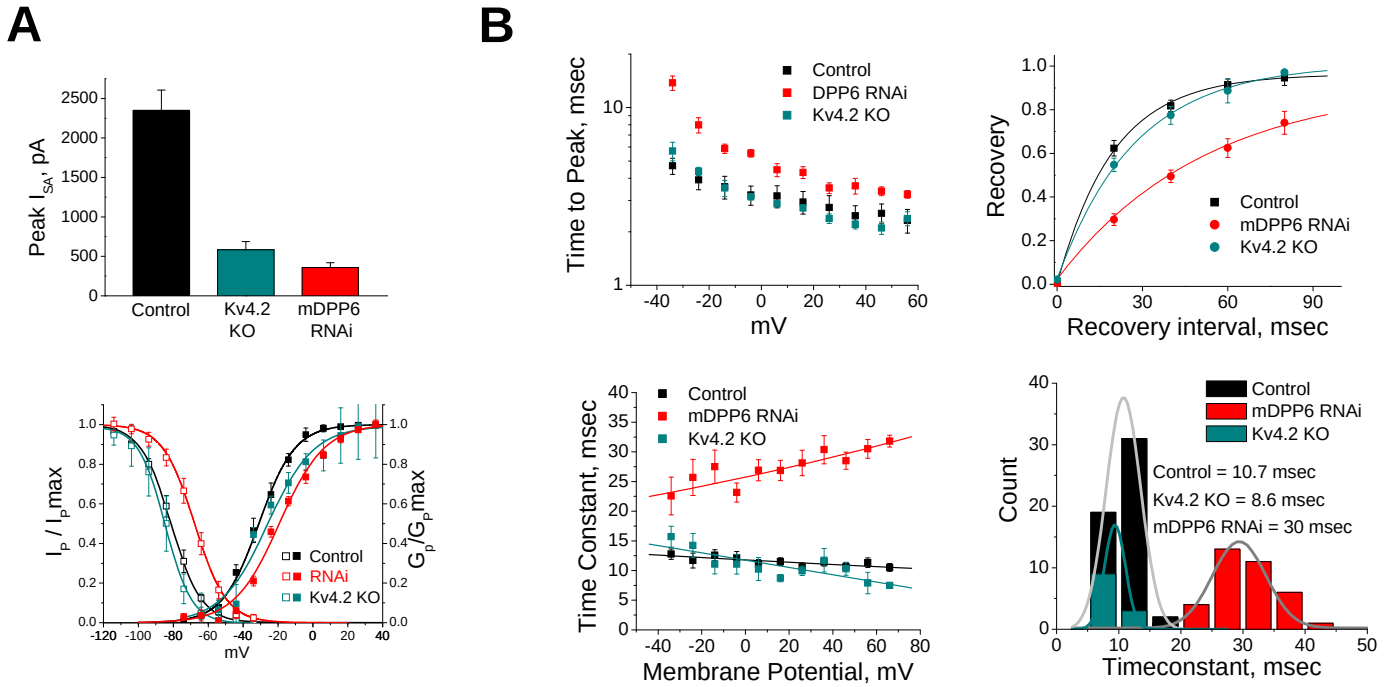




Supplemental Figure 1: Specificity of mDPP6 RNAi and quantitation of rescue with rDPP6 constructs. HEK cells were transfected with the indicated DPP6 expression vector then treated with control or mDPP6 RNAi vectors. Western blots of expressed DPP6 protein and normalizing GAPDH levels. **A)** Triplicate Westerns showing RNAi has a strong selective suppression of mouse DPP6 with no effects on rat or human DPP6 constructs. **B)** Quantitation of Westerns blots following normalization by GAPDH shows that mDPP6 RNAi selectively suppresses mDPP6 protein expression by over 90%. **C)** Specific rescue vector expresses rat DPP6 constructs along with mDPP6 RNAi to produce a change in expressed DPP6 protein from mouse to rat. Mouse HA-DPP6 was co-expressed in HEK cells with the indicated rescue vector. Western blots show that the rescue vector suppresses mDPP6 producing a loss of HA-tag immunoreactivity and replaces it with a similar level of rat DPP6 expression. **D)** Quantitation of these results shows that nearly all the mDPP6 protein can be replaced by co-expressed rat protein.



Supplemental Figure 2: Comparing the importance of different changes in NEURON modeling of CG cells at 10 days in culture. The importance of different effects produced by mDPP6 RNAi on time to first spike were compared to the control CG cell model: 1) Change in I_{SA} amplitude only, 2) Adding in the change in leak conductance, and 3) Adding in the effects on gating, (I_{SA} steady state properties shifted by +13 mV) and (I_{SA} activation and inactivation kinetics slowed by 2x). The reduction in I_{SA} amplitude alone is able to produce most of the observed decrease in time to first spike. Adding in the reduction of leak conductance completes the shift to the observed time to first spike. Only a slight further reduction in time to first spike occurs by adding in gating property changes, although the model suggest that the cell is expected to be more excitable than we actually observe.



Supplemental Figure 3: Elimination of Kv4.2 significantly reduces I_{SA} in CG cells but the remaining current is rapid and kinetically indistinguishable from control I_{SA} . **A)** Peak I_{SA} values from Kv4.2 KO CG cells represent a 75% reduction relative to control. Voltage-dependence of steady-state inactivation and steady-state activation of remaining I_{SA} in Kv4.2 KO are similar to that of I_{SA} from control cells. **B)** Voltage-dependence of time to peak, recovery from inactivation at -114mV and voltage dependence of inactivation of remaining I_{SA} in Kv4.2 KO CG cells is markedly different from residual I_{SA} in mDPP6 RNAi treated CG cells and indistinguishable from I_{SA} in control CG cells, suggesting that DPP6 in Kv4.2 KO CG cells mediates the rapid kinetics of the remaining I_{SA} through effects on other Kv4 subunits.