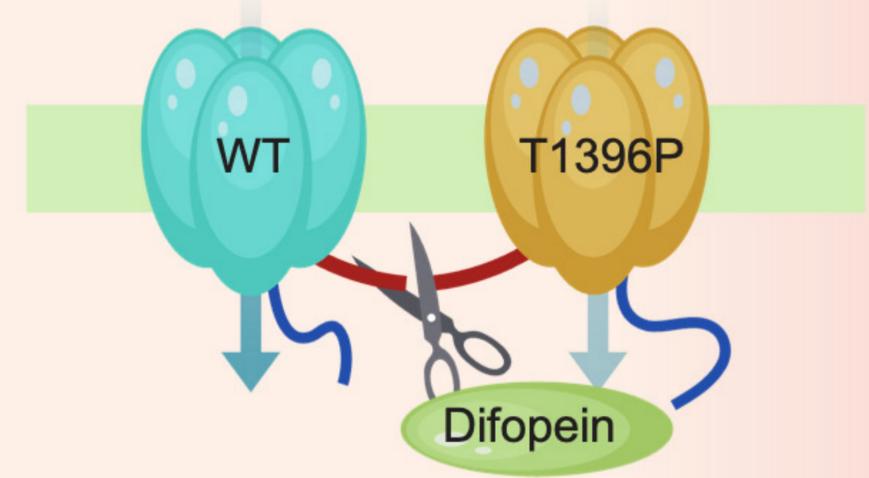
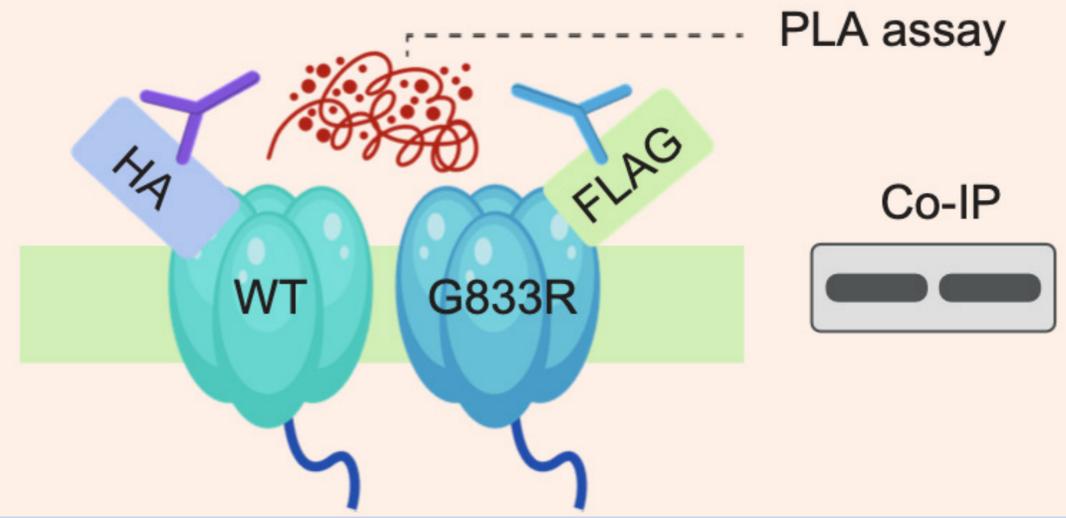


**Coupled gating may be a necessary physiological mechanism**

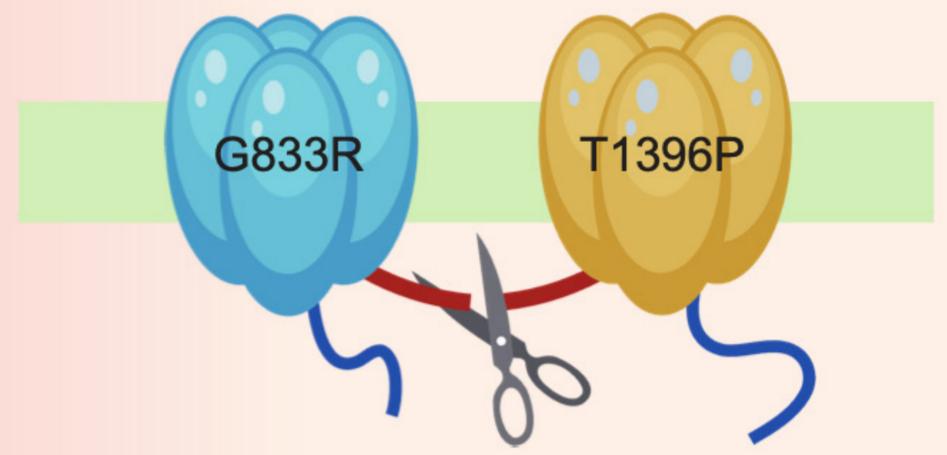
### Electrophysiological uncoupling by difopein



### Physical dimerization intact in both



### Uncoupling variant G833R



WT: wild-type; Co-IP: co-immunoprecipitation; PLA: proximity ligation assay

**Na<sub>v</sub>1.5 channel physical interaction is functionally independent of coupled gating**