

➤ Background

Nav1.5 ion channel is a voltage-gated sodium channel expressed primarily in the myocardium. The currents passed by this channel are responsible for the depolarization phase of the ventricular action potential. Mutations in this channel are associated with long QT syndrome, potentially resulting in the development of arrhythmias.

➤ Nav1.5 Assay specifics

- Compound profiling against the voltage-gated calcium channel Nav1.5 to evaluate potential cardiac liability
- Manual and Automated Patch Clamp with QPatch HTX and QPatch 16
- Positive control and vehicle control in every assay
- Single concentration profiling and full concentration response curves (5 pt. curves; n=3 cells).

➤ Nav1.5 ion channel currents and current-voltage (I-V) relationship

The raw current traces and the corresponding current-voltage relationship is consistent with that reported for Nav1.5 ion channel.

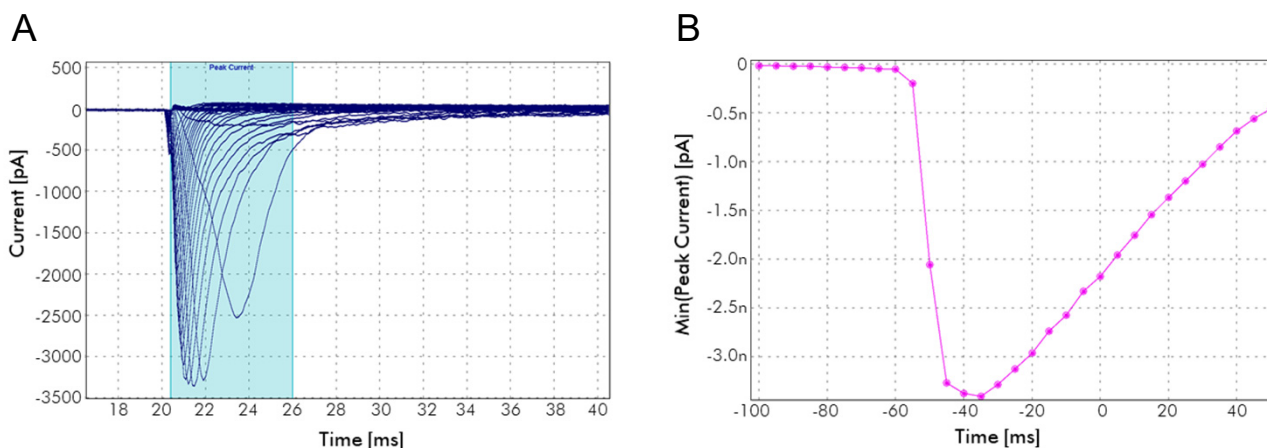


Figure 1. Example of Nav1.5 ion channel activation currents (A) and Current/Voltage (I/V) relationship (B). Currents were elicited by stepping from -100 mV to + 50 mV in 5 mV increments, from a holding potential of -100 mV.

➤ Inhibition of ATXII-induced late current in Nav1.5 ion channel by Ranolazine

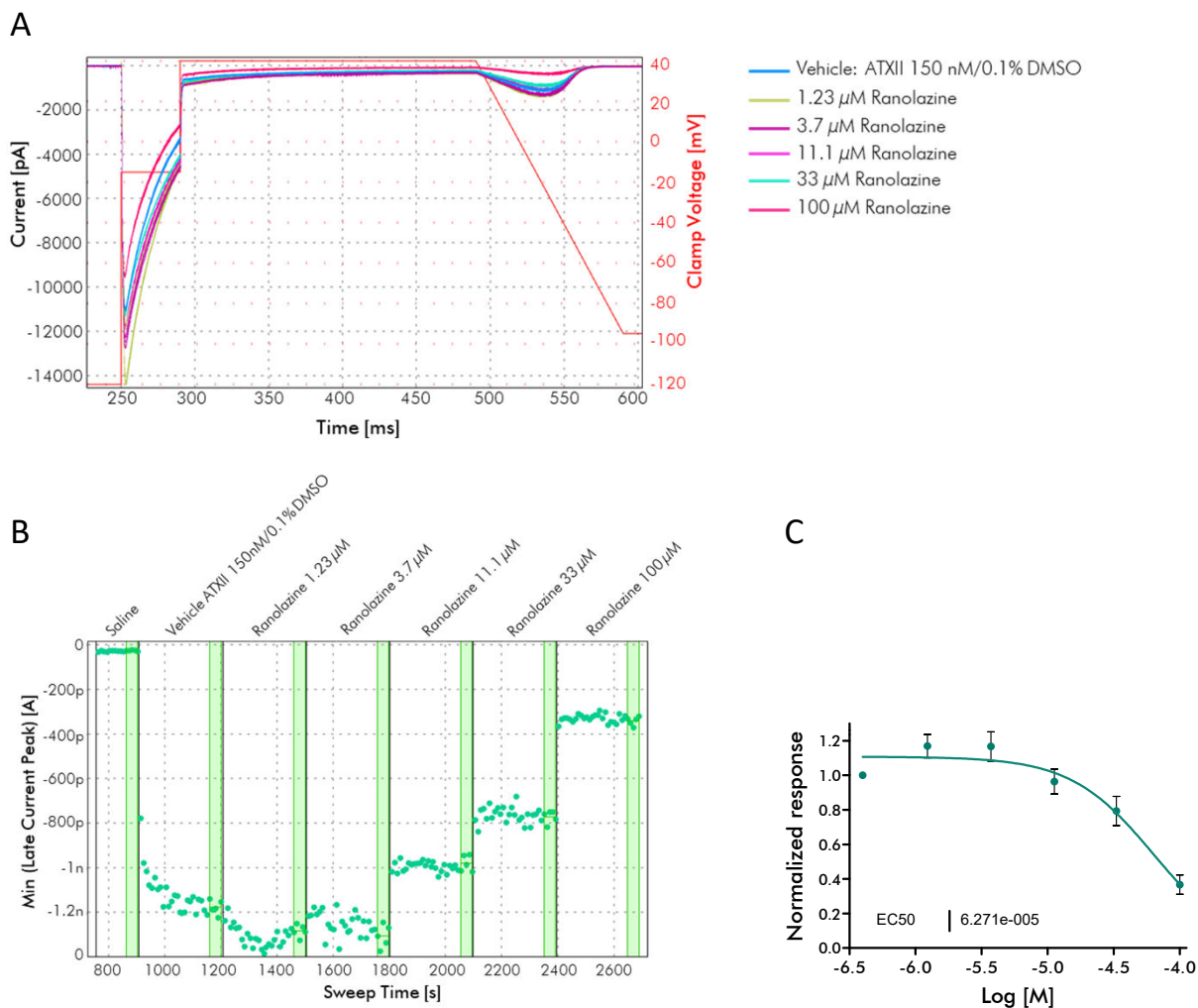


Figure 2. (A) Example of inhibition of ATXII-induced late current in Nav1.5 ion channel by the reference compound Ranolazine. Late current was elicited during the ramp down phase from +40 mV to -20 mV in the presence of ATXII. (B) Resulting time-current plots from QPatch HTX. Currents were normalized to the negative control peak current and plotted as % inhibition (C, below).