

➤ Background

Cav1.2 is an L-type voltage-gated calcium channel that is expressed in the heart, smooth muscle, neurons and other tissues. The channel passes L-type calcium currents that play a role in the release of calcium from the sarcoplasmic reticulum thereby modulating cardiac muscle contractility. Cav1.2 is included in the panel of ion channels to be tested for cardiac safety because of the role it plays in shaping the ventricular action potential.

➤ Cav1.2 Assay specifics

- Compound profiling against the voltage-gated calcium channel Cav1.2 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 (4 pt. curves, n=3 cells)

➤ Cav1.2 ion channel currents and current-voltage (I-V) relationship

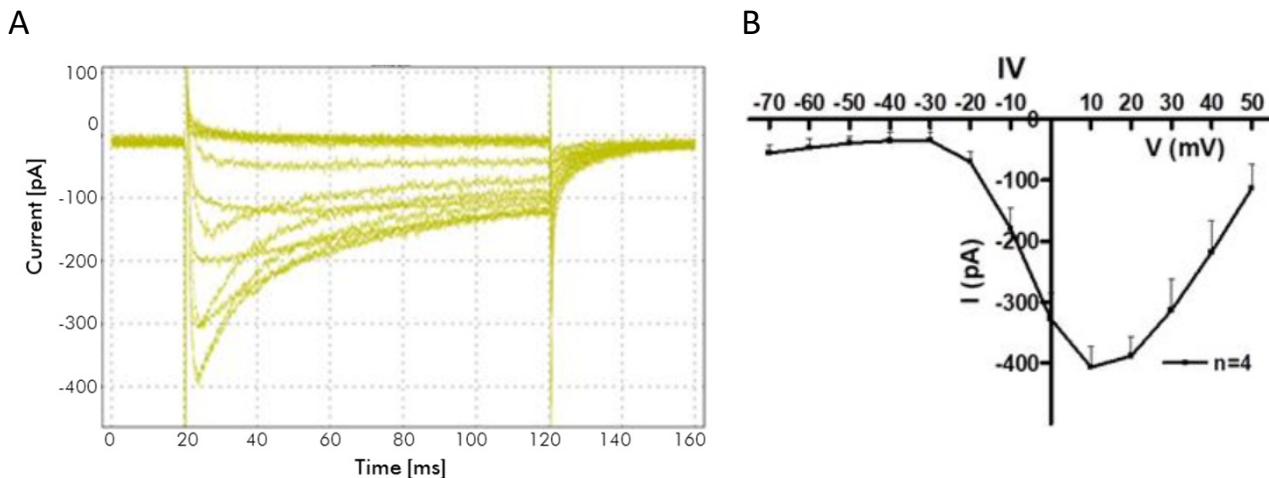


Figure 1. Example of Cav1.2 ion channel activation currents (A) and Current/Voltage (I/V) relationship (B). Currents were elicited by stepping from -70 mV to + 50 mV in 10 mV increments, from a holding potential of -90 mV.

➤ Example of reference compound isradipine on Cav1.2 ion channel inhibition

ADME & SAFETY SERVICES

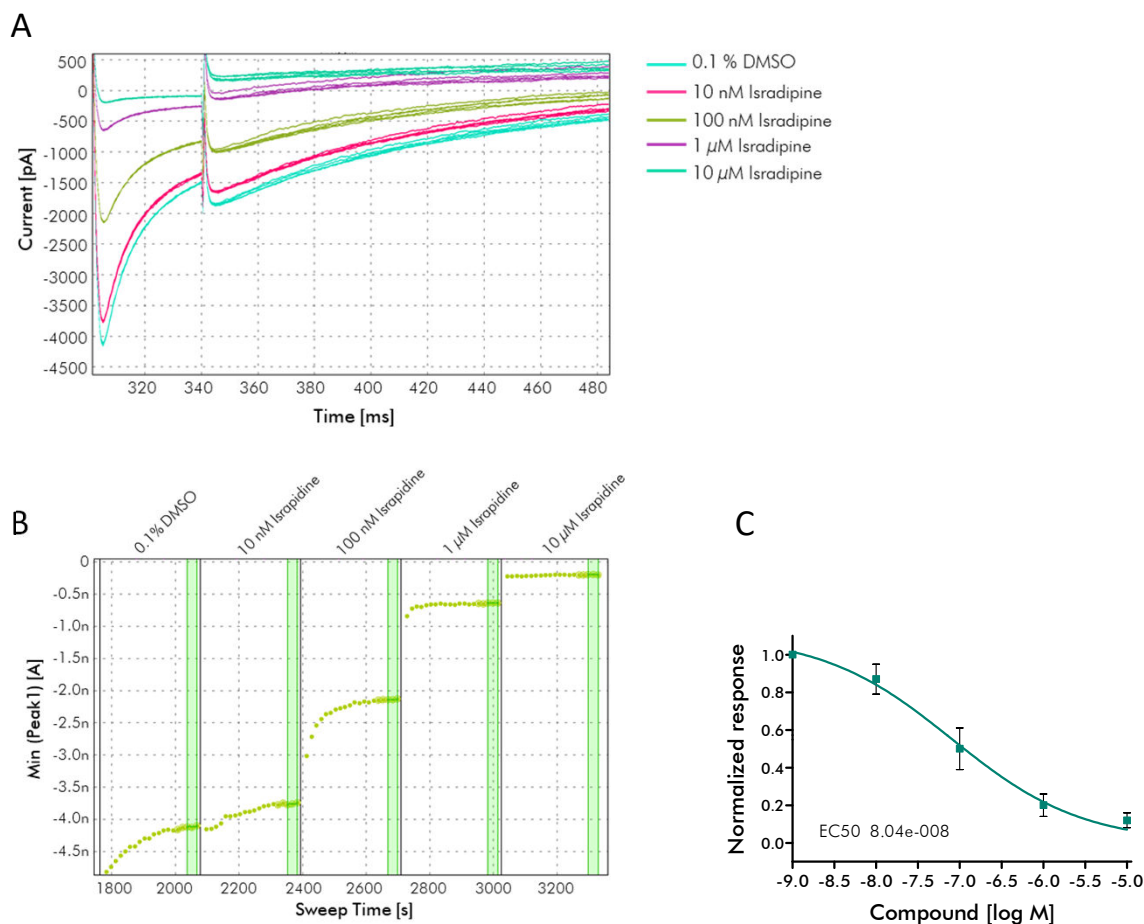


Figure 2. (A) Example of inhibition of Cav1.2 ion channel currents by the reference compound Isradipine. Peak Cav1.2 currents were elicited by a step-change in membrane potential from -90 mV to +0 mV. (B) Resulting time-current plots from QPatch HTX. Currents were normalized to the negative control peak current and plotted as % inhibition (C, below).