

➤ Background

hERG ion channel is a voltage-gated potassium channel that is expressed in the heart and the nervous system. The channel passes I_{Kr} , the rapidly activating, delayed rectifier cardiac current, and the currents play an essential role in the generation of the ventricular action potential. Inhibiting hERG channel activity by small molecules or mutations can lead to long QT syndrome; the prolongation of the QT segment can lead to the development of life-threatening arrhythmias. For this reason, regulatory bodies such as the FDA and EMA, mandate that molecules be tested against hERG to identify possible cardiac liability.

➤ hERG Assay specifics

- Compound profiling against the voltage-gated potassium channel hERG 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 (6 pt. curves; n=3 cells).

➤ hERG ion channel currents and current-voltage (I-V) relationship

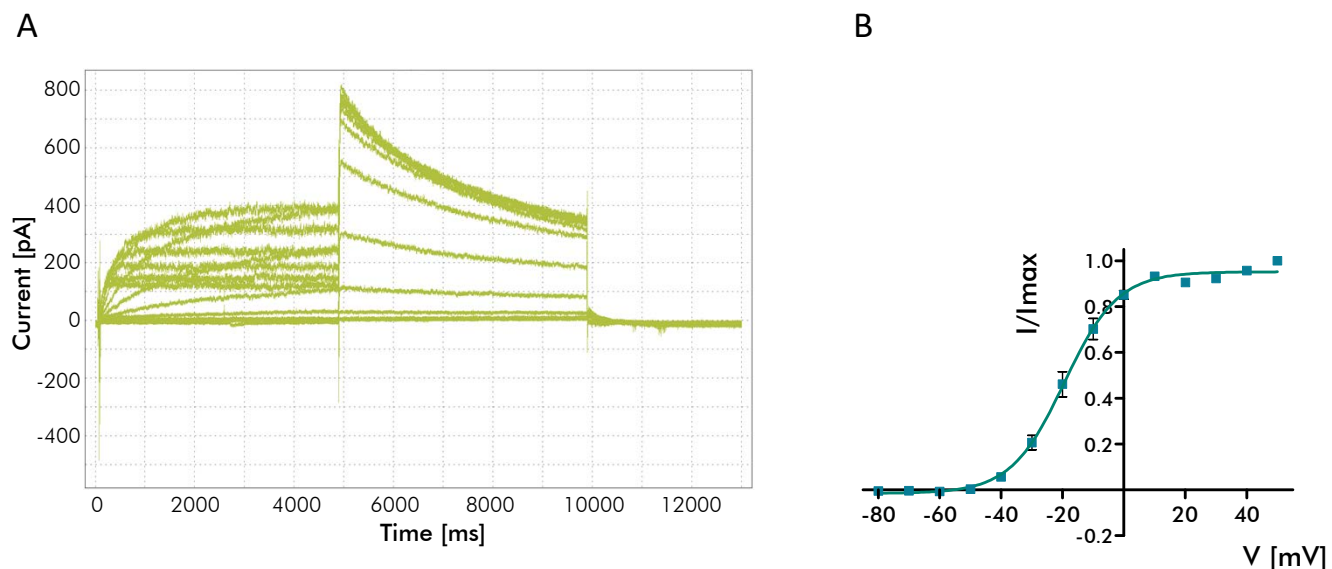


Figure 1. Example of hERG ion channel (A) and Current/Voltage (I/V) relationship (B). Currents were elicited by stepping the voltage from -80 mV to +50 mV in 10 mV increments, from a holding potential of -80 mV.

➤ Quinidine inhibition of hERG ion channel

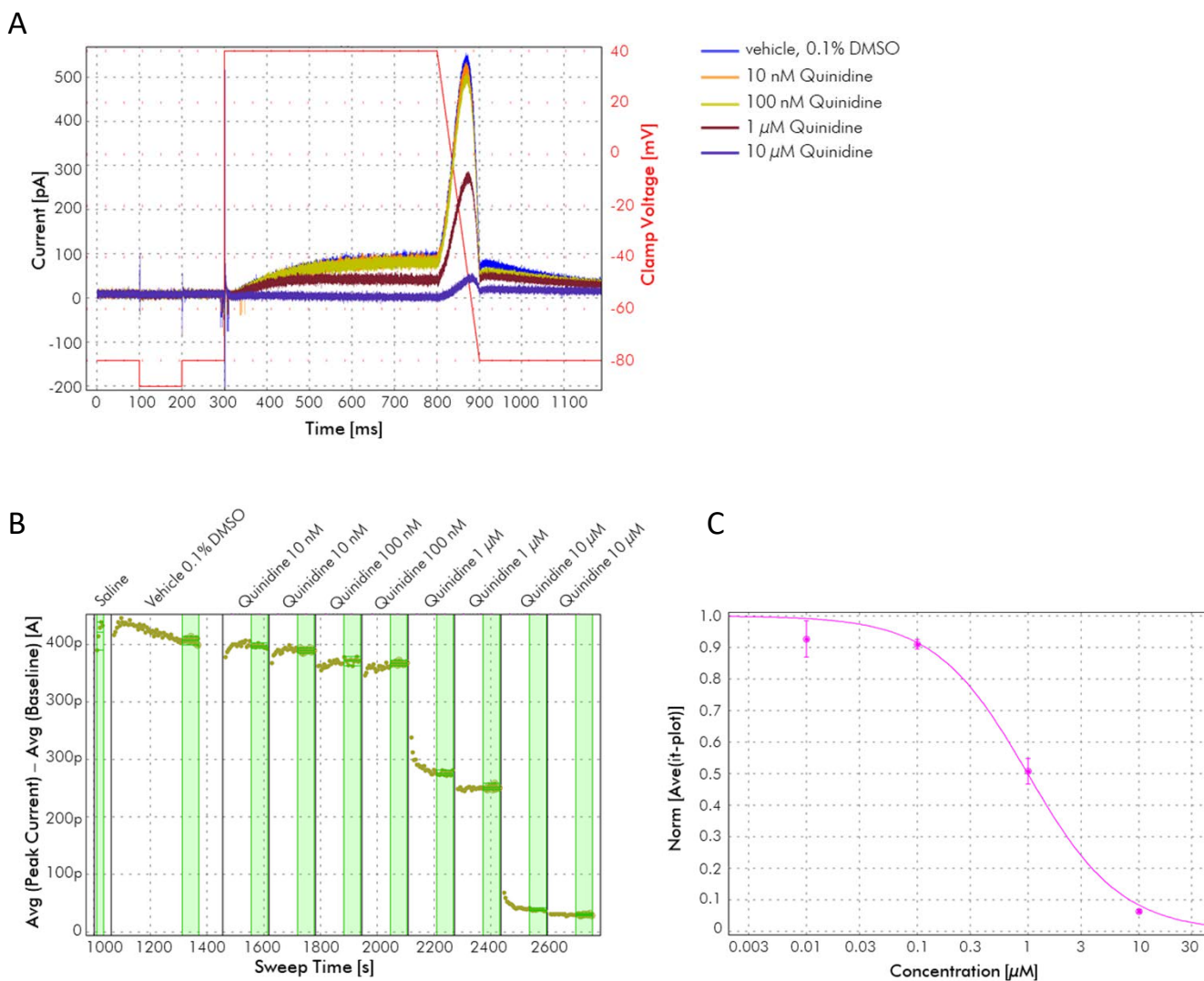


Figure 2. (A) Example of inhibition of hERG ion channel currents by Quinidine. Peak hERG currents were elicited by a ramp down from +40 mV to -80 mV. (B) Resulting time/current plots from QPatch HTX. Currents were normalized to the negative control peak current and plotted as % inhibition (C).