

Customer Story: Cav1.2 Cell Line, Biophysical and Pharmacological Properties

Abstract

Cav1.2 ion channels are expressed in heart, smooth muscle and neurons. Therefore, they are therapeutic targets in cardiac arrhythmia and hypertension. Furthermore, due to their key role in shaping the cardiac action potential, they are part of the CiPA-compliant panel of human ion channel to be tested for cardiac safety. Thus, the generation of a cell line stably expressing all three subunits of the Cav1.2 channel is crucial. Since it is a general knowledge that high expression levels of Ca²⁺ channels have a negative impact on the growth and health of cultured cells, we developed a CHO cell line with inducible expression of Cav1.2 using our proprietary IGAMI[®] expression system. We successfully created an inducible cell line stably expressing all three subunits of the Cav1.2 channel with a high performance in automated patch clamp assays.

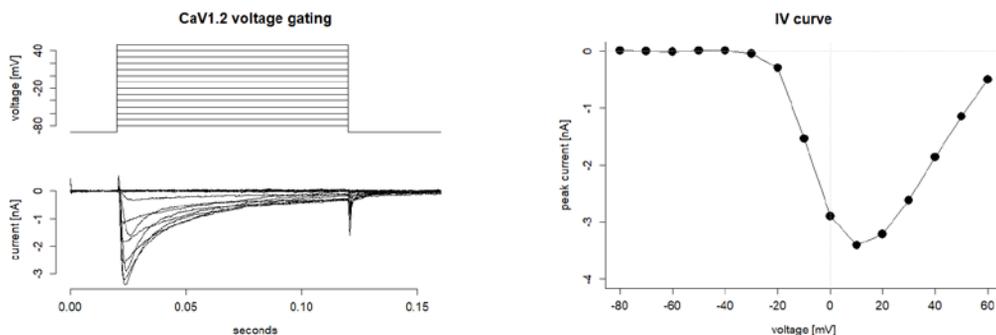


Figure 1. Voltage-dependent gating. Representative current traces elicited by a voltage clamp step protocol. The holding potential was set to -90 mV and the cells were stimulated with 100 ms pulses ranging from -70 to +50 mV in 10 mV increments. The right panel shows a typical Cav1.2 I/V curve, where the amplitude of the current starts increasing at -20 mV and reaches the highest peak at 10 mV.

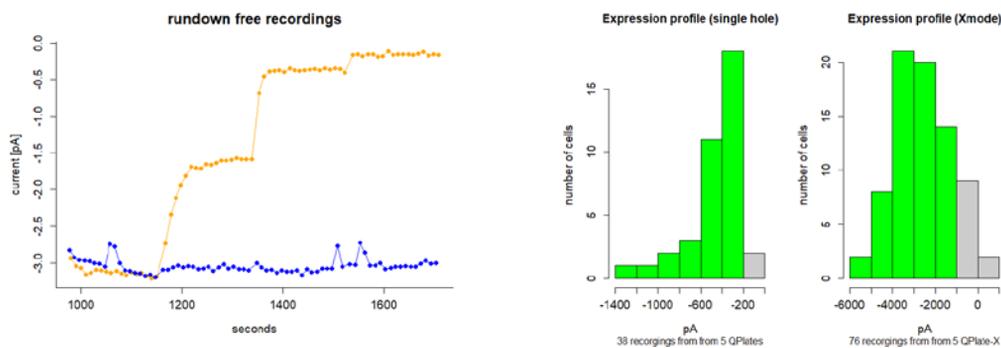
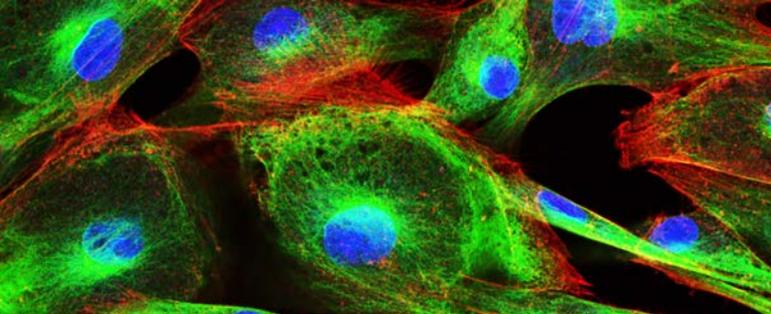


Figure 2. Assay performance. The left panel shows the current at the peak over time. The blue trace shows a down-free current recording in control conditions and the orange trace shows the dose dependent inhibition by Nifedipine, a well-known CaV1.2 inhibitor. The right panel shows expression profile histograms of the Cav1.2 cell line recorded in the Qpatch platform in single- and multi-hole mode.



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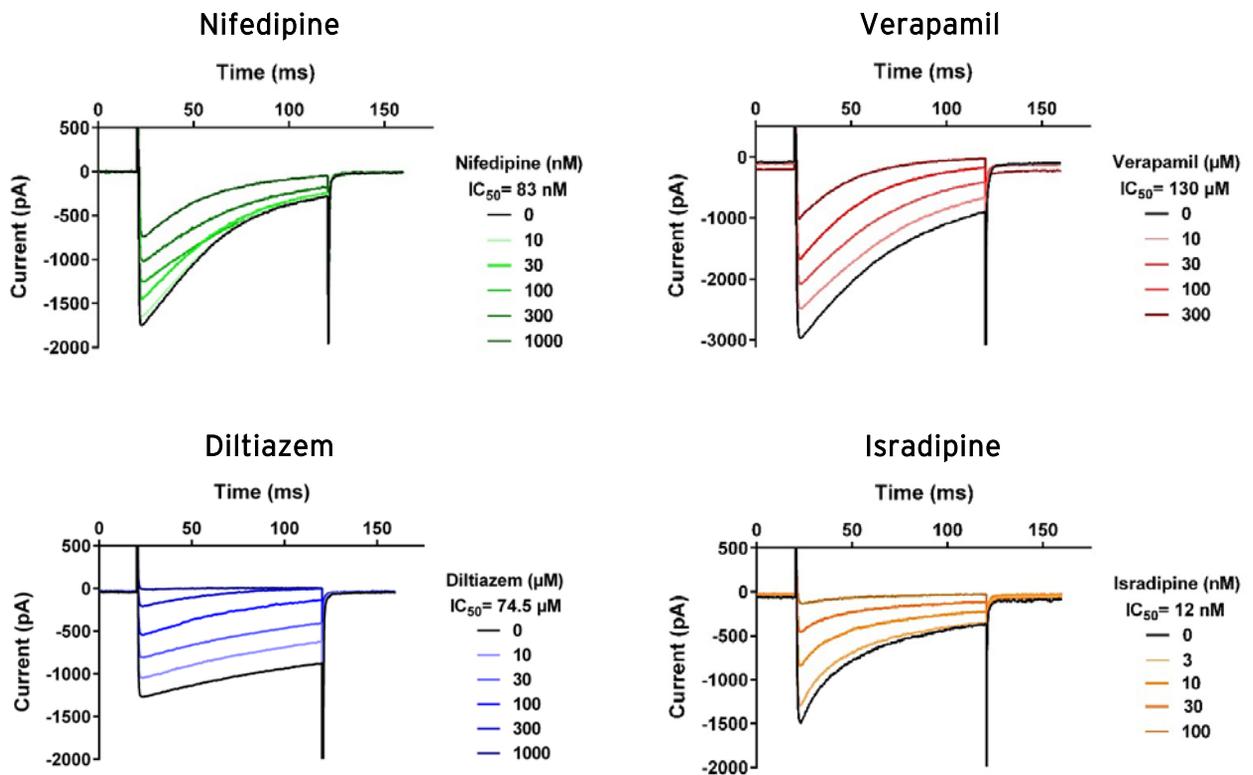


Figure 3. Pharmacological validation. Dose response analysis made with four well-known CaV1.2 inhibitors. Nifedipine in green with an IC_{50} of 83 nM, Verapamil in red with an IC_{50} of 130 μM , Diltiazem in blue with an IC_{50} of 74.5 μM , and Isradipine in orange with an IC_{50} of 12 nM.

Conclusion

Our cell line has an excellent performance in manual and automated patch clamp systems with high success rates and excellent data quality. Furthermore, by varying the duration of the induction phase, our system allows you to regulate the desired CaV1.2 channel expression level and ensures healthy and easy-to-maintain cultures.