

Cardiac Ion Channel Applications of PatchXpress Automated Electrophysiology

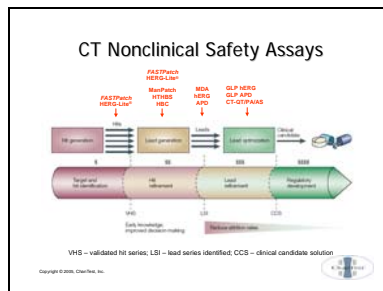
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Nonclinical evaluation of compounds for potentially cardiotoxic interaction with ion channels has undergone rapid progress with the commercial release of automated patch clamp systems. We selected PatchXpress® (PX) as a platform (FASTPatch™) for the development of accurate, rapid voltage clamp analysis of cardiac ionic currents, expressed in either heterologous cell lines, or in native cardiomyocytes. Validation of our automated HERG potassium channel assay has been performed using a panel of eight well-characterized compounds in a side-by-side comparison with manual patch clamp (MPC). PX IC50 values varied no more than two-fold from those obtained in MPC, with the exception of astemizole (2.8-fold less potent in PX). The discrepancy may be attributed to hydrophobicity-related (astemizole cLogP = 5.7) loss due to adsorption within the PX apparatus. In addition to HERG channels, the PX system has been adapted successfully to record hKv1.5 potassium channel currents and hNav1.5 sodium channel currents heterologously expressed in L cells and HEK293 cells, respectively. Neonatal rat ventricular myocytes also have been shown to be amenable to sodium channel current recording, demonstrating the utility of the system for recording native ionic currents. We conclude that the PX system is suitable for the purpose of rapid assessment of cardiac ion channel safety pharmacology.



- ### FASTPatch Validation Criteria for Data Acceptance
- Gigaseal
 - Membrane resistance (R_m) $\geq 200 \text{ M}\Omega$
 - Access resistance (R_a) $\leq 8 \text{ M}\Omega$ (after 60% compensation)
 - Peak hERG tail current $\geq 200 \text{ pA}$
 - Leak current $\leq 25\%$ of the peak current
 - Run down of peak current $\leq 2.5\%$ per min.

