Introduction

For reliable identification of cardiac safety risk, compounds should be screened for effects on cardiac ion channels in addition to HRG, including Na\textsubscript{v}1.5 and Ca\textsubscript{v}1.2. Automated patch clamp (APC) protocols are increasingly adapted for cardiac safety measurements but cross-site and cross-platform comparisons of IC\textsubscript{50} values has identified the need for standardized protocols for reliable pharmacology. In this study, we identified different parameters that might affect IC\textsubscript{50} values of compounds on Na\textsubscript{v}1.5 peak and late currents recorded using APC.

Effect of voltage protocol on Na\textsubscript{v}1.5

Cultured cells versus frozen stocks and correlation across platforms

Persistant and late Na\textsubscript{v}1.5 current

Comparison with literature

Conclusions

- CTA step-ramp protocol should be used for safety pharmacology testing. This allows effects on both peak and late current to be studied.
- Temperature affects biophysical properties and pharmacology and, at the very least, should be carefully controlled. Best experiments should be performed at physiological temperature (where possible).
- A minimum compound incubation time of 3 min is required to reliably IC\textsubscript{50} measurement longer is preferred for sticky compounds.
- The use of standardized protocols for APC experiments e.g. voltage protocol, incubation time, replicate number etc. is critical to be able to compare IC\textsubscript{50} values across platforms, sites and with the literature.

References: Data shown in this paper has been accepted into JPM/ pending revisions.