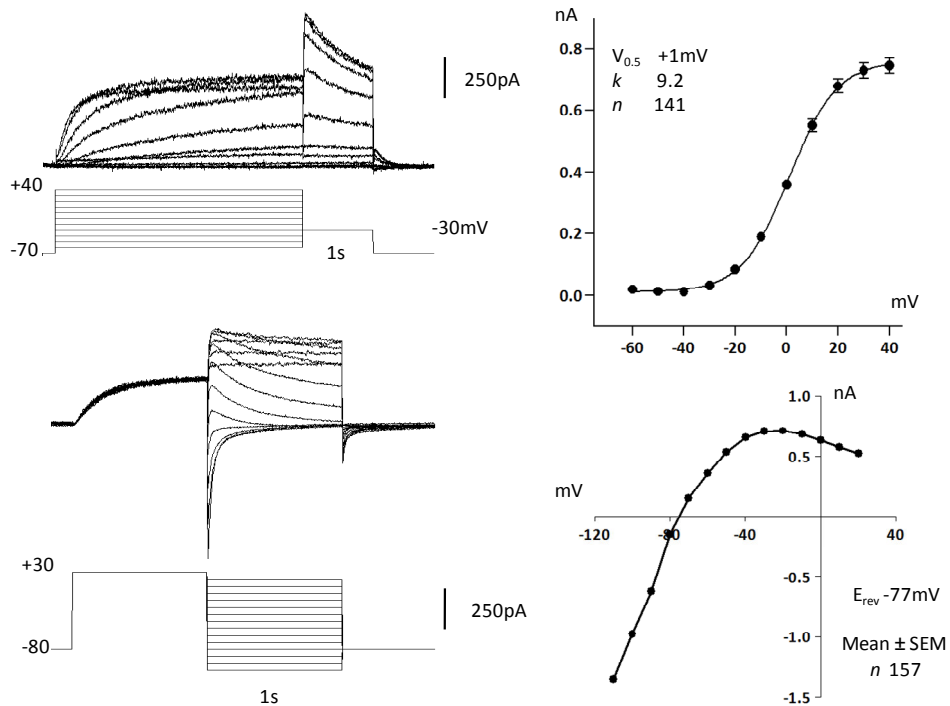


## hERG automated patch-clamp electrophysiology assay

- **Assay** hERG automated patch clamp electrophysiology
- **Channel** Human ether-a-go-go-related gene (hERG),  $K_v11.1$
- **Gene Name** *KCNH2*
- **Synonyms** ERG1, LQT2, erg1, HERG, SQT, H-ERG, HERG1, Erg1, ERG
- **Assay format** 96-well IonWorks<sup>HT</sup> automated electrophysiology
- **Cell Host** Chinese Hamster Lung (CHL)
- **Stimulus** Repeated gating steps,  $V_h$  -70 mV,  $V_{step}$  +40 mV,  $V_{tail}$  0 mV
- **Controls** Quinidine, 0.1-0.3% DMSO



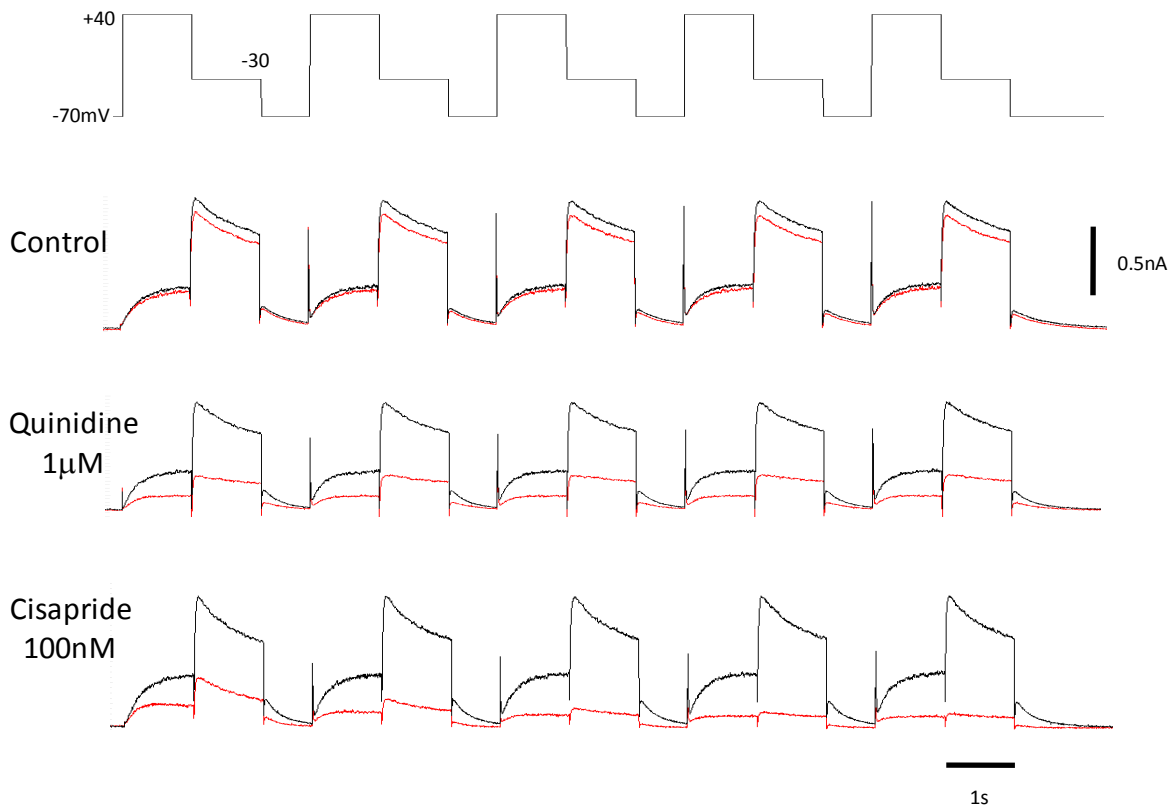
**Biophysical validation** IonWorks<sup>HT</sup> recordings from CHL-hERG cells using standard gating protocols

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**Background** Several marketed pharmaceutical agents that have been associated with adverse cardiac safety events (cardiac arrhythmias and sudden death) have been shown to be potent inhibitors of the delayed rectifying potassium channel (IKr) encoded by the human ether-a-go-go (hERG) gene. Indeed, in 2005, the International Conference on Harmonization (ICH) published technical guidelines that require an *in-vitro* test on the activity of potential new drugs prior to Phase I clinical testing.

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**Pharmacology** Compound inhibition in screening protocol: control, quinidine & cisapride



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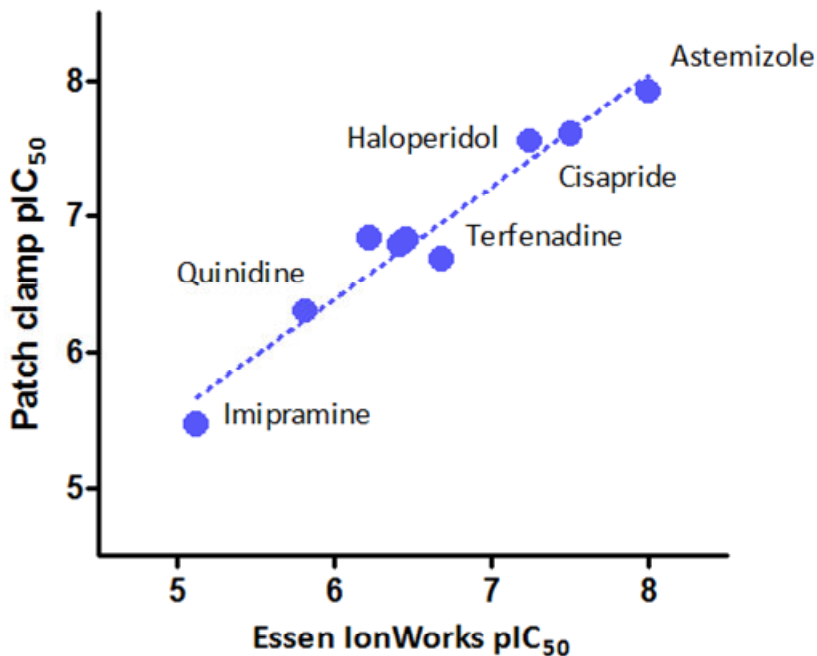
**Assay QC**

Cell, Curve fit, Solubility & Plate QC parameters applied:

**Cell:**  $I_{hERG} > 250 \text{ pA}$ , baseline & seal resistance stability filters

**Plate QC:** Minimum 250 cells, Quinidine  $pIC_{50}$  5.7-6.3.

**Typical assay precision:** compound  $pIC_{50}$  values  $\pm 0.25$  log units



**Why Essen?** The protocol for the hERG assay takes into account several critical factors which can affect compound potency. These include careful compound preparation/handling, standardized cell preparation procedures, and recording solutions and voltage protocols designed to maximize sensitivity. The assay is designed to accurately assess the widest array of pharmacological and chemical entities, including use-dependent and hard-to-handle (sticky) compounds. We offer high data fidelity, competitive pricing and turn-around times difficult to match by CRO's who are simply end-user's of the IonWorks technology.

**References** Kiss, L. *et al.*, (2003) High throughput ion-channel pharmacology: planar-array-based voltage clamp. *Assay & Drug Development Technologies*, **1**, 1-2.

M.H. Bridgland-Taylor *et al.*, (2006). Optimisation and validation of a medium-throughput electrophysiology-based hERG assay using IonWorks HT. *Journal of Pharmacological and Toxicological Methods*. **54**, 189-199.

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