Cross-site reliability in a cardiac safety assay using multiwell microelectrode array (MEA) technology: preliminary results from the CiPA Pilot Study

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I. Introduction
- Current safety testing standards evaluate the lethality of the K+ efflux potassium channel to inform cardiac liability.
- The CiPA initiative aims to facilitate the adoption of a new paradigm for assessment of clinical TdP, including integrated human cellular studies.

II. The Maestro Multiwell MEA Platform
- Label-free and non-invasive recording of intracellular voltage from multiwell culture conditions up to 96 wells.
- Environmental control provides a stable benchtop environment for short- and long-term toxicity studies.
- High data collection rate (12.5 KHz) allows for rapid identification of critical events.

III. Cell Culture Protocol
- Cells were plated according to manufacturer recommended specifications in an 8-well plate and media added to achieve a well volume of 300 uL.
- Media was changed the evening prior to the experiment and then moved straight from the incubator to the Maestro on the day of recording. The EMRini was used to supply 2% O2 and maintain pH buffering, while the embedded heater plate kept the MEA culture plate at 37°C.

IV. Analysis Methods
- A grid of microelectrode interfaces with a 50-µm pitch was defined from bivariate analysis of extracellular voltage from the continuous recording.

V. Baseline Reliability
- Consistency in the baseline electrophysiology across wells, plates, and sites is critical for potassium channel current safety testing standards.
- Baseline activity was highly consistent across wells, plates, and sites.

VI. Signal Analysis Workflow
- Field potential duration (FPD) changes, and arrhythmic events were accurately detected using multiwell processing.
- Raw measures of repolarization agree across well replicates and display consistent changes in field potential duration for a given cell type.

VII. Compound Case Studies
- consistency across cell type.
- High consistency in depolarization spike, repolarization, and arrhythmia occurrence for a set of 8 compounds with known mechanism of action.

VIII. Maestro Results Compilation and Conclusions
- The CiPA pilot study results from the Maestro platform demonstrated high reliability across replicates and sites for each cell type, while accurately detecting phenotypic changes in depolarization, repolarization, and arrhythmia occurrence for a set of 8 compounds with known mechanism of action.

IX. Conclusions
- Predictability of the myocyte-MEA assay
- Reliable response trends were observed across sites and cell types for each compound.

References

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