BACKGROUND

Historically, animal EEG studies have been the standard for preclinical assessment of drug induced seizures. Furthermore, in a typical ex vivo study, cortical neurons derived from rat forebrain must be extracted and cultured on microelectrode arrays (MEA) for roughly 4 weeks before mature functional network activity can be utilized for seizure assessment. With recent advances in human stem cell technologies, iPS-derived neurons can provide for roughly 4 weeks before mature functional network activity can be utilized for seizure assessment. With recent advances in human stem cell technologies, iPS-derived neurons can provide a number of advantages over current models for seizure predictivity within the 12 drug set and allowed for significantly faster " assay ready" culture times than typical murine ex vivo preparations. In conclusion, human iPS neurons + astrocytes provide a number of advantages over current models for seizure liability and anti-epileptic drug screening efforts and should be further explored to develop a more comprehensive library to better understand their predictivity for drug induced seizures.

METHODS

Calcium transient flux

- Instrument: Hamamatsu FDS5/jCell, 384 format
- Density: 30,000 cells/well
- Buffer - Ncardia Ca Oscillations buffer
- Ca Dye: Cal520 (AAT Bio)
- Density 3.6-7.2 x 10^4 cells/well
- Recording time: Day 33 in vitro post-thaw

Pro-seizurogenic Drug Liability Assessment using 3 Different hiPSC-derived neural co-cultures for the HESI Neutox Consortium

CONCLUSIONS

- Large lot numbers and stringent (and MEA based functional) QC parameters by Ncardia results in high quality hiPSC-derived neuronal cells ideal for translational large scale studies and guarantees robust electrical activity
- Experiments reveal suitability of Ncardia hiPSC-derived neurons (+ astrocytes) for seizure liability assays given their long-term synchronous network activity and reactivity to seizure-active or - suppressive compounds
- The high acquisition rate camera on the Hamamatsu FDS5/jCell detects calcium flux in neurotransmitter stimulated hiPSC-derived neurons labeled with Cal520 thus providing a new translatable neuron screening system for high throughput studies in up to 384 well format for pharmacology safety studies. This may present a novel screening strategy for seizure activity as well.