Safety Pharmacology Society
Annual Meeting, September 23-26, 2019

Sponsored Presentation
Wednesday, September 25th, 2019 | 12.30-13.30 | Room 121

hiPSC for Drug Development and Safety Assessment Using Live Kinetic and Electrophysiological Readouts

Attend to learn how drug discovery challenges are being reduced by using iPSC-derived neurons, cardiomyocytes and 3D-neural spheroids with real-time, high-throughput functional methodologies to identify potential drug-induced effects and improve predictivity.

Stay with us after the talks for a discussion and refreshments!

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Dr. Udo Kraushaar

Bringing Human Neuronal Biology to HTS: Functional Drug Screening with iCell GlutaNeurons and Astrocytes on the Hamamatsu FDSS/µCELL

The drug discovery field is strongly moving towards hiPSC-derived neurons as primary animal neurons partially lack predictivity. We developed live-cell Ca imaging screening assays on the Hamamatsu µCell using Cellular Dynamics' iCell Glutaneurons. Intracellular Ca dynamics was recorded as an indicator of neuronal network activity using different pharmacological tool compounds. We focused on three experiment classes: seizurogenic compounds, mGluR modulators, and addition of amyloid-beta peptide, which plays a major role in Alzheimer's disease. We also compared data obtained from a pure iCell GlutaNeuron culture and coculture with iCell Astrocytes. iCell GlutaNeurons, in parts, expressed higher sensitivity compared to the primary cell system. Furthermore, cocultivation with iCell Astrocytes substantially impacted network activity after compound treatment.

Dr. Blake Anson

Implementing 3D Neural Spheroids in Drug Discovery: Disease Modeling, Screening, and Toxicity Testing

3-dimensional cellular preparations are gaining increased traction as more biologically appropriate in-vitro experimental models. However, as with many complex cellular systems, preparation and implementation can be quite laborious. StemoniX has removed this barrier with microBrain®3D, ready-to-use neural spheroids containing a mixture of hiPSC-derived cortical GABAergic and glutamatergic neurons and astrocytes. MicroBrain 3D is provided in standard 96 or 384 well plates that can be assayed within a few days of receipt. Here we present case studies demonstrating how microBrain 3D is being used to bring high throughput, relevant human biology into disease modeling, screening, and toxicity studies with a variety of biochemical and functional assays.

Dr. Stéphane Bedut

Early evaluation of drug candidates proarrhythmic potency: combining throughput and information level with voltage/calcium-sensitive dyes and fast imaging device

Preclinical proarrhythmic evaluation of drug candidates requires predictive in vitro as well as in vivo assays and are often performed after "lead-optimization" phases due to insufficient throughput and/or cost reasons. As cardiac safety remains one of the major causes of drug development attrition, some efforts could also be carried out during "hit-to-lead" or "lead-optimization" phases, to help classify the compounds according to their proarrhythmic risks. Usually, the number of compounds to be tested at these phases necessitates higher throughput assays with a reasonable cost per data point to fulfill this challenge. The multiwell fluorescence recording of the electrical activity of hiPSC-derived cardiomyocytes with a fast imaging plate reader allows getting an integrative overview of the dose-related effects of compounds on cardiac electrical functionality. Moreover, the concomitant use of a calcium-sensitive fluorescent dye adds information on the possible alteration of calcium cycling by the drug candidates. Beyond clinical predictivity, this assay represents a good opportunity for early identification of the "concentrations at risk" for each compound.