Cardiac Arrhythmia Mechanisms
Gordon Research Conference

Model Systems, Emerging Technologies and Precision Medicine in
Arrhythmia Research and Therapeutic Development

Gordon Research Conferences
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Preclinical Cytotoxicity Investigations in Stem Cells for Primary and Secondary Assays with an "All Inclusive" Approach

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Human stem cell-derived cardiomyocytes (hIPSC-CMs) have recently proven to recapitulate key features of human cardiac electrophysiology in vitro.

Chip-based approaches allow parallel patch clamp recordings without compromising data quality or technical sophistication. We present high-throughput voltage and current clamp recordings of CiPA reference compounds. Since drug efficacies may vary with temperature, we present recordings at room and at physiological temperatures.

In addition to patch-clamping experiments, we present hybrid impedance (cell contractility) with MEA-like extracellular field potential (EFP) recordings. Experiments were complemented with optical stimulation of monolayers of hiPSC-CMs expressing the light-gated cation channel Channelrhodopsin2. This approach allows frequency-dependent drug screening and detection of potential side effects on Na^+-, Ca^{2+}- and repolarizing K^+ channels. Furthermore, investigations of potential breaks in excitation-contraction coupling can accompany the ion channel screening with the final aim to enable a reliable automatized cardiac toxicity screening platform. As a proof-of-principle, pharmacological effects of CiPA compounds from each risk category will be presented.

Cytotoxic responses of cell monolayers involve metabolic or biochemical changes that affect the morphology of the cells, or reduce their overall viability. In that regard, effects of a number of reference compounds tested for long-term cytotoxicity in hepatocyte-like cells (i.e. Paracetamol), will be presented.