Cytotoxicity Monitoring for Safety Assessments: iPS Cardiomyocytes and Cancer Cells

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Human stem cell-derived cardiomyocytes (hIPSC-CMs), among other hIPSCs, have recently proven to recapitulate key features of human physiology in vitro. Here, we show a comprehensive overview of the complete list of CiPA compounds and their effects on the impedance and EFP signal of diverse spontaneously beating hIPS-CMs. We focus on concentration-dependent effect of compounds such as nifedipine, pentamidine, dofetilide, E4031, isoproterenol and mexiletine on the impedance and EFP. Effect of these compounds was depicted by plotting crucial parameters into spider charts, enabling easy visual data evaluation. In addition to data obtained from spontaneously beating cells, recent optical stimulation techniques have been shown extremely useful in specific compound safety screenings. Therefore, we also demonstrate optical stimulation with an advantage over electrical stimulation due to the highly precise timing and simultaneous delivery of the light stimulus to all cells of the beating network. This optogenetic assay approach delivered optical pacing of hIPSC-CMs in a range from 1Hz to 3Hz, impedance and EFP traces adapting to the paced beat rate will be compared.

In addition, we describe the development and optimization of a label-free cytotoxicity assay using impedance measurements in combination with extracellular field potential (EFP) recordings. This assay provides reproducible results for safety pharmacology, toxicity screens of adherent, proliferating (e.g. cancer) or non-proliferating cells. Changes in the impedance signal indicate effects on cell contractility, cell morphology and proliferation over prolonged periods of time, giving a crucial advantage of this technique over standard cytotoxicity assays as it allows continual monitoring of the development of cytotoxicity. We will focus on the data obtained from testing the concentration dependent effects of chemotherapeutic drugs on cancer cells and their proliferation patterns.

In summary, our data and technical innovations strengthen the importance of testing compounds in assays complementary to patch clamp electrophysiology, to provide an all-inclusive safety and toxicity compound profile.