

Tentative Outline

Title of thematic issue: Utilization of iPSC technologies for drug-induced risk and drug efficacy evaluation during drug development

Guest Editor: Dr. Norimasa Miyamoto, Ph.D.

Aims & Scope: Many pharmaceutical companies are interested in to use induced pluripotent stem cell (iPSC) technologies not only for regenerative medicine, but also drug-induced risk evaluation. It is difficult to do collaboration for drug efficacy evaluation among pharmaceutical companies, but it is easy for drug safety purpose to organize cooperative collaboration with joint ownership of protocols by both technological advancement and including policy recommendations. The Comprehensive in Vitro Proarrhythmia Assay (CiPA) initiative in US was established to develop a new paradigm for assessing proarrhythmic risk with an international multi-disciplinary team of regulatory, industry and academic scientists. The CiPA has a stem-cell-derived cardiac myocyte team to check for missed or unanticipated effects of torsades de pointes (TdP) risk prediction results from in silico modeling using current inhibition data by drugs on 7 types cardiac ion channels. The Translational Biomarkers of Neurotoxicity (NeuTox) Committee of Health and Environmental Science Institute (HESI) in US created the NeuTox Micro-Electrode Array (MEA) Subteam to investigate the potential of MEA technology to predict the seizure liability of drugs. The team launched a multi-site pilot study, and is promoting engagement in scientific discussion utilizing the results of the multi-site pilot study. Similar organizations are collaborating in Japan, Japan iPS Cardiac Safety Assessment (JiCSA), iPS Non-clinical Experiments for Nervous System (iNCENS) as national projects, Consortium for Safety Assessment using Human iPS Cells (CSAHi) as a consortium of industry, government and academia. The CSAHi is originally established by Japan Pharmaceuticals Manufacturers Association to realize the application of human PSC-derived cardiomyocytes, hepatocytes and neurons for drug safety evaluations. These organizations had been published their research results, then global cross-organizational discussion is promoting. This special thematic issue mainly focused on introduction of the latest research for utilization of iPSC-derived cells for drug-induced risk evaluation from basic science of academia to applied research of industry. Some of technologies have potency to use commonly in drug safety and efficacy evaluation. Healthy, disease iPSC differentiation methodology and in vitro modeling research is also pick up in this issue. Then, potential impact for drug development in the pharmaceutical companies using iPSC technologies will be discussed.

Keywords: iPS, QT, Seizure, drug safety, non-clinical, in vitro modeling

The subtopics to be covered within this issue are listed below:

- A Utilization of iPSC-derived cardiomyocytes for drug-induced heart risks
- B Utilization of iPSC-derived neurons for drug-induced seizure risks
- C Utilization of iPSC-derived hepatocytes for drug-induced toxicity and metabolism
- D Nobel methodology for *in vitro* evaluation
- E Differentiation methodology and *in vitro* modeling of iPSC-derived cells
- F Potential impact of iPSC technologies for drug development in the pharmaceutical companies

Schedule:

Schedule:

- ◇ Manuscript submission deadline: September 4, 2019
- ◇ Peer Review Due: October 30th, 2019

- ✧ Revision Due: November 7, 2019
- ✧ Announcement of acceptance by the Guest Editor: December 2, 2019
- ✧ Final manuscripts due: December 10, 2019

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Special Thematic Issue for Current Pharmaceutical Biotechnology

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Many pharmaceutical companies are interested in to use induced pluripotent stem cell (iPSC) technologies not only for regenerative medicine, but also drug-induced risk evaluation. It is difficult to do collaboration for drug efficacy evaluation among pharmaceutical companies, but it is easy for drug safety purpose to organize cooperative collaboration with joint ownership of protocols by both technological advancement and including policy recommendations. The Comprehensive in Vitro Proarrhythmia Assay (CiPA) initiative in US was established to develop a new paradigm for assessing proarrhythmic risk with an international multi-disciplinary team of regulatory, industry and academic scientists. The CiPA has a stem-cell-derived cardiac myocyte team to check for missed or unanticipated effects of torsades de pointes (TdP) risk prediction results from *in silico* modeling using current inhibition data by drugs on 7 types cardiac ion channels. The Translational Biomarkers of Neurotoxicity (NeuTox) Committee of Health and Environmental Science Institute (HESI) in US created the NeuTox Micro-Electrode Array (MEA) Subteam to investigate the potential of MEA technology to predict the seizure liability of drugs. The team launched a multi-site pilot study, and is promoting engagement in scientific discussion utilizing the results of the multi-site pilot study. Similar organizations are collaborating in Japan, Japan iPS Cardiac Safety Assessment (JiCSA), iPS Non-clinical Experiments for Nervous System (iNCENS) as national projects, Consortium for Safety Assessment using Human iPS Cells (CSAHi) as a consortium of industry, government and academia.

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Schedule:

- ✧ Manuscript submission deadline: October 31th, 2018
- ✧ Peer Review Due: November 30th, 2018
- ✧ Revision Due: January 31th, 2019
- ✧ Announcement of acceptance by the Guest Editor: February 28th, 2019
- ✧ Final manuscripts due:

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List of possible contributing authors (Just list correspondence author)

1. Non-invasive phenotyping and drug testing in living cardiomyocytes by calcium imaging and optogenetics

Dr. Matthew Daniels, University of Oxford, UK

2. Using functionally enhanced human iPSC-derived cardiomyocytes for preclinical cardiac safety assessment of drugs and evaluation of inotropic compounds

Dr. Xiaoyu Zhang, ACEA Biosciences, US

3. New iPSC-based neural in vitro approach for seizure liability testing

Dr. Jonathan Davila, NeuCyte, US

4. Epileptiform activities in cultured human iPSC-derived neuronal networks and pharmacological analysis

Dr. Ikuro Suzuki, Tohoku Institute of Technology, Japan

5. *In vitro* disease modeling using patient related iPSC-derived cells

Dr. Haruhisa Inoue, Center for iPS Cell Research and Application (CiRA), Kyoto University, Japan

6. Trial for drug-induced risk assessments using iPSC-derived cells under the CSAHi consortium collaboration

Dr. Norimas Miyamoto, Eisai Co., Ltd., Japan

7. Development of standardized test for drug safety evaluation using iPSC-derived cells from the regulatory aspect-CiPA, JiCSA, iNCENS

Dr. Yasunari Kanda, Director of Pharmacology Department, National Institute of Health Science, Japan

and more under the discussion