HESI CARDIAC SAFETY COMMITTEE WORKSHOP:

STEM CELL-DERIVED CARDIOMYOCYTES AS MODELS OF CARDIAC PATHO BIOLOGY AND TOXICITY

MARCH 18-19, 2013
CAMBRIDGE, MA, AMGEN, INC.

Workshop Co-Chairs: Hugo Vargas (Amgen), Dr. Kevin Dreher (EPA)

Objective: To bring together an international and multi-disciplinary group of scientists to evaluate the use of stem cell platforms and associated technologies in the nonclinical cardiovascular risk assessment of pharmaceuticals and environmental chemicals.

This scientific program will achieve the following:

➢ Provide an interdisciplinary forum for exchange of information regarding current approaches and experiences across organizations applying or developing stem cell-derived cardiomyocyte assay platforms in pharmaceutical and environmental chemical hazard identification;
➢ Raise awareness of the development of the science with respect to the cellular substrates and technologies used to evaluate cardiomyocyte systems;
➢ Identify key areas of consensus regarding application of this technology for cardiovascular risk assessment/screening as well as areas of uncertainty or specific future research/evaluative initiatives that may be needed;
➢ Begin to identify recommendations for minimum quality standards to be associated with the use of these cells for safety evaluations;
➢ Result in an important contribution to the scientific literature in the form of a manuscript that captures key presentations, discussions, consensus, and recommendations regarding current and possible future use of this technology and available preparations;
➢ Generate informed and broadly vetted proposals for consideration by the HESI Committee on Cardiovascular Safety as well as SPS/other forums interested in acting upon the recommendations generated within this forum;
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www.hesiglobal.org

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HESI Workshop Agenda of Events

Monday March 18, 2013

9:00 a.m. – 10:00 a.m.  Session I: Introduction and Keynote Address

Agenda and goals for the workshop
_Dr. Hugo Vargas, Director, Safety & Exploratory Pharmacology, Amgen, Inc - Host and Co-Chair_

Stem cell-derived cardiomyocytes: State of the Science
_Dr. Tim Kamp, Professor of Medicine and Co-Director, Stem Cell and Regenerative Medicine Center University of Wisconsin_

_Moderator: Dr. Hugo Vargas_

10:00 a.m. – 11:00 a.m.  Session II: Stem cell-derived cardiomyocytes as assay substrates

Characterization of stem cell systems as models - i.e. what makes a cardiomyocyte a cardiomyocyte?
_Dr. Kyle Kolaja, Vice President, Business Development, Cellular Dynamics International, formerly with Roche_

Quality standards for stem cell assay platforms
_Dr. Byungdoo Alexander Yi, Research Fellow, Harvard Stem Cell Institute_

_Moderator – Dr. Kyle Kolaja_

11:00 a.m. – 12:30 p.m.  Session III: Application of Stem Cell Derived Cardiomyocytes

Evaluation of cellular impedance measures of cardiomyocyte cultures for drug screening applications
_Dr. Matt Peters, Principal Scientist, Molecular Toxicology, AstraZeneca_

Cardiac stem cell electrophysiology: Strengths, limitations, and challenges for cardiac safety evaluations
_Dr. Gary Gintant, Research Fellow, Department of Integrative Pharmacology, Global Pharmaceutical Research and Development, Abbott Laboratories_

_Stem cell-derived cardiomyocytes for measures of contractility_
Prof. Mark Mercola, Professor and Director at the Muscle Development and Regeneration Program, Sanford-Burnham Medical Research Institute

Moderator – Dr. Gary Gintant

12:30 p.m. – 2:00 p.m.  LUNCH & OPEN POSTERS

2:00 p.m. – 3:30 p.m.  Session III Continued: Application of Stem Cell Derived Cardiomyocytes

Cardiomyocyte cytotoxicity/structural cardiotoxicity stem cell assays
Dr. Yvonne Will, Senior Principal Scientist, Exploratory Medicinal Science, Pfizer

On-chip cardiomyocyte network screening assay for predictive cardiotoxicity
Prof. Kenji Yasuda, Professor, Biomedical Science Program, Tokyo Medical and Dental University

Human iPS/ES cell technology and its application to toxicology testing with a focus on in vitro cardiac function toxicity
Dr. Atsushi Sanbuissho, Head of the Medicinal Safety Research Laboratories, Daiichi Sankyo

Moderator – Ms. Syril Pettit, HESI Executive Director

3:30 p.m. – 3:45 p.m.  BREAK

3:45 p.m. – 5:30 p.m.  Session IV: Potential for Use in Regulatory or Risk/Safety Decision-making Applications

ICCVAM and Cell-based Assay Systems
Dr. Warren Casey, Deputy Director, NICEATM, NIEHS, ICCVAM

EPA and Cardiovascular Hazard Identification
Dr. Kevin Dreher, Principal investigator, US EPA, NHEERL

Human iPS-derived cardiomyocyte for development of in vitro pre-clinical testing
Dr. Yuko Sekino, Head of the Division of Pharmacology, Japan National Institute of Health Sciences
FDA Research Perspective
Dr. Xi Yang, US FDA, NCTR, Innovative Safety and Technologies Branch

Moderator – Dr. Kevin Dreher

5:30 p.m. – 6:30 p.m. Poster Session
Tuesday March 19, 2013

8:00 a.m. – 9:30 a.m.  
Session V: Future Opportunities for Stem cell-derived Assay Systems

Stem cell derived from diseased patients: potential utility for clinical modeling  
Dr. Craig January, Professor, Division of Cardiovascular Medicine, University of Wisconsin-Madison

Regenerative therapies for the treatment of cardiovascular disease: Failure to meet expectations but hope for the future.  
Dr. Frank Sellke, Karlson Professor and Chief of Cardiothoracic Surgery, Brown Medical School and the Lifespan Hospitals

Micro-engineered hydrogels for tissue engineering and stem cell bioengineering  
Dr. Mehdi Nikkhah, Postdoctoral Fellow, Khademhosseini Lab, Massachusetts Institute of Technology

Moderator – Dr. Hugo Vargas

9:30 a.m. – 11:45 a.m.  
Session VI: Gaps and Opportunities Roundtable Discussions  
The introductory talk in each of these mini-sessions will tee up key issues raised during Day 1 of the workshop as well as critical challenges in moving the field forward. The floor will then be opened to the panelists and all participants for discussion. The panel discussions will address:

- Where are the gaps in the science?
- What is needed to further implementation and acceptance?
- Where are the opportunities for benefit to public health?
- Where is the need for future work

Session VI a: Electrophysiology (40 minutes)  
Moderator Introduction: Challenges and Opportunities for Stem cells as in vitro measures of electrophysiology  
Dr. Gary Gintant, Research Fellow, Department of Integrative Pharmacology, Global Pharmaceutical Research and Development, Abbott Laboratories

Electrophysiology Panel Discussion
Dr. Norman Stockbridge, Director of the Division of Cardiovascular and Renal Products, US FDA, CDER
Dr. Craig January, Professor, Division of Cardiovascular Medicine, University of Wisconsin-Madison
Dr. Kyle Kolaja, Senior Leader/Global Head Predictive Toxicology Screens and Mechanistic Toxicology, Hoffmann-La Roche
Dr. Colette Strnadova, Senior Scientific Advisor, Therapeutic Products Directorate of Health Canada

Session VI b: Contractility
Moderator Intro: Challenges and Opportunities for Stem cells as in vitro measures of contractility
Prof. Mark Mercola, Professor and Director at the Muscle Development and Regeneration Program, Sanford-Burnham Medical Research Institute

Contractility Panel Discussion
Dr. John Koerner, Senior Pharmacologist, US FDA, CDER
Dr. Khuram Chaudhary, Investigator, Safety Pharmacology, GlaxoSmithKline
Dr. Gul Erdemli, Head of Ion Channel Group, Novartis

Session VI c: Structural Cardiotoxicity
Moderator Intro: Challenges and Opportunities for Stem cells as in vitro measures of cardiomyocyte toxicity
TBD

Structural Cardiotoxicity Panel Discussion
Dr. Yvonne Will, Senior Principal Scientist, Pfizer
Dr. Donna Mendrick, Director, Division of Systems Biology, US FDA, NCTR
Dr. Warren Casey, Deputy Director, NICEATM, NIEHS, ICCVAM
Dr. Sarah Bacus, Senior Vice President and Chief Scientific Officer of the Translational R&D Oncology, Quintiles

10:15 a.m. – 10:30 a.m. BREAK

11:45 a.m. – 12:30 p.m. Session VII: Bringing it all Together

Applications: Where do we need to go as a scientific community to facilitate application for public health benefit?
Where are opportunities to bridge across applications?
Moderated group discussion – Dr. Hugo Vargas, Director, Safety & Exploratory Pharmacology, Amgen, Inc – Workshop Host and Co-Chair and Dr. Kevin Dreher, Principal investigator, US EPA – Workshop Co-Chair

12:30 p.m.  Closing Comments and Adjourn