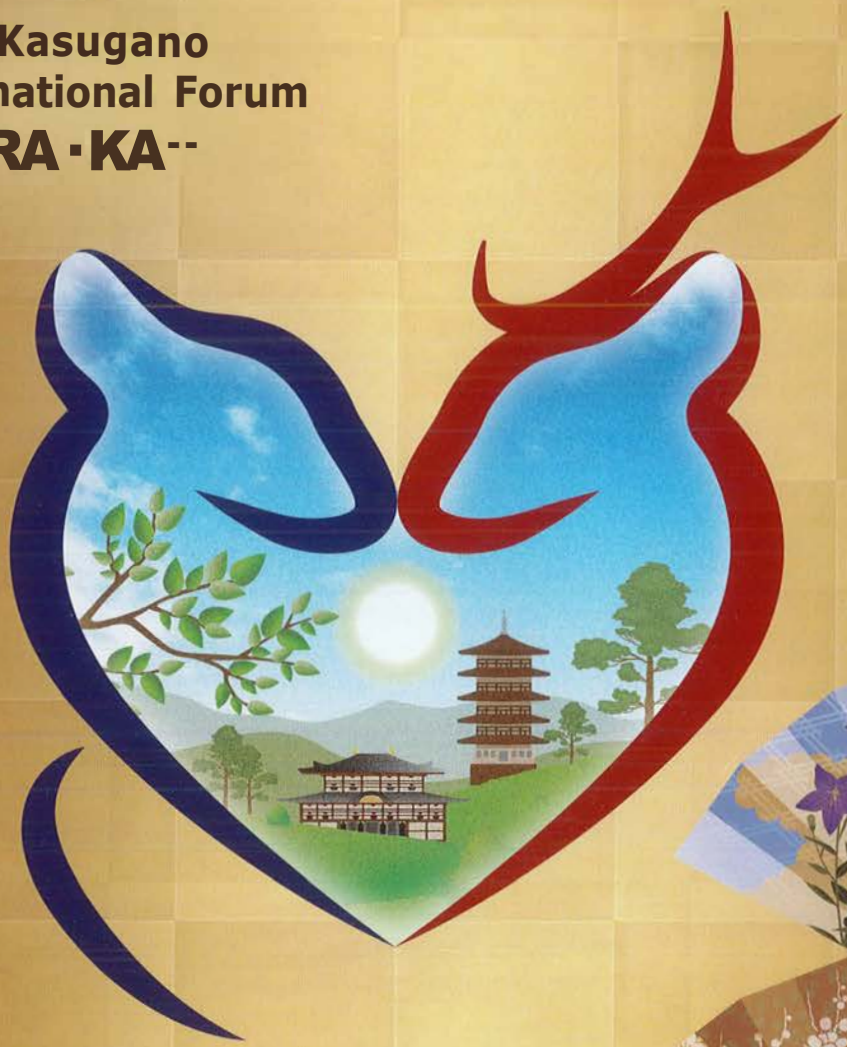
Weins tein 2018

NARA, JAPAN -1.

May 16-18, 2018

Venue | **Nara Kasugano International Forum -- I･RA･KA--**



KEYNOTE LECTURE 1

SHINYA YAMANAKA, MD, PhD

Professor. Shinya Yamanaka is most recognized for his discovery of induced pluripotent stem (iPS) cells, which are differentiated cells chat have been reprogrammed to the pluripotent scare. He is the Director of the Center for iPS Cell Research and Application (CiRA) and a Principal lnvestigator at the Institute for Integrated Cell-Material Sciences, borh at Kyoto University. Dr. Yamanaka is also a Professor of Anatomy at the University of California, San Francisco, as well as a Senior Investigator and the L.K. Whittier Foundation lnvestigator in Stem Cell Biology at the Gladstone Institutes. Dr. Yamanaka studied for his medical degree ac Kobe University and lacer earned his PhD from Osaka City University. He took his current position as a professor ac Kyoto University in 2004 and was appointed as a Senior Investigator at the Gladstone Institutes in 2007. Since 2008, he has directed CiRA. In 2012, Dr. Yamanaka was awarded the Nobel Prize in Physiology or Medicine for his discovery chat adule somatic cells can be reprogrammed into pluripotent cells. By introducing the genes for four factors chat turn genes on and off, he induced the skin cells of adule mice to become like embryonic stem cells, which he called induced pluripotent stem (iPS) cells. This iPS cell technology represents an entirely new platform for fondamental studies of developmencal biology. In addition to the Nobel Prize, Dr. Yamanaka has received many awards and honors, including the Albert Lasker Basic Medical Research Award, the Wolf Prize in Medicine, the Millennium Technology Award, the Shaw Prize, the Kyoto Prize for Advanced Technology, the Gairdner International Award, the Robert Koch Award and the March of Dimes Prize.

RECENT PROGRESS IN iPS CELL RESEARCH AND APPLICATION

SHINYA YAMANAKA, MD, PhD

Induced pluripotent stem cells (iPSCs) can proliferate almost indefinitely and differentiate into multiple cell lineages, giving chem wide medical application. As a resulc, rhey are being used for new cell-based rherapies, disease models and drug development around the world.

We are establishing technologies for the efficient generation of safe iPSCs. TIle original iPSCs were made from the retroviral transduction of four genes, Occ3/4, Sox2, c-Myc and Klf4. We have since reported an integration-free merhod using episomal vectors chat does not cause chromosomal damage and proposed using L-Myc as an alternative to oncogenic c-Myc to reduce the risk of cumorigenicicy. We have also developed a recombinant laminin-based matrix and developed a culture medium free of animal-derived constituencs (xeno-free) to generate iPS cells chat satisfy regularory requirements for medical practice.

In 2014, the world's firsc clinical study using iPSCs began for the treacment of age-relaced macular degeneration. One year afcer the surgery, the patienc's vision in the treated eye had srabilized and even showed improvement. TIle results of this clinical scudy indicate chat the use of iPSCs as a source for cell-based cherapy. To push rhese efforts, we are proceeding wich an iPSC stock project. TIle building of an iPS cell stock for regenerative medicine involves the collection of cells from healchy donors wich homozygous HLA (human leukocyte ancigen) haplotypes. Homozygous HLA haplotypes

KEYNOTE LECTURE 2

MITINORI SAITOU, MD, PhD

Professor Mitinori Saitou focusing on understanding the mechanism of germ cell development in mice, primates, and humans, and reconstituting the process of their development in vitro with pluripotent stem cells. He is a leader of the Department of Anatomy and Cell Biology, Graduate School of Medicine, Kyoto University. He was an undergraduate student in School of Medicine, Kyoto University and received an MD. After graduating in 1995, he pursued a PhD under the late professor Shoichiro Tsukita who was the pioneer of tight junction research at Kyoto University. Dr. Saitou next moved to Cambridge to join professor Azim Surani's lab in the Gurdon Institute where he met the study of germ cell development. Since rhen, his research over the last two decades has focused on understanding mechanisms to regulate specification, proliferation, development, and fonction of germ cells and he has been ac the forefront of rhis field. After completion of his postdoctoral work in Cambridge, Dr. Saitou moved back to Japan as a group leader in the RIKEN Centre for Developmemal Biology (Kobe) and then took up a professorship at Kyoto University in 2009.

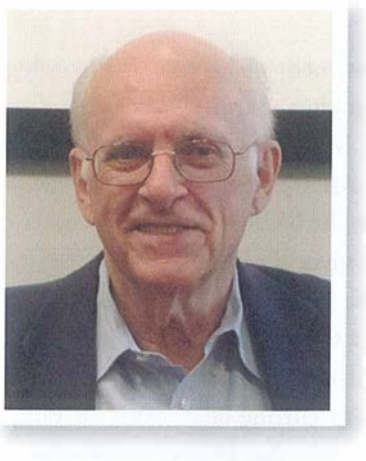
Dr. Saitou's lab firsdy succeeded in the reconstitution of the mouse germ cell specification in vitro and production of functional sperms as well as oocytes from embryonic stem (ES) cells and induced pluripotent stem (iPS) cells in mice. More importandy, he has expanded rhese groundbreaking achievements to primates and humans. ln addition, Dr. Saitou now explores where human and primate germ cells originate in vivo and the difference in pluripotency between mice and primates (including humans).

MECHANISM AND RECONSTITUTION IN VITRO OF GERM CELL DEVELOPMENT IN MICE, MONKEYS, AND HUMANS

MITINORI SAITOU, MD, PhD

The germ cell lineage ensures the creation of new individuals, perpetuating/diversifying the genetic and epigenetic information across the generations. We have been investigating the mechanism for germ cell development, and have shown that mouse embryonic stem cells (mESCs)/induced pluripotent stem cells (miPSCs) are induced into primordial germ cell-like cells (mPGCLCs) with a robust capacity both for spermatogenesis and oogenesis. We have also shown that human iPSCs (hiPSCs) with a primed pluripotency robusdy generates human PGCLCs (hPGCLCs) with a property of human early PGCs. Moreover, by investigating the development of cynomolgus monkeys, we have defined a developmental coordinate of the spectrum of pluripotency among mice, monkeys, and humans, and have made an unexpected finding that the germ cell lineage in primates is specified in the amnion. I would here discuss our efforts towards understanding the mechanism of and reconstituting in vitro of germ cell development in mice, monkeys, and humans.

THE 25TH MEMORIAL LECTURE



ROGER R. MARKWALD, PhD

Dr. Roger Markwald is the Distinguished University Professor of the Medical University of South Carolina and Professor of Regenerative Medicine and Cell Biology. In 1994, Dr. Markwald organized the first independent meeting at MUSC in Charleston, one year before this meeting was formally named the " Weinstein Cardiovascular Development Conference".

Dr. Markwald's laboratory has pioneered cell and molecular mechanisms of heart development and their relationship to pediatric and adule onset of cardiovascular diseases. A major focus has been to apply the principles of developmental biology to cell and tissue signaling, regulation and bioengineering in combination with generating animal genetic models or 3D bioprinted complex tissues to srudy disease mechanisms. Afi:er his discoveries duringl 970's chat the valve and septal mesenchyme progenitor cells chat serve to divide a simple tubular heart into a 4-chambered organ were derived from the endocardium following an inductive interaction with the myocardium, Dr. Markwald has continued to contribute to the cardiovascular filed of science, including recognition of the novel anterior (secondary) heart forming field, and published over 230 papers to date. Dr. Markwald has had 33 years of experiences in departmental chair administration including working with multiple NIH programmatic and center grants including directing an NIGMS COBRE Center in Cardiovascular Developmental Biology and serving as the institutional PI for an NIGMS Bioengineering COBRE in Regenerative Medicine. Dr. Markwald is also a recipient of Henry Gray Lifetime Research Achievement Award.

WEINSTEIN CONFERENCES: "25 YEARS OF DISCOVERY IN HEART DEVELOPMENT & DISEASE: WHAT'S NEXT?"

CONDENSED CONFERENCE SCHEDULE

Scienti:fic Sessions will be held in the Noh 1heater (First Floor (Ground Level) 0fMain Bldg)
Poster Sessions will be held on the Second Floor ofMain Bldg and on the Second Floor ofAnnex Bldg

WEDNESDAY 16TH MAY, 2018

10:00	Registration Opens
13: 10-13:30	Opening Remarks
13:30-14:50	Platform Session 1: Cardiac Progenitors
14:50-15:10	Break
15:10-16:30	Platform Session 2: Heart Fields
16:30-16:40	Break
16:40-17:25	Hot Topics Pick Up
17:25-17:50	Special Lecture 1
17:50-18:00	Break
18:00-19:00	Keynote Lecture 1: Shinya Yamanaka, MD, PhD
19:00-21:00	Poster Session I: (Odd nurnbers) (Cocktail reception)

THURSDAY 17TH MAY, 2018

8:40-10:00	Platform Session 3: Cardiovascular Morphogenesis
10:00-10:20	Break
10:20-11:20	Platform Session 4: Ductus and Pulmonary Artery
11:20-11:25	Break
11:25-11:55	25th Memorial Lecture: Roger R. Markwald, PhD
11:55-13:00	Lunch & Poster Viewing
13:00-14:00	Platform Session S: Heart Valve
14:00-14:05	Break
14:05-15:05	Platform Session 6: Epicardium and Conduction
15:05-15:20	Break
15:20-16:20	Keynote Lecture 2: Mitinori Saitou, MD, PhD
16:20-18:20	Poster Session Il: (Even nurnbers)
18:20-21:00	Museum Tour & Reception@Museum Restaurant (BI)

FRIDAY 18TH MAY, 2018

8:40-9:40	Platform Session 7: Epigenetic Regulation
9:40-9:45	Break
9:45-11:05	Platform Session 8: Genetie Technology for CHD
11 :05-11 :25	Break
11:25-12:25	Special Lecture 2
12:25-14:30	Lunch & Poster Viewing, Business Meeting
14:30-15:50	Platform Session 9: Cell Fate
15:50-16:10	Break
16:10-17:30	Platform Session 10: Cardiovascular Regeneration
17:30-17:45	Closing Remarks & Information for Weinstein 2019
18:30-21:00	Gala Dinner with Attractions @ Convention Hall Garden

DETAILED CONFERENCE PROGRAM

Scientific Sessions *Will be held in the Noh Theater (First Floor (Ground Level) of Main Bldg)*
Poster Sessions *Will be held on the Second Floor of Main Bldg and on the Second Floor of Annex Bldg*

WEDNESDAY 16TH MAY, 2018

10:00 **Registration Opens, First Floor of Main Bldg**

13: 10-13:20 **Opening Remarks by Co-organizer, Yamada Science Foundation**

13:20-13:30 **Opening Remarks: Local Committee**

13:30-14:50 **Platform Session 1: Cardiac Progenitors**
Moderators: Nicole Dubois (Mount Sinai, USA),
Kenta Yashiro (Osaka University. JPN)

13:30-13:50 1.1 Richard Tyser, University of Oxford
Defining Cardiac Progenitor Cell Types Genetically and Anatomically at the Single Cell Level during Cardiac Crescent Development

13:50-14:10 1.2 Tarja Yvanka de Soysa, University of California, San Francisco/ J. David Gladstone Institutes
Single Cell Analysis of Early Mouse Cardiogenesis and Perturbation upon Hand2 Loss

14: 10-14:30 1.3 Xuefei Yuan, University of Toronto
Gata5/6 Regulate the Early Specification of Diverse Mesoderm Lineages

14:30-14:50 1.4 Clayton Elliott Friedman, University of eensland, Institute for Molecular Bioscience
Single Cell Transcriptional Landscape of Cardiac Differentiation

14:50-15: 10 Break

15:10-16:30 **Platform Session 2: Heart Fields**
Moderators: Robert Kelly (Aix Marseille Univ, France),
Deborah Yelon (University of California San Diego, USA)

15:10-15:30 2.1 Aibin He, Peking University
Single-Cell Transcriptomics Reveals Lineage Hierarchies and Interlineage Communications for Tubb Heart Fields

15:30-15:50 2.2 Peter Andersen, Johns Hopkins University
Heart Fields Are Induced by Coordinated Activities of Wnt and Bmp Signaling and Identified by Cxcr4 Expression

15:50-16:10 2.3 Yuntao Charlie Song, Cincinnati Children's Hospital Medical Center
HDAC1-Mediated Repression of the Retinoic Acid-Responsive Gene Ripply3 Promotes Second Heart Field Development

16:10-16:30 2.4 Hiroko Nomaru, Albert Einstein College of Medicine
Tbx1 Cell Lineage Analysis in the Second Heart Field

16:30-16:40 Break

16:40-17:25 **Hot Topics Pick Up**
Moderator: Bin Zhou (Chinese Academy of Sciences, China)

16:40-16:55 HT.1 Wataru Kimura, RIKEN BDR
Hypoxia and Cardiac Regeneration

16:55-17:10 HT.2 Guo Huang, University of California San Francisco
Hormonal Control of Cardiac Regenerative Potential in Development and Evolution

17:10-17:25 HT.3 Gonzalo del Monte, Victor Chang Cardiac Research Institute
NOTCH1/NRG1 Control of Cardiac Jelly Dynamics Defines the Building Plan for Trabeculation

17:25-17:50 **Special Lecture 1**

Moderator: Margaret Buckingham (Pasteur Institute, France)

SL.1 James F. Martin, Baylor College of Medicine

Induction of Cardiogenesis in Mammals

17:50-18:00 Break

18:00-19:00 **Keynote Lecture 1**

Moderator: Deepak Srivastava (Gladstone Institutes, USA)

KL.1 Shinya Yamanaka, MD, PhD, CiRA, Kyoto University, Gladstone Institute

Recent Progress in iPS Cell Research and Application

19:00-21:00 **Poster Session I (Odd numbers), Cocktail Reception**

THURSDAY 17TH MAY, 2018

8:40-10:00 **Platform Session 3: Cardiovascular Morphogenesis**

Moderators: Henry Sucov (University of Southern California, USA), Michiko Watanabe (Case Western Reserve Univ, USA)

8:40-9:00 3.1 Sigolene Meilhac, Imagine-Institut Pasteur
Le.ft-Right Asymmetry of the Heart:Jrom the Regulation of the Embryonic Loop Shape to Congenital Heart Dejècts

9:00-9:20 3.2 Kelly Smith, University of eensland
Myosin Vb-Mediated Endosomal Tra.fficking of N-Cadherin is Required for Cardiac Chamber Ballooning

9:20-9:40 3.3 Mingfu Wu, Albany Medical College
Numb Modulates Cardiac Morphogenesis by Regulating N-Cadherin Endocytic Tra.fficking to Membrane

9:40-10:00 3.4 Yusuke Watanabe, National Cerebral and Cardiovascular Center Research Institute
Signifi,cance of Hey 1 Transcription Factor in Pharyngeal Arch Artery Formation and Regulatory Mechanisms of its Expression during Embryonic Development

10:00-10:20 Break

10:20-11 :20 **Platform Session 4: Ductus and Pulmonary Artery**

Moderators: Sophie Astrof (TI1omas Jefferson University, USA), Utako Yokoyama (Yokohama City University, JPN)

10:20-10:40 4.1 Satoko Ito, Cardiovascular Research lnstitute, Yokohama City University
Prostaglandin E-EP4 Signaling-Mediated Fibulin-1 Integrates Extra-Cellular Matrices to Promote Smooth Muscle Cel! Migration of the Ductus Arteriosus

10:40-11:00 4.2 Adriana Gittenberger-de Grooc, Leiden University Medical Cencer
Contribution Of Neural Crest and Second Heart Field to Ductus Arteriosus and Pulmonary Arteries: Clinical Implications

11 :00-11 :20 4.3 Takashi Shimizu, University of Tokyo
PERK Inhibition Improves Pulmonary Arterial Hypertension with BMPR2 Mutation in Mice

11:20-11:25 Break

11 :25-11 :55 **25th Memorial Lecture**

Moderator: Adriana Gittenberger-de Groot (Leiden University Medical Center, Netherland)

ML.1 Roger R. Markwald, PhD, Medical University of South Carolina
Weinstein Coriferences: 25 Years of Discovery in Heart Development & Disease: What's Next?

11:55-13:00 **Lunch** & **Poster Viewing**

13:00-14:00 **Platform Sessioh 5: Heart Valve**

Moderators: AndyWessels (Medical University of South Carolina, USA), Hiroki Kokubo (Hiroshima University,JPN)

13:00-13:20 5.1 Salim Abdelilah-Seyfried, Potsdam University
Biomechanics of Zebrajish Cardiac "Valve Morphogenesis

13:20-13:40 5.2 Ayako Shigeta, University of California, Los Angeles
Endocardially-Derived Macrophages are Essential for "Valvular Remodeling
"Developmencal Dynamics Sponsored Speakers"

13:40-14:00 5.3 Maiko Matsui, Weill Cornell Medicine
Increased Ca^{2+} Influx Through Cacnal c Promotes Progressive Aortic "Valve Stenosis in Mice

14:00-14:05 Break

14:05-15:05 **Platform Session 6: Epicardium and Conduction**

Moderators: Takashi Mikawa (University of California San Francisco, USA), Vincent Christoffels (University of Amsterdam, Netherland)

14:05-14:25 6.1 Marina Peralta, IGBMC
Intraflagellar Transport Proteins Modulate the Activity of the Hippo Pathway Effector Yap1 during Proepicardium Development

14:25-14:45 6.2 Laurence Celine Garric, Hubrecht Institute
Islet-1 is the Key Regulator in Pacemaker Cells Development and Function

14:45-15:05 6.3 Martina Gregorovicova, Institute of Physiology, the Czech Academy of Science
Evolutionary Origin of the Ventricular Septum and Conduction System in Squamate Reptiles

15:05-15:20 Break

15:20-16:20 **Keynote Lecture 2**

Moderator: Hiroki Kurihara (University of Tokyo, JPN)

KL.2 Mitinori Saitou, MD, **PhD,** Graduate School of Medicine and Faculty of Medicine, Kyoto University
Mechanism and Reconstitution In Vitro of Germ Cell Development in Mice, Monkeys, and Humans

16:20-18:20 **Poster Session II (Even numbers)**

18:20-21:00 **Museum Tour & Reception@Museum Restaurant (BI of National Museum of Nara)**

FRIDAY 18TH MAY, 2018

8:40-9:40 **Platform Session 7: Epigenetic Regulation**

Moderators: William T Pu (Boston Children's Hospital, USA),
Bin Zhou (Albert Einstein College of Medicine, USA)

- 8:40-9:00 7.1 Yahui Lan, Weill Cornell Medicine
Epigenetic Regulation of Cardiogenesis by Tissue-Specifi,c Tet-Dependent Demethylation of Target Genes Controlling AVC and Epicardial Morphogenesis

9:00-9:20 7.2 Karl Degenhardt, Children's Hospital of Philadelphia
Acetylation by NATIO Protects against Cardiac Dejècts in the Setting of Maternai Diabetes

9:20-9:40 7.3 Lauren Wasson, Harvard Medical School
Modeling Chromatin Modifying Congenital Heart Disease Patient Mutations in iPSCs Using CRJSPR

9:40-9:45 Break

9:45-11:05 **Platform Session 8: Genetie Technology for CHD**

Moderators: Rolf Bodmer (SBP Medical Discovery lnstitute, USA),
Vidu Garg (Nationwide Children's Hospital, USA)

9:45-10:05 8.1 Min-Su Kim, Medical College of Wisconsin
CRISPR/Cas9-Mediated Genome Editing in Patient Derived iPSC-Cardiomyocytes Recapitulate MYH6-R443P Phenotype in HLHS Family

10:05-10:25 8.2 Eva Lana-Elola, Francis Crick lnstitute, London
Genetie Dissection and Transcriptomic Profiling of Congenital Heart Dejècts in Down Syndrome Identifi,es a Minimal Causative Genetie Region and Implicates a Pathological Mechanism

10:25-10:45 8.3 Georg Vogler, Sanford Burnham Prebys Medical Discovery Institute
High-Throughput Cardiac in Vivo Platform to Functionally Vàlidate Genome-Wide Candidate Genesfor Congenital Heart Disease

10:45-11 :05 8.4 Anne M Moon, Geisinger Clinic and The University of Utah
Swine Models of Congenital Heart Diseasefor Basic and Translational Research

11:05-11:25 Break

11:25-12:25 **Special Lecture 2**

Moderator: Naoki Mochizuki (National Cerebral and Cardiovascular Cencer,JPN)

11:25-11:55 SL2.l Didier Stainier, Max Planck Institute
Cardiomyocyte Behavior during Development and Regeneration

11:55-12:25 SL2.2 Paul Riley, University of Oxford
Lymphatic-Macrophage Interactions during Heart Development and Repair

12:25-14:30 **Lunch & Poster Viewing, Poster Removal (14:00-14:30), Business Meeting (14:00-14:30@Noh Theater)**

14:30-15:50 **Platform Session 9: Cell Fate**

Moderators: Brian L. Black (University of California San Francisco, USA),
Jose Luis de la Pompa (Centro Nacional de Investigaciones Cardiovasculares Carlos III, Spain)

14:30-14: 50 9.1 Estelle Jullian, Institut de Biologie de Developpement, Marseille
Jnvestigating Myogenic Cell Fate Choice between Heart and Head Muscles in Murine Cardiopharyngeal Mesoderm

14:50-15:10	9.2	Wei Wang, New York University *A Single Cel! Transcriptional Roadmapfor Cardiopharyngeal Fate Diversification* "Developmental Dynamics Sponsored Speakers"
15:10-15:30	9.3	Jun Takeuchi, TMDU *Conversion ofthe Heart Cellsftom the Ectoderm/Endoderm Lineage*
15:30-15:50	9.4	Antonio Fernandez-Perez, U T Southwestern Medical Center *Dissecting Mechanismsfor Hand2-Dependent Pacemaker Cel! Reprogramming*
15:50-16:10	Break	
16:10-17:30	**Platform Session 10: Cardiovascular Regeneration** Moderators: Alexandre Colas (SBP Medical Discovery lnstitute, USA), Eldad Tzahor (Weizmann lnstitute ofScience, Israel)	
16:10-16:30	**10.1**	Masahide Sakabe, Cincinnati Children's Hospital Medical Center *G-Protein Signaling Regulation ofthe HIPPO Pathway in Neonatal Cardiomyocyte Regeneration*
16:30-16:50	10.2	William Thomas Stockdale, University ofOxford *Heart Regeneration in the Mexican Cavefish*
16:50-17:10	10.3	Maria Azzurra Missinato, SBP Medical Discovery lnstitute *High-Throughput Screening Identifies a Novel Combination Of Synergistically-Acting Barriers to Cardiac Reprogramming*
17:10-17:30	10.4	Shugo Tohyama, Keio University School ofMedicine *Metabolic Selection Systemfor Large Numbers ofHuman iPSC-Derived Cardiomyocytes*
17:30-17:45	**Closing Remarks & Information for Weinstein 2019**	
18:30-21 :00	**Gala Dinner with Attractions @ Convention Hall Garden**