UC San Diego - Kyoto University Joint Symposium

Cancer & Drug Development
Regenerative Medicine & Biology
Advanced Energy Research




March 14-15, 2016
UC San Diego

Contents

Welcome Message

Dear Colleagues and Friends:

UC San Diego is pleased to partner with Kyoto University to host our second Kyoto University – UC San Diego Joint Symposium. From our first partnership five decades ago, to our ongoing collaboration today, we continue to build on our foundation of innovation and partnership.

Through this symposium as well as our exchange of talent and resources, we are advancing the frontiers of knowledge and propelling our research, particularly in the areas of regenerative medicine and biology, cancer, drug development, biomedical research, and advanced energy research. The presentations and discussions at this symposium will further strengthen the ties between our universities.

This event is a mark of our teamwork and a grand addition to our existing collaborations. Over the next two days, you will hear from faculty and leaders at the forefront of their fields. It is our hope that these meetings will educate, inspire and advance the connections between our universities.

Thank you for attending the symposium.

With kind regards,

Pradeep K. Khosla
Chancellor
UC San Diego

I am delighted to see this 2nd UC San Diego-Kyoto Symposium realized thanks to the great efforts of researchers from both institutions. I feel that this symposium embodies both continuity and innovation. Continuity, as we strengthen and develop the ongoing collaboration between our two institutions, and innovation, build on the new developments that have been produced in the UC San Diego-Kyoto research community since last year.

The origins of this symposium go back to 2013, when Project La Jolla, an initiative to promote interdisciplinary research and education collaboration between Kyoto University and UC San Diego was launched under Kyoto University's SPIRITS (Supporting Program for Interaction-based Initiative Team Studies) program. Project La Jolla seeks to promote diverse global research collaboration by uniting researchers in life sciences, the humanities, and cognitive science. The launch of Project La Jolla was followed up by the signing of a formal Memorandum of Understanding (MOU) for academic cooperation and exchange between Kyoto University and UC San Diego in February 2014. The momentum gathered through the MOU and the two years of initiatives under Project La Jolla was then continued with the 1st joint symposium and satellite symposium between Kyoto University and UC San Diego, held in Kyoto in March 2015. Since then, several impressive collaborative research and education projects have been initiated, some of which have already produced jointly authored publications. This 2nd joint symposium will further accelerate our collaboration and facilitate yet more new developments.

In addition to the more established scholars in our growing academic network, we also have many up-and-coming young researchers joining us this year. The symposium will provide a great platform for this new generation to exchange ideas, learn about developments at the front line of their fields, and form networks which will support their future careers.

Kyoto University is one of the oldest and most reputed research-oriented universities in Japan. As a national university, we are committed to contributing to the national and international communities. UC San Diego is a service-oriented public institution with a mission to provide all of its members with the opportunity to realize their full academic potential. The meeting of keen academic minds that this symposium represents will contribute to the missions of both institutions, advance cutting-edge research in diverse fields, and help us to work for the benefit of our local and global communities.

I wish all participants the best for an enjoyable and fruitful symposium.

Juichi Yamagiwa
President
Kyoto University

2nd UC San Diego – Kyoto University Joint Symposium

March 14-15, 2016 – UC San Diego, La Jolla, California

Organizing Committee

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Breakout Session Steering Committees

Cancer & Drug Development

Scott M. Lippman, Professor, Department of Medicine; Director, Moores Cancer Center, UC San Diego

James H. McKerrow, Professor, Pharmaceutical Sciences; Dean, Skaggs School of Pharmacy and Pharmaceutical Sciences

Masakazu Toi, Professor, Department of Breast Surgery, Graduate School of Medicine, Kyoto University

David R. Vera, Professor, Department of Radiology; Director, Molecular Imaging, UC San Diego

Tomoko Hayashi, Project Scientist, Moores Cancer Center, UC San Diego

Regenerative Medicine & Biology

Lawrence S. B. Goldstein, Professor, Department of Cellular & Molecular Medicine; Scientific Director, Sanford Consortium for Regenerative Medicine

Catriona H. Jamieson, Associate Professor, Department of Medicine; Chief, Division of Regenerative Medicine, UC San Diego

Martin Marsala, Professor, Department of Anesthesiology, UC San Diego; Sanford Consortium for Regenerative Medicine

Jun Takahashi, Deputy Director, Center for iPS Cell Research and Application, Kyoto University

Advanced Energy Research

Farhat N. Beg, Professor, Department of Mechanical and Aerospace Engineering; Director, Center for Energy Research, UC San Diego

Satoshi Konishi, Professor, Institute of Advanced Energy, Kyoto University

Carlos Coimbra, Professor, Department of Mechanical and Aerospace Engineering, UC San Diego

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KURA

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JOINT SYMPOSIUM

2016

J. R. BEYSTER AUDITORIUM
Rady School of Management

MAR 14 MONDAY — **PLENARY SESSION**

MAR 15 TUESDAY — **CANCER & DRUG DEVELOPMENT**

VILLAGE 15
Building 1, The West Village

MAR 15 TUESDAY — **ADVANCED ENERGY RESEARCH IN SAN DIEGO & KYOTO**

DUANE J. ROTH AUDITORIUM
Sanford Consortium

MAR 15 TUESDAY — **REGENERATIVE MEDICINE & BIOLOGY**

AGENDA

J.R. Beyster Auditorium, Rady School of Management

8:00-9:00 **Registration**

9:00-9:30 **Symposium Series Introduction and Welcome**

Vice Chancellor Sandra A. Brown, UC San Diego (Introduction)

Chancellor Pradeep K. Khosla, UC San Diego (Welcome)

Executive Vice-President Nagahiro Minato, Kyoto University (Leadership Remarks)

Executive Vice-President Kayo Inaba, Kyoto University (International Affairs Remarks)

9:30-11:45 **Breakout Session Introductions** (Chairman, **Paul K. L. Yu**, Provost, Revelle College)

9:30-10:15 **Cancer & Drug Development**

Scott M. Lippman, Director, Moores Cancer Center, UC San Diego
"Research Highlights and New Initiatives at the Moores Cancer Center"

James H. McKerrow, Dean, Skaggs School of Pharmacy and Pharmaceutical Sciences, UC San Diego
"Research and Programmatic Initiatives at the UC San Diego Skaggs School of Pharmacy & Pharmaceutical Sciences"

Masakazu Toi, Professor, Breast Cancer Unit and Breast Surgery, Kyoto University
"Cancer Research at Kyoto University Graduate School of Medicine and Kyoto University Hospital"

10:15-10:45 **Coffee Break & Networking**

10:45-11:15 **Regenerative Medicine & Biology**

Lawrence S. B. Goldstein, Scientific Director, Sanford Consortium for Regenerative Medicine
"Research Highlights and New Initiatives at the Sanford Consortium for Regenerative Medicine"

Jun Takahashi, Deputy Director, Center for iPS Cell Research and Application (CiRA), Kyoto University
"Current Research Activities and Future Perspectives at Kyoto University CiRA"

11:15-11:45 **Advanced Energy Research**

Farhat N. Beg, Director, Center for Energy Research, UC San Diego
"Research and Programmatic Initiatives at the UC San Diego Center for Energy Research"

Satoshi Konishi, Professor, Institute of Advanced Energy, Kyoto University
"Current Research Activities and Future Perspectives at Kyoto University Institute of Advanced Energy"

11:45-14:00 **Lunch & Networking**

14:00-16:00 **Nobel Laureate Introductions & Lectures**

Introduction by Chancellor Pradeep K. Khosla, UC San Diego

Professor Roger Y. Tsien, UC San Diego
"Molecules for Multicolor Imaging and for Long-Term Memory Storage"

Introduction by Executive Vice-President Nagahiro Minato, Kyoto University

Professor Shinya Yamanaka, Director, CiRA, Kyoto University
"New Era of Medicine with iPS Cells"

16:00-16:30 **Health Sciences Overviews and Strategies**

Vice Chancellor David A. Brenner, UC San Diego
"UC San Diego Health Sciences: Overview & Strategies"

Executive Vice-President Nagahiro Minato, Kyoto University
"Present and Future of Health Sciences and Biomedical Research at Kyoto University"

16:30-17:00 **Networking**

J.R. Beyster Auditorium, Rady School of Management

8:30-8:40 **Opening Address**

Professor Scott M. Lippman, Director, Moores Cancer Center, UC San Diego

8:40-9:20 **Keynote Session**

Introduction & Chair: **Professor Quyen T. Nguyen**, (UC San Diego)

Professor Roger Y. Tsien, (UC San Diego)
"Molecules for Imaging and Radiosensitizing Cancer"

9:20-10:10 **Session 1: Molecular Imaging**

Chair: **Professors Quyen T. Nguyen & David R. Vera**, (UC San Diego)

Professor Masakazu Toi, (Kyoto University)
"Axillary Surgery Using Fluorescence Lymphatic Mapping for Primary Breast Cancer"

Professor Anne M. Wallace, (UC San Diego)
"Molecular Imaging of the Sentinel Lymph Node"

Coffee Break

10:25-11:45 **Session 2: Tumor Microenvironment**

Chair: **Professor Scott M. Lippman**, (UC San Diego)

Professor Makoto Mark Taketo, (Kyoto University)
"Molecular Mechanisms of Colon Cancer Metastasis: Toward Clinical Applications"

Professor Napoleone Ferrara, (UC San Diego)
"Regulation of Angiogenesis"

Lunch Break

13:00-14:10 Collaboration Update

Chair: **Professor Kumar Sharma**, (UC San Diego)

Professor Motoko Yanagita, (Kyoto University)
"Crosstalk Inside the Kidney Determines Kidney Plasticity"

14:10-14:20 Introduction to Japan Society for the Promotion of Science (JSPS)

Mr. Junji Oshima, (Japan Society for the Promotion of Science)
"Mechanisms of JSPS Support of International Collaborations"

14:20-15:40 Session 3: Inflammatory Response – Its Regulation and Application

Chair: **Professor Kayo Inaba**, (Kyoto University)

Professor Osamu Takeuchi, (Kyoto University)
"Targeting Posttranscriptional Regulators in Inflammation"

Professor Dennis A. Carson, (UC San Diego)
"Prevention and Treatment of Infectious Diseases and Cancer with Synthetic Toll-like Receptor Activators"

Coffee Break

15:50-17:10 Session 4: Innate Immune Cell-Targeted Immunotherapy

Chair: **Dr. Yasunori Yamaguchi**, (Kyowa Hakko Kirin California, Inc.)

Professor Maripat Corr, (UC San Diego)
"Dendritic Cells as a Target for Treatment of Autoimmune Diseases"

Professor Kayo Inaba, (Kyoto University)
"Initiation and Regulation of Immune Responses by Dendritic Cells"

Duane J. Roth Auditorium, Sanford Consortium Building

7:45-8:00 **Opening Address**

Dr. Edward W. Holmes, President, Sanford Consortium for Regenerative Medicine

8:00-9:30 **Keynote Session**

Chair: **Professor Lawrence S. B. Goldstein**, (Sanford Consortium; UC San Diego)

Professor Shinya Yamanaka, (CiRA, Kyoto University)
"Recent Progress in iPS Cell Research and Application "

Professor Fred H. Gage, (Sanford Consortium; Salk Institute)
"Modeling Human Psychiatric Diseases in Vitro"

Coffee Break

9:45-11:45 **Session 1: In Vitro Disease Modelling and Epigenetics**

Chair: **Professor Alysson R. Muotri**, (UC San Diego)

Professor Bing Ren, (Sanford Consortium; UC San Diego)
"The 3-Dimensional Organization of Genomes"

Professor Alysson R. Muotri, (Sanford Consortium; UC San Diego)
"Modeling MeCP2 Disorders with iPSCs"

Professor Haruhisa Inoue, (CiRA, Kyoto University)
"Dissecting Neurodegenerative Diseases with iPSC Technology"

Professor Hirohide Saito, (CiRA, Kyoto University)
"Synthetic RNA Switches and Circuits to Detect and Purify Target Live Cells"

Lunch Break

13:00-14:45 Session 2: Cell and Tissue Differentiation and Behavior

Chair: **Professor Catriona H. Jamieson**, (Sanford Consortium; UC San Diego)

Professor Juan Carlos Izpisua Belmonte, (Sanford Consortium; Salk Institute)
"Crossing Xeno-Barriers: the Hidden Dimension of Distinct Flavors of Pluripotency"

Professor Kelly A. Frazer, (Sanford Consortium; UC San Diego)
"Genetic Determinants of Gene Expression in a Collection of 215 Human iPSCs"

Professor Dan S. Kaufman, (Sanford Consortium; UC San Diego)
"Anti-Cancer Therapies Derived from Human Pluripotent Stem Cells"

14:45-15:00 Introduction to Japan Society for the Promotion of Science (JSPS)

Mr. Junji Oshima, (Japan Society for the Promotion of Science)
"Mechanisms of JSPS Support of International Collaborations"

Coffee Break

15:15-17:15 Session 3: Clinical Application of Cell Replacement-Based Therapies

Chairs: **Professors Martin Marsala**, (Sanford Consortium: UC San Diego) & Alexander Norbash (UC San Diego)

Professor Jun Takahashi, (CiRA, Kyoto University)
"Challenges Towards Stem Cell-Based Therapy for Parkinson's Disease"

Professor Carl K. Hoh, (UC San Diego)
"Quantitative Measurements of Biologic Processes with PET"

Professor Martin Marsala, (Sanford Consortium, UC San Diego)
"Spinal Cell-Replacement Therapies for Treatment of Spinal Traumatic Injury: An Update"

Professor Catriona H. Jamieson, (Sanford Consortium, UC San Diego)
"Role of RNA Editing in Leukemia Stem Cell Evolution"

17:15 Reception: Bella Vista Social Club & Caffé (adjacent to Duane J. Roth Auditorium)

Breakout Session – Tuesday, March 15 – Advanced

The West Village, Building 1, 15th Floor

9:00-9:10 **Opening Address:**

Professor Albert P. Pisano, Dean, Jacobs School of Engineering

9:10-10:30 **Keynote Session**

Chair: **Professor Farhat N. Beg**, (UC San Diego)

Professor George R. Tynan, (UC San Diego)
"Energy Challenges and Fusion Research"

Professor Satoshi Konishi, (Kyoto University)
"Fusion Energy and its Future Deployment"

10:35-11:40 **Session 1: Solar Energy and Energy Materials**

Chair: **Professor Y. Shaya Fainman**, (UC San Diego)

Professor Carlos F. Coimbra, (UC San Diego)
"Resource and Power Forecasting for Large Scale Solar Plants"

Professor Hiroshi Sakaguchi, (Kyoto University)
"New Carbon-Nanowires for Energy Utilization"

Lunch Break

13:00-13:10 **Message from Japan Society for the Promotion of Science (JPSP)**

Mr Junji Oshima, (Japan Society for the Promotion of Science)
"Mechanisms of JSPS Support of International Collaborations"

13:15-14:15 **Session 2: Energy Storage**

Chair: **Professor George R. Tynan**, (UC San Diego)

Professor Ping Liu, (UC San Diego)
"Energy Storage Innovation for Vehicle and Grid Applications"

Professor Toshiyuki Nohira, (Kyoto University)
"Sodium Secondary Batteries Using Amide Ionic Liquid Electrolytes"

14:20-15:20 Session 3: Ultrafast Phenomena

Chair: **Professor Satoshi Konishi**, (Kyoto University)

Professor Y. Shaya Fainman, (UC San Diego)
"Ultrafast Processing with Nanophotonics"

Professor Takashi Nakajima, (Kyoto University)
"Discovering a New Aspect of Laser-Nanobubble Interactions"

Coffee Break

15:50-16:50 Session 4: The Future of Energy

Chair: **Mr. William V. Torre**, (UC San Diego)

Professor David G. Victor, (UC San Diego)
"A Decentralized Future for the Electric Power System?"

Professor Seiichi Ogata, (Kyoto University)
"Expanding Renewable Energy in Japan: Research Progress and Anticipated Solutions from Kyoto University"

16:55-17:55 Session 5: Fusion

Chair: **Professor Carlos F. Coimbra**, (UC San Diego)

Professor Farhat N. Beg, (UC San Diego)
"Why Do We Need an Advanced Inertial Fusion Energy Concept?"

Professor Shinichiro Kado, (Kyoto University)
"Topical Studies on Plasma-Material Interactions with MAP-II Linear Divertor Simulator and Heliotron J"

17:55-18:10 Concluding Remarks

Professor Farhat N. Beg, (UC San Diego)

Professor Satoshi Konishi, (Kyoto University)

PRESENTATION ABSTRACTS

Nobel Laureate Lectures

ROGER Y. TSIEN

Molecules for Multicolor Imaging and for Long-Term Memory Storage

I have moved on from my historical involvement in fluorescent proteins of many colors to two current interests, engineered far-red fluorescent proteins and multicolor electron microscopy.

We are testing the hypothesis (Tsien, 2013) that life-long memories are stored as the pattern of holes in the perineuronal net (PNN), a specialized form of extracellular matrix deposited around neurons during critical periods of brain development. The PNN contains very long-lived molecules, can be modified by proteolysis, and is interrupted by holes where synapses occur. We postulate that new memories are recorded by proteases carving new holes to form novel synapses or expanding existing holes to strengthen old synapses. Experimental tests are underway including time-lapse fluorescence and electron microscopy of the PNN, 15N pulse-14N chase measurement of the age of PNN components compared to traditional synaptic molecules, and selective amnesia induced by pharmacological or genetic inhibition of proteases.

Tsien, R.Y. 2013. Very long-term memories may be stored in the pattern of holes in the perineuronal net. Proc Natl Acad Sci USA 110: 12456-61.

SHINYA YAMANAKA

New Era of Medicine with iPS Cells

The appeal of induced pluripotent stem cells (iPSCs) is that they can proliferate almost indefinitely and differentiate into multiple lineages. This property means that a small number of iPSCs can be used to make a large number of any desired cell type. Moreover, iPSCs can in theory be made using any cell from the human body, which significantly expands their availability and medical application. As a result, cell-based therapies, disease mechanisms and new drug development are being studied worldwide using iPSCs, with iPSC technology evolving at an accelerated pace.

We are currently establishing optimal technologies for the efficient generation of safe iPSCs. The original iPSCs were made from the retroviral transduction of four genes, Oct3/4, Sox2, c-Myc and Klf4. Retroviral transduction is not suitable for clinical use, however, because it results in gene integration, which risks chromosomal damage. We have since reported an integration-free method using episomal vectors. Another consideration is the four genes themselves. c-Myc is oncogenic, but is considered key to the efficient generation of iPSCs. Therefore, we have explored the use of L-Myc as an alternative to c-Myc, so as to reduce the risk of tumorigenicity while at the same time maintaining iPSC induction at high efficiency. Conventionally, iPSC induction uses feeder cells or culture materials from different species. These materials also make the resulting iPSCs incompatible with clinical use. Accordingly, we have replaced feeder cells with a recombinant laminin-based matrix and developed a culture medium free of animal-derived constituents (xeno-free). Regarding quality control, genes that mark defective iPSC clones have been identified, indicating the possibility of screening out low-quality iPSCs before use, which would expedite application for regenerative medicine.

In 2014, the world's first clinical study using iPSCs was initiated to study the transplantation of iPSC-derived RPE (retinal pigment epithelium) sheets for age-related macular degeneration. In addition, iPSC studies have recently shown major progress for other disorders, such as corneal diseases, blood diseases and Parkinson's disease, giving expectation that iPSC-based regenerative medicine will be widely used in the near future. To push these efforts, we are proceeding with an iPSC stock project in which iPSC clones are being established from donors with a homologous HLA haplotype, which is associated with decreased immune response and therefore less risk of transplant rejection. The iPSC stock is being designed with the intention of providing quality-assured cells for medical treatments around the world. In 2015, we started distributing an iPSC stock clone to organizations in Japan.

Other applications of iPSCs include drug screening, toxicity studies and the elucidation of disease mechanisms using disease-specific iPSCs from patients with intractable diseases. In addition, iPSCs may be resourceful for preventative measures, as they make it possible to predict the patient condition and provide a preemptive therapeutic approach to protect against the onset of the disease or to establish personalized medicine. Finally, accumulating evidence is demonstrating the benefits of iPSCs in drug repositioning or better assessing drug candidates that succeeded animal testing but failed in patients (false-positives) or have clinical benefits that were not seen in animal tests (false-negatives).

Keynote Session

ROGER Y. TSIEN

Molecules for Imaging and Radiosensitizing Cancer

For cancer diagnosis and therapy, we are developing activatable cell penetrating peptides (ACPPs), synthetic molecules with a novel amplifying mechanism for homing to diseased tissues. ACPPs are polycationic cell penetrating peptides whose cellular uptake is minimized by a polyanionic inhibitory domain and restored if the peptide linker connecting the two domains is cleaved. Local activity of specific proteases cuts the linker and causes amplified adhesion and uptake in tumors. ACPPs sensitive to matrix metalloproteinases -2 and -9 enable magnetic resonance imaging (MRI), fluorescence-guided surgery, delivery of chemotherapy, and (most recently) radiosensitization (Buckel, 2015). We have also developed fluorescent peptides that light up peripheral nerves to show surgeons where not to cut.

Buckel, L., et al. 2015. Tumor radiosensitization by monomethyl auristatin E: mechanism of action and targeted delivery. Cancer Res 75: 1376-87.

Session 1: Molecular Imaging

MASAKAZU TOI

Axillary Surgery Using Fluorescence Lymphatic Mapping for Primary Breast Cancer

The indocyanine green fluorescence (fICG) technique enables to visualize axillary lymphatic pathway and sentinel node(s) mapping during primary breast cancer surgery. In order to assess diagnostic performance of sentinel lymph node (SNs) using fICG method, we have carried out multiple clinical studies, compared with blue dye method, and with radioisotope (RI) method.

In the initial study, it was demonstrated that high rate of SN detection was achievable using the fICG method. Next, we studied the sensitivity of the fICG method to detect tumor-positive SNs as compared with the RI method in clinically node-negative breast cancer patients who underwent SN biopsy. This prospective study, including 821 patients for the per-protocol analysis, showed that the overall detection of SNs using fICG was identical to RI (97.2 vs. 97.0 %), and the combination of both methods achieved a significant improvement compared with RI alone (99.8 vs. 97.0 %, $P < 0.001$). The detection rate for tumor-positive SN was 93.3 % for fICG and 90.0 % for RI, and the sensitivity of the fICG was 95.7 %. The additional use of fICG significantly improved positive SN detection for RI (97.2 vs. 90.0 %, $P < 0.001$). These study results suggested that the fICG method can be used as a standard for SN mapping as well as the RI-based method and the combined use of fICG and RI improve SN diagnosis for primary breast cancer patients.

It has been widely accepted that surgical axillary clearance/dissection should be avoided if SN contains no or only isolated tumor cells. Currently it is also accepted that axillary clearance is avoidable if node-metastasis is limited, such as a few node involvement. Using the fICG method, which visualizes lymphatic flow from the breast and provides multiple nodes mapping in axilla, the number of axillary nodes to resect can be personalized in each patient. The combined use of fICG and RI helps to make axillary staging and surgical management more precise. It promises better quality of life for primary breast cancer patients.

ANNE M. WALLACE

Molecular Imaging of the Sentinel Lymph Node

Lymphoseek (Tc-99m tilmanocept) is a receptor-targeted agent designed for lymphatic mapping in patients with solid tumors. Initially approved in 2011 by the United States Food and Drug Administration (FDA) for lymph node mapping in breast and melanoma cancer, Lymphoseek has continued to gain expanded approval. Additionally, Lymphoseek is approved for guiding sentinel lymph node biopsy (SLNB) using a handheld gamma counter in patients with clinically node negative squamous cell carcinoma (SCC) of the oral cavity, breast cancer or melanoma. Recently, Lymphoseek was approved for use by the European Union (EU).

Two phase III trials in breast and melanoma patients demonstrated within-patient concordance of Lymphoseek with vital blue dye for sentinel lymph node imaging. In these studies, Lymphoseek identified more sentinel lymph nodes and this localization represented a higher number of metastatic breast cancer and melanoma lymph nodes than that of vital blue dye. Another Phase III trial examined the false negative rate (FNR) of sentinel lymph node biopsy relative to the pathologic nodal status in patients with intraoral or cutaneous head and neck squamous cell carcinoma. In 101 enrolled patients, the FNR was 2.6% and overall accuracy was 98.8%.

Recent laboratory studies have demonstrated that Lymphoseek may be labeled with fluorescent dye to be used for near infrared (NIR) image guided lymph node mapping. Studies have demonstrated successful pelvic sentinel lymph node biopsy in dogs that were injected with fluorescent-Lymphoseek in both the prostate and the bladder. Additionally, fluorescent Lymphoseek was recently labeled with both Ga-68 and Tc-99m for tri-modal imaging to perform PET images for pre-operative SLN mapping, fluorescence imaging, and quantitative radiometric measurements of SLN accumulation after excision.

Session 2: Tumor Microenvironment

MAKOTO MARK TAKETO

Molecular Mechanisms of Colon Cancer Metastasis: Toward Clinical Applications

The direct cause of cancer death is often its metastasis to the vital organs. Metastasis is achieved through a multistep cascade of events, and therefore inefficient as a whole. Despite efforts to find mutations that are responsible for metastasis, relatively few such genetic changes have been found, leading to the speculation that metastasis is driven by the mechanisms for physiological and/or pathological body reactions.

Recently, we have shown that AES/Aes (Amino-terminal enhancer of split) gene encodes colorectal cancer (CRC) metastasis suppressor Aes that functions as an endogenous inhibitor of Notch signaling that plays a variety of roles in cancer in a context-dependent manner. Expression of Aes is decreased in liver metastases compared with primary colon tumors in both mice and humans. Upon introduction of homozygous Aes knockout mutation into adenomatous epithelium of Apc+/Δ716 intestinal polyposis mice, their tumors become malignant due to Notch signaling activation, showing submucosal invasion and intravasation. Consistently, transendothelial migration (TEM) is increased significantly, when CRC cells are activated for Notch signaling and placed on an endothelial cell (EC) layer in culture. Thus, reduced level of Aes and stimulation of Notch signaling are implicated in the invasion and intravasation of CRC cells during metastasis.

Next, we have investigated how Notch signaling stimulates CRC metastasis. One of the genes induced by Notch signaling in CRC is DAB1/Dab1. Genetic depletion of Dab1 suppresses cancer invasion and metastasis in the Notch signaling-activated mice. Dab1 is phosphorylated by Abl tyrosine kinase, and phosphorylated Dab1 activates Abl reciprocally. Consistently, inhibition of Abl suppresses cancer invasion in mice. Furthermore, we show that one of the targets of Abl Tyr-kinase is Rac/Rho-GEF protein Trio, and that phosphorylation at its Tyr residue 2681 (pY2681) causes Rho activation in CRC cells. The Tyr-to-Phe mutation Trio(Y2681F) reduces the RhoGEF activity, and inhibits invasion of CRC cells. Importantly, Trio(pY2681) correlates with significantly poorer prognosis of CRC patients after surgery.

These results indicate that Trio(pY2681) is one of the downstream effects by Notch signaling activation in CRC, and can be a prognostic marker, helping determine the therapeutic modality of CRC patients.

NAPOLEONE FERRARA

Regulation of Angiogenesis

Tumors consist of a wide variety of cell types, including normal host cells such as immune cells, fibroblasts and vascular endothelial cells, in addition to cancer cells. They communicate with each through a network of cytokines, chemokines and angiogenic factors. The development of a vascular supply within the tumor microenvironment is a critical step for cancer cells to survive and proliferate because blood vessels carry the necessary nutrients and oxygen. Vascular endothelial growth factor (VEGF) is one of the most important regulators of tumor angiogenesis, and it works not only as a mitogen of endothelial cells, but at least in some circumstances, also as a stimulant on cancer cells to proliferate, migrate and survive in the tumor microenvironment. Therefore, angiogenesis is an attractive therapeutic target for various types of cancer. Bevacizumab, an anti-VEGF antibody, and several VEGF pathway inhibitors, including the small molecule tyrosine kinase inhibitors sorafenib and sunitinib, are FDA-approved as therapy for multiple tumor types. We have been recently studying the mechanisms of resistance to anti-VEGF therapies in various tumor models. These studies indicate that multiple pro-angiogenic mechanisms may be implicated. We identified factors produced by myeloid cells and by fibroblasts as key mediators of angiogenesis. We also identified IL-17, a key product of Th17 Helper T cell, as a key factor mediating angiogenic escape and resistance to VEGF inhibitors. Efforts are ongoing to determine the translational and clinical significance of such findings.

Collaboration Update

MOTOKO YANAGITA

Crosstalk Inside the Kidney Determines Kidney Plasticity

Tubular injury and interstitial fibrosis are the hallmarks of chronic kidney disease (CKD) and the degree of these two features correlate with kidney prognosis. Previously we demonstrated that interstitial fibrosis and the reduction of erythropoietin (Epo) production in CKD are caused by the transdifferentiation of resident fibroblasts to myofibroblasts, however the trigger of this transdifferentiation remained unclear. Recently we generated a mouse strain expressing proximal tubule specific inducible form of Cre recombinase, Ndrg1CreERT2 mice, in which Cre is activated in proximal tubules by the administration of tamoxifen at the desired time point.

Using this mouse strain and another mouse strain expressing diphtheria toxin receptor under the control of Cre recombinase (iDTR mice), we generated a novel mouse model to induce proximal tubule-specific injury. Administration of high-dose diphtheria toxin (DT) faithfully causes severe proximal tubule-specific injury, associated with interstitial fibrosis and reduction of Epo production. Mild proximal tubule injury triggers reversible fibrosis, whereas repeated mild injuries cause sustained interstitial fibrosis, inflammation, glomerulosclerosis and atubular glomeruli. Proximal tubule-specific injury also triggers distal tubule injury, implying the proximal-distal tubule crosstalk. Our data provide new evidence that proximal tubule injury triggers several features of CKD. This work was done in collaboration with Prof. Kumar Sharma from UC San Diego. We are currently analyzing the role of fibrosis on tubular regeneration and would like to discuss our unpublished data in this joint symposium.

Session 3: Inflammatory Response – Its Regulation & Application

OSAMU TAKEUCHI

Targeting Posttranscriptional Regulators in Inflammation

Inflammation is initially evoked by the innate immune system in response to microbial infection and other cellular stresses. Proinflammatory cytokines produced by innate immune cells upon sensing of pathogens by Toll-like receptors (TLRs) are the mediators important for inflammation. The cytokine levels in innate immune cells are tightly controlled to prevent the development of septic shock and autoimmune diseases. The expression of genes involved in inflammation is controlled both transcriptionally and post-transcriptionally. Cytokine mRNAs tend to be degraded rapidly by a set of RNA binding proteins (RBPs) recognizing cis-elements such as AU rich elements and stem-loop structures present in the mRNA 3'-untranslated region (UTR). Among RBPs, Roquin recognizes stem-loop structures present in mRNAs encoding inflammatory proteins and degrades them by recruiting a CCR4-NOT deadenylase complex to its target mRNAs. Roquin-mutant mice spontaneously develop autoimmunity by elevated expression of ICOS on T cells and enhanced production of TNF in innate immune cells. We have identified Regnase-1 (also known as Zc3h12a or MCPIP1) as an RNA binding protein essential for degradation of inflammation-related mRNAs induced by TLR stimuli in innate immune cells. Regnase-1 is also critical for suppressing activation of T cells and maintenance of immune homeostasis in mice. Regnase-1 harbors an endonuclease activity to directly degrade immune response-related mRNAs such as IL-6 mRNA. Although both Regnase-1 and Roquin are critical for controlling cytokine mRNA degradation in innate immune cells, their mechanistic relationship has yet to be clarified. In the present study, we found that Regnase-1 and Roquin regulate an overlapping set of mRNAs via a common stem-loop structure. However, Regnase-1 and Roquin function in distinct subcellular locations: ribosome/endoplasmic reticulum and processing-body/stress granules, respectively. Moreover, Regnase-1 specifically cleaves and degrades translationally active mRNAs and requires the helicase activity of UPF1, similar to the decay mechanisms of nonsense mRNAs. In contrast, Roquin controls translationally inactive mRNAs, independent of UPF1. Defects in both Regnase-1 and Roquin in mouse cells lead to large increases in their target mRNAs, although Regnase-1 tends to control the early phase of inflammation when mRNAs are more actively translated. Taken together, our findings reveal that differential regulation of immune-related mRNAs by two RNA binding proteins, Regnase-1 and Roquin, depends on their translation status and enables elaborate control of inflammation. In this session, I will discuss mechanisms of posttranscriptional regulation of inflammation, and strategies for controlling inflammation.

DENNIS A. CARSON

Prevention and Treatment of Infectious Diseases and Cancer with Synthetic Toll-like Receptor Activators

The innate immune system is the first line of defense against infectious diseases and cancers. Pathogenic viruses and malignant tumors have mechanisms to avoid innate immune activation. To overcome this problem, our laboratory has synthesized specific activators of Toll-like Receptor 7 (TLR7) and TLR4, that potently activate innate immune cells in both mice and man. When used as an adjuvant for a universal influenza vaccine, a synthetic TLR7/4 drug combination induced quick and long-lasting protection against multiple strains of the virus. When delivered to the lungs as an immunotherapeutic, a TLR7 activating nanoparticle protected mice from lethal influenza challenge, and from infection with West Nile virus, a Flavivirus related to the Zika virus. In mouse models of head and neck cancer, breast cancer, and melanoma, the same drug inhibited tumor growth and metastasis without causing an inflammatory cytokine syndrome. The TLR7 agonist synergized with inhibitors of PD-1 and CTLA-4, without causing increased toxicity. These results indicate the diverse therapeutic potential of the new innate immune modulators, that are being advanced toward clinical trials.

Session 4: Innate Immune Cell-Targeted Immunotherapy

MARIPAT CORR

Dendritic Cells as a Target for Treatment of Autoimmune Diseases

Persistent inflammation has been implicated in the pathogenesis of diverse chronic inflammatory and autoimmune diseases such as rheumatoid arthritis, multiple sclerosis and diabetes. Pharmacologic manipulation of the immune system by targeting antigen presenting cells (dendritic cells) would be desirable to abate organ damage in different autoimmune diseases. The Toll-like receptor (TLR) family members are highly expressed on dendritic cells and are potential targets. These receptors respond to pathogen-associated molecular patterns, or PAMPs, which are released by bacteria and viruses. The TLRs can also sense endogenous ligands and have been implicated in perpetuating deleterious cascades in sterile inflammation. Although activation of TLRs contributes to the initiation and maintenance of chronic inflammation in autoimmune diseases, repeated exposure to a TLR agonist can induce hypo-responsiveness to subsequent TLR stimulation. Identifying agents capable of attenuating inflammation without increasing susceptibility to severe infection is an area of intense investigation. Hence, we have examined several series of small molecular weight synthetic compounds that are TLR agonists. Promising compounds were selected that at low doses reduced damage in murine autoimmune models, including arthritis, diabetes and multiple sclerosis. The activity of the compounds was not dependent on T or B lymphocytes, but did require bone marrow derived cells. Further ex-vivo experiments with ovalbumin (OVA) as a test antigen demonstrated the compounds limited the activation of bone marrow derived dendritic cells (BMDC) and attenuated their ability to stimulate an antigen specific recall response and did not directly affect the recall ability of T cells. In vivo and in vitro, the compounds only modestly limited dendritic cell surface expression of activation markers such as MHC class II, CD80, and CD86; however, the expression of negative regulatory molecules, such as programmed death ligand 1 (PD-L1) were markedly increased. Multiple mechanisms contributed to the reduction in dendritic cell activation including the up-regulation of two inhibitors of TLR signaling: Interleukin 1 Receptor Associated Kinase (IRAK) M, and Src homology 2 domain-containing inositol polyphosphate phosphatase (SHIP)-1. Pharmaceutical modulation of DC maturation and function in situ, thus represents an opportunity to treat autoimmune disease and might be a new therapeutic approach to subdue inflammation in autoimmune diseases.

KAYO INABA

Initiation and Regulation of Immune Responses by Dendritic Cells

Dendritic cells (DCs) are a member of leukocytes derived from hematopoietic stem cells and are known to play essential roles in the initiation and regulation of immune responses. They distribute not only in the body surface, such as the skin and various mucosal tissues, but also lymphoid as well as nonlymphoid organs. DCs patrol to find infectious and noninfectious agents in periphery and transport antigenic information to the draining lymphoid organs, where antigen specific lymphocytes are activated or inactivated by DCs. Crucial roles of antigen presenting cells in the induction of immune response were first revealed as adherent cells in spleen cell suspension at the time when in vitro culture system was established. In the beginning, macrophages were believed to be a responsible cell type, because of abundance in the body. Even after discovering DCs by Ralph Steinman, most researchers in the immunology field were skeptical to accept the idea that DCs capture and process antigens for presentation. However, development of cell and molecular biology along with development of new methods and the increase in knowledge on immunological phenomena have cleared and solved such queries, issues and controversial points. The important steps for appreciation of DC functions in immunology are 1) the understanding of DC maturation, 2) the recognition of DC potency to evoke specific immune responses not only in vitro but also in situ, and 3) establishment of a method to generate a large number of DCs from precursor cells.

I will give an overview of the advancement of DC research concerning histological aspects and discuss present and future subjects in clinical therapy as well as basic research.

Keynote Session

SHINYA YAMANAKA

Recent Progress in iPS Cell Research and Application

Induced pluripotent stem cells (iPSCs) can proliferate almost indefinitely and differentiate into multiple lineages, giving them wide medical application. Also, they can be made from various types of somatic cells. As a result, cell-based therapies, disease mechanisms and new drug development are being studied worldwide using iPSCs at an accelerated pace.

We are establishing technologies for the efficient generation of safe iPSCs. The original iPSCs were made from the retroviral transduction of four genes, Oct3/4, Sox2, c-Myc and Klf4. We have since reported an integration-free method using episomal vectors that does not cause chromosomal damage and proposed using L-Myc as an alternative to oncogenic c-Myc to reduce the risk of tumorigenicity. We have also developed a recombinant laminin-based matrix and developed a culture medium free of animal-derived constituents (xeno-free) to generate iPS cells that satisfy regulatory requirements for medical practice. Regarding quality control, we are innovating technologies to screen out low-quality iPSCs before use, which would expedite application for regenerative medicine.

In 2014, the world's first clinical study using iPSCs began for the treatment of age-related macular degeneration. iPSC studies have also made major progress for other disorders, giving expectation that iPSC-based regenerative medicine will be widely used in the near future. To push these efforts, we are proceeding with an iPSC stock project in which iPSC clones are being established from donors with a homologous HLA haplotype, which is associated with decreased immune response and therefore less risk of transplant rejection.

Other applications of iPSCs are drug screening, toxicity studies and the elucidation of disease mechanisms. Additionally, iPSCs may be resourceful for preventative measures, as they make it possible to predict the patient condition and provide a preemptive therapeutic approach. Finally, accumulating evidence is demonstrating the benefits of iPSCs in drug repositioning.

FRED H. GAGE

Modeling Human Psychiatric Diseases in Vitro

Although psychiatric disorders affect a number of brain regions to produce a complex array of clinical behavioral and cognitive symptoms, we hypothesize that basic phenotypes at the level of single neurons and simple networks may ultimately lie at the heart of these disorders. Being highly heritable, we hypothesize that these disorders are amenable to cell-based studies in vitro. Using induced pluripotent stem cell-derived neurons and/or induced neurons from fibroblasts, limitless numbers of live human neurons, can now be generated with a genetic background known to produce the disease state. Our prediction is that cell-based studies will ultimately contribute to our understanding of the initiation, progression and treatment of psychiatric disorders.

Session 1: In Vitro Disease Modelling and Epigenetics

BING REN

The 3-Dimensional Organization of Genomes

The 3-dimensional chromatin organization plays a critical role in gene regulation. Great strides have been made recently to characterize and identify cis regulatory elements from epigenome profiles in different cell types and tissues, but efforts have just begun to functionally characterize these long-range control elements. Mapping interactions between enhancers and promoters, and understanding how the 3D landscape of the genome constrains such interactions is fundamental to our understanding of genome function. I will present recent findings related to 3D genome organization in mammalian cells, with a particular focus on how chromatin organization contributes to transcriptional regulation. I will describe higher-order organizational features that are observed at the level of both the whole chromosome and individual loci. I will highlight changes in genome organization that occur during the course of differentiation, and discuss the functional relationship between chromatin architecture and gene regulation. Taken together, mounting evidence now shows that the genome organization plays an essential role in orchestrating the lineage-specific gene expression programs through modulating long-range interactions between enhancers and target genes.

ALYSSON R. MUOTRI

Modeling MeCP2 Disorders with iPSCs

We generated iPSC models to study the consequences of the Methyl CpG binding protein 2 (MeCP2) gene dosage in human neurons. Rett Syndrome (RTT), caused by loss of MECP2 function, is a severe neurodevelopmental disorder characterized by regression with loss of language and hand skill, and autistic features during regression. Interestingly, increased dosage of MeCP2 also results in a dramatic neurodevelopmental phenotype with onset at birth. Treatment for these disorders is entirely symptomatic: there are no curative or disease modifying therapies. We hypothesized that variation in MECP2 expression affects the transcriptional network of the cell, leading to defects in synaptogenesis and neuronal connectivity.

HARUHISA INOUE

Dissecting Neurodegenerative Diseases with iPSC Technology

Neural cells derived from iPS cells, which had previously been inaccessible, show promise for multiple purposes related to understanding disease mechanisms and treatment.

In neurodegenerative diseases, selective neurons are vulnerable and degenerate. The greatest risk for these diseases is aging, and every person faces this unavoidable risk. For the coming aging society, prevention and control of these diseases will be social imperatives. Various research efforts up to now have been contributing to advancing their outcome, including neuropathological findings, discoveries of causative genes with functional analysis, and the generation of model animals. However, solving the diseases still remains. To understand these diseases, analysis of the neural cells of the patients has been required. iPS cell technology is able to provide us with patient neural cells. Using these new materials, we are modeling the diseases, analyzing the disease markers for patient stratification, or cell transplantation research.

Session 1: In Vitro Disease Modelling and Epigenetics

HIROHIDE SAITO

Synthetic RNA Switches and Circuits to Detect and Purify Target Live Cells

The precise identification and purification of living cell types is critical to both study cell function and prepare cells for medical applications. However, intracellular information to distinguish live cells remains largely inaccessible. Here, we develop a method for high-resolution identification, separation, and purification of cell types by quantifying multiple microRNA (miRNA) activities in live cell populations. We designed synthetic mRNAs encoding a protein of interest tagged with target sequences of miRNAs. We found that a set of miRNA-responsive, in vitro synthesized mRNAs identify a specific cell population as a sharp peak and clearly separate different cell types based on less than two-fold differences in miRNA activities. These "miRNA switches" purified variety of target cells differentiated from human pluripotent stem cells with high efficiency, accuracy, and safety. In addition, the miRNA switches encoding an apoptosis inducer Bim automatically enriched the target cells without cell sorting. I will also explain synthetic RNA circuits to control mammalian cell fate based on miRNA activities. Our RNA switches and circuits can detect and purify desired cell types for which other isolation strategies are unavailable.

Session 2: Cell and Tissue Differentiation and Behavior

JUAN CARLOS IZPISUA BELMONTE

Crossing Xeno-Barriers: The Hidden Dimension of Distinct Flavors of Pluripotency

Embryonic pluripotency can be recapitulated in vitro by a spectrum of pluripotent stem cell states captured by different synthetic niches. Their distinct spatio-temporal characteristics provide an unprecedented tool towards the study of early human development as well as evolution. The newly unveiled ability of some stem cell types to cross xeno-barriers will facilitate the generation of cross-species chimeric embryos from distant species, including humans. When combined with efficient zygote gene editing technologies, xenogeneic human pluripotent stem cells may also open new frontiers for regenerative translational medicine applications including the possibility of generating human organs in animals via interspecies chimeric complementation.

KELLY A. FRAZER

Genetic Determinants of Gene Expression in a Collection of 215 Human iPSCs

In this study, we examined gene expression regulation in a collection of 215 human induced pluripotent stem cells (iPSC). We systematically reprogrammed fibroblasts from a diverse set of 215 individuals and performed transcriptome sequencing for the iPSC as well as germline whole genome sequencing (WGS). Using these data, we identified 5,628 genes with expression quantitative loci (eQTL) including 80 genes whose lead variant was a biallelic copy number variant (CNV). We also identified 98 genes whose expression was associated with multi-allelic CNVs. Transcription factor binding sites for NANOG, SP1, JUND, and JUN were highly enriched for disruption by lead eQTL variants implicating these factors as important regulators of gene expression in iPSCs. We used various functional genomics data sets to fine map putative causal eQTL variants and found variants that disrupt transcription factor binding sites for 2,388 genes. Additionally, we used allele specific expression to investigate the rate of X chromosome reactivation after reprogramming and showed that it is heterogeneous across the X chromosome and correlated with XIST and TSIX expression. We also found evidence that imprinting can be retained in iPSCs suggesting that reprogramming does not completely erase imprinting. This work defines key regulators of gene expression in iPSCs, provides information on the heterogeneity of X reactivation after reprogramming, and helps define the role of CNVs in the regulation of gene expression.

Dan S. Kaufman

Anti-Cancer Therapies Derived from Human Pluripotent Stem Cells

Adoptive transfer of anti-tumor lymphocytes has been rapidly gaining increased interest in cancer therapeutics. Human natural killer (NK) cells are a promising source of lymphocytes for anti-cancer immunotherapy. NK cells are part of the innate immune system and exhibit potent anti-tumor and anti-viral activity without need for HLA matching and without prior antigen exposure. Clinical trials using allogeneic NK cells isolated from peripheral blood demonstrate efficacy against chemotherapy-refractory tumors, mainly acute myelogenous leukemia. Derivation of NK cells from pluripotent stem cells could provide an unlimited source of lymphocytes for “off-the-shelf” therapy. We have developed a two-stage culture system to efficiently produce NK cells from human embryonic stem cells (hESCs) and induced pluripotent stem cells (iPSCs) that does not require cell sorting and without need for xenogeneic stromal cells. This approach combines hematopoietic organoid formation using defined conditions and membrane-bound IL21-expressing artificial antigen presenting cells to produce mature and functional NK cells from several different hESC and iPSC lines. While different hESC/iPSC lines had varying efficiencies in hematopoietic development, all cell lines could produce functional NK cells. The hESC/iPSC-derived NK cells have phenotype and function similar to NK cells isolated from peripheral blood. This includes potent anti-tumor and anti-viral activity both in vitro and in vivo. These methods can be used to generate enough cytotoxic NK cells to treat a single patient from less than 250,000 input hESCs/iPSCs. More recent studies demonstrate that hESCs/iPSCs can be stably engineered to express chimeric antigen receptors (CARs) to derive NK cells able to better target and kill more refractory tumors. Other cellular engineering studies to enhance anti-tumor activity of hESC/iPSC-derived NK cells are in progress. We now aim to translate these hESC/iPSC-derived NK cell to clinic trials to provide a novel standardized strategy to better treat and potentially cure refractory cancers and chronic viral infections.

Session 3: Clinical Application of Cell Replacement-Based Therapies

JUN TAKAHASHI

Challenges Towards Stem Cell-Based Therapy for Parkinson's Disease

Human embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs) can provide a promising source of midbrain dopaminergic (DA) neurons for cell replacement therapy for Parkinson's disease (PD). To evaluate safety and efficacy of the human ESC-derived DA neurons, we induced neural progenitor cells from human ESCs by a modified SDIA (stromal cell-derived inducing activity) method. When the cells were transplanted into the bilateral striatum of monkey models of PD, they did not form tumors and survived as DA neurons as long as 12 months proved by immunofluorescence and PET studies. In addition, the monkeys showed behavioral improvement after 3 months post-transplantation. We also generated DA neurons from human induced pluripotent stem cells (iPSCs) without feeder cells, and confirmed that these cells could survive as long as 6 months in the monkey brain. These results support the idea that human ESCs/iPSCs can be used as a source for cell replacement therapy of PD. However, ESC/iPSC-derived donor cells may inevitably contain tumorigenic or inappropriate cells. Therefore, as a next step, we have developed a method for 1) scalable DA neuron induction on human laminin fragment and 2) sorting DA progenitor cells using a floor plate marker, CORIN. The grafted CORIN+ cells survived well and functioned as midbrain DA neurons in the 6-OHDA-lesioned rats, and showed minimal risk of tumor formation. For the clinical application of iPSCs, the scalability and reproducibility of the donor cell preparation is critical. These results suggest that our strategy is advantageous in terms of scalability, safety and efficiency, and can be applied to the cell replacement therapy for Parkinson's disease. The sorting of DA progenitor cells is favorable in terms of both safety and efficacy of the transplantation, and we have now established a protocol for the clinical application of human iPSCs to treat Parkinson's disease.

CARL K. HOH

Quantitative Measurements of Biologic Processes with PET

Positron emission tomography (PET) involves the intravenous injection of a trace amount of radiopharmaceutical that closely resembles a biologic molecule. The PET scanner acquires a volume of transaxial images where the image pixel intensity is proportional to the regional radiopharmaceutical concentration in the tissues. If the images are acquired in a dynamic mode, then the temporal changes in tissue radiopharmaceutical concentration can be used in various mathematical techniques for modeling the underlying pharmacokinetic processes at the cellular or receptor level.

In the study of Parkison's disease, there are several radiopharmaceuticals that have been used to help elicit the underlying disorders in the dopaminergic and non-dopaminergic systems in the pre and post synaptic regions.

Dopaminergic presynaptic activity of aromatic amino acid decarboxylase can be performed with 18F-6-fluoro-L-DOPA (18F-DOPA), which gets converted to 18F-dopamine. The striatal uptake of 18F-DOPA follows a tracer kinetic model allowing in-vivo estimation of the rate of cellular decarboxylase activity. 18F-DOPA PET has been used to monitor the outcome of striatal graft transplantation. The presynaptic dopamine uptake transporter (DAT) can be image with either PET or SPECT radiolabeled tracers, such as 18F-CFT or 123I-ioflupane (DATscan). The dopaminergic postsynaptic system can be imaged with a D2 receptor antagonist, 11C-raclopride. A two-scan raclopride PET procedure has been reported to show the effect of dopamine on the striatal D2 receptors with oral dopamine therapy.

The non-dopaminergic involvement in Parkinson's has been studied with 11C-DASB, a radiotracer which binds specifically to the serotonin transporter (SERT, 5-HTT) in the presynaptic terminals. Recent studies demonstrate decreased 11C-DASB uptake in various brain structures suggesting a serotonergic dysfunction in Parkinon's disease. 11C-DASB imaging of graft induced dyskinesias has lead to the suspicion of excessive sertonertic innervation in the grafted striatum and that serotonin terminals possess the ability to convert L-DOPA to dopamine.

MARTIN MARSALA

Spinal Cell-Replacement Therapies for Treatment of Spinal Traumatic Injury: An Update

In previous experimental studies, we have demonstrated a functional-treatment effect after spinal grafting of GMP grade human fetal spinal cord-derived neural precursors in a rat model of traumatic spinal cord injury. This functional improvement corresponded with robust cell engraftment, neuronal differentiation, axonal sprouting, and development of putative synaptic contacts with the persisting host neurons. Using the same clinical grade neural precursors grafted spinally in naïve non-injured pigs, we have also demonstrated long-term safety and defined the optimal cell injection dose to be used in future human clinical trials. The currently ongoing human clinical trial (UC San Diego) in patients with chronic spinal cord injury receiving a direct spinal injection of neural precursors shows that multiple spinal grafts are well tolerated and show no detectable functional side effects at intervals up to 1 year after cell grafting. These data show the feasibility of cell-replacement-based therapy for treatment of trauma-induced spinal cord injury in humans.

CATRIONA H. JAMIESON

Role of RNA Editing in Leukemia Stem Cell Evolution

Recently RNA editing, particularly in the context of primate specific Alu sequences that represent 10% of the human genome, has emerged as an important arbiter of human transcriptomic diversity by introducing novel splice acceptor sites, editing 5' and 3' UTR sequences and modulating mRNA, microRNA and long non-coding RNA stability. As the most abundant human RNA editing enzyme, adenosine deaminase associate with RNA (ADAR) is usually activated in stem cell populations during embryogenesis or as a component of an innate anti-viral immune response in hematopoietic stem cells. While ADAR-mediated adenosine to inosine (A-to-I) RNA editing likely evolved to prevent propagation of RNA viruses in primitive stem cell populations, cumulative RNA sequencing analyses show that ADAR activation contributes to therapeutic resistance and relapse of a broad array of human malignancies. Recently, we discovered that ADAR1 activation enhances malignant reprogramming of chronic myeloid leukemia (CML) progenitors into self-renewing cancer stem cells by inducing missplicing of GSK3b thereby preventing b-catenin degradation. Convergence of BCR-ABL1 and JAK2/STAT signaling on ADAR1 activation disrupts the let-7/LIN28B self-renewal axis by impairing let-7 biogenesis in an editase dependent manner thereby further enhancing the self-renewal potential of CML progenitors. Dual inhibition of JAK2 and BCR-ABL1 restored let-7 biogenesis and reduces cancer stem cell self-renewal both in vitro and in humanized mouse models of CML. Together these studies suggest that inhibition of ADAR1 activation may represent a key component of clinical strategies aimed at eradicating cancer stem cells that contribute to both therapeutic resistance and relapse.

Keynote Session

GEORGE R. TYNAN

Energy Challenges and Fusion Research

Access to adequate sources of clean, low-carbon energy sources is critical for sustaining human development and providing a good quality of life for all of humanity in the 21st century. Nuclear fusion has long been put forward as a possible technological solution to this need, but progress has been slow. This talk will introduce the challenge and promise of controlled fusion as an energy source, review the current status of the magnetic and inertially confined approaches to fusion energy, and summarize the open issues that must be resolved if fusion is to ever become a practical energy source. The talk will then look at recent progress in other clean energy technologies such as advanced nuclear fission and renewables, discuss prospects for those technologies, and look at their ability to provide a significant fraction of global energy demand in the coming decades. Finally, given the status of these other energy technologies, the talk concludes with a few speculations on the viability of fusion as a practical energy technology.

SATOSHI KONISHI

Fusion Energy and its Future Deployment

Institute of Advanced Energy, Kyoto University has started plasma confinement experiment in 1959, and is one of the first fusion research facilities in Japan. Although significant progress was been made since then, the commercialization of fusion energy is expected around the middle of this century. This talk overviews the possible deployment scenario of fusion based on the analysis of the future energy system considering sustainability aspects, and introduce a viable strategy for fusion contribution to the sustainable energy systems.

While stable large scale electricity grid is common in the industrialized countries, majority of the electricity market in this century would be in developing countries with grids far smaller than 100GW. Difficulty is anticipated in accommodating fusion that requires large starting power from the grid and would induce an instability in an unexpected shut down event such as plasma disruption. Also the future grid would be more vulnerable due to the larger fraction of renewables and nuclear, both do not respond to the change of demand. Free electricity market with dual directional power flow without the single strong controller of the grid will make the stabilization more difficult. Criteria for fusion introduction was numerically analysed and expressed as the multi-dimensional function of grid size, composition, and the generation capacity of fusion plant. Typical 1GW fusion plant will have a difficulty in most of the cases. An innovative concept of electricity storage that will make the impact of fusion will be addressed as a mitigation.

This study also introduces the biomass-fusion hybrid concept developed by the authors. Waste biomass (typically cellulose and lignin) can be converted to CO and hydrogen gas by the endothermic reaction at high temperature and the measured efficiency was above 90%. Gaseous products can further be converted to either hydrogen or diesel equivalent substituting fossil fuel. Because of the high energy efficiency without thermal cycle and the assistance of biomass chemical energy, requirements for fusion energy balance so called “Lawson Criteria” can be relaxed by this energy multiplication. Market of fuel is much larger than electricity in the total energy consumption, and unlike in the case of electricity generation where renewable and nuclear are available, almost all the fuels are carbon emitting fossil. Substituting fossil with carbon neutral biofuel is effective in reducing carbon dioxide emission. At the same time, providing fuels from fusion energy to dispersed electricity sources such as fuel cells makes local grids to be cleaner and more stable. For fusion introduction, above mentioned difficulty to connect small size grid is avoided, and large contribution to the primary energy supply for future sustainable world can be expected.

Finally, environmental impact analysis of fusion by tritium emission will be presented, and possible social acceptance issue after Fukushima, and its possible mitigation strategy will be suggested.

Session 1: Solar Energy and Energy Materials

CARLOS F. COIMBRA

Resource and Power Forecasting for Large Scale Solar Plants

Integration of variable energy resources into the power grid requires advanced knowledge of both the availability of and the demand for power. My research group at UC San Diego is the world's leading developer of forecasting engines for solar power integration, with a particular interest in large-scale solar plants. In this talk, I will show some of the methods used to ingest large amounts of data from local telemetry, remote sensing and numerical weather prediction, and how to use these data sets to develop stochastic learning forecasting engines that are able to predict solar irradiance, power output and load demand for a wide variety of temporal horizons.

HIROSHI SAKAGUCHI

New Carbon-nanowires for Energy Utilization

Carbon-based nanowires, called graphene nanoribbons (GNRs) having a 1D graphitic structure are of great interest in materials science not only for their fundamental aspects but also for their potential applications. They also have a large potential to be applied to energy-related fields such as photovoltaics and electronic devices with low energy consumption. One of the main challenges in this field is the fabrication of new GNRs with the desired edge structures and widths, because theory has predicted that the armchair-edged GNRs would provide a nice semiconductor performance, whereas zigzag-edged GNRs would become the excellent carbon-based spin-devices due to significant low spin-orbit coupling. Surface-assisted synthesis of GNRs categorized in the bottom-up fabrication process, has attracted much attention because it is capable of synthesizing the various types of GNRs by the chemical reactions of designed precursors on the metal surface. This synthetic method is believed so far to be based on "heterogeneous catalysis," which it exploits the electronic interactions between the precursor and the metal surface, resulting in the acceleration of the chemical reactions such as dehydrogenation into GNRs. Recently, we demonstrate a totally new principle of "conformation-controlled heterogeneous catalysis" in which the transformation of precursors on metal surface can accelerate the chemical reactions into novel GNRs. We discovered our designed "Z-bar-linkage" precursor molecule could transform into a special asymmetrical conformation on a 2D surface, and can afford self-assembled homochiral polymers with a special planar conformation by our developed 2-zone chemical vapor deposition technique, followed by efficient step-wise dehydrogenation to form the new type of GNRs having a wide width. These unprecedented findings of "conformation-driven heterogeneous catalysis" which is analogous to the optimization algorism in nature, present a new concept of creating new nanocarbon materials that has never been reported so far.

Session 2: Energy Storage

PING LIU

Energy Storage Innovation for Vehicle and Grid Applications

Rechargeable batteries have enabled the emerging revolution in electric vehicles and grid storage. However, continued improvements in performance, life, safety, and cost effectiveness are still needed. We will analyze the fundamental limitations of state of the art lithium-ion batteries and outline opportunities in cell chemistry, architecture, and system design for next generation batteries. Highlighted technologies include batteries with aqueous and solid state electrolytes as well as multifunctional batteries which can simultaneously serve energy storage and other system functions.

TOSHIYUKI NOHIRA

Sodium Secondary Batteries Using Amide Ionic Liquid Electrolytes

Sodium secondary batteries are now attracting much attention mainly as a candidate for large-scaled secondary battery owing to abundant sodium resource and expected high performance. We have developed several FSA-based (FSA: bis(fluorosulfonyl)amide) ionic liquids for sodium secondary battery electrolytes. Since, these ionic liquids have high thermal stabilities, high ionic conductivities, and wide electrochemical windows, the development of safe and high-performance sodium batteries is well expected. First, we developed Na[FSA]-K[FSA] inorganic ionic liquids, and reported the performances of $NaCrO_2$ positive electrode and several tin-based negative electrodes. Secondly, we developed several organic-inorganic hybrid ionic liquids such as Na[FSA]-[C3C1pyrr][FSA] (C3C1pyrr: N-methyl-N-propylpyrrolidinium) and Na[FSA]-[C2C1im][FSA] (C2C1im: 1-ethyl-3-methylimidazolium). We also confirmed excellent cycle performances, rate capabilities, and wide operating temperatures for batteries using the Na[FSA]-[C3C1pyrr][FSA] ionic liquid as an electrolyte and a $NaCrO_2$ positive electrode. In this ionic liquid, hard carbon (HC) negative electrodes also exhibited very good cycle performances, rate capabilities, and wide operating temperatures.

In this presentation, we explain the fundamental charge-discharge characteristics of $NaCrO_2$ positive electrodes and HC negative electrodes in Na[FSA]-[C3C1pyrr][FSA] ionic liquids using coin-type half-cells at 273-363 oK. Then, we also present the full cell performance, including the long-term cycle life, of a 1.5 mAh HC/$NaCrO_2$ coin-type cell over the temperature range of 273–363 oK. Finally, we describe the performance of a large-sized prismatic full cell with a capacity of 27 Ah.

Session 3: Ultrafast Phenomena

Y. SHAYA FAINMAN

Ultrafast Processing with Nanophotonics

Various future system applications that involve photonic technology rely on our ability to integrate it on a chip to augment and/or interact with other signals (e.g., electrical, chemical, biomedical, etc.). For example, future computing and communication systems will need integration of photonic circuits with electronics and thus require miniaturization of photonic materials, devices and subsystems. Another example, involves integration of microfluidics with nanophotonics, where former is used for particle manipulation, preparation and delivery, and the latter in a large size array form parallel detection of numerous biomedical reactions useful for healthcare applications. To advance the nanophotonics technology we established design, fabrication and testing tools. The design tools need to incorporate not only the electromagnetic equations, but also the material and quantum physics equations to include near field interactions. These designs are integrated with device fabrication and characterization to validate the device concepts and optimize their performance. Our research work emphasizes the construction of passive (e.g., engineered composite metamaterials, filters, etc.) and active (e.g., nanolasers) components on-chip, with the same lithographic tools as electronics. In this talk, we discuss some of the passive metamaterials and devices that recently have been demonstrated in our lab. These include our recent results on nanoscale engineering optical nonlinearities with SOI material platform and design, fabrication and testing of nanolasers constructed using metal-dielectric-semiconductor resonators confined in all three dimensions.

TAKASHI NAKAJIMA

Discovering a New Aspect of Laser-Nanobubble Interactions

Intense studies on the nanoparticles (NPs) in recent years have brought us a lot of interesting phenomena in many fields. In many cases the surrounding medium of NPs is a solution (usually water), and the plasmonic heating of metallic NPs by the irradiation of resonant laser results in the formation of nanobubbles (NBs). It is usually called plasmonic NBs, since NBs are produced by the plasmonic heating of NPs. The dynamics of NPs and NBs depend not only on the incident laser fluence but also the laser wavelength, pulse durations, etc. Until now, however, very little attention has been paid to the number density of NPs in the solution. It is as if there is a wide belief in the community that the number density of NPs in the solution does not play any important role.

In this paper we investigate the time-dependent dynamics of plasmonic NBs upon irradiation of single nanosecond laser pulses onto the Ag NPs solution, and show that the growth speed and the size of plasmonic NBs strongly depends on the number density of NPs. This phenomenon cannot be explained by the commonly accepted physical picture, and we propose a new model in which the bubble growth is strongly influenced by the pressure waves produced by the surrounding NPs. To justify the validity of this new model, we perform the numerical calculations by solving the Rayleigh-Plesset equation, which is commonly used to study the dynamics of cavitation bubbles, with an additional time-varying external pressure term, and obtain the good agreement with our experimental results. Similar effects should be found for other kind of NPs regardless of the pulse duration (fs, ps, and ns). Our findings indicate that the number density can serve as a new doorknob to control laser-NBs/NPs interactions.

Session 4: The Future of Energy

DAVID G. VICTOR

A Decentralized Future for the Electric Power System?

For decades the electric power industry has been grounded in the logic of central power stations connected to customers via large transmission and distribution networks. That model may now be changing with the advent of new technologies that allow a larger role for distributed generation as well as new regulatory and business models aimed at accelerating that transition. Still, the ratio of bold talking about transformation in the power industry to actual transformation remains high. This talk will focus on one dimension of that change—the possible rise of microgrids—and present new UC San Diego research on the business and financial viability of microgrids in different configurations. We find that while much of the popular attention to microgrids is rooted in the potential for expanded use of renewables as well as consumer demand response, the core business logic for microgrids in the United States is based on the potential for expanded use of natural gas. Whether that shift will make it easier or harder to cut emissions from the electric power system overall remains an area of intense ongoing investigation.

SEIICHI OGATA

Expanding Renewable Energy in Japan: Research Progress and Anticipated Solutions from Kyoto University

Japan experienced the Great East Japan Earthquake and Tsunami on March 11, 2011. The Tsunami subsequently caused the Fukushima Nuclear Plant Accident. This changed the energy situation dramatically in Japan, as the Nuclear Plant Accident revealed various problems in the electricity sector.

Although future energy planning and related discussions have been quite chaotic, the necessity to diversify Japan's energy mix and increase the role of renewable energy has been recognized by many.

In August 26, 2011, the Diet passed the Act on Special Measures concerning the Procurement of Renewable Electric Energy by Operators of Electric Utilities (the FIT Act). Under this new FIT Act, the electricity power companies (EPCOs) are obligated to purchase solar, wind, hydro, geothermal, and biomass generated electricity at prices to be set by the METI (Ministry of Economy, Trade and Industry). The act took effect on July 1, 2012. (The FIT Procurement Price Calculation committee chairman: Prof. Kazuhiro Ueta, Graduate School of Economics, Kyoto University).

Newly certified renewable energy capacity soared in March 2013, reaching 23GW by the end of June 2013. The most remarkable growth was seen in the certification of non-residential PV, but wind power and biomass have also shown steady growth.

Out of such certified capacity, 1.8GW actually started operation in 9 months since July 2012 (when FIT started in Japan) till the end of FY2012 (March 2013). RE power plants, especially Non-residential PV started accelerating in April-June 2013, adding 1.9GW in 3 months and leading the total RE operating capacity to 3.7GW by the end of June 2013. It is expected to grow even more rapidly.

Session 5: Fusion

FARHAT N. BEG

Why Do We Need an Advanced Inertial Fusion Energy Concept?

The Fast Ignition (FI) concept for Inertial Confinement Fusion has the potential to provide a significant advance in the technical attractiveness of Inertial Fusion Energy. In the fast ignition (FI) scheme of inertial confinement fusion (ICF), compression of the fuel to high density and heating are achieved in separate processes. Similar to conventional ICF, a number of long pulse lasers can be used to compress the fuel shell to create high density plasma. Subsequently, a high energy (over 100 kJ), high intensity (over 1020 W/cm2), short (~10 ps) laser pulse is used to create high-energy (MeV) particles: electrons or ions, which then heat the compressed fuel plasma to initiate ignition. The requirements on the symmetry of the target are less stringent in FI compared to conventional ICF due to the external heating source. In addition, higher gain is expected with the FI scheme because more fuel mass can be assembled with less compression energy.

This scheme involves some of the most challenging and complex physics of laser-matter interactions and energetic particle transport in varying density plasmas. In recent experiments and modeling, critical issues related to electron source, transport through plasma and target design have been identified. In this talk, these issues will be discussed and a path forward will be proposed.

SHINICHIRO KADO

Topical Studies on Plasma-Material Interactions with MAP-II Linear Divertor Simulator and Heliotron J

Plasma facing components (PFCs) in magnetic fusion-relevant toroidal devices, such as tokamak and stellarator/heliotron, encounter a significant amount of particle and heat fluxes. Producing recombining plasma in the volume of divertor/edge region, known as “divertor detachment”, can function as a sink of these fluxes due to the neutralization of the plasma before reaching the divertor plate. However, determining the appropriate parameters from the spectroscopy or from the particle measurements includes many difficulties.

We have measured the electron temperature far below 1 eV in the detached plasma in MAP (material and plasma)-II linear divertor simulator in the University of Tokyo using the laser Thomson scattering (LTS) system. Also, we have proposed a novel Doppler-Stark spectrometry for atomic/ionic temperature in which the line profiles of several atomic helium spectra (He I) are analyzed, i.e. the lines from 31P, 71P and 73D.

In the detached plasma for helium discharge in MAP-II, the temperature of the electrons, ions and atoms became close to each other, suggesting the achievement of the thermal equilibrium. In the ionizing plasmas, on the other hand, the temperature of the excited states of the atomic helium was revealed to be dependent on the states, exhibiting the disequilibrium feature.

Heliotron J in Kyoto University is a medium-sized helical-axis heliotron device (major radius R0 = 1.2 m, minor radius a = 0.1-0.2 m, and magnetic field at the magnetic axis B0 ≤ 1.5 T). The divertor region is kept “open” without a baffle plate to compress the neutral gas, i.e. basically the “attached” condition.

PFCs in Heliotron J are cleaned by main plasma discharges. In order to monitor the long-term progress in the conditioning of the PFCs, vacuum ultraviolet (VUV) spectroscopy is applied to the line spectra of highly charged ions such as Fe, Cr, Ti, O, and C in the wavelength of 17 - 39 nm.

SPEAKERS & SESSION CHAIRS

Speakers & Session Chairs

FARHAT N. BEG

Professor, Department of Mechanical & Aerospace Engineering, UC San Diego

Farhat Beg is the Director of the Center for Energy Research and Professor at the UC San Diego Jacobs School of Engineering. Farhat Beg received the Ph.D. degree in plasma physics from Imperial College, London in 1995. In 2003, he joined the faculty at the Department of Mechanical and Aerospace Engineering, UC San Diego. He has been a fellow of the American Physical Society since 2009 and the Institute of Electronics and Electrical Engineers (IEEE) since 2011. Farhat Beg is the recipient of the IEEE Early Career Award and the Department of Energy Junior Faculty Award. He has published over 200 articles in refereed journals and conference proceedings including, Nature, Nature Physics, Nature Communications, and Physical Review Letters among others. His research interests include ultra high intensity laser matter interactions, inertial confinement fusion, astrophysical plasmas and bright x-ray sources.

DAVID A. BRENNER

Vice Chancellor, Health Sciences, UC San Diego

David Brenner is Vice Chancellor for Health Sciences and Dean of the School of Medicine at UC San Diego. In this role, he leads the School of Medicine, Skaggs School of Pharmacy and Pharmaceutical Sciences at UC San Diego, and UC San Diego Health System. Dr. Brenner has oversight of more than 1,300 faculty physicians, pharmacists and scientists; 7,500 staff; more than 750 medical and pharmacy students, and a health system that cares for approximately 125,000 patients annually. Dr. Brenner first joined UC San Diego in 1985 as a gastroenterology fellow, later joining the School of Medicine faculty, and serving as a physician at the Veterans Affairs (VA) San Diego Healthcare System. He was ultimately recruited to UC San Diego from the Columbia University College of Physicians and Surgeons, where from 2003 to 2007 he was Samuel Bard Professor, chair of the Department of Medicine, and physician-in-chief of New York Presbyterian Hospital/Columbia.

SANDRA A. BROWN

Vice Chancellor, Research, UC San Diego

Sandra Ann Brown, Professor of Psychology and Psychiatry, was named the Vice Chancellor for Research at UC San Diego in December 2010. She oversees the Office of Research Affairs, which is charged with creating opportunities, enhancing the research experience, developing tools and training to improve research administration, and supporting and promoting university innovations. Under her leadership, UC San Diego has achieved yearly billion-dollar investments in research and has maintained the university's top-five ranking as one of the nation's premier public research universities. She has also overseen a major transformation of research-related processes, saving researchers valuable resources and time in a competitive funding environment.

DENNIS A. CARSON

Professor Emeritus, Department of Medicine, UC San Diego

Dr. Dennis Carson has spent his career discovering new targets and developing therapeutics in the fields of oncology, autoimmune, and infectious diseases. At the Scripps Clinic for 14 years, he developed the drug cladribine from bench to bedside for the effective treatment of hairy cell leukemia, as well as two approved clinical diagnostic agents, advancing to become head of the clinical immunology division. He directed the Stein Institute for Research on Aging for 13 years, and then the Moores Cancer Center for eight years. Dr. Carson also co-founded several biotechnology companies in the vaccine and oncology areas (Vical, Triangle, Dynavax, Salmedix, Samumed) that successfully developed new drugs. At this stage in his career, he applies his expertise and experience to help younger basic and clinical scientists in the difficult process of drug discovery and development.

CARLOS F. COIMBRA

Professor, Dept of Mechanical & Aerospace Engineering, UC San Diego

Dr. Coimbra received his PhD in Mechanical and Aerospace Engineering from UC Irvine. He joined the Jacobs School of Engineering at UC San Diego in July of 2011, and is now the Co-Director of the UC San Diego Center for Excellence in Renewable Resource Integration (CERRI) and an Associate Director of the Center for Energy Research (CER) at UC San Diego. Professor Coimbra explores the intersection between experimental, theoretical and fieldwork methods to analyze and develop new technologies to harvest solar power in its diverse forms (direct, wind, hydro-potential, and others).

MARIPAT CORR

Professor, Department of Medicine, UC San Diego

Maripat Corr, MD is a trained rheumatologist and research immunologist. She received her medical degree from the University of North Carolina, Chapel Hill and pursued further training in internal medicine at UC San Diego. Afterward, she was a fellow at the National Institutes of Health in the Laboratory of Immunology. She then completed her clinical training in rheumatology at UC San Diego and joined the faculty. She is currently the rheumatology section head, serves on the American College of Rheumatology Division Director's Committee and is a liaison for the ACR Government Affairs Committee.

Y. SHAYA FAINMAN

Distinguished Professor, Electrical & Computer Engineering, UC San Diego

Dr. Fainman received a PhD from Technion – Israel Institute of Technology in 1983. He is Cymer Professor of Advanced Optical Technologies and Distinguished Professor of ECE at the UC San Diego. His current research involves near field optical science and technology, nanophotonics, nanolasers, nanoiplasmonics and ultrafast optics. He is a Fellow of OSA, IEEE, and SPIE. He is a recipient of the Miriam and Aharon Gutvirt Prize, Technion, Haifa, Israel (1982), Lady Davis Fellowship (2006), Brown Award (2006), Gabor Award (2012) and E. Leith Medal (2015).

NAPOLEONE FERRARA

Distinguished Professor, Department of Pathology, UC San Diego

Dr. Napoleone Ferrara is Distinguished Professor of Pathology and a Distinguished Adjunct Professor of Ophthalmology in the School of Medicine at UC San Diego. The main research theme of his lab is the regulation of angiogenesis (the formation of new blood vessels). In 1989, they reported the isolation and cDNA cloning of vascular endothelial growth factor (VEGF). He is presently focusing on investigating mechanisms of tumor angiogenesis alternative to VEGF, in particular the role of the microenvironment and of factors produced by immune cells and fibroblasts in resistance to VEGF inhibitors. Among his many awards is the 2013 Life Sciences Breakthrough Prize. In 2015, Professor Ferrara was elected to the National Academy of Medicine.

Speakers & Session Chairs

KELLY A. FRAZER

Professor, Department of Pediatrics, UC San Diego

Dr. Frazer is Professor and the Founding Chief of the Division of Genome Information Sciences in the Department of Pediatrics, and Director of UC San Diego's Institute for Genomic Medicine. A large part of the Frazer laboratory is involved in the NextGen Program of the National Human Genome Research Institute (NHGRI) and the Heart, Lung, and Blood Institute (NHLBI), which is aimed at generating and utilizing iPSC to investigate the biological mechanisms underlying disease association with genetic variants. Dr. Frazer's laboratory has specifically been funded to link cardiac molecular phenotypes to genotypes through the generation of iPSC-derived cardiomyocytes from 222 individuals in the CARDiPS collection.

FRED H. GAGE

Adjunct Professor, Department of Neurosciences, UC San Diego

Fred H. Gage, PhD, a Professor in the Laboratory of Genetics, joined The Salk Institute in 1995. He received his PhD in 1976 from The Johns Hopkins University. Dr. Gage's work concentrates on the adult central nervous system and unexpected plasticity and adaptability to environmental stimulation that remains throughout the life of all mammals. In addition, he models human neurological and psychiatric disease in vitro using human stem cells. Prior to joining Salk, Dr. Gage was a Professor of Neuroscience at UC San Diego.

LAWRENCE S. B. GOLDSTEIN

Distinguished Professor, Cellular & Molecular Medicine, UC San Diego

Dr. Goldstein is Distinguished Professor in the Departments of Cellular and Molecular Medicine and Neurosciences at UC San Diego, as well as Director of the UC San Diego Stem Cell Program, Scientific Director of the Sanford Consortium for Regenerative Medicine, and Director of the Sanford Stem Cell Clinical Center. His research is focused on understanding the molecular mechanisms of intracellular transport in neurons and how transport failures may lead to neurodegenerative diseases. Current projects use human stem cells to understand and treat AD, Niemann-Pick Type C, and ALS.

CARL K. HOH

Professor, Department of Radiology, UC San Diego

Dr. Carl Hoh has a background in chemical engineering and was involved in the development of the whole body PET technique. His area of research has been in the development and clinical application of various software tools for the analysis of nuclear medicine and dynamic PET image data: Tracer kinetic modeling, Logan analysis, Patlak analysis, factor analysis, independent component analysis, and multimodality image co-registration.

EDWARD W. HOLMES

President, Sanford Consortium for Regenerative Medicine

Dr. Holmes was appointed Vice Chancellor for Health Sciences and Dean of the School of Medicine at UC San Diego in 2000 and served in this role until October 2006. He is currently a Distinguished Professor of Medicine, Vice Chancellor/Dean of Health Sciences Emeritus at UC San Diego, and CEO/President of the Sanford Consortium for Regenerative Medicine. Dr. Holmes became the Executive Deputy Chairman of the Biomedical Research Council and the Executive Chairman of the National Medical Research Council in Singapore in October 2006. He also holds an appointment as the Lien Ying Chow Professor of Medicine at the Yong Loo Lin School of Medicine, National University of Singapore.

KAYO INABA

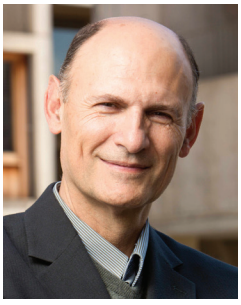
Executive Vice-President, Kyoto University

Dr. Inaba served as Dean of the Graduate School of Biostudies from April 2003 to March 2005, and Director of the Center for Women Researchers in Kyoto University from October 2007 to March 2014. Dr. Inaba received her doctorate in science from Kyoto University in 1978 and became the first female associate professor at Kyoto University in Faculty of Science. She received the L'Oréal-UNESCO for Women in Science Award 2014 and Takeda Medical Prize 2015. Prof. Inaba is known for her work on demonstrating the importance of dendritic cells, which act as "sentinels" of the immune system. She has also shown that these cells can be treated outside the body, and then reinfuse into the body to stimulate immune responses. In addition, she developed a method to generate dendritic cells from bone marrow precursor cells — a key advance that could lead to a new type of anticancer treatment or open a new path for cellular therapy.

HARUHISA INOUE

Professor, Center for iPS Cell Research & Application, Kyoto University

Haruhisa Inoue did his PhD at National Center for Neurology and Psychiatry, and RIKEN Brain Science Institute where he studied neurodegenerative diseases using model animals. He then did his post-doctoral work with Prof. Ole Isacson at Harvard Medical School working on neuroregenerative medicine. He started his independent lab in 2009 and is currently a principal investigator at CiRA, and also one of the research directors for the Core Research for Evolutional Science and Technology (CREST) research program funded by the Japan Science and Technology Agency. His focus is to unravel neurodegenerative diseases using iPS cell technology for the curative development.



JUAN CARLOS IZPISUA BELMONTE

Adjunct Professor, Department of Cell & Developmental Biology, UC San Diego

Dr. Izpisua Belmonte's early work was pivotal to understand fundamental genetic and cellular principles that govern vertebrate development. His observations have later been key towards elucidating the cellular and molecular basis of tissue/organ regeneration. He has contributed to the regenerative medicine field with key discoveries including: dedifferentiation and epigenetic modifications that allow for organ regeneration; novel pluripotent stem cell states that may allow for generation of human organs; and, novel drivers and stem cell models of human aging and prevention of mitochondrial diseases. Overall, his scientific interests are in discovering new molecules and specific gene/cell treatments to cure diseases affecting mankind.

Speakers & Session Chairs

CATRIONA H. JAMIESON

Associate Professor, Department of Medicine, UC San Diego

Catriona Jamieson, MD, PhD, is Associate Professor of Medicine, Chief of the Division of Regenerative Medicine, Co-Leader of the Hematologic Malignancies Program in the Division of Hematology-Oncology and Director of Stem Cell Research at the Moores UC San Diego Cancer Center. Dr. Jamieson specializes in myeloproliferative neoplasms (MPNs) and leukemia. Myeloproliferative neoplasms are a family of clonal bone marrow disorders in which the body overproduces blood cells. Dr. Jamieson studies the mutant stem cells and progenitor cells in myeloproliferative neoplasms. Her goal is to find more selective, less toxic therapies.

SHINICHIRO KADO

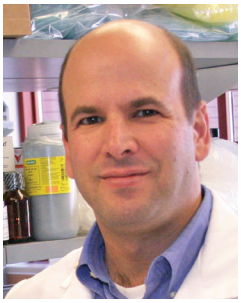
Associate Professor, Institute of Advanced Energy, Kyoto University

Shinichiro Kado is Associate Professor in the Institute of Advanced Energies (IAE) at Kyoto University. After finishing his PhD work on one of the laser-aided plasma diagnostics, the phase-contrast imaging technique, in Kyushu University, he started his carrier as a "fusion plasma spectroscopist." During 1997-1999 at National Institute for Fusion Science, he developed the charge-exchange recombination spectroscopy system for CHS and LHD heliotron-type devices. Previously at the University of Tokyo, he conducted the experimental study of the atomic and molecular processes being particularly relevant to the heat-flux mitigation in fusion edge/divertor plasmas by making use of the MAP (material and plasma)-II linear divertor simulator.

MAKOTO KATO-AZUMA

Director & Senior University Research Administrator, Kyoto University

Dr. Makoto Kato-Azuma, PhD is currently Director and Senior University Research Administrator (URA) at South-West Yoshida Main Campus URA Office, Kyoto University. He leads the University's URA team in research fund acquisition, planning and supporting domestic and international research and educational collaboration, strategic planning and promotion on international academic alliances, and social outreach of the university's research activities. Before returning to Kyoto University in January 2013, he had been working for Nihon Medi-Physics Co. Ltd. where he served as Director of Research Center, Executive Officer until December 2012.



DAN S. KAUFMAN

Professor, Department of Medicine, UC San Diego

Dr. Kaufman joined UC San Diego in 2016 from the University of Minnesota. He did undergraduate work at Stanford University and then completed an MD and PhD (Immunology) at the Mayo Medical School and Mayo Graduate School in Rochester, MN. He then completed both residency training in Internal Medicine and fellowship training in Hematology at the University of Wisconsin-Madison. Dr. Kaufman led a laboratory in the Stem Cell Institute and Masonic Cancer Center focused on using human stem cells to better understand development of blood cells and related cell types. He is also working to translate new stem cell-based therapies to clinical trials for treatment of cancer, chronic infectious disease, vascular disease, and bone repair.

PRADEEP K. KHOSLA

Chancellor, UC San Diego

Pradeep K. Khosla became UC San Diego's eighth Chancellor on August 1, 2012. As UC San Diego's Chief Executive Officer, he leads a campus with more than 30,000 students, six undergraduate colleges, five academic divisions, and five graduate and professional schools. Before his current appointment, Khosla served as Dean of the College of Engineering and Philip and Marsha Dowd University Professor at Carnegie Mellon University. There, he set the strategic direction for undergraduate and graduate education and research, and initiated undergraduate curriculum reform, successful diversity efforts, multidisciplinary research centers and graduate offerings, and international programs.

SATOSHI KONISHI

Professor, Institute of Advanced Energy, Kyoto University

Satoshi Konishi was born in Tokyo, and graduated the University of Tokyo in 1979. He studied chemistry and plasma physics. He started his research career at the Japan Atomic Energy Institute in 1981, involved in various fusion technology projects. Since 2003, he has been the Professor at the Institute of Advanced Energy, Kyoto University, and involved in the research and education on fusion technology particularly breeding blanket, divertor, energy conversion, energy application, tritium fuel cycle, safety, socio-economics and externality analysis that also covers energy systems other than fusion. As one of the leading scientist in fusion technology area, he served as the Chair of the ITER TBM Program Committee from 2009 to 2012. As one of the leading scientists in fusion technology area, he served as the Chair of the ITER TBM Program Committee from 2009 to 2012."

SCOTT M. LIPPMAN

Director, Moores Cancer Center, UC San Diego

Scott Lippman, MD is Professor of Medicine and Senior Associate Dean and Associate Vice Chancellor for Cancer Research and Care at UC San Diego. He brings more than 25 years of experience as principal investigator of translational research involving investigator-initiated clinical trials and maintains an active clinical practice. His research interests include clinical and translational research focused on head and neck and lung cancer; genetic drivers of cancer; predictive molecular signatures, biomarkers for clinical response in solid tumors; design of trials using molecular targets and markers for cancer prevention and therapy.

PING LIU

Associate Professor, Department of Nanoengineering, UC San Diego

Prior to joining the Jacobs School faculty, Professor Ping Liu has been a Program Director at the Advanced Research Projects Agency – Energy (ARPA-E) since 2012, where he initiated and managed research programs in energy storage for electric vehicles and thermal management technologies to improve building energy efficiency. He was the manager of the Energy Technology Department at HRL Laboratories and was a research staff member with the National Renewable Energy Laboratory. He received his PhD in Chemistry from Fudan University in China and was a Distinguished Inventor in multiple years at HRL.

Speakers & Session Chairs

MARTIN MARSALA

Professor, Department of Anesthesiology, UC San Diego

Dr. Marsala is Professor in the Department of Anesthesiology at UC San Diego. During the past 20 years, Martin Marsala has been involved in the development and characterization of several spinal and brain ischemia and trauma models using rodents and mini-pigs. In the course of these studies, his laboratory has characterized the behavioral, electrophysiological and histopathological changes in the spinal cord and brain of animals after transient ischemia or trauma and developed a well-defined scientific base for the initiation of cell replacement-based therapies to modulate spinal-injury-induced motor dysfunction and muscle spasticity.

JAMES H. McKERROW

Dean, Skaggs School of Pharmacy & Pharmaceutical Sciences, UC San Diego

Dr. James "Jim" McKerrow is the Dean of UC San Diego's Skaggs School of Pharmacy and Pharmaceutical Sciences. Dr. McKerrow came to UC San Diego from UC San Francisco, where he served as Professor of Pathology and Director of the Center for Discovery and Innovation in Parasitic Diseases, a consortium of academic and industry scientists dedicated to the discovery and development of new drugs for neglected tropical diseases. Dr. McKerrow founded and served as Chief Executive Officer of Demeter Pharmaceuticals, a nonprofit company focusing on acquisition and screening of the largest marine natural products library in the United States.

NAGAHIRO MINATO

Executive Vice-President, Kyoto University

Dr. Minato graduated from Kyoto University School of Medicine in 1975, studied as an associate researcher at Albert Einstein College of Medicine from 1977 to 1980, was appointed to the Professor of Immunology and Cell Biology at Kyoto University Graduate School of Medicine in 1992, and served as Dean of the Graduate School of Medicine from 2010 to 2014. He received his doctorate in medicine (MD, PhD) from Kyoto University in 1981. His main research interests have been focused on understanding the central issues in immunology, including the development of immune system, mechanisms of tumor immunity, autoimmunity, and he has published over 180 original papers in immunology and cancer fields. He is currently the Executive Vice President for Research, Planning and Hospitalization Administration.

ALYSSON R. MUOTRI

Associate Professor, Department of Pediatrics, UC San Diego

Dr. Muotri earned a BSc in Biological Sciences from the State University of Campinas in 1995 and a PhD in Genetics in 2001 from University of Sao Paulo, in Brazil. He moved to the Salk Institute as Pew Latin America Fellow in 2002 for a postdoctoral training in the fields of neuroscience and stem cell biology. He has been Professor at the School of Medicine, UC San Diego since 2008. His research focuses on modeling neurological diseases, such as Autism Spectrum Disorders, using human induced pluripotent stem cells. His lab has developed several techniques to culture human neurons and glia for basic research and drug-screening platforms.

TAKASHI NAKAJIMA

Associate Professor, Institute of Advanced Energy, Kyoto University

Dr. Takashi Nakajima is Associate Professor at Institute of Advanced Energy of Kyoto University. He received the B.E. and M.E. degrees from Kyoto University, and the Ph.D. degree in physics from the University of Southern California. After doing a postdoc for a few years at the Max-Planck-Institute in Germany and RIKEN in Japan, he joined the Institute of Advanced Energy, Kyoto University. Currently he is working on the ultrafast phenomena induced by X-ray pulses, and the time-dependent study of nanoparticles and polymer films.

QUYEN T. NGUYEN

Associate Professor, Department of Surgery, UC San Diego

Dr. Nguyen is Associate Professor in the Department of Surgery at UC San Diego and is a staff investigator of the Moores Cancer Center. She received her combined MD/PhD degree from Washington University, School of Medicine in St. Louis, MO. Her PhD focus, while in the lab of Jeff Lichtman, MD/PhD, was on synaptic maintenance and nerve regeneration. She developed an in-vivo fluorescence time-lapse imaging system to visualize motor nerve regeneration using transgenic mice expressing neuron-specific GFP-variant following transection injury. She showed that Schwann cell pathways persist following axonal degeneration to guide the regenerating neurites back to their original target muscle fibers.

TOSHIYUKI NOHIRA

Professor, Institute of Advanced Energy, Kyoto University

Toshiyuki Nohira is Professor in the Advanced Energy Utilization Division of the Institute of Advanced Energy at Kyoto University where he has been since 2015. He was an Associate Professor during 2007-2014 and an Assistant Professor during 1998-2006 in the Graduate School of Energy Science at Kyoto University. He received the degree of Doctor of Engineering from Kyoto University in 1998. Recently, he has been working on the development of new sodium ion batteries using amide ionic liquids as electrolytes. He has also been researching and developing new production methods of solar-grade silicon using molten salt electrolysis.

ALEXANDER NORBASH

Professor, Department of Radiology, UC San Diego

Alexander Norbash joined UC San Diego, as Chair and Professor of Radiology in September 2015. He previously served as Chair and Professor of Radiology at Boston University from 2004 to 2015. He is an interventional neuroradiologist with an active endovascular neurosurgical practice, having an active practice since 1993 with a focus on arteriovenous vascular malformations, intracranial aneurysms, and stroke therapy. Prior to joining Boston Medical Center, Dr. Norbash was Associate Professor of Radiology at Harvard Medical School, directing the Diagnostic and Interventional Neuroradiology Service at Brigham and Women's Hospital, and founding the Interventional Neuroradiology and Endovascular Neurosurgical practices at Brigham and Women's Hospital.

Speakers & Session Chairs

SEIICHI OGATA

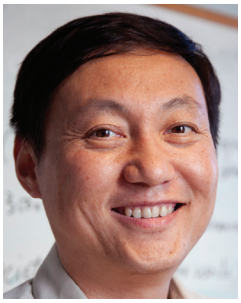
Assistant Professor, Department of Environmental Economics, Kyoto University

Seiichi Ogata is Assistant Professor of Environmental Economics at Kyoto University. He received his PhD in Policy Sciences from Ritsumeikan University in 2005. He then became a research associate for community development at Nagoya University. His research focuses on the political economics of renewable energy and policy studies. He has implemented a joint research project on renewable energy through collaboration between the natural science and social science departments at Kyoto University.

ALBERT P. PISANO

Dean, Jacobs School of Engineering, UC San Diego

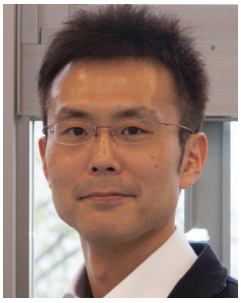
Albert P. Pisano began his service as Dean of the Jacobs School of Engineering on September 1, 2013. Pisano holds the Walter J. Zable Chair in Engineering and serves on the faculty of the departments of Mechanical and Aerospace Engineering and Electrical and Computer Engineering. Prior to his appointment at UC San Diego, Pisano served on the UC Berkeley faculty for 30 years where he held the FANUC Endowed Chair of Mechanical Systems. Pisano was the senior co-director of the Berkeley Sensor & Actuator Center (an NSF Industry-University Cooperative Research Center), director of the Electronics Research Laboratory (UC Berkeley's largest organized research unit), and faculty head of the Program Office for Operational Excellence, among other leadership positions.



BING REN

Professor, Department of Cellular & Molecular Medicine, UC San Diego

Dr. Ren is currently a member of the Ludwig Cancer Research (LCR) and Professor of Cellular and Molecular Medicine at UC San Diego School of Medicine. He is also a Co-Director of the UC San Diego Bioinformatics and Systems Biology Graduate Program. Dr. Ren obtained his PhD from Harvard University in 1998, and subsequently conducted postdoc research at the Whitehead Institute. He joined the faculty at LCR and UC San Diego in 2001, and was promoted to Associate Professor in 2007 and to Full Professor in 2009. Dr. Ren has made important contributions to the understanding of gene regulatory mechanisms and chromatin organization in mammalian cells.



HIROHIDE SAITO

Professor, Center for iPS Cell Research and Application, Kyoto University

Dr. Hirohide Saito is Professor at the Center for iPS Cell Research and Application (CiRA), Kyoto University. After completing pre-doctoral training at the University of Tokyo and SUNY Buffalo in the U.S., he received his PhD from the University of Tokyo in 2002. He is interested in the field of RNA synthetic biology & nanotechnology. He aims to understand design principle of living systems and develop new biotechnologies for cell research. Recently he developed "RNA switches" to detect and purify target live cells, and "RNA-protein nanodevices" to control cell fate.

HIROSHI SAKAGUCHI

Professor, Institute of Advanced Energy, Kyoto University

Hiroshi Sakaguchi is Professor at Molecular Nanotechnology Research Section, Energy Utilization Division, Institute of Advanced Energy at Kyoto University. His current interest is the chemistry of energy-related materials, especially surface-assisted growth of carbon-based nanowires. Dr. Sakaguchi received a PhD from Kyushu University and was an associate professor in the Institute of Electronics at Shizuoka University and a professor in the Chemistry Department at Ehime University.

KUMAR SHARMA

Professor, Department of Medicine, UC San Diego

Kumar Sharma, MD is Professor of Medicine and Director of Translational Research in Kidney Disease at UC San Diego. Dr. Sharma's research efforts have focused on the pathogenesis of diabetic kidney disease (DN). His laboratory helped define the central role of the cytokine Transforming Growth Factor-b (TGF-b) in DN using cell culture and animal models and translated these findings to the human condition. These studies contributed to the development of the highly innovative anti-fibrotic approaches that are currently being tested in clinical research trials under Dr. Sharma's guidance. Recently, Dr. Sharma has focused his attention on the contribution of the kidney to cardiovascular disease in diabetes and obesity.

JUN TAKAHASHI

Deputy Director, Center for iPS Cell Research and Application, Kyoto University

Jun Takahashi is Professor at the Center for iPS Cell Research and Application (CiRA) at Kyoto University. He graduated from Kyoto University Faculty of Medicine in 1986, and started his career as a neurosurgeon at Kyoto University Hospital. After he earned his PhD from Kyoto University Graduate School of Medicine in 1993, he worked as a postdoctoral research fellow at the Salk Institute (Dr. Fred Gage's laboratory, 1995 & 1996) where he started research on neural stem cells. He became an associate professor at Institute for Frontier Medical Sciences, Kyoto University in 2007. In 2012, he moved to CiRA as a full professor pursuing clinical application of a stem cell therapy for Parkinson's disease patients.

MAKOTO MARK TAKETO

Professor, Institute for Liberal Arts and Sciences, Kyoto University

Dr. Taketo was educated at Kyoto University (MD, PhD, 1978). After postdoctoral training and faculty positions in the U.S. (Jackson Laboratory and Duke University Medical Center), he returned to Japan (Banyu-Merck). In 1996, he accepted a professorship at the University of Tokyo, and moved to Kyoto University in 2000. In 2013, due to the age-based mandatory retirement by-law, he switched to the Institute for Liberal Arts and Sciences from Graduate School of Medicine where he is still keeping his research lab. For ~20 years, he has been working on mouse models of colon cancer. For the last ~10 years, he has investigated the molecular mechanisms of colon cancer invasion and metastasis.

Speakers & Session Chairs

OSAMU TAKEUCHI

Professor, Institute for Virus Research, Kyoto University

Osamu Takeuchi, MD, PhD, is Professor in the Institute for Virus Research at Kyoto University. After receiving his MD from Osaka University and clinical training, he entered the Graduate School of Medicine, Osaka University, where he started working on innate immunity with Prof. Shizuo Akira. Takeuchi discovered that different Toll-like receptors (TLRs) recognize different microbial components, and received his PhD degree. He became an assistant professor in Osaka University, and worked on functional roles of TLR signaling molecules and RIG-I-like receptors in inflammation. In 2012, he moved to Kyoto University as a full professor. He is currently focusing on the posttranscriptional regulation of inflammation by a set of RNA binding proteins.

MASAKAZU TOI

Professor, Department of Surgery, Kyoto University

Masakazu Toi, MD, PhD, is Professor of Surgery in the Graduate School of Medicine at Kyoto University. He received his MD from Hiroshima University School of Medicine and his PhD from Hiroshima University, Medical Science. Dr. Toi is currently the Director of the Breast Cancer Unit at Kyoto University Hospital and Professor of Drug Delivery System Center in the School of Pharmacy at the Science University of Tokyo.

WILLIAM V. TORRE

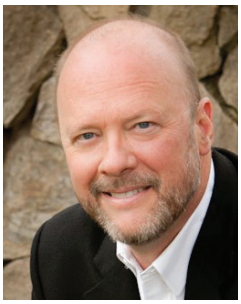
Program Director, Center for Energy Research, UC San Diego

William Torre serves as UC San Diego Program Director of Energy Storage and Systems with oversight of power system research, development and testing of advanced energy storage systems, and integration of renewable energy systems. In November 2011, he retired from San Diego Gas and Electric Co. (SDG&E) after 30 years, and his last assignments from 2010-2012 were as SDG&E's Manager of Research and Development, Manager of Technology Innovation and Development group in Transmission & Distribution Engineering division where he led the installation of several energy storage projects as part of the SDG&E smart grid program.

ROGER Y. TSIEN

Professor, Department of Chemistry & Biochemistry, UC San Diego

Roger Y. Tsien, born in 1952, received his A.B. in Chemistry and Physics from Harvard College in 1972. He received his Ph.D. in Physiology in 1977 from the University of Cambridge and remained as a Research Fellow until 1981. He then became an Assistant, Associate, then full Professor at the University of California, Berkeley. In 1989, he moved to UC San Diego where he is an Investigator of the Howard Hughes Medical Institute and Professor in the Depts. of Pharmacology and of Chemistry & Biochemistry. His honors include Artois-Baillet-Latour Health Prize (1995), Gairdner Foundation International Award (1995), Award for Creative Invention from the American Chemical Society (2002), Heineken Prize in Biochemistry and Biophysics (2002), Wolf Prize in Medicine (shared with Robert Weinberg, 2004), Rosenstiel Award (2006), E.B. Wilson Medal of the American Society for Cell Biology (shared with M. Chalfie, 2008), and Nobel Prize in Chemistry (shared with O. Shimomura and M. Chalfie, 2008). He is a member of the National Academy of Sciences and the Royal Society. Dr. Tsien is best known for designing and building molecules that either report or perturb signal transduction inside living cells. These molecules, created by organic synthesis or by engineering naturally fluorescent proteins, have enabled many new insights into signaling. Extension of these methods to electron microscopy aims to reveal biochemistry at nanometer resolution. At mm-cm scales, he is exploiting new ways to target contrast agents and therapeutic agents to tumors and sites of inflammation based on their expression of extracellular proteases, and to highlight peripheral nerves to aid surgery. Also he is testing the hypothesis that life-long memories are stored as the pattern of holes in the perineuronal net, a specialized form of extracellular matrix deposited around selected neurons during critical periods of brain development.



GEORGE R. TYNAN

Professor, Dept of Mechanical & Aerospace Engineering, UC San Diego

George R. Tynan servers as an Associate Dean of the Jacobs School of Engineering at UC San Diego. He received his PhD in 1991 from the Department of Mechanical, Aerospace, and Nuclear Engineering at UC Los Angeles. He then spent several years studying the effect of sheared flows on plasma turbulence on experiments located in the Federal Republic of Germany and at Princeton Plasma Physics Laboratory. He then worked in industry developing plasma sources for use in investigating the creation of nano-meter scale semiconductor circuits, and joined the UC San Diego faculty in 1999. Professor Tynan's current research is focused on the plasma physics of controlled nuclear fusion as an energy source.

DAVID R. VERA

Professor of Radiology & of Surgery, UC San Diego

Dr. David R. Vera is presently Professor of Radiology and of Surgery at UC San Diego and Director of the UC San Diego In Vivo Cancer and Molecular Imaging Center, one of seven NCI-sponsored centers nationwide. His research focus is the design and synthesis of targeted diagnostic agents capable of measuring receptor density and affinity. Dr. Vera began his career at UC Davis, where he contributed to the development Tc-99m-galactosyl-neoglycoalbumin, the first technetium-99m labeled receptor-binding radiopharmaceutical and the first to be approved for commercial human-use as TcGSA, a product of Nihon Mediphysics. Dr. Vera's current research uses receptor-binding technology for sentinel node mapping of melanoma, breast, GI, and urologic cancers.

Speakers & Session Chairs

DAVID G. VICTOR

Professor, School of Global Policy & Strategy, UC San Diego

David G. Victor is Professor of International Relations and Director of the Laboratory on International Law and Regulation. His research focuses on highly regulated industries, such as electric power, and how regulation affects the operation of major energy markets. He is author of "Global Warming Gridlock," which explains why the world hasn't made much diplomatic progress on the problem of climate change while also exploring new strategies that would be more effective. Prior to joining the faculty at UC San Diego, Victor served as director of the Program on Energy and Sustainable Development at Stanford University where he was also a professor at Stanford Law School and taught energy and environmental law.

ANNE M. WALLACE

Professor of Clinical Surgery, Department of Surgery, UC San Diego

Dr. Anne Wallace is a Professor of Clinical Surgery in the Department of Surgery at UC San Diego. She is the Director, of the Comprehensive Breast Health Center at the Moore's Cancer Center, which received accreditation from NAPBC as an official Accredited Breast Program in 2009. She has extensive experience in all aspects of breast health, specifically breast cancer and breast reconstruction, also involved with other types of cancer reconstruction. Other specialties are melanoma diagnosis and treatment as well as all forms of cosmetic breast and body contouring surgery. She earned her medical degree at Creighton University and her bachelor's degree with honors at Georgetown University.

YASUNORI YAMAGUCHI

President, Kyowa Hakko Kirin California

Dr. Yasunori Yamaguchi is President and CEO of BioWa, Inc. and President of Kyowa Hakko Kirin California, Inc. With more than 25 years of research and business experience, Dr. Yamaguchi has been appointed to lead these two wholly owned subsidiaries of Kyowa Hakko Kirin, Co., Ltd. to the next stage of corporate development. Before joining BioWa, Dr. Yamaguchi worked in the immunology therapeutic area as Deputy Director of the Strategic Product Planning Department in Tokyo. Dr. Yamaguchi received his master's degree and his doctorate in Immunobiology from the Graduate School of Science, Kyoto University under the supervision of Professor Kayo Inaba (Executive Vice President, Kyoto University).

SHINYA YAMANAKA

Director, Center for iPS Cell Research and Application, Kyoto University

Professor Shinya Yamanaka is most renowned for his discovery of induced pluripotent stem cells (iPSC), which are differentiated cells that have been reprogrammed back to the pluripotent state. He is Director of the Center for iPS Cell Research and Application (CiRA), which was founded in 2008 in response to his discovery, at Kyoto University, and named Senior Investigator at the Gladstone Institutes from 2007. In recognition of his work, he has been the recipient of many prestigious awards including the Albert Lasker Basic Medical Research Award, the Canada Gairdner International Award, the 100th Imperial Prize and Japan Academy Prize, the Kyoto Prize, the Wolf Prize, the Japan Order of Cultural Merit, and the Life Sciences Breakthrough Prize. The significance of iPSC was culminated with Dr. Yamanaka being co-recipient of the Nobel Prize in Physiology or Medicine in 2012.

MOTOKO YANAGITA

Professor, Department of Nephrology, Kyoto University

Motoko Yanagita, MD, PhD is the first Professor of Department of Nephrology at Kyoto University Graduate School of Medicine since the department was established in 2011. She received her MD and PhD at Kyoto University and residency training at Kyoto University Hospital. Dr. Yanagita is a physician scientist conducting basic and clinical research. Her basic research area is the elucidation of the pathophysiology of kidney injury and repair process, and her current research focuses on the identification of cellular origin of kidney regeneration and fibrosis as well as the epithelial-fibroblast crosstalk in the progression of kidney disease. Her clinical research area is Onconephrology, a new area connecting oncology and nephrology.

PAUL K. L. YU

Provost, Revelle College, UC San Diego

Paul Yu is Distinguished Professor of Electrical and Computer Engineering at UC San Diego where he is the inaugural holder of the William S.C. Chang Endowed Chair at the Jacobs School of Engineering. Currently, he is the Provost of UC San Diego's Revelle College. At UC San Diego, Professor Yu has been developing optoelectronic and electronic devices, such as laser and optical modulator and photodetector, and GaN HEMTs that enhance the performance of fiber optic networks. His work on advanced semiconductor materials and components have brought about major advancements to high data rate for digital fiber-optic communications as well as wide bandwidth, high linearity analog fiber optic transmission.

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