

ESO
2021

From Basic to Bedside

EXCHANGE PROGRAM SEMINAR BETWEEN FRANCE & JAPAN

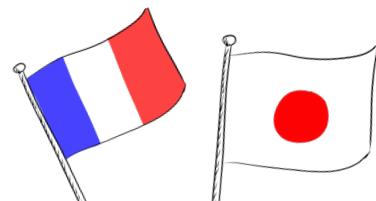
FRONTIERS OF STEM CELL AND ORGANOID TECHNOLOGY : FROM BASIC TO BEDSIDE

MONDAY, JANUARY 25 TO THURSDAY, JANUARY 28, 2021

The program will begin at 8:00 CET
The program will begin at 16:00 JST

ORGANIZERS:

Maxime M. Mahe, PhD, INSERM TENS (UMR 1235), Nantes, FRANCE
Takanori Takebe, MD, Tokyo Medical and Dental University, JAPAN
Daisuke Hishikawa, PhD, Tokyo Medical and Dental University, JAPAN
Rie Ouchi, PhD, Tokyo Medical and Dental University, JAPAN





MAX



TAKA



RIE



DAISUKE



ASUKA



LUCIE

Dear Participants,

Welcome to the Symposium :

Frontiers of stem cell and organoid technology (FSO2021): From Basic to Bedside.

This event was originally designed to foster the cooperation of a small group of French and Japanese scientists. However, the recent pandemic precluded us from organizing an in-person meeting and put significant organizational challenges. This change brought the opportunity to connect even further with a broader community of scientists working on stem cells and organoids. Our organizing team leveraged a virtual opportunity to attract a broader breath of speakers and, excitingly, bring onboard outstanding artists to design an artistic and graphical booklet summarizing FSO2021 at a glance.

This is the first virtual joint-symposium between France and Japan with a main focus on stem cell and organoid science. The event will include four exciting scientific sessions of three hours each and each hosted simultaneously in France and Japan. We are very pleased to welcome distinguished speakers and rising stars in multi-disciplinary talks. We hope the outcome of this event will have evolved our friendship and come to very productive collaboration and exchange driven by junior scientists between our countries.

We would like to thank *Rie Ouchie*, *Daisuke Hishikawa* for their commitment and *Lucie Clarysse* and *Asuka Kodaka* for their substantial help on graphic design and art . We also would like to thank our official sponsors for this year's symposium : **The Japan Society for the Promotion of Science (JSPS) and the French Institute of Health and Medical Research (INSERM)**. None of this would be possible without their support !

We look forward to seeing you on January 25th!

Max & Taka on behalf of FSO2021 organizing committee.



SEMINAR'S PROGRAM

8:15-9:00* Paris time (in blue)
16:15-17:00** Tokyo time (in red)

DAY 1 - Monday, January 25 | 2021

8:30-8:45 Self-introduction & photo time
16:30-16:45

8:45-9:30 **Ayuko Hoshino** - Exosomal proteins: Roles in cancer detection and pre-metastatic niche formation
16:45-17:30

9:30-10:15 **Laurent David** - Programming and reprogramming cell fate to study human preimplantation development
17:30-18:15

10:15-11:00 **5-min flash talks** (8-9 students & staff)
18:15-19:00

DAY 2 - Tuesday, January 26 | 2021

8:30-9:15 **Hans J. Becker** - Defined expansion platforms complement HSC gene editing.
16:30-17:15

9:15-10:00 **Maxime M. Mahé** - Generating human innervated intestinal tissue from pluripotent stem cells.
17:15-18:00

10:00-10:45 **Anne Camus** - Generation of human intervertebral disc progenitor cells: from induced pluripotent stem cells on the road to disc organoids
18:00-18:45

10:45-11:30 **Hiroyuki Koike** - Engineering human hepatobiliary-pancreatic organoids from pluripotent stem cells.
18:45-19:30

DAY 3 - Wednesday, January 27 | 2021

8:30-9:15 **Catherine Le Visage** - Stem cell-based therapies for osteoarthritis.
16:30-17:15

9:15-10:00 **Kazuo Takayama** - Human bronchial organoids for COVID-19 research.
17:15-18:00

10:00-10:45 **Oumeya Adjali** - Gene transfer using AAV-based viral vectors: Recent advances and remaining challenges.
18:00-18:45

10:45-11:30 **5-min flash talks** (5-6 students & staff)
18:45-19:30

DAY 4 - Thursday, January 28 | 2021

8:30-9:15 **Vianney Delplace** - "Click" Hydrogels: past, present, and mostly future.
16:30-17:15

9:15-10:00 **Shizuka Miura** - Generation of mouse and human intestinal progenitor cells using direct reprogramming.
17:15-18:00

10:00-10:15 **Maxime M. Mahé** - Flash talks award announcement.
18:00-18:15

10:15-11:00 **Takebe Takanori** - Promise and Impact of Organoid Medicine.
18:15-19:00

11:00-11:15 **Takebe Takanori** - Concluding Remarks.
19:00-19:15

EACH RESEARCHER'S 30 MIN-TALK WILL BE FOLLOWED BY 15 MIN ASK & QUESTION TIME

EXOSOMAL PROTEINS: ROLES IN CANCER DETECTION AND PRE-METASTATIC NICHE FORMATION

AYUKO HOSHINO

Tokyo Institute of Technology

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Associate Professor, Tokyo Institute of Technology

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Research Interests:

Exosome Biology, Cancer Metastasis, Neurodevelopmental Disease, Autism, Biomarker



Education:

Ph.D. in Cell and Molecular Biology, 2011
M.Sc. in Cell and Molecular Biology, 2008
University of Tokyo

Professional Career:

2011-2015

Postdoctoral Associate. Weill Cornell Medicine, New York.

2015-2016

Research associate. Weill Cornell Medicine, New York.

2016-2019

Instructor. Weill Cornell Medicine, New York.

2019-current

Adjunct Assistant Professor. Weill Cornell Medicine, New York
Department of Pediatrics

2019-2020

Lecturer. IRCN, The University of Tokyo

2019-current

PRESTO researcher

2020-current

Associate Professor. Department of Life Science and
Technology, Tokyo Institute of Technology



Monday, January 25 | 2021

8:45-9:30 Paris

16:45-17:30 Tokyo



For over 130 years, metastatic organotropism remained as one of the greatest mysteries in cancer biology. Experimental evidence indicates that tumor-derived microvesicles, referred to as exosomes, released by lung-, liver- and brain-tropic tumor cells fuse with cells at their future metastatic sites preparing the pre-metastatic niche. Proteomic profiling of exosomes revealed integrin expression patterns associated with lung and liver metastasis, whereas CEMIP in brain tropic exosomes enhanced metastasis in the brain. To gain a more comprehensive understanding of the exosomal protein cargo and tumor progression, we investigated the proteomic profile of exosomes in 426 human samples from tissue explants, plasma and other bodily fluids. Machine learning classification of plasma-derived exosome proteomes revealed 95% sensitivity/90% specificity in identifying cancer-associated exosomes. We found that the protein signatures that determine cancer types were derived from a variety of sources, including tumor tissue, distant organs, as well as the immune system, emphasizing the importance of using non-cancer cell-derived exosomal signatures to identify cancer-associated alterations and define tumor-associated biomarkers. Finally, we defined a panel of tumor-type specific exosomal proteins in plasma, which may help classify tumors of unknown primary origin. These data suggest that tumor-associated exosomal proteins could be used as biomarkers for early-stage cancer detection and potentially for diagnosing tumors of unknown primary origin.



Monday, January 25 | 2021

9:30- 10:15 Paris

17:30-18:15 Tokyo

PROGRAMMING AND REPROGRAMMING CELL FATE TO STUDY HUMAN PREIMPLANTATION DEVELOPMENT



Education & Professional Career :

Dr. David received his Ph.D. from University Joseph Fourier, Grenoble, France, in 2007. During his PhD, he discovered that BMP9 and BMP10 are physiological ligands of the receptor ALK1, which stemmed an active field of research in angiogenesis, and led to new therapeutic strategies for HHT, a disease caused by mutations of ALK1.

Dr. David started to work on somatic cell reprogramming during his post-doc in Jeff Wrana lab, in Toronto, Canada. His work led to a better understanding of the mechanisms of somatic cell reprogramming, such as the characterization of the mesenchymal-to-epithelial transition that initiates the reprogramming of fibroblasts.

In 2013, Dr. David joined the Medical School of University of Nantes as an Associate Professor. His lab is particularly interested in studying the regulation of pluripotency in human pluripotent stem cells and in human embryos. His lab combines stem cells, bioinformatics, developmental biology and clinical approaches to unravel human preimplantation development. Dr David is the director of Nantes iPSC core facility. Dr David is also treasurer of the French society for stem cell research (FSSCR).

The goal of our lab is to identify regulators of fate decisions driving the first cell type commitment of the human development. These cell fate choices lead to the establishment of trophectoderm (TE), epiblast (EPI) and primitive endoderm cells in preimplantation blastocysts. In particular, we aim to identify novel clues to understand how lineage specification is regulated. Single-cell RNAseq coupled to morphokinetic analysis of human embryos identified key determinants of lineage specification. Cellular models are necessary to study human preimplantation development: we have already established human naive iPSC, counterparts of EPI, and have recently successfully generated human induced trophoblast stem cells, counterparts of TE. In this presentation, we will summarize our results coupling cellular models and human embryos.

LAURENT DAVID
INSERM UMR 1229, RMeS, Université de Nantes, ONIRIS,
Nantes, France

Affiliation:

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Research Interests:

Stem cells, Pluripotency, Human embryo, Preimplantation development



DEFINED EXPANSION PLATFORMS COMPLEMENT HSC GENE EDITING



Tuesday, January 26 | 2021
8:30-9:15 Paris
16:30-17:15 Tokyo



Education :
2013.9 **M.D.**
University of Cologne, Germany

Professional Career :

2014-2017

Resident physician, Dept. of Internal Medicine, Hematology and Oncology, University Hospital Cologne, Germany

2014-2017

Research associate, Cologne Interventional Immunology, Cologne, Germany

2017-present

Visiting scientist, The University of Tokyo, Center for Stem Cell Biology and Regenerative Medicine, Division of Stem Cell Biology, Japan (Prof. Satoshi Yamazaki)

2018-present

DFG fellow



HANS JIRO BECKER

The University of Tokyo

Affiliation:

DFG fellow, Institute of Medical Science,
The University of Tokyo

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Research Interests:

Hematopoietic stem cells, gene therapy, gene editing, hematologic disorders

Due to their potency, hematopoietic stem cells (HSCs) are a particularly attractive target for gene therapy. Indeed, the rapid adoption of genetic precision tools, such as CRISPR/Cas9, has put HSCs on center stage of therapeutic genome editing applications. However, due to the low frequency of functional HSCs, protocols for their ex vivo expansion are crucial for the generation of gene edited HSC grafts. Unfortunately, attempts to induce proliferation of HSCs outside of their physiologic niche often result in the loss of self-renewal.

Over the past years, our group has focused on establishing culture conditions permissive to bone fide HSC expansion. Recently, we have reported that serum replacement by synthetic polymers combined with all-recombinant cytokine supplementation greatly enhances ex vivo HSC proliferation while maintaining their self-renewal properties. We succeeded in applying our culture system to gene editing, demonstrating that Cas9-edited, expanded HSCs corrected the immunodeficient phenotype in a murine SCID model. Further work has established a novel polymer-based system which supports the expansion of edited HSCs to the single cell level, allowing for marker-free selection strategies. This talk will highlight the encouraging potential of our defined HSC expansion platform and demonstrate its utility to gene editing and other HSC-centric therapeutic strategies.

GENERATING HUMAN INNERVATED IN TESTINAL TISSUE FROM PLURIPOTENT STEM CELLS.



Tuesday, January 26 | 2021
9:15-10:00 Paris
17:15-18:00 Tokyo

MAXIME MAHÉ

INSERM UMR 1235, TENS,
Université de Nantes, Nantes, France



Education & Professional Career :

In 2012, Dr. Maxime Mahe obtained his PhD from the University of Nantes in Neurogastroenterology. In 2012, he joined the Division of Pediatric General and Thoracic Surgery at CCHMC, under the leadership of Michael Helmrath, MD, MS and Jim Wells, PhD, and worked on developing new methodologies for the study of murine and human intestinal stem cells. The aim of my research was to develop and use intestinal stem cell culture techniques to study the mechanisms that result in regional specific intestinal stem cell patterning. With the goal of studying regional patterning in the small intestine, they were the first group to successfully generate 3-dimensional intestinal human PSCs and show functional maturation following engraftment into mice. In 2017, Dr. Mahe has been recruited as an assistant professor (Inserm CRCN) to establish a research program on the effects of the enteric nervous system on intestinal development using innovative approaches.

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Research Interests:

Stem cells, enteric nervous system, intestinal organoid, bioengineering

The use of pluripotent stem cells offers great avenues to generate human tissues. The understanding of intestinal development and its translation to human pluripotent stem cells, had allow the field to move forward in understanding intestinal development and gastrointestinal diseases. In this talk, I will highlight our previous work which had focused on generating functional human intestinal organoids (HIOs) from embryonic stem cells and induced pluripotent stem cells. Building on this model, I will highlight the additional complexity we were able to engineer in order to gain insights into intestinal physiology and diseases. In this context, the development of human intestine with an enteric nervous system (ENS) represents a real opportunity to expand our knowledge into the effect of ENS on intestinal development and toward the understanding of pathophysiological processes leading to functional gastrointestinal neuropathies. Finally, I will delineate the forthcoming strategies that could be used to create a fully functional intestine for intestinal regenerative medicine.



ANNE CAMUS
INSERM UMR 1229,
RMeS,
Université de Nantes,
ONIRIS, Nantes, France

GENERATION OF HUMAN INTERVERTEBRAL DISC PROGENITOR CELLS: FROM INDUCED PLURIPOTENT STEM CELLS ON THE ROAD TO DISC ORGANOIDS

Monday, January 25 | 2021

10:00- 10:45 Paris
18:00-18:45 Tokyo



Education & Professional Career :

Anne Camus, PhD, studied Genetics and Embryology at University Paris XI, followed by a PhD with C. Babinet, at the Pasteur Institute, Paris, France. In 1997, she carried out postdoctoral training with P. Tam at the Children's Medical Research Institute, Sydney, Australia. In 2000, she joined J. Collignon in the Jacques Monod Institute, Paris. In 2001, she was appointed as senior scientist at C.N.R.S. She has a long-standing interest in deciphering basic mechanisms that regulate cell fates and tissue patterning during embryogenesis and in stem cells differentiation studies. In 2013, she joined, the Regenerative medicine and skeleton research lab -INSERM UMR1229-RMeS- in Nantes, France, headed by J. Guicheux, as the «Stem Cells and Axial Skeleton Development» group leader. Her current research focuses on studying the cellular and molecular mechanisms of axial skeleton development using genetic tools in the mouse model to address the biological causes of disc degeneration and on human stem cells tissue engineering to develop innovative regenerative strategies for the intervertebral disc. She is developing systems biology approaches to identify gene networks and signaling pathways associated with notochordal cells differentiation as progenitors and regulators of the intervertebral disc in human and mouse. She is coordinating the "DevStem" scientific cluster at Nantes University to promote regional collaboration between researchers and strengthen the developmental and stem cell biology field.

Low back pain is one of the most common musculoskeletal disorders often (40%) associated to the degeneration of the intervertebral disc. There is no effective treatment for this disease that leads to irreversible deterioration of disc function. This is largely due to a lack of basic knowledge of the molecular and cellular controls of disc development, growth and differentiation during embryogenesis and at different stages of life.

The founder cells of the centre of the disc, originate from an axial embryonic structure, the notochord. After birth, these notochord cells have matured and behave as key regulators to keep the disc healthy. With ageing or injury, the observation is made that notochordal cells disappear leaving room for imbalance and tissue degeneration. Increasing research studies have demonstrated that native notochord cells exert rejuvenating effects on degenerated disc. As such, a better understanding of human notochord biology has great potential in disc degenerative disease and as a regenerative-cell source.

By translating fundamental knowledge from mouse developmental biology to human pluripotent stem cells research, we developed a two-step method to generate a stable human notochord-like

population with a distinct molecular signature (RNA-Sequencing DGE-seq). Time-course analysis of lineage-specific markers shows that WNT pathway activation and transfection of the notochord-related transcription factor NOTO are sufficient to induce high levels of mesendoderm progenitors and favour their commitment toward notochordal lineage instead of paraxial and lateral mesodermal or endodermal lineages. Our work advances the understanding of the regulatory network controlling human notochord cell fate and differentiation program.

We pursue our research efforts to identify key molecules associated with cell fate decisions, morphogenesis and maturation of the notochordal cells that may also be essential players for healthy adult disc maintenance. In particular we investigate the intricate role between signalling pathways, tissue growth and mechanical forces using specific scaffold mimicking healthy disc characteristics in 3D models as steps toward the disc organoid.

Affiliation:

Senior researcher (CRCN CNRS), INSERM UMR 1229, RMeS, Université de Nantes, ONIRIS

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Research Interests:

Stem cell and developmental biology, Skeleton, Regenerative Medicine

ENGINEERING HUMAN HEPATO-BILIARY-PANCREATIC ORGANOID FROM PLURIPOTENT STEM CELLS



Tuesday, January 26 | 2021
10:45-11:30 Paris
18:45-19:30 Tokyo



Education :

2014.3 **Ph.D.**

Graduate School of Medicine,
Yokohama City University

Professional Career :

2014.4-2015.11

Postdoctoral Fellow, Institute of Stem Cell Biology and Regenerative Medicine, Stanford University

2015.11-2018.2

Research Fellow, Division of Gastroenterology, Hepatology and Nutrition and Division of Developmental Biology, Cincinnati Children's Hospital Medical Center

2018.3-2019.3

Assistant Professor, Medical Research Institute, Tokyo Medical and Dental University

2019.4-present

Assistant Professor, Department of Biochemistry & Molecular Biology, Nippon Medical School



HIROYUKI KOIKE
Nippon Medical School

Affiliation:

Assistant Professor, Department of Biochemistry & Molecular Biology, Nippon Medical School

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Research Interests:

Stem cell and developmental biology

Human organoids are emerging as a valuable resource to investigate human organ development and disease. The applicability of human organoids has been limited, partly due to the oversimplified architecture of the current technology, which generates single-tissue organoids that lack inter-organ structural connections. Thus, engineering organoid systems that incorporate connectivity between neighboring organs is a critical unmet challenge in an evolving organoid field. Here, we describe a protocol for the continuous patterning of hepatic, biliary and pancreatic (HBP) structures from a three-dimensional culture of human pluripotent stem cells (PSCs). After differentiating PSCs into anterior and posterior gut spheroids, the two spheroids are fused together in one well. Subsequently, self-patterning of multi-organ (i.e. HBP) domains occurs within the boundary region of the two spheroids, even in the absence of any extrinsic factors. Long-term culture of HBP structures induces differentiation of the domains into segregated organs complete with developmentally relevant invagination and epithelial branching. This in-a-dish model of human hepato-biliary-pancreatic organogenesis provides a unique platform for studying human development, congenital disorders, drug development, and therapeutic transplantation. More broadly, our approach could potentially be used to establish inter-organ connectivity models for other organ systems derived from stem cell cultures.



Wednesday, January 27 | 2021
8:30-9:15 Paris
16:30-17:15 Tokyo

Education & Professional Career :

Catherine Le Visage (Research Director, 71 publications in ISI-indexed journals, h-index 29, 2000 citations, 11 patents) is the Deputy Director of the Regenerative Medicine and Skeleton (RMeS) laboratory, headed by J. Guicheux at the University of Nantes, France (www.rmes.univ-nantes.fr). She was trained as a Pharmacist and received her PhD in Pharmaceutical Technologies in 1999. She then performed a post-doctoral training in the BME Department of the Johns Hopkins University (Baltimore, USA) in Prof. K. Leong's laboratory with a focus on stem cells regenerative approaches for intervertebral disc (IVD).

In 2007, she joined with a tenured position the French National Institute of Health and Medical Research (INSERM) to investigate chemically cross-linked polysaccharide hydrogels. Her most recent works have focused on innovative hydrogels as i) carriers of cells or bioactive molecules in the context of IVD disease and osteoarthritis and ii) tools for stem cell-based organogenesis.

She is an elected member of the TERMIS-EU Council and has been appointed Chair of the communication committee. She gave 60 invited lectures/seminars at national and international conferences.

Osteoarthritis (OA), the most common inflammatory and degenerative joint disease, is a multifaceted rheumatic disease that has become a major socio-economic problem in industrialized societies. A large proportion of this burden is due to hip and knee OA, with prevalent cases of 300 million in the world. OA is characterized by progressive alterations, including cartilage erosion, subchondral bone remodeling, and synovial inflammation. Despite the disability and the significant impairment of quality of life, existing therapeutic solutions provide symptomatic relief of pain at best but fail to prevent joint tissue damages.

Mesenchymal Stromal Cells (MSCs), derived from bone marrow or fat tissue, have recently been proposed as a relevant therapeutic approach to prevent joint OA. MSCs have been contemplated for their protective effect on chondrocytes, their anti-inflammatory and immunoregulatory properties. In this presentation, we will highlight the pre-clinical and clinical studies that have shown that IA injection of MSCs in OA knees was safe and well-tolerated. Unfortunately, the issue of MSC long-term persistence in an OA joint has been raised, since IA injection suffers from 2 limitations, i.e a massive cell death after injection, and cell leakage outside of the articular space.

STEM CELL-BASED THERAPIES FOR OSTEOARTHRITIS

CATHERINE LE VISAGE

INSERM UMR 1229, RMeS,
Université de Nantes, ONIRIS, Nantes, France

In this context, cell protection in biocompatible and permeable hydrogels has been envisioned as a way to i) protect the MSCs and enhance their local retention, ii) provide a suitable microenvironment supporting their biological activity, and (iii) extend the diseased tissue exposure to MSC-derived anti-OA molecules. We will first review conventional microencapsulation approaches with natural polymers (hyaluronic acid, alginate) as well as droplet-based microfluidics and micromolding ones. We will then present our recent studies where we demonstrated that alginate microparticles support human MSC viability and ability to sense and respond to a pro-inflammatory environment (TNF/INF, pathological synovial fluids). The anti-OA efficacy of encapsulated MSCs in a post-traumatic osteoarthritis model in rabbits will also be discussed. Finally, this stimuli-sensitive cell-based system, able to provide an "on-demand" release of biological factors could pave the way of future developments for a wide variety of inflammation-, age- and trauma-associated disorders particularly for osteoarticular tissues including, bone, tendons, ligaments and intervertebral disc.

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Professor, University of Nantes

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Research Interests:

Stem cell, biomaterials, IVD disease and osteoarthritis,
Regenerative Medicine

HUMAN BRONCHIAL ORGANOIDS FOR COVID-19 RESEARCH



Wednesday, January 27 | 2021

9:15- 10:00 Paris

17:15-18:00 Tokyo



Education :

2015.3 **Ph.D.**

Graduate School of Pharmaceutical Sciences,
Osaka University

Professional Career :

2015.4-2018.1

Specially appointed assistant professor, Graduate School of
Pharmaceutical Sciences, Osaka University

2016.11-2020.3

PRESTO researcher, JST

2018.2-2020.2

Assistant professor, Graduate School of Pharmaceutical
Sciences, Osaka University

2020.3-present

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

The development of new drugs is expected to eradicate COVID-19 (coronavirus disease 2019). For efficient drug development, it is necessary to conduct non-clinical studies using excellent model cells. We aimed to develop model cells that can not only reproduce the life cycle of SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) but also evaluate COVID-19 drug candidates. Because SARS-CoV-2 is easily infected and replicated in the upper part of the lung (bronchi), we generated a human bronchial organoid. Our human bronchial organoids consist of basal cells, goblet cells, club cells, and ciliated cells. Human bronchial organoids strongly expressed ACE2 (angiotensin-converting enzyme 2) and TMPRSS2 (transmembrane protease serine 2) essential for SARS-CoV-2 infection. After infection with patient-derived SARS-CoV-2, replication of the viral genome, expression of viral spike protein, and release of progeny virus were observed. Next, drug screening using human bronchial organoids was performed. We confirmed that several drugs including Camostat, Remdesivir, and Interferon-beta exert a strong antiviral effect. From the above, it was shown that our human bronchial organoids can not only reproduce the life cycle of SARS-CoV-2 but also evaluate COVID-19 drug candidates.

Affiliation:

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

Contact:

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Research Interests:

SARS-CoV-2, lung development and disease, organ-on-a-chip

KAZUO TAKAYAMA
Kyoto University



GENE TRANSFER USING AAV-BASED VIRAL VECTORS: RECENT ADVANCES AND REMAINING CHALLENGES.



Education & Professional Career :

Oumeya Adjali (MD, PhD), is a senior scientist (Research Director) at the French Institute of Health and Medical Research INSERM. She is the head of Translational Gene Therapy laboratory (INSERM UMR 1089) in Nantes University since January 2017. She has been working at the interface of cell and gene therapies and immunology for more than 18 years. Since 2007, her research focuses on the use of recombinant Adeno-Associated Viral (AAV) vectors for retinal, muscular and liver gene transfer. Her research activity covers the translation chain of a gene therapy product development from viral vector design to its preclinical evaluation using relevant in vitro and in vivo models. Oumeya Adjali is also involved as an immunology expert in AAV gene therapy clinical trials.



OUIMEYA ADJALI

Translational gene therapy laboratory,
INSERM and University of Nantes, France

Affiliation:

Senior scientist, laboratory head, Translational gene therapy laboratory, INSERM and University of Nantes

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Research Interests:

Recombinant adeno-associated virus, gene therapy, rAAV-based gene transfer products, Regenerative medicine

Recombinant adeno-associated virus (rAAV) provides a clinically relevant platform for efficient and sustained *in vivo* gene therapy as illustrated by recent market approvals for neurological, metabolic and retinal genetic diseases. More recently, rAAV vectors have been also used successfully for *in vitro* stem cell gene transfer and editing. Despite a wide panel of rAAV applications and an increasing number of preclinical and clinical studies, there are still hurdles to overcome to enable a successful clinical translation of rAAV-based gene transfer products. Among them, the limited packaging size of rAAV, and their immunogenicity are both the subject of large number of developments. In addition, large scale manufacturing of rAAV products is another issue that still needs breakthrough innovations. During this oral presentation, new directions in the field to overcome current challenges will be presented.

Wednesday, January 27 | 2021

10:00-10:45 Paris

18:00-18:45 Tokyo



“CLICK” HYDROGELS: PAST, PRESENT, AND MOSTLY FUTURE



VIANNEY DELPLACE
INSERM UMR 1229, RMeS,
Université de Nantes,
ONIRIS, Nantes, France

Thursday, January 28 | 2021

8:30-9:15 Paris

16:30-17:15 Tokyo



Education & Professional Career :

In 2011, Vianney Delplace completed a master's degree in chemical engineering from ESCOM, in parallel with a cross-disciplinary master of science from Chimie ParisTech and Sorbonne University. He then joined the team of Prof. Patrick Couvreur, at Institut Galien Paris-Sud (CNRS 8612), and completed a PhD in polymer science and nanomedicine, with a thesis dedicated to the development of innovative synthetic strategies for the design of biodegradable and biofunctional vinyl polymers. In 2015, he joined the team of Prof. Molly Shoichet, at the University of Toronto, as a post-doctoral fellow, where he developed a variety of hydrogel-based systems for the investigation and treatment of retinal degenerations. Member of the RMeS Lab (INSERM 1229) in Nantes since 2018, his current research focuses on the design of injectable synthetic extracellular matrices for 3D cell culture, bioprinting and material-assisted cell therapy.

Hydrogel design is a booming field of research. The last ten years have seen the development of many new crosslinking strategies tailored to address specific roadblocks to further advance biomedical applications, in particular 3D cell culture and material-assisted cell therapy. Yet, most of them require external stimuli or catalysts, are not entirely bioorthogonal, or have inherent limitations (e.g., limited stability, slow gelation rate). Thus, hydrogels that would be fully tunable, fast-gelling, biocompatible and, yet, easy to synthesize and use, remain to be designed. In this context, innovative “click” and bioorthogonal reactions are being explored.

In this presentation, biomaterial challenges and design criteria related to cell encapsulation for various biomedical applications will be discussed. The concept of “click” chemistry will be introduced, and a critical state-of-the-art of the existing “click” crosslinking strategies will be presented. Focusing on polysaccharide-based hydrogels, I will then present our most recent work on universally applicable network platforms and their potential applications, including the use of the inverse electron-demand Diels-Alder (IEDDA) reaction, the strain-promoted azide-alkyne cycloaddition (SPAAC) and novel dynamic covalent networks.

Using hyaluronic acid as a polymer of interest, I will demonstrate how we successfully synthesized a variety of hydrogel precursors in single-step reactions from commercially available compounds, and how these precursors form hydrogels upon simple mixing under physiological conditions. I will then present a roadmap for the physicochemical characterization and optimization of hydrogels and how it allowed us to design gels that are minimally-swelling, fast-forming, and cytocompatible, with stiffness tunable over orders of magnitude. Various applications of these “click” hydrogels, spanning from explant two-photon imaging to bioprinting, will be presented as a demonstration of their versatility.

Finally, new concepts in hydrogel design for advanced biomimicry, such as programmable hydrogels and peptide/protein patterning, will be introduced, paving the way toward new generations of hydrogels to come.

Affiliation:

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Research Interests:

Biomaterials, Hydrogels, Bioprinting, Regenerative Medicine



Thursday, January 28 | 2021
9:15- 10:00 Paris
17:15-18:00 Tokyo

GENERATION OF MOUSE AND HUMAN INTESTINAL PROGENITOR CELLS USING DIRECT REPROGRAMMING TECHNOLOGY



SHIZUKA MIURA

Post-doctoral Fellow,
Université de Nantes, Oniris, INSERM,
Regenerative Medicine and Skeleton,
RMeS, UMR 1229



Education :
2018.3 **Ph.D. in Medecine**
Kyushu University

Professional Career :

2018.4-present

Specially appointed assistant professor, Medical Institute of Bioregulation, Kyushu University

Recent studies have demonstrated establishment of culture systems about adult tissue stem cells. Particularly, intestinal stem cells were difficult to maintain for a long term in vitro, but it became possible to maintain them by using Matrigel culture system. However, it is difficult to collect the intestinal tissue from patients. So, it is expected to develop the less invasive method. Meanwhile, recently, direct reprogramming technology enables us to convert into the other types of cells from the differentiated cells. For example, myoblasts, neurons and hepatocytes can be generated directly from fibroblasts using this technology. In our previous study, we have succeeded to generate induced fetal intestine-derived progenitor cells (iFIPCs) from mouse embryonic fibroblasts and human umbilical vein endothelial cells. Similar to FIPCs, iFIPCs can form spherical organoids (SOs), and iFIPC-derived SOs can develop into budding organoids (BOs). iFIPC-derived BOs contain cells with the properties of ISC_s, designated as induced ISC_s (iISC_s), which have self-renewal capacity and multi-lineage differentiation potential. Upon transplantation into the injured colon, iFIPC-derived SOs functionally reconstitute colonic epithelial tissues. Therefore, iFIPCs may be useful in the study of intestinal development and applications toward drug screening and regenerative therapy.

Affiliation:

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Research Interests:

Development, regeneration, reprogramming

PROMISE AND IMPACT OF ORGANOID MEDICINE



Education :

2019.1 Ph.D.
2011.4 M.D.

Yokohama City University School of Medicine

Professional Career :

2011.4-2013.9

*Research Associate, Department of Regenerative Medicine,
Yokohama City University*

2013.10-2018.1

*Associate Professor, Department of Regenerative Medicine,
Yokohama City University,*

2015.12-present

*Assistant Professor, Division of Gastroenterology, Hepatology
and Nutrition and Division of Developmental Biology, Cincinnati
Children's Hospital Medical Center*

2017.6-present

*Director of Commercial Innovation, Center for Stem Cell and
Organoid Medicine (CuSTOM), Cincinnati Children's Hospital
Medical Center, USA*

2018.1-present

*Professor & Founding Director, Communication Design
Center, Yokohama City University*

2018.2-present

*Professor, Institute of Research, Tokyo Medical Dental
University*

Scientific Activities:

2018-present

*Deputy to the Chairman, Japanese Society for Regenerative
Medicine (JSRM)*

2018-present

*Board of Directors, International Society for Stem Cell
Research (ISSCR)*



TAKEBE TAKANORI

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Research Interests:

Stem cell and developmental biology, organoid medicine

Organoids are multicellular structures that can be derived from adult organs or pluripotent stem cells. Early versions of organoids range from simple epithelial structures to complex, disorganized tissues with large cellular diversity. The current challenge is to engineer cellular complexity into organoids in a controlled manner that results in organized assembly and acquisition of tissue function. These efforts have relied on studies of organ assembly during embryonic development and have resulted in development of organoids with multilayer tissue complexity and higher order functions. For example, we show that antero-posterior interactions recapitulate the foregut and the midgut boundary *in vitro*, modeling the inter-coordinated specification and invagination of the human hepato-biliary-pancreatic system from human pluripotent stem cells. Coupled with patient-derived stem cells, my group studied the mechanisms of human hepatic diseases that includes viral hepatitis, steatohepatitis, recently extended to drug induced liver injury (DILI), wherein organoid modelled the clinical phenotype and genotype are correlated. Here I will summarize the next generation of organoid by design, and discuss its promise and impact to elucidate personalized disease mechanisms and understand drug reactions underlying individual variations in humans.

Thursday, January 28 | 2021

10:15-11:00 Paris

18:15-19:00 Tokyo



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