ASHBi SEMINAR

Transcriptome plasticity & progressive lineage restriction in stem cell systems

Lecturer: Rahul Sinha Ph.D.

Senior Research Scientist,
Stanford University

Date Thursday, 9 June 2022

Time 11:00 – 12:00 [JST]

Venue Zoom Online Meeting*

*Register via the right QR code

Abstract

Within the Weissman lab (Stanford School of Medicine) my major focus has been on elucidating the role of global transcriptome plasticity that governs the progressive lineage restriction of the stem/progenitor fractions within the developing fetal brain and blood systems during ontogeny and post-natal aging.

Normal hematopoiesis: I have used single-cell RNA sequencing (scRNAseq) to thoroughly study first, the development, then aging within the stem cell compartments of brain and blood.
In the hematopoietic system I confirmed the existence of diverse hematopoietic stem cell (HSC) subsets based on mRNA expression in young mice. As the mice aged, the diversity of HSCs diminished with most HSCs expressing mRNAs indicative of myeloid biased HSCs.
A parallel study where I profiled HSC and progenitor fractions during multiple stages of human fetal development and 7 decades of post-natal life also revealed clonal selection and expansion of certain HSC subsets that were present in young individual.

Normal neuropoiesis: The human brain undergoes rapid development at midgestation from a pool of neural stem and progenitor cells (NSPCs), which give rise to the neurons, oligodendrocytes, and astrocytes of the mature brain. Functional study of these cell types has been hampered by a lack of precise purification methods. We describe a method for prospectively isolating nine distinct NSPC types from the developing human brain using combinations of cell surface markers. CD24−THY1−/lo cells were enriched for radial glia, which robustly engrafted, migrated, and differentiated into all three neural lineages in the mouse brain. THY1hi cells marked unipotent oligodendrocyte precursors committed to an oligodendroglial fate, and CD24+THY1−/lo cells marked committed excitatory and inhibitory neuronal lineages. Notably, we identify and functionally characterize a transcriptomically-distinct THY1hiEGFRhiPDGFRA− bipotent glial progenitor, which is lineage-restricted to astrocytes and oligodendrocytes, but not neurons. Our study provides a framework for the functional study of distinct cell types in human neurodevelopment.

Organizer：Graduate School of Medicine
Institute for the Advanced Study of Human Biology (WPI-ASHBi)
Contact: Associate Prof. Ryo Yamamoto
[E-mail] yamamoto.ryo.2c@kyoto-u.ac.jp

ASHBi SEMINAR

Exploring evolutionary immunogenomics: Lessons from primates and recent pandemics

Lecturer: Luis Barreiro Ph.D.

Associate Professor, University of Chicago

Date Thursday, 16 June 2022

Time 11:00 – 12:00 [JST]

Venue Zoom Online Meeting*

*Register via the right QR code

Abstract

Humans display remarkable immune response variation when exposed to identical immune challenges. However, our understanding of the genetic, evolutionary, and environmental factors that impact immune response heterogeneity across species and human populations is still in its early days. In this seminar I will address three fundamental questions concerning the evolution of the human immune system: 1. the degree to which innate immune responses have evolved during primate evolution; 2. the degree to which individuals from different populations vary in their innate immune responses and the genetic variants accounting for such differences; and 3. the evolutionary mechanisms that led to the establishment of these variants in modern human populations. How past selective events might have contributed to the uneven distribution of immune-related disorders across populations will also be considered.

Organizer : Graduate School of Medicine

Institute for the Advanced Study of Human Biology (WPI-ASHBi)

Contact: Prof. Guillaume Bourque

[E-mail] guil.bourque@mcgill.ca

ASHBi SEMINAR

Mechanical symmetry breaking in C. elegans dorsal-ventral axis establishment

Lecturer: Masatoshi Nishikawa Ph.D.

Associate Professor, Hosei University

Date Wednesday, 22 June 2022

Time 13:30 – 14:30 [JST]

Venue Hybrid* *Register via the right QR code

Zoom Online / Conference Room

B1F, Faculty of Medicine Bldg. B

Abstract

The major body axes are specified during early development. These relies on complex interplay between intra/inter-cellular biochemical reactions and cell mechanics which break symmetry of the embryo spontaneously. In Caenorhabditis elegans development, the initial event of spontaneous symmetry breaking that gives rise to embryonic polarity is the midbody remnant in the two-cell embryo being off-centered, which specifies the dorsal-ventral axis. This results from the asymmetric ingression of cytokinetic furrow in first cleavage, but their underlying mechanisms remain largely unexplored. Here I demonstrate that a hydrodynamic coupling between the cell cortex and cytoplasm facilitates asymmetric furrow ingression. I identified two prerequisites for this symmetry breaking: cortical contractility to drive cytoplasmic flow, and the link between the cortex and the mitotic spindle to set long-ranged cytoplasmic flow, suggesting that cytoplasmic flow influences the cytokinetic furrow ingression.

Organizer：Graduate School of Medicine

Institute for the Advanced Study of Human Biology (WPI-ASHBi)

Contact: Prof. Sungrim Seirin Lee

[E-mail] lee.seirin.2c@kyoto-u.ac.jp

ASHBi SEMINAR

Dissecting cell identity via network inference and in silico gene perturbation

Lecturer: Samantha A Morris Ph.D.

Associate Professor of Developmental Biology and Genetics, Washington University in St. Louis

Date Wednesday, 29 June 2022

Time 16:00 – 17:00 [JST] *New!*

Venue Zoom Online Meeting*

*Register via the right QR code

Abstract

Cell identity is governed by the complex regulation of gene expression, represented as Gene Regulatory Networks (GRNs). Here, we leverage GRNs inferred from single-cell multi-omics data to perform in silico transcription factor (TF) perturbations, simulating the consequent changes in cell identity without requiring experimental perturbation data. We apply this machine learning-based approach, CellOracle, to two well-established paradigms: mouse hematopoiesis and zebrafish embryogenesis, correctly simulating reported phenotypic changes due to TF perturbation. Via systematic in silico TF perturbation in the developing zebrafish, we simulate and experimentally validate a previously unreported phenotype upon loss of noto, an established notochord regulator. Further, we reveal a novel axial mesoderm regulator, lhx1a. Following validation of our approach in these well-characterized systems, we integrate CellOracle analysis with lineage tracing of fibroblast to induced endoderm progenitor (iEP) conversion, a prototypical direct lineage reprogramming paradigm. By linking early network state to reprogramming success or failure, we reveal distinct network configurations underlying different reprogramming outcomes. Using these network analyses and in silico simulation of TF perturbation, we identify new factors to coax cells into successfully converting cell identity, uncovering a central role for the AP-1 subunit Fos with the Hippo signaling effector, Yap1. Together, these results showcase CellOracle's ability to dissect TF-regulation of cell identity, enabling new mechanistic insights into development, differentiation, and reprogramming.

Organizer：Graduate School of Medicine
Institute for the Advanced Study of Human Biology (WPI-ASHBi)

Contact: Associate Prof. Ryo Yamamoto
[E-mail] yamamoto.ryo.2c@kyoto-u.ac.jp

ASHBi
DISTINGUISHED SEMINAR

Engineering Organoid Development

Lecturer: **Matthias Lutolf PhD**

Director Roche Institute for Translational Bioengineering
Professor EPFL Lausanne, Switzerland

Date: **Monday, 11 July 2022**

Time: **17:00 – 18:00**

Venue: **Zoom Online** Register via the right QR code

Eligibility: **Researchers and Students in Kyoto University**

Most organoids form through poorly understood morphogenetic processes in which initially homogeneous ensembles of stem cells spontaneously self-organize in suspension or within permissive three-dimensional extracellular matrices. Yet, the absence of virtually any predefined patterning influences such as morphogen gradients or mechanical cues results in an extensive heterogeneity. Moreover, the current mismatch in shape, size and lifespan between native organs and their in vitro counterparts hinders their even wider applicability. In this talk I will discuss some of our ongoing efforts in developing next-generation organoids that are assembled by guiding cell-intrinsic self-patterning through engineered stem cell microenvironments.

Organizer : Institute for the Advanced Study of Human Biology (WPI-ASHBi)

Contact: Associate Prof. Cantas Alev
[E-mail] alev.cantas.8m@kyoto-u.ac.jp

ASHBi SEMINAR

Paleogenomic analysis on human demography and adaptation in insular East Asia

Lecturer: Shigeki Nakagome Ph.D.

Assistant Professor, School of Medicine, Trinity College Dublin

Date Monday, 1 Aug 2022

Time 13:00 – 14:00 [JST]

Venue Hybrid* *Register via the right QR code

Zoom Online / Conference Room

B1F, Faculty of Medicine Bldg. B

Abstract

Most of the world's population is fed by farming today. In the past, however, human ancestors lived as foragers for tens of thousands of years before subsistence practises transformed from food collection to food production in the Holocene period. This agricultural revolution is a relative blip on the evolutionary timescale, but its impacts on human demography and adaptation were enormous. Given that agriculture emerged in different ways, at different times, and for different reasons, it is crucial to understand regional uniqueness in the impacts of this transition. Our research focuses on Japanese prehistory, where its lifeway transitions were characterised by many thousands of years of insular isolation of foragers followed by recent but radical shifts to wet rice farming and then to the rise of the state. Generating 12 ancient Japanese genomes from pre- and post-farming periods, we found a tripartite structure of Japanese genomic origins, in which each of the three distinct ancestors derived from the hunting-gathering, agrarian, and state formation phases made a significant contribution to the formation of modern Japanese populations. We further employed genome-wide selection scans to identify the adaptive genes and traits that were hardwired into the pre-agricultural populations or that continue to characterise the modern populations. This talk will discuss the power and applicability of ancient human genomes in untangling the genetic legacy of the cultural transitions and its impacts on phenotypic variation in Asia today.

Organizer：Graduate School of Medicine
Institute for the Advanced Study of Human Biology (WPI-ASHBi)

Contact: Junior Associate Prof. Taro Tsujimura
[E-mail] tsujimura.taro.4m@kyoto-u.ac.jp

ASHBi SEMINAR

Programmable DNA integration by CRISPR-associated transposase

Lecturer: Makoto Saito Ph.D.

Postdoctoral fellow,
Broad Institute of MIT and Harvard

Date **Tuesday, 2 August 2022**

Time **11:00 – 12:00 [JST]**

Venue **Zoom Online Meeting***

***Register via the right QR code**

Abstract

Genome engineering has revolutionized biomedical research. Although diverse CRISPR-Cas genome editing tools are currently available, general methodology for programmable DNA integration in living cells has been a long-standing challenge. For example, Cas9-mediated knock-in relies on target cell DNA repair machinery, which does not work efficiently in post-mitotic cells including neurons. Exploring the biological diversity of CRISPR systems, we recently identified CRISPR-associated transposase (CAST) systems, which precisely insert DNA in an RNA-guided manner at specific target sites on the genome of prokaryotic cells. In this seminar, I will discuss the basics of CAST systems and our approach to apply the systems for genome engineering in mammalian cells.

Organizer：Graduate School of Medicine
Institute for the Advanced Study of Human Biology (WPI-ASHBi)
Contact: Associate Prof. Tomoyuki Tsukiyama
[E-mail] ttsuki@belle.shiga-med.ac.jp

ASHBi SEMINAR

Fate-mapping blood cells (HSC and T cells) to explore their *in vivo* dynamics

Lecturer: Munetomo Takahashi

Student, The University of Tokyo, Faculty of Medicine

Date **Monday, 8 August 2022**

Time **16:45 – 17:45 [JST]**

Venue **Zoom Online Meeting***

***Register via the right QR code**

Abstract

Blood cells form a dynamic system wherein hematopoietic stem cells (HSCs) maintains homeostasis through hematopoiesis and T cells prevent infection through clone expansions. Important questions remain as to how HSCs and T cells behave *in vivo* to mediate these functions. For instance, in hematopoiesis, the contribution of HSCs toward maintaining steady state hematopoiesis is unknown. Equally, in immune responses, how T cell clones localise tolerance against tumours is unknown. This seminar will present two works modelling HSC flux experiments and fate-mapping T cells from activation to address these key questions.

Organizer：Graduate School of Medicine

Institute for the Advanced Study of Human Biology (WPI-ASHBi)

Contact: Associate Prof. Ryo Yamamoto

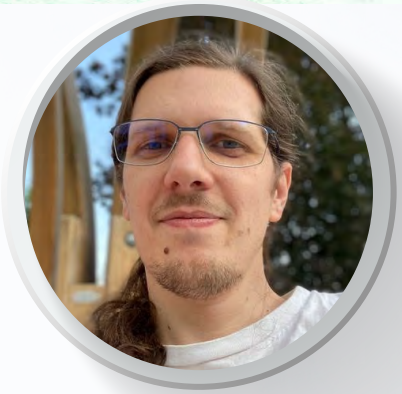
[E-mail] yamamoto.ryo.2c@kyoto-u.ac.jp

ASHBi SEMINAR

Controlled temporal variability facilitates spatial robustness in early mouse development

Lecturer: Dimitri Fabrèges Ph.D.

Post-doc, Hubrecht Institute



Date Thursday, 1 September 2022

Time 16:00 – 17:00 [JST]

Venue Zoom Online Meeting*

* Register via the right QR code

Abstract:

Living systems are noisy. Nonetheless, they achieve precision in form and function. How they do this and whether the variability has any role are fundamental yet open questions in biology. In this study, we use pre-implantation mouse embryos to measure and manipulate temporal as well as spatial variabilities and show that they are functionally linked and controlled to an optimal level facilitating robust morphogenesis and patterning. As we found that the timing of divisions of blastomeres desynchronized passively without compensation, we investigated the effect of the division asynchrony on cell packing. By using geometrical cell shape descriptors, we established a morphomap of embryogenesis, which shows that embryos converge to a certain 3D structure that cannot be explained by compaction alone. A physical model of the compacting 8-cell stage, based on surface tension minimization, recapitulates the geometrical convergence and revealed, both theoretically and experimentally, that noise generated by cortical contractility may be required to escape from local minimum and achieve topological transitions. On the other hand, experimental synchronization of cell divisions using Nocodazole generates a significantly higher number of spatially mis-allocated cells, suggesting that too much spatial noise is no good – the mitosis desynchronization reduces the spatial perturbations resulting from the divisions and allows the embryos reaching an optimal geometry and topology. Remarkably, the desynchronization rate was unique to species in mice, rabbits and monkeys, and may therefore be an important evolutionary treat to ensure developmental robustness.

Organizer：Graduate School of Medicine

Institute for the Advanced Study of Human Biology (WPI-ASHBi)

Contact: Prof. Takashi Hiiragi

[E-mail] hiiragi.takashi.7w@kyoto-u.ac.jp

ASHBi SEMINAR

Mechanisms of Necroinflammation and Nephron Loss

Lecturer: Andreas Linkermann M.D., Ph.D.

Deputy director of Nephrology and Heisenbergprofessor, Division of Nephrology, University Hospital Carl Gustav Carus at the Technische Universität Dresden, Dresden, Germany

Date Friday, 9 September 2022

Time 16:00 – 17:10 [JST]

Venue Zoom Online Meeting*

*Register via the right QR code

Abstract

Understanding nephron loss is a primary strategy for preventing CKD progression. Death of renal tubular cells may occur by apoptosis during developmental and regenerative processes. However, during AKI, the transition of AKI to CKD, sepsis-associated AKI, and kidney transplantation ferroptosis and necroptosis, two pathways associated with the loss of plasma membrane integrity, kill renal cells. This necrotic type of cell death is associated with an inflammatory response, which is referred to as necroinflammation. Importantly, the necroinflammatory response to cells that die by necroptosis may be fundamentally different from the tissue response to ferroptosis. Although mechanisms of ferroptosis and necroptosis have recently been investigated in detail, the cell death propagation during tubular necrosis, although described morphologically, remains incompletely understood. Here, we argue that a molecular switch downstream of tubular necrosis determines nephron regeneration versus nephron loss. Unraveling the details of this "switch" must include the inflammatory response to tubular necrosis and regenerative signals potentially controlled by inflammatory cells, including the stimulation of myofibroblasts as the origin of fibrosis. Understanding in detail the molecular switch and the inflammatory responses to tubular necrosis can inform the discussion of therapeutic options.

Organizer：Graduate School of Medicine
Institute for the Advanced Study of Human Biology (WPI-ASHBi)

Contact: Prof. Motoko Yanagita

[E-mail] kidney2011@kuhp.kyoto-u.ac.jp

ASHBi SEMINAR

Synthetic Ex Utero Embryogenesis: from Naive Pluripotent Stem Cells to Embryos

Lecturer: Jacob Hanna M.D., Ph.D.

Associate Professor, Department of Molecular Genetics, Weizmann Institute of Science, Israel

Date Thursday, 15 September 2022

Time 16:00 – 17:00 [JST]

Venue Zoom Online Meeting*

*Register via the right QR code

Abstract

The identity of somatic and pluripotent cells can be epigenetically reprogrammed and forced to adapt a new functional cell state by different methods and distinct combinations of exogenous factors. The aspiration to utilize such ex vivo reprogrammed pluripotent and somatic cells for therapeutic purposes necessitates understanding of the mechanisms of reprogramming and elucidating the extent of equivalence of the *in vitro* derived cells to their *in vivo* counterparts. In my presentation, I will present my group's recent advances toward understanding these fundamental questions and further detail our ongoing efforts to generate developmentally unrestricted human naive pluripotent cells with embryonic and extra-embryonic developmental potential. I will conclude by highlighting new avenues for utilizing custom made electronically controlled ex utero platforms and novel optimized conditions for growing natural mammalian embryos ex utero until advanced stages, for better studying of stem cell transitions during embryogenesis and organogenesis. The latter platforms offered an exclusive technical platform to unleash the self-organizing capacity of mouse naïve PSCs to generate post-gastrulation whole synthetic embryos with both embryonic and extraembryonic compartment ex utero. Collectively, I will be highlighting prospects for new platforms for advancing human disease and developmental modelling.

Organizer：Graduate School of Medicine
Institute for the Advanced Study of Human Biology (WPI-ASHBi)

Contact: Associate Prof. Cantas Alev
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ASHBi
DISTINGUISHED SEMINAR

Modelling early human development using stem cells:
Exploring regulatory considerations and anticipating societal response

日本語同時通訳 SIMULTANEOUS INTERPRETATION

Lecturer: **Megan Munsie PhD**

Professor, University of Melbourne
Group leader, Murdoch Children's Research Institute

Date & Time: 2022. 12.5 MON 9:30 – 11:00

Venue: Zoom Online
Register via the right QR code

Eligibility: Academic Researchers and Students

Recent reports of the use of pluripotent stem cells to create 3D models of early embryonic development have sparked concern amongst some in the community, and reignited discussions around how this area of research should be regulated. Many jurisdictions across the globe already have clear regulations in place that define how human embryos should be used in research, including how and from where they can be obtained, and considerations around experimental design such as the length of time an embryo should be maintained in culture. Whether existing human embryo research laws are, or should be, relevant to experiments designed to model early human development *in vitro* has become increasingly topical as scientific capability advances.

In this presentation I will share a 2021 interpretation of Australian law that effectively equates embryo models made from reprogrammed human somatic cells as equivalent to a sperm-egg embryo[1], and contrast this ruling with regulations in other jurisdictions and the recently revised recommendations on this topic by the International Society for Stem Cell Research[2].

This is an area of stem cell research that is likely to provide invaluable insights into the earliest stages of human development, the so-called 'black-box' stage of embryogenesis that has been difficult to study until now. While such knowledge may be transformative, for some in the community this remains an area of research that if allowed, should demand the highest level of scrutiny. There is a clear need for a reflexive, anticipatory and deliberative approach to ethical and regulatory considerations raised[1] and I welcome the opportunity to explore how to implement such an approach during this lecture.

1. Ankeny R et al. *American Journal of Bioethics* doi.org/10.1080/15265161.2021.1974976
2. Clark A et al. (2021) *Stem Cell Reports* doi.org/10.1016/j.stemcr.2021.05.008

Hosted by Institute for the Advanced Study of Human Biology (WPI-ASHBi)
Co-organized by Uehiro Research Division for iPS Cell Ethics at CiRA

Contact: Prof. Misao Fujita
[E-mail] uehiro-contact@cira.kyoto-u.ac.jp

ASHBi SEMINAR

2022
12.08
Thursday

Time 13:00 - 14:30

Hybrid

Venue Conference Room / Zoom
B1F, Faculty of Medicine Bldg. B

*Register via the right QR code

"Expected Harm: A Translational Pathway for Reproductive Genome Editing"

Lecturer: **Julian Savulescu** Ph.D.
Professor, National University of Singapore

"The Ethics of Polygenic Genome Editing"

Lecturer: **Christopher Gyngell** Ph.D.
Senior Lecturer, The University of Melbourne
Team Leader, Murdoch Children's Research Institute

Hosted by Institute for the Advanced Study of Human Biology (WPI-ASHBi)
Co-organized by Uehiro Research Division for iPS Cell Ethics at CiRA

Contact: Prof. Misao Fujita
[E-mail] uehiro-contact@cira.kyoto-u.ac.jp

ASHBi SEMINAR

Visualizing and manipulating nonhuman primate brain circuits and functions

Lecturer: Dr. Takafumi Minamimoto

Chief, Section on Systems and Neural Circuits
National Institutes for Quantum Science and Technology

Date Friday, 23 December 2022

Time 16:00 – 17:00 [JST]

Venue Hybrid* *Register via the right QR code

Conference Room / Zoom online
B1F, Faculty of Medicine Bldg. B

Abstract

Non-human primates, especially macaque and marmoset monkeys are excellent models for elucidating highly organized brain function and behavior. However, the application of optogenetics or chemogenetics to monkeys is still limited, preventing a network-level understanding of the higher brain functions. We have been working on the application of a chemogenetic technology Designer Receptors Exclusively Activated by Designer Drugs (DREADDs) to non-human primates. DREADDs afford a means of reversibly and remotely controlling the activity of a neuronal population expressing designer receptors through delivery of their agonist. Combined with PET and MR imaging, DREADDs are now a powerful and attractive tool for non-human primate research to visualize and manipulate specific brain circuits and monitor induced network activity changes. I will summarize the current status and prospects of chemogenetic technology that links primate brain circuits and behavior and opens up possibilities for developing therapeutic applications.

Organizer：Graduate School of Medicine
Institute for the Advanced Study of Human Biology (WPI-ASHBi)

Contact: Dr. Ken-ichi Amemori
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ASHBi SEMINAR

HD Video Recorder of the Cell

Lecturer: Nozomu Yachie Ph.D.

Associate Professor, School of Biomedical Engineering,
The University of British Columbia

Date Wednesday, 11 January 2023

Time 10:00 – 11:30 [JST]

Venue Zoom Online Meeting*

*Register via the right QR code

Abstract

The dynamic behaviors of cells during development, tumorigenesis, and other disorders remain largely unclear. Our lab is developing "DNA event recording" systems by which high-resolution information of cells is progressively stored in cell-embedded "DNA tapes." Using high-throughput single-cell sequencing, such a system enables access to molecular and cellular history information of cells at the time of observation and provides a way of observing the dynamics of complex biological systems in high resolution. We envision mapping the whole-body cell lineage and differentiation trajectories of mouse development and have been actively progressing towards this goal. I will share our grant vision and recent progresses in developing new genome editing tools and high-performance computing technologies.

Organizer：Graduate School of Medicine
Institute for the Advanced Study of Human Biology (WPI-ASHBi)

Contact: Prof. Masatsugu Ema
[E-mail] mema@belle.shiga-med.ac.jp

ASHBi SEMINAR

Spatiotemporal regulation of gene expression: from description to perturbation and back

Lecturer: Ivano Legnini Ph.D.

Group Leader at Human Technopole, Milan

Date Friday, 20 January 2023

Time 16:00 – 17:00 [JST]

Venue Zoom Online Meeting*

*Register via the right QR code

Abstract

Gene expression is tightly regulated in time and space to ensure cellular homeostasis and, for example in development, to coordinate cellular transitions. To study these phenomena, we combine high-resolution sequencing technologies - such as long-read sequencing, single-cell RNA sequencing and spatial transcriptomics - with organoid models of neurodevelopment and optogenetic perturbations of gene expression. In this seminar, I will talk about our latest research efforts in the fields of gene regulation, neural organoids and genomic technologies.

Organizer : Graduate School of Medicine
Institute for the Advanced Study of Human Biology (WPI-ASHBi)

Contact: Prof. Yasuhiro Murakawa

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ASHBi SEMINAR

Rapid Research Autopsy: Genesis, Operation, and Collaborations of Programs at 3 United States Universities

日本語同時通訳 SIMULTANEOUS INTERPRETATION

Lecturer: **Jody E. Hooper, MD**

Associate Professor of Pathology, Stanford University

Director of Autopsy, Stanford University School of Medicine

Date **Wednesday, 25 January 2023**

Time **10:00 – 11:30 [JST]**

Venue **Zoom Online Meeting***

*Register via the right QR code

Abstract

Tissue samples are essential to medical research, particularly in the era of tumor heterogeneity. "Rapid" or research autopsy means conducting a postmortem examination of a patient on an urgent basis (measured in hours) to collect tissue (mostly cancers) to support different types of research. This activity allows for the investigation of large volumes of tumor or diseased tissue at a unique time point in the evolution of the tumor from a genetic and immunologic standpoint, when aggressive local and distant spread has occurred. Starting and operating a research autopsy program requires institutional infrastructure, dedicated resources and people, and involves considerable logistical and ethical considerations. To elucidate these factors, Dr. Hooper will review the characteristics of three research autopsy programs she helped to create and run at U.S. universities, including Oregon Health and Science University in Portland, Oregon; Johns Hopkins University in Baltimore Maryland; and a new program just opened at Stanford University in Palo Alto, California. She will discuss creating collaborations, legal and ethical guidelines, and critical procedures pre, during, and after the autopsy. Research autopsy can provide unique samples that cannot be obtained in any other way and offers patients and families the chance to meaningfully contribute to science and the treatment of future patients.

Organizer：Graduate School of Medicine

Institute for the Advanced Study of Human Biology (WPI-ASHBi)

Contact: Dr. Go Okui

[E-mail] okui.go.5x@kyoto-u.ac.jp

ASHBi SEMINAR

Human spinal cord organoid for disease modeling and drug screening

Lecturer: Woong Sun, Ph.D.

**Professor at the Department of Anatomy,
Korea University College of Medicine**

Date Wednesday, 8 February 2023

Time 16:00 – 17:00 [JST]

Venue Hybrid* *Register via the right QR code

Conference Room / Zoom online
B1F, Faculty of Medicine Bldg. B

Abstract

Spinal cord is generated by the folding of the neural plate along anterior-posterior axis via an embryonic process called neurulation. Perturbation of this process often leads to a common congenital malformation, neural tube defects, highlighting the importance to develop in vitro model recapitulating human neurulation. The advent of organoid technology, which produces 3D structure resembling parts of organs from ESCs/iPSCs, has provided ways to study human organogenesis and to model human diseases. Recently, we developed a novel organoid model that exhibits specific morphogenetic features of spinal cord development, such as neural tube formation. The human spinal cord organoids (hSCOs) exhibited tube-forming morphogenesis, and differentiation into the major types of caudal spinal-cord cells, and functional maturations such as synaptic contacts and synchronized neural activities. Furthermore, optimization of the process allowed quantifiable and scaleable organoid production, suitable for the high contents drug screening. In this talk, I will present an example that the hSCOs were used to toxicology screen for drugs that might cause neural-tube defects.

Organizer : Graduate School of Medicine
Institute for the Advanced Study of Human Biology (WPI-ASHBi)

Contact: Prof. Cantas Alev
[E-mail] alev.cantas.8m@kyoto-u.ac.jp

ASHBi SEMINAR

Developments and applications of ex vivo hematopoietic stem cell expansion cultures

Lecturer: Ms. Kyomi J. Igarashi

Ph.D. Student, Stanford University School of Medicine

Date Friday, 17 February 2023

Time 16:00 – 17:00 [JST]

Venue ~~Conference Room~~
~~B1F, Faculty of Medicine Bldg. B~~
[New!]→Memorial Auditorium
(Faculty of Medicine Campus Map #7)

*Register QR code

Abstract

While the self-renewing and multipotent hematopoietic stem cells (HSCs) can maintain and reconstitute the blood and immune system, their scarcity in vivo has hindered its use in blood disease treatment and in vitro characterization. Despite developments in ex vivo expansion methods, achieving high HSC selectivity in these cultures remains difficult. We have previously introduced a polyvinyl alcohol (PVA)-based HSC culture system that can expand mouse bone marrow HSCs 236-899-fold over the span of a month. However, HSCs comprise < 10% of the total culture, with the majority being differentiated progenitors and mature hematopoietic cells. We have now significantly increased the HSC selectivity of this system by decreasing oxygen (O2) culture concentrations from the standard 20% to hypoxic 5%. This system further depletes differentiated progenitors and mature hematopoietic cells, while also affording selective expansion of HSCs from heterogeneous populations (unfractionated bone marrow and fetal hematopoietic tissues). To investigate the mechanism of this selectivity, we performed various transcriptomic analyses, revealing an upregulation of sterol and cholesterol metabolism pathways in the 5% O2 cultures. This highly selective culture system can be used to develop powerful new ex vivo assays for HSC activity, while also providing potential time- and cost-efficient alternatives to in vivo stem cell assays.

Organizer：Graduate School of Medicine
Institute for the Advanced Study of Human Biology (WPI-ASHBi)

Contact: Dr. Ryo Yamamoto
[E-mail] yamamoto.ryo.2c@kyoto-u.ac.jp

ASHBi SEMINAR

2023
03.13
Monday

Time 10:00 - 11:00

Venue #114 Conference Room
1F, Faculty of Medicine Bldg. A
*Register via the right QR code

Lecturer: **Norihiro Takakuwa** Ph.D

Postdoc
Max Planck Institute for Brain Research,
Frankfurt am Main, Germany

Decision-invariant memory traces of spatial goals in the dopamine-striatal system

Organizer：Graduate School of Medicine
Institute for the Advanced Study of Human Biology (WPI-ASHBi)

Contact: Prof. Tadashi Isa
[E-mail] isa.tadashi.7u@kyoto-u.ac.jp

ASHBi SEMINAR

A cell model to study embryonic genome activation

Lecturer: Juha Kere, MD, Ph.D.

Professor of Molecular Genetics,
Department of Biosciences and Nutrition, Karolinska Institutet

Date Friday, 24 March 2023

Time 10:00 – 11:00 [JST]

Venue Hybrid*
Conference Room / Zoom online
B1F, Faculty of Medicine Bldg. B

*Register via the right QR code

Abstract

In human, Embryonic Genome Activation (EGA) occurs during days 2-3 after fertilization, at 4-8 cell stages, when the combined genome of the zygote start to be transcribed. EGA coincides with the reprogramming of the oocyte transcriptome to the totipotent cell phenotype of the 4-8 cell stage cells. We have earlier studied human EGA by single-cell RNA sequencing of oocytes, zygotes, and single cells from 4- and 8-cell stage embryos[1]. This study allowed us to list 32 genes activated at 4-cell stage compared to oocytes (minor EGA), 129 genes activated at 8-cell stage compared to 4-cell stage (major EGA), and thousands of specifically degraded mRNAs until the 4-cell stage, corresponding to ≈75% of oocyte mRNA content. We cloned new paired-like (PRDL) homeobox family genes not detected earlier active in any human tissues[2] . Recently, we have continued to characterize the roles of key genes[3]. Our results implicated DUX4 functions to include chromatin modification, enhancer activation, transcriptional activation, and regulation of oocyte mRNA degradation. However, work to understand human EGA in detail has been hampered not only by technical aspects, but also by that work destroying human embryos is not allowed in all legislations. Therefore, cell models to study human EGA and the genes involved in it are badly needed. Toward this aim, we succeeded in reprogramming human embryonic stem cells (hESCs) to 8-cell-like cells (8CLC, called by us as induced blastomeres, iBM) by a brief pulse of DUX4 expression[4]. Human 8CLCs had recently been derived also by chemical induction[5]. The cell models now also open up new routes to study human EGA without harming human embryos, allowing manipulations such as inactivation of selected genes, studying effects of chemical compounds and biochemical changes, and drawing the complete landscape of human EGA.

[1] Töhönen & al. 2015; DOI: 10.1038/ncomms9207)
[2] Töhönen & al. 2015; Jouhilahti & al. 2016; DOI: 10.1242/dev.134510; Madissoon & al. 2016; DOI:10.1038/srep28995)
[3] Vuoristo & al. 2022; DOI: 10.1016/j.isci.2022.104137
[4] Yoshihara & al. 2022; DOI: 10.1016/j.stemcr.2022.06.002
[5] Mazid & al. 2022; DOI: 10.1038/s41586-022-04625-0

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