ASHBi
DISTINGUISHED SEMINAR

Decoding the mechanisms of human development and diseases by single cell genomics approaches

Lecturer: **Dr. Fuchou Tang**

Professor, BIOPIC, College of Life Sciences, Peking University
Associate Director, Beijing Advanced Innovation Center for Genomics (ICG)

Date: Tuesday, 6th April 2021

Time: 15:30～17:00

Venue: Zoom Online Register via the right QR code

Eligibility: Researchers and Students in Kyoto University

Profile

Dr. Fuchou Tang is Professor at BIOPIC, College of Life Sciences, Peking University. He is also Associate Director of Beijing Advanced Innovation Center for Genomics (ICG). He set up his own lab as a principal investigator at Peking University in 2010. Dr. Fuchou Tang's lab focuses on the epigenetic regulation of gene expression network during human early embryonic development and germline development. His lab pioneered the single cell sequencing field and has systematically developed a serial of single cell functional genomic sequencing technologies. His work has been cited for more than 10,000 times. He has been invited to give presentations at AGBT, ISSCR, ICHG, Gordon Conferences, HCA, etc. He organized the Cold Spring Harbor Asia conference of Frontiers in Single Cell Genomics in 2016, 2018 and 2020.

Abstract

Human germline cells are crucial for maintenance of the species. Our understanding of these cell types is limited by the difficulty of analyzing the precious and heterogeneous germline tissue samples. The rapid development of single-cell omics sequencing technologies provides a chance for comprehensive profiling of the omics dynamics of human germline development. I will discuss progress in analyzing the development of human germline cells, including preimplantation and implantation embryos, fetal germ cells (FGCs), and adult spermatogenesis by single-cell omics sequencing technologies. I will also discuss progress in analyzing the critical molecular features of colorectal cancer.

[NOTE] The lecturer will also cover Chinese regulations surrounding the research use of fetal tissues and how they are obtained for research.

Organizer : Prof. Misao Fujita, Prof. Mitinori Saitou

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

Co-organized by Uehiro Research Division for iPS Cell Ethics at CiRA

ASHBi SEMINAR

Correlative Light and Electron Microscopy

Lecturer: Dr Bruno M Humbel

Section leader at Okinawa Institute of Science and Technology (OIST)

Date Friday, 9 April 2021

Time 2:00pm – 3:00pm

Venue Zoom Online Meeting*

*Register via the right QR code

Abstract

In recent years correlative microscopy, combining the power and advantages of light and electron microscopy, has become an important tool for biomedical research. Light microscopy has the advantage of easily searching large areas, even volumes, for the cells of interest, e.g., a special cell type in tissue, astrocytes in brain or for cells that have been modified either by transfections or by RNAi in a large population of nonmodified cells. Also on thin sections, the low magnification of light microscopy and therefore ease of searching large areas are very beneficial to speed-up the analysis of rare events. The predominant disadvantage of this technique, however, is that only the fluorescently labelled structures can be imaged in relation to each other. Electron microscopy reveals the cellular ultrastructure a high resolution and individual organelles, even large protein polymers like cytoskeletal filaments or ribosomes can unequivocally identified. Macromolecules of interest can be labelled with colloidal gold. Searching for a few gold particles within a few cells of a large tissue, however, is very cumbersome and can be extremely time consuming. In addition, labelling with colloidal gold particles can be very inefficient and barely get over background level. Seen the advantages of light and electron microscopy suggests that the optimal approach is to combine both techniques for cell biology and biomedical research. Localisation of rare cellular events are followed and identified by (fluorescence) light microscopy, the high-resolution data and fine localisation to cellular substructures are done by electron microscopy. In combination with super-resolution light microscopy, the fluorescence signal can also be used to label macromolecules by overlying the fluorescence signal with the electron micrograph. In this presentation we willdescribe the approach we have chosen to follow the cell(s) of interest from sampling the tissue until the analysis by electron microscopy.

Organizer : Dr Akiko Oguchi, Prof Yasuhiro Murakawa

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

ASHBi
DISTINGUISHED SEMINAR

Haematopoietic Stem/Progenitor Cell Development and Function

Lecturer: Dr Bertie Göttgens

Professor of Moleculr Haematology and Deputy Director of the Cambridge Stem Cell Institute.
Associate Editor of the journal BLOOD

Date: **Monday, 19 April 2021**

Time: **4:00pm - 5:30pm**

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

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

Homeostasis of the haematopoietic system is achieved through carefully balanced proliferation, differentiation and cell death, to maintain appropriate numbers of all the various haematopoietic cell types. Malignant as well as non-malignant diseases impact the very same cellular processes, thus disrupting the overall balance between cell types. Historically, it has been difficult to connect "molecular scale" processes, such as leukaemogenic mutations, with their likely "tissue scale" consequences, such as the resulting dynamic alterations of the entire haematopoietic system.

The advent of high throughput single cell molecular profiling promises to transform our ability to map blood development as well as interpret perturbations of the haematopoietic system, because molecular level information can now be obtained for tens of thousands of cells. This presentation will provide an update of the Göttgens group's efforts on enhancing our understanding of haematopoiesis based on representations of the haematopoietic differentiation landscape generated from single cell expression profiles. High-throughput CrispR gene knock-out experiments are complemented with tissue modelling to identify comprehensive information on gene regulatory interactions in haematopoietic progenitor cells, as well as infer parameters that underpin normal homeostasis and allow the simulation of leukaemogenic mutations and possible treatments.

Organizer : Assoc Prof Ryo Yamamoto
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Hosted by Institute for the Advanced Study of Human Biology (WPI-ASHBi)

ASHBi
DISTINGUISHED SEMINAR

How cohesin folds the genome by loop extrusion

Lecturer: **Dr. Jan-Michael Peters**

Scientific Director, Research Institute of Molecular Pathology (IMP), Vienna

Date: Friday, 28 May 2021

Time: 5:00pm - 6:00pm

Venue: Zoom Online

Register via the right QR code

Eligibility: Researchers and Students in Kyoto University

Genomic DNA is folded over long distances into loops and topologically associating domains (TADs), which serve important structural and regulatory functions. We and others discovered that these genomic structures depend on cohesin complexes and are positioned in the genome by the DNA binding protein CTCF. It has been proposed that cohesin and related "structural maintenance of chromosomes" (SMC) complexes form chromatin loops and TADs by a loop extrusion process. According to this hypothesis cohesin reels DNA into loops, which grow in size until they encounter CTCF bound to DNA, or until cohesin is released from DNA by the protein WAPL. We recently provided evidence for this hypothesis by reconstituting and imaging cohesin mediated DNA loop extrusion at the single molecule level. In my seminar I will provide an overview about how cohesin forms chromatin loops and TADs by loop extrusion, explain how loop extrusion mediated by cohesin enables V(D)J recombination in mouse pro-B cells, and will present an outlook on our recent efforts to understand the mechanism of loop extrusion.

Organizer : Prof. Mitinori Saitou

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

ASHBi SEMINAR

Investigating the function of the non-canonical SMC protein SMCHD1 in regulating X chromosome inactivation

Lecturer: **Dr. Marnie Blewitt**

Bellberry-Viertel Senior Medical Research Fellow
Walter and Eliza Hall Institute

Date **Friday, 27 August 2021**

Time **2:00pm – 3:00pm**

Venue **Zoom Online Meeting***

***Register via the right QR code**

Abstract

SMCHD1 is a large chromosomal ATPase critical for gene silencing in normal development. Heterozygous mutations in SMCHD1 are associated with four distinct diseases. Therefore, we have been interested to understand how SMCHD1 contributes to epigenetic silencing at the molecular level so that we can understand its roles in normal development and consider how its function might be targeted to treat disease.

Using the inactive X chromosome as a model of epigenetic silencing, we have found that SMCHD1 is first recruited to chromatin dependent on polycomb repressive complex 1-mediated H2AK119, but independent on polycomb repressive complex 2-mediated H3K27me3. Once at the chromatin SMCHD1 mediates long range interactions, without SMCHD1 H3K27me3 spreads to cover more of the inactive X than is normally the case. These data suggest SMCHD1 plays a role in insulating the inactive X from other epigenetic regulators, potentially via the steric constraints of the long range interactions. With these data in mind, I will discuss our recent unpublished work on a neomorphic allele of SMCHD1, which are able to refine our model of SMCHD1 silencing. We are now extending our studies to how SMCHD1 functions at its autosomal targets including the Hox clusters, imprinted genes and other clustered gene families.

Organizer : Prof. Mitinori Saitou

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

ASHBi SEMINAR

Rare begets Common

Lecturer: Prof Bruno Reversade

IMB & IMCB, A*STAR, Singapore
Amsterdam UMC, Netherlands
Koç University, Turkey

Date **Friday, 3 September**

Time **15:00 – 16:00**

Venue **Zoom Online Meeting***

***Register via the right QR code**

Abstract

Over the last 10 years, a revolution in the speed and accessibility of high volume sequencing has introduced a paradigm shift in human genetics and medicine. Rare diseases – the human experiment – are a primary tool for assigning function to the human genome.

By identifying the genes responsible for rare diseases, we are best positioned to pinpoint the subverted biological pathways which not only underlie the pathology of a specific condition but which will, in many cases, reveal biological nodes whose perturbation contributes to more common pathologies – i.e. rare begets common.

I will illustrate this paradigm by highlighting how we have gone from discovering mutations in genes controlling early organogenesis in humans to the development of therapeutic drugs for oncology indications.

Organizer : Prof Takashi Hiiragi

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

ASHBi SEMINAR

Mapping human fibrotic diseases on a single cell level

Lecturer: Dr Rafael Kramann

Professor of Medicine and Chair of Nephro-Cardiology
RWTH Aachen University, Germany

Date Friday, 5 November 2021

Time 18:00 – 19:00

Venue Zoom Online Meeting*

*Register via the right QR code

Abstract

Tissue fibrosis occurs in virtually every organ after chronic repetitive injury and destroys the architecture of the tissue leading to organ failure. Fibrosis represents a large and growing healthcare burden. It has been estimated that fibrosis contributes to as much as 45% of deaths in the developed world. However, for fibrosis in most organs, there are currently no approved therapies available. This dire innovation gap can be explained by the lack of deep cellular and molecular understanding of the disease pathophysiology. Novel single cell genomic and spatial transcriptomic technologies allow to map human disease at unprecedented resolution. The seminar will present how these technologies can be utilized in an integrated manner to understand fibrotic disease and identify novel therapeutic targets with a particular focus on the kidney and the heart. Identified mechanisms and targets are validated in novel cell culture systems and organoids.

Organizer : Prof Motoko Yanagita

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

ASHBi SEMINAR

Deciphering Mental Conflict in Decision-Making from Animal Behavioral Data

Lecturer: Dr Naoki Honda

Professor,
Graduate School of Integrated Sciences for Life, Hiroshima University
Exploratory Research Center on Life and Living Systems (ExCELLS),
National Institutes of Natural Sciences

Date Tuesday, 30 November 2021

Time 16:00 – 17:00

Venue Zoom Online Meeting*

*Register via the right QR code

Abstract

Humans and animals are not optimal agents and often behave irrationally. They do not only rationally exploit rewards, but also explore the environment even without rewards so as to minimize uncertainty of the environment owing to their curiosity. However, the mechanism by which their curiosity is regulated has been largely unclear. Here, we developed a new decision-making model by extending the free energy principle. This model successfully described conservative, rational, and explorative behaviors depending on the level of curiosity. Furthermore, we have developed a machine learning method to infer fluctuations in curiosity and confidence from behavioral data. Therefore, comparison between neural activities and curiosity estimated by our method could enable us to reveal the neural basis for controlling mental temporal dynamics such as conflicts between reward and curiosity.

Organizer : Associate Prof Ken-ichi Amemori

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

ASHBi SEMINAR

Generation and comparative analysis of primate iPS cells

Lecturer: **Dr Mari Ohnuki**

Post-Doc

Anthropology and Human Genomics, Department Biology II

Ludwig Maximilians University Munich

Date **Friday, 17 December 2021**

Time **17:00 – 18:00**

Venue **Zoom Online Meeting***

*Register via the right QR code

Abstract

Comparing the molecular and cellular properties among primates is crucial to better understand human evolution and biology. However, it is difficult or ethically impossible to collect matched tissues from many primates including human, especially during development. Induced pluripotent stem cells (iPSCs) from primates allow experimental access to various cell types and differentiation stages and thus allow to compare cellular differentiation programs in humans and their closest relatives. Here we generated primate iPSCs and maintained them under the same feeder-free culture conditions. We first validated the Sendai virus-vector based reprogramming method and applied that to primate fibroblasts and urinary cells obtained in a non-invasive manner. Transcriptomic analysis revealed that the urine-derived primate iPSCs are well comparable to the human iPSCs. To study expression conservation throughout a dynamic process we analyzed the human, gorilla and cynomolgus macaque cells during neural differentiation by single-cell RNA sequencing. As constantly upregulated genes in all species we identified 18 core transcription factors. Thus the series of primate iPSCs have a huge potential to better understand human-specific traits as well as conserved regulatory networks.

Organizer : Associate Prof Takuya Yamamoto

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

ASHBi /HBRC
JOINT DISTINGUISHED SEMINAR

Using the Oculomotor System to Identify Biomakers of Neurological and Psychiatric Disease

Lecturer: **Douglas P. Munoz PhD**

Professor, Canada Research Chair in Neuroscience,
Queen's University, Canada

Date: **Wednesday, 5 January 2022**

Time: **21:00 - 22:00**

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

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

Dr. Munoz is a world leader in his research field of understanding eye saccades in relation to brain function. His lab combines eye tracking with neurophysiology and neuroimaging to study the brain pathways that control these voluntary eye movements. Using these techniques, his research team aims to understand child development and aging in healthy people as well as in patients with neurological and psychiatric disorders, and to identify potential biomarkers and therapeutic applications to improve cognitive function. Specifically, the research team combines human clinical research, functional brain imaging, and basic animal neurophysiology to understand brain circuits that control oculomotor behaviour and how dysfunction in specific brain circuits produces biomarkers of disease that can be studied with video-based eye tracking.

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

Contact: Prof Tadashi Isa
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ASHBi SEMINAR

Organoid based My Medicine

Lecturer: **Takanori Takebe** M.D., Ph.D.

Associate Professor, Cincinnati Children's Hospital

Professor, Tokyo Medical and Dental University

Date Friday, 7 January 2022

Time 16:00 – 17:00

Venue Hybrid*: Zoom Online/Memorial Auditorium

Faculty of Medicine Campus Map #7

* Registration required (Please register via QR code).
* Onsite participants will be individually informed from the organizer.

Abstract

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. Coupled with patient-derived stem cells, my group studied the mechanisms of human liver development and diseases, wherein organoid modelled a remarkable correlation between the clinical phenotype and genotype. Here, I will discuss our recent efforts to advance organoid development and inform personalized traits for chronic liver disease investigation by combining genetic-, cellular-, organoid- and human-scale evidence that might potentially inform designs of safer, more efficient, and robust clinical trials.

Organizer : Graduate School of Medicine

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

Contact: Prof. Mitinori Saitou

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ASHBi SEMINAR

Computational mass spectrometry to deepen the understanding of metabolisms

Lecturer: **Hiroshi Tsugawa** Ph.D.

Associate Professor, Tokyo University of Agriculture and Technology

Date Monday, 14 February 2022

Time 14:00 – 15:00

Venue Zoom Online Meeting*

*Register via the right QR code

Abstract

The metabolome is the complete set of small molecules present within a living organism, formed as a result of metabolism reflecting biological phenotypes. Untargeted metabolomics studies using mass spectrometry (MS) show that metabolites are deeply involved in the body's physiology and homeostasis. Yet, only 100-200 metabolites out of thousands of ions detected by MS are identified by modern computational techniques. Currently, most metabolomics data are "dark matter" and biological mechanisms are discussed based on information from only 2-3% of the metabolome (#1). Small biomolecules are thought to comprise over one million chemical species. Illuminating the 'dark matter of metabolomes' will expand our understanding of metabolic diseases and lead to the discovery of innovative drugs. Here I have established a new field of research called computational MS (CompMS) (#2-6). Employing CompMS, I was able to (A) develop a data processing pipeline for complex MS data and (B) identify unknown metabolites. Advancing CompMS can improve our knowledge of fundamental biology and open the door to the development of new biomarkers, drugs, and clinical applications.

References

1. da Silva, R.R. et al., PNAS, 112, 12549–12550, 2015
2. Tsugawa, H. et al. Nature Methods 12, 523–526, 2015
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5. Tsugawa, H. et al. Nature Methods 16, 295–298, 2019
6. Tsugawa, H. et al. Nature Biotechnology 38, 1159–1163, 2020

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

Contact: Prof. Yasuhiro Murakawa

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ASHBi
DISTINGUISHED SEMINAR

Stem cells, embryos and embryo models

Lecturer: Janet Rossant PhD
Chief of Research Emeritus, Senior Scientist,
The Hospital For Sick Children

Date: Wednesday, 2 February 2022

Time: 10:00 - 11:30

Venue: Zoom Online Register via the right QR code

Eligibility: Researchers and Students in Kyoto University

I will discuss the molecular pathways underlying the transition from totipotency to pluripotency during mouse embryo development and related this to the properties of the stem cell lines that derived from the blastocyst. These cell lines have recently been used to make stem cell-derived embryo models in the mouse and in the human. It is becoming clear that mouse and human embryo and stem cell development show important differences that need to be understood if stem cell-based embryo models are to be used more routinely to model human development.

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

Contact: Prof Masatsugu Ema
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ASHBi SEMINAR

A genome editing technology CRISPR-Cas3 in gene therapy

Lecturer: Tomoji Mashimo Ph.D.

Professor, Institute of Medical Science,
The University of Tokyo

Date Tuesday, 15 February 2022

Time 16:00 – 17:00

Venue Zoom Online Meeting*

*Register via the right QR code

Abstract

Although single-component Class 2 CRISPR systems, such as type II Cas9 or type V Cas12a, are widely used for genome editing in eukaryotic cells, the application of multi-component Class 1 CRISPR has yet to be developed. Recently we demonstrated that type I-E CRISPR, which is composed of Escherichia coli Cascade, Cas3, and programmable pre-crRNA, mediates distinct DNA cleavage activity in human cells. Notably, Cas3, which possesses helicase and nuclease activity, predominantly triggered several thousand base pair deletions upstream of the 5-ARG PAM, without prominent off-target activity. This Cas3-mediated directional and broad DNA degradation can be used to introduce functional gene knockouts and knock-ins. As an example of potential therapeutic applications, we show Cas3-mediated exon-skipping of the DMD gene in patient-iPSCs. We also highlight potential use for Cas3-mediated rapid, low-cost, instrument-free detection method for SARS-CoV2. This Cas3-based assay is comparable with Cas12- and RT-PCR-based assays in its speed and sensitivity but offers greater specificity for single-base-pair discrimination while negating the need for highly trained operators.

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

Contact: Associate Prof. Tomoyuki Tsukiyama

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ASHBi SEMINAR

Deciphering heterogeneity in liver diseases using mathematical models and data science

Lecturer: Naotoshi Nakamura M.D., Ph.D.

Specially Appointed Associate Professor,
Group of interdisciplinary Biology Laboratory (iBLab),
Graduate School of Science, Nagoya University

Date **Friday, 4 March 2022**

Time **15:00 – 16:00**

Venue **Zoom Online Meeting***

*Register via the right QR code

Abstract

The elucidation of cellular and individual heterogeneity is a central issue in modern life science and medicine, and various research approaches are attempted. Mathematical models are capable of describing nonlinear phenomena based on molecular mechanisms, while data science is good at deciphering systems with many variables. The combination of mathematical models and data science is an attractive approach to utilize the advantages of both. In this seminar, I will discuss mathematical data analyses that I have been working on recently, especially on the malignant transformation of hepatocellular carcinoma cells and on the determinants of therapeutic effects in chronic hepatitis patients. I will also touch on the importance of domain knowledge in data-driven mathematical medicine.

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

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