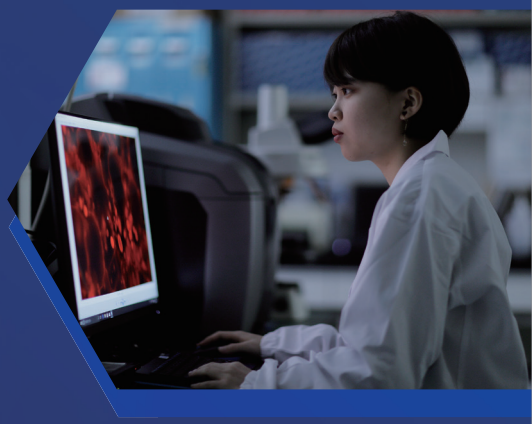
KANAZAWA UNIVERSITY

Cancer Research Institute
Kanazawa University

International Symposium

on Tumor Biology in Kanazawa 2021

Nov. 26, 2021



Program and Abstract

International Symposium on Tumor Biology in Kanazawa 2021

November 26(Fri), 2021
Cancer Research Institute, Kanazawa University(KU CRI), Japan

Venue: NanoLSI Main Conference Room, Kanazawa University (on-site),
zoom webinar (online)

Program

17:00-17:10(JST)　Opening Remarks
Takashi Wada (Vice President, KU)

Session I : Stem Cell, Embryogenesis and Development
(Chair: Masanobu Oshima, KU CRI, NanoLSI, Masaya Ueno, KU CRI)

17:10-17:40(JST)
Kim Jensen (Biotech Research & Innovation Centre & Novo Nordisk Foundation Center for Stem Cell Biology, University of Copenhagen, Denmark)
Intestinal Stem Cells in Development and Disease

17:40-18:05(JST)
Yusuke Miyanari (KU NanoLSI)
Dissecting Molecular Mechanisms to Regulate Chromatin Structure

18:05-18:35(JST)
Maria Elena Torres-Padilla (IES, Helmholtz Zentrum, Munich, Germany)
Epigenetic Mechanisms of Cellular Plasticity and Reprogramming to Totipotency

BREAK

Session II : Cellular Functions and Tumor Biology
(Chair: Chiaki Takahashi, KU CRI, Ryu Imamura, KU CRI)

18:50-19:15(JST)
Atsuko Kasahara (KU CRI, InFiniti)
Mitochondrial Dynamics: A New Therapeutic Target to Beat Malignant Tumour Cells

19:15-19:40(JST)
Eishu Hirata (KU CRI)
Multifaceted Interactions Between Cancer Cells and Glial Cells in Brain Metastasis

19:40-20:10(JST)
Erik Sahai (The Francis Crick Institute, UK)
A New Player in the Tumour Microenvironment of Dormant Cancer Cells

20:10-20:20(JST)　Closing Remarks
Kunio Matsumoto (Director, KU CRI)

Organizing committee: Atsushi Hirao, Kazuhiro Murakami, Yusuke Miyanari, Eishu Hirata, Yoshio Endo

Kim B Jensen

Biotech Research and Innovation Center (BRIC)
Novo Nordisk Foundation Center for Stem Cell Biology (DanStem)
Faculty of Health and Medical Sciences University of Copenhagen

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Education:

2000 M.Sc. in Molecular biology and chemistry, Department for Molecular and Structural Biology, University of Aarhus, Denmark

2003 Ph.D. in Science, Department for Molecular and Structural Biology, University of Aarhus, Denmark

Professional Career:

2003-2010 Research fellow with Dr Fiona Watt in London and Cambridge, UK

2010-2014 Group leader, The Cambridge Stem Cell Institute, University of Cambridge, UK

2013- Group Leader BRIC and DanStem, University of Copenhagen

Research Interests:

Kim Jensen is a Professor at the University of Copenhagen, Denmark. Kim Jensen did his PhD at the University of Aarhus, and joined Fiona Watt's group for his postdoctoral training. He held his first faculty position at the Stem Cell Institute, University of Cambridge, UK, before moving to Copenhagen in 2013, where he in 2019 was promoted to full Professor. Dr Jensen is interested in the molecular mechanisms that govern stem cell fate specification, and how extracellular signals integrates with gene regulatory networks to control tissue maturation and cellular plasticity in developing and adult epithelia. By combining studies using mouse models and clinical specimens the long-term aim of the research in the Jensen lab is to translate result from in vitro and in vivo models into regenerative therapies.

Selected Awards and Honors:

2015 ERC consolidator award

2021 EMBO Member

Publications:

1. Bornholdt, J., et al., (2020) Personalized B cell response to the Lactobacillus rhamnosus GG probiotic in healthy human subjects: a randomized trial. Gut Microbes 12:1-14.

2. Andersen, M.S. et al., (2019) Tracing the cellular dynamics of sebaceous gland development in normal and perturbed states. Nature Cell Biology 21: 924–32

3. Guiu, J. et al. (2019) Tracing the origin of adult intestinal stem cells. Nature 570: 107–111

Intestinal Stem Cells in Development and Disease

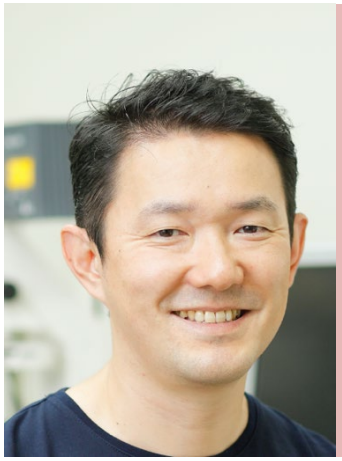
Kim B. Jensen
Biotech Research and Innovation Center (BRIC) and
Novo Nordisk Foundation Center for Stem Cell Biology (DanStem)
Faculty of Health and Medical Sciences
University of Copenhagen

The intestine is essential for digestion and absorption of nutrients. Moreover, the epithelium, which lines the luminal surface, constitutes a barrier that protects our body from gut microbiota. Adult stem cells located at the bottom of crypts are responsible for the life-long replenishment of the epithelium by giving rise to differentiated offspring. Using a combination of mouse models and tissue biopsies from human fetuses, we recently outlined the relationship between fetal progenitors in the developing epithelium and adult stem cells (Guiu et al., 2019, Nature). Here we observed that fetal cells are not organised in a strict cellular hierarchy as has been observed for adult epithelium and appear to be inherently more plastic. Moreover, during injury of the adult epithelium, which is associated with cellular dedifferentiation, the adult epithelial cells transition into a fetal-like state (Yui et al., 2018, Cell Stem Cell). Given the complexity of the intestinal epithelium along its axis it will be important to understand the mechanisms that fuel the first rudimental patterning of the epithelium providing spatial context for a differentiated and a proliferative state, and also to address whether similar mechanisms are recapitulated in diseases such as cancer.

References:

Guiu, J., Hannezo, E., Yui, S., Demharter, S., Ulyanchenko, S., Maimets, M., Jorgensen, A., Perlman, S., Lundvall, L., Mamsen, L.S., et al. (2019). Tracing the origin of adult intestinal stem cells. Nature 570, 107-111.

Yui, S., Azzolin, L., Maimets, M., Pedersen, M.T., Fordham, R.P., Hansen, S.L., Larsen, H.L., Guiu, J., Alves, M.R.P., Rundsten, C.F., et al. (2018). YAP/TAZ-Dependent Reprogramming of Colonic Epithelium Links ECM Remodeling to Tissue Regeneration. Cell stem cell 22, 35-49 e37.



Yusuke Miyanari

Nano Life Science Institute (WPI-NanoLSI), Kanazawa University

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Education:

2006 PhD, Department of Human Tumor Viruses, Graduate School of Biostudies, Kyoto University

Professional Career:

2006-2009 Postdoc, National Institute of Genetics (NIG), JAPAN (Hiro Sasaki Lab)

2009-2014 Postdoc, IGBMC, Strasbourg, FRANCE (Maria-Eleana TP Lab)

2014-2020 Associate Professor (PI), National Institute of Basic Biology (NIBB), JAPAN

2020-present Associate Professor (PI), NanoLSI, Kanazawa U.

Scientific Activities:

2001-2006 Studies on Hepatitis C virus

2006-present Epigenetic regulation of cell lineage allocation

Research Interests:

Epigenetics, Stem cell, chromatin, transcription

Honors:

2015 The Young Scientists' Prize, The Commendation for Science and Technology by the MEXT

2015 Takenaka Promotion Prize

Publications:

1. Miyanari Y. et al, Nature. 483.470-473. 2012
2. Miyanari Y. et al, Nature Structural & Molecular Biology, 2013 Nov;20(11):1321-4
3. Kurihara M. et al, Molecular Cell, S1097-2765(20)30230-6. 2020

Dissecting Molecular Mechanisms to Regulate Local Chromatin Structure

Yusuke Miyanari

NanoLSI, Kanazawa University

Chromatin is organized in a non-random fashion within 3D nuclear space. During developmental processes, the nuclear architecture is dramatically reconstructed, resulting in the establishment of cell-type specific nuclear organization. Defects in structural components of the nucleus are responsible for developmental aberrations and several human diseases. Remodeling of the nuclear architecture leads to spatial arrangement of genes, which could affect genome functions including gene expression. We aim to reveal the role of chromatin dynamics in cell lineage-allocation by deciphering the molecular mechanisms underlying the remodeling of nuclear organization and their effects on developmental gene expression, using mouse early embryos and embryonic stem (ES) cells as model systems. We recently conducted genome-wide screening to discover novel players involved in regulation of chromatin accessibility, and found that some key players have significant roles to establish global chromatin accessibility. Manipulation of these key players allowed us to boost genetic and epigenetic reprogramming of cells.

Maria-Elena Torres-Padilla

Director, Institute of Epigenetics & Stem Cells Helmholtz Zentrum Munich
Professor, Chair of Stem Cell Biology at the Faculty of Biology
Ludwig-Maximilians-University Munich

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Education:

1998 University Degree in Biology. Faculty of Sciences, National University of Mexico, Mexico
2002 Ph.D. Institut Pasteur/University of Paris V, France
2008 Habilitation. Université Louis Pasteur, Strasbourg, France

Professional Career:

2002-2006 Postdoctoral EMBO fellow, The Gurdon Institute, University of Cambridge, UK
2006-2008 Senior Scientist, IGBMC, Strasbourg, France
2007 Nominated Chargee de Recherche (INSERM)
2009 Independent Group leader, IGBMC, Strasbourg, France
2010-2012 Deputy Director of Developmental and Stem Cell Biology Department, IGBMC,Strasbourg, France
2012 Nominated Director of Research (INSERM)
2016- Professor, Chair of Stem Cell Biology, Faculty of Biology, Ludwig-Maximilians-University Munich, Germany
2016- Director, Institute of Epigenetics & Stem Cells,Helmholtz Zentrum Munich, Germany

Selected Awards and Honors:

2015 Elected EMBO Member
2018 Female Award of the German Stem Cell Network
2019 Honorary Professor, University of Aarhus Denmark

Selected Publications:

1. Canat A. & Torres-Padilla ME. 2021. Retrotransposing a promoter for development. ***Nature Cell Biology,*** *In press (2021)*

2. Burton A. & Torres-Padilla ME. 2021. Deconfining heterochromatin for expression. ***Nature Cell Biology,*** Aug;23(8):814-816. (2021)

3. Iturbide A. Ruiz Tejeda Segura ML. Noll C. Schorpp K. Rothenaigner I. Ruiz-Morales ER. Lubatti G. Agami A. Hadian K. Scialdone A & Torres-Padilla ME. 2021. Retinoic acid signalling is critical during the totipotency window in early mammalian development. ***Nature Structural & Molecular Biology,*** Jun;28(6):521-532. (2021)

Epigenetic Mechanisms of Cellular Plasticity and Reprogramming to Totipotency

Maria-Elena Torres-Padilla
Institute of Epigenetics & Stem Cells,
Helmholtz Centre Munich, Munich,
Germany

Totipotency is a fundamental cellular feature. In mammals, the terminally differentiated sperm and oocyte fuse to create a totipotent zygote upon fertilisation. The mechanisms underlying the epigenetic reprogramming towards totipotency that follows fertilisation are not fully understood, and the molecular features of totipotent cells remain scarce. Embryonic cells remain totipotent only for a restricted time window. During this time, embryonic cells are characterised by an atypical chromatin structure and reactivation of specific families of retrotransposons. Recently, it was reported that totipotent-like cells arise in ES cell cultures in vitro. Like in the embryo, these cells are characterized by the expression of MERVL LTR retrotransposons. To address how the expression of these elements is regulated during the transition between totipotent and pluripotent states, we first examined histone modifications and chromatin structure in early mouse embryos. Remarkably, we have found that specific features of embryonic chromatin are also present in totipotent-like cells in vitro. Based on this analysis, we have begun to decipher key molecular regulators of repetitive elements in the embryo, and how they contribute to shaping the regulatory programme of the newly formed embryo. Our results have identified candidate pathways that regulate chromatin function and expression of these elements and show that they can promote totipotency. We will present our latest results that reveal a new role for chromatin integrity in promoting epigenetic reprogramming and sustaining molecular features of totipotent cells *in vivo*.

Atsuko Kasahara

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Education

2002	B.Sc.	Biological Science Degree, University of Tsukuba, Japan
2004	M.Sc.	Dept. of Biosystem Studies, University of Tsukuba, Japan (Molecular and Cellular Biology)
2006	Ph.D.	Dept. of Biological Sciences, University of Tsukuba, Japan (Molecular and Cellular Biology)

Professional Career

2006-2008 Postdoctoral Research Fellow, Graduate School of Life and Environmental Sciences, Institute of Biological Sciences and Center for Tsukuba Advanced Research Alliance, University of Tsukuba, Japan

2008-2013 Postdoctoral Research Fellow, Department of Physiology and Metabolism, Centre Médical Universitaire (CMU), University of Geneva, Switzerland

2013-2014 Postdoctoral Research Fellow, Department of Pathology and Immunology, Centre Médical Universitaire (CMU), University of Geneva, Switzerland

2015 Postdoctoral Research Fellow, Department of Biology, University of Padua, Italy, Lab of Molecular Neuropharmacology, Graduate School of Pharmaceutical Sciences, Osaka University, Japan

2016- Assistant Professor, Cancer Research Institute, Institute for Frontier Science Initiative, Kanazawa University, Japan

Research Interests:

Mitochondrial dynamics, organeller communications

Publications:

1. Bassoy EY*, **Kasahara A*,** Chiusolo V, Jacquemin G, Boydell E, Zamorano S, Riccadonna C, Pellegatta S, Hulo N, Dutoit V, Derouazi M, Dietrich PY, Walker PR, Martinvalet D. ER-mitochondria contacts control GSC surface glycan expression and sensitivity to killer lymphocytes. ***EMBO J.*** 2017 36: 1493-1512. *Contributed equally to this work
2. **Kasahara A**, Scorrano L. Mitochondria: from cell death executioners to regulators of cell differentiation. ***Trends Cell Biol***. 2014 24: 761-770. Review
3. **Kasahara A**, Cipolat S, Chen Y, Dorn GW 2nd, Scorrano L. Mitochondrial fusion directs cardiomyocyte differentiation via calcineurin and Notch signaling. ***Science***. 2013 342: 734-737.

Mitochondrial Dynamics: A New Therapeutic Target to Beat Malignant Tumour

Atsuko Kasahara

Cancer Research Institute, Institute for Frontier Science Initiative, WPI Nano Life Science Institute (WPI-Nano LSI), Kanazawa University

Mitochondria are the power supply of the cell, also in cancer cells to maintain their continuous proliferation. In addition to ATP production through oxidative phosphorylation, mitochondria play crucial roles in metabolic pathways, calcium and redox homeostasis, and apoptosis. These multiple mitochondrial functions are reflected by their extremely dynamic morphology in the cells, which is modulated and maintained by their fusion and division. The dynamin-related GTPases Mitofusin (Mfn) 1 and 2, and Optic Atrophy 1 (OPA1) fuse mitochondria, and the cytosolic dynamin-related protein 1 (DRP1) divides mitochondria.

These "mitochondria-shaping proteins" also play roles in the malignant characteristics of cancer cells. In glioblastoma cell lines, we found that mitochondria are fragmented with up-regulation of DRP1 in a tumorigenic stem-like population, and down-regulation of DRP1 lose their tumorigenic potential (Bassoy EY, **Kasahara A**, et al., *EMBO J* 2017). Glioma stem-like populations (GSCs) are resistant to chemotherapy, therefore, targeting GSCs is crucial for the complete eradication of glioblastoma. Interestingly, cytotoxic T lymphocytes (CTL) kill more preferentially GSCs than glioma differentiated cells (GDCs). Mitochondria in GSCs are fragmented, distant from the endoplasmic reticulum (ER), and show fewer contact sites with the ER compared to GDCs. This specific mitochondrial morphology and the distance between ER and mitochondria are important for sialylated glycan expressions at the plasma membrane, which directly influence the CTL physiological contact to the target glioma cells (Bassoy EY, **Kasahara A**, et al., *EMBO J* 2017).

Epidermal Growth Factor Receptor (EGFR) tyrosine kinase inhibitors (EGFR-TKIs) are commonly used molecular target drugs against non-small-cell lung cancer; however, the appearance of resistant lung adenocarcinoma cells after a certain period of treatment hinders the complete eradication of the cancer cells. Although several molecular mechanisms underlying this acquired resistance to the EGFR-TKIs have been demonstrated, the mitochondrial dynamics and functions can also be one of the molecular mechanisms used by lung adenocarcinoma cells for acquiring resistance to the EGFR-TKIs. In fact, we have identified the up-regulation of mitochondrial inner membrane profusion protein OPA1 in a gefitinib-resistant lung adenocarcinoma cell line, which contributes to the maintenance of the resistance. OPA1 protects cells from apoptosis by keeping the cristae junction tight to prevent cytochrome *c* release. OPA1 is also required for the stabilisation of the respiratory chain supercomplexes, and efficient respiration activity. We have observed elongated mitochondria and tightened cristae lumen in the resistant cells compared to that in the sensitive cells. The resistant cells showed anti-apoptotic cell death induced by gefitinib as well as intrinsic apoptotic stimuli via OPA1 up-regulation. The resistant cells also showed increased mitochondrial respiration; thus, inhibition of mitochondrial respiration restored the sensitivity to gefitinib. Ablation of OPA1, as well as a small molecule specific OPA1 inhibitor, restored the sensitivity to gefitinib (manuscript in preparation).

Our results suggest that "mitochondria-shaping proteins", which regulate the shape and structure of the organelle for efficient activities of the enzymes embedded, can be used to target the malignant cancer cells.

Eishu Hirata

Division of Tumor Cell Biology and Bioimaging, Cancer Research Institute of Kanazawa University

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Education:

2002	Kyoto University School of Medicine (MD)
2010	Kyoto University Graduate School of Medicine (PhD)

Professional Career:

2002	Resident, Kyoto University Hospital
2003	Resident, Ako City Hospital
2004	Medical Staff, Kokura Memorial Hospital
2005	Medical Staff, Shinko Hospital
2010	Assistant Professor, Kyoto University
2011	Research Fellow, Cancer Research UK London Research Institute
2015	Research Fellow, Francis-Crick Institute
2015	Senior Assistant Professor, Kanazawa Medical University
2018-present	Associate Professor, Kanazawa University

Scientific Activities:

2010-	Board certified neurosurgeon, Japanese Neurosurgical Association
2022-	Councilor, Japanese Cancer Association

Publications:

1. Hirata et al., The brain microenvironment induces DNMT1 suppression and indolence of metastatic cancer cells. ***iScience.*** 23(9):101480, 2020.
2. Hirata et al., Intravital imaging reveals how BRAF inhibition generates drug tolerant microenvironments with high integrin β1/FAK signaling. ***Cancer Cell.*** 27: 1-15, 2015.
3. Hirata et al., In vivo fluorescence resonance energy transfer imaging reveals differential activation of Rho-family GTPases in glioblastoma cell invasion. ***J Cell Sci.*** 125: 858-68. 2012.

Multifaceted Interactions Between Cancer Cells and Glial Cells in Brain Metastasis

Eishu Hirata

Division of Tumor Cell Biology and Bioimaging,
Cancer Research Institute of Kanazawa University

The tumor microenvironment is deeply involved in cancer cell growth, invasion, metastasis, and resistance to therapy. It is composed of a variety of stromal cells, including fibroblasts, vascular endothelial cells, and cells of the immune system. There are also some organ-specific cell types, such as osteoblasts in the bone tissue, and glial cells in the brain tissue. In the process of brain metastasis formation, the emerging and progressive interactions between cancer cells and glial cells play a very important role; however, there are few methods to stably analyze these events for a long period in vitro. Recently, we have developed a simple and stable culture method for prolonged observation of astrocytes and microglia. Mixed-glial culture on soft substrate (MGS) not only enables long-term culture of primary microglia, but also maintains the reactive expression of glial fibrillary acidic protein in astrocytes, a characteristic response observed in disease-related astrocytes, including those in cancer brain metastasis. These astrocytes maintain astrocytic gene expression signatures compared to those prepared and cultured using a conventional method. The growth abilities of cancer cells in mouse brains positively correlate with those in MGS, and cancer cells cultured in MGS for a long period acquire growth ability in mouse brains. These results suggest that MGS well mimics the brain microenvironment for cancer cells and is a useful system to investigate cancer-glia interactions. Three-dimensional live imaging with chemical and/or genetic manipulations in the co-culture system reveals complicated and multifaceted interactions between cancer cells, astrocytes, and microglia, which collectively configurates cancer-promotive and/or -suppressive microenvironment.

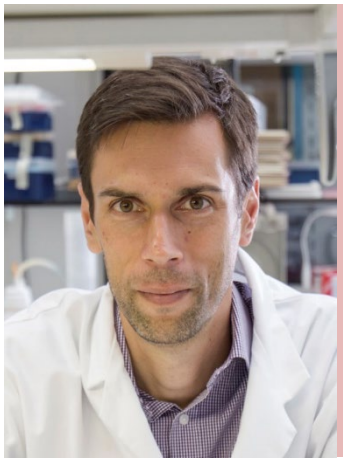
References:

[1] Hirata E, Ishibashi K, Kohsaka S, Shinjo K, Kojima S, Kondo Y, Mano H, Yano S, Kiyokawa E, Sahai E. The brain microenvironment induces DNMT1 suppression and indolence of metastatic cancer cells. ***iScience.*** 23(9):101480, 2020.

[2] Hirata E and Sahai E. Tumor Microenvironment and Differential Responses to Therapy. ***Cold Spring Harb Perspect Med.*** 7(7):a026781, 2017.

[3] Seifert H, Hirata E, Gore M, Khabra K, Messiou C, Larkin J, Sahai E. Extrinsic factors can mediate resistance to BRAF inhibition in CNS melanoma metastases. ***Pigment Cell Melanoma Res.*** 29(1):92-100, 2016.

[4] Hirata E, Girotti MR, Viros A, Hooper S, Spencer-Dene B, Matsuda M, Larkin J, Marais R and Sahai E. Intravital imaging reveals how BRAF inhibition generates drug tolerant microenvironments with high integrinβ1/FAK signaling. ***Cancer Cell.*** 27: 1-15, 2015.



Erik Sahai

The Francis Crick Instiute

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Education:

1991 - 1994	Emmanuel College, University of Cambridge First Class degree – Zoology
1994 - 1998	University College London, University of London Doctor of Philosophy - Biochemistry

Professional Career:

Nov '98 – June '03	Post-doc - Institute of Cancer Research, 237 Fulham Road, London, UK
June '03 – June '04	Research Fellow - Albert Einstein College of Medicine, 1300 Morris Park Ave, Bronx, New York, USA
Aug '04 – March '15	Group Leader - Cancer Research UK London Research Institute 44 Lincoln's Inn Fields, London, UK
April '15 – present	Senior Group Leader - The Francis Crick Institute 1 Midland Road, London, NW1 1AT UK

Honors:

Elected to the Academy of Medical Sciences – 2021
Elected Fellow of the European Academy of Cancer Sciences – 2017
Elected EMBO member – 2014
British Society for Cell Biology Hooke Medal - 2009
EMBO Young Investigator Programme Member – 2008
UICC Translational Cancer Research Fellowship - 2003-2004
University of Cambridge Frank Smart Prize for Zoology - 1994

Top 3 Publications in last 3 years:

(selected from >100 papers published during career, h-index 72, >28000 citations Google Scholar metrics)

1. Arwert EN, Milford EL, Rullan A, … Sahai E. Nature Cell Biology. 2020 Jul;22(7):758-766. doi: 10.1038/s41556-020-0527-7

2. Montagner M, …Sahai E. Nature Cell Biology 2020 Mar;22(3):289-296. doi: 10.1038/s41556-020-0474-3 PMID: 32094692

3. Park D, … Sahai E. Nature Materials 2020 Feb;19(2):227-238. doi: 10.1038/s41563-019-0504-3.. PMID: 31659294

A New Player in the Tumour Microenvironment of Dormant Cancer Cells

Erik Sahai

The Francis Crick Institute

Delayed relapses at distant sites are common for certain types of cancers after removal of primary tumor, such as breast and prostate cancer. This implies that disseminated cancer cells can persist in an indolent or dormant state for long periods of time. Because of the asymptomatic nature of this phenomenon, isolation, and analysis of disseminated dormant cancer cells from clinically disease-free patients is ethically and technically highly problematic. To overcome this major limitation, we have developed in vitro models of the metastatic niche for different organs and different types of cancers. In particular, we have developed a lung 'organotypic' system and used this in combination with in vivo assays of breast cancer dormancy. This reveals how the behaviour of indolent breast cancer cells in the lung is determined by their interactions with alveolar epithelial cells, in particular alveolar type 1 cells. This promotes the formation of fibronectin fibrils by indolent cells that drive integrin-dependent pro-survival signals. Combined in vivo RNA sequencing and drop-out screening identified secreted frizzled-related protein 2 (SFRP2) as a key mediator of this interaction. Sfrp2 is induced in breast cancer cells by signals from lung epithelial cells and promotes fibronectin fibril formation and survival, whereas blockade of Sfrp2 expression reduces the burden of indolent disease. Subsequent analyses show that that the TFEB-lysosomal axis is activated in dormant cancer cells (DCCs) and that it is modulated by the pro-survival ephrin receptor EphB6. TFEB lysosomal direct targets are enriched in DCCs in vivo and correlate with relapse in ER+ breast cancer patients. Direct coculture of DCCs with alveolar type I-like lung epithelial cells and dissemination in the lung drive lysosomal accumulation and EphB6 induction. EphB6 contributes to survival, TFEB transcriptional activity, and lysosome formation in DCCs in vitro and in vivo. Furthermore, signaling from EphB6 promotes the proliferation of surrounding lung parenchymal cells in vivo. Our data provide evidence that EphB6 is a key factor in the crosstalk between disseminated dormant cancer cells and the lung parenchyma and that the TFEB-lysosomal pathway plays an important role in the persistence of DDCCs.

References

EphB6 Regulates TFEB-Lysosomal Pathway and Survival of Disseminated Indolent Breast Cancer Cells. Zangrossi M, Romani P, Chakravarty P, Ratcliffe CDH, Hooper S, Dori M, Forcato M, Bicciato S, Dupont S, Sahai E, Montagner M. Cancers (Basel). 2021 Mar 3;13(5):1079. doi: 10.3390/cancers13051079.

A Lung Organotypic Coculture Reveals a Role for TFEB-Lysosomal Axis in the Survival of Disseminated Dormant Cancer Cells. Zangrossi M, Chakravarty P, Romani P, Dupont S, Hooper S, Sahai E, Montagner M. Cancers (Basel). 2021 Feb 28;13(5):1007. doi: 10.3390/cancers13051007.

In vitro Models of Breast Cancer Metastatic Dormancy. Montagner M, Sahai E. Front Cell Dev Biol. 2020 Mar 3;8:37. doi: 10.3389/fcell.2020.00037.

Crosstalk with lung epithelial cells regulates Sfrp2-mediated latency in breast cancer dissemination. Montagner M, Bhome R, Hooper S, Chakravarty P, Qin X, Sufi J, Bhargava A, Ratcliffe CDH, Naito Y, Pocaterra A, Tape CJ, Sahai E. Nat Cell Biol. 2020 Mar;22(3):289-296. doi: 10.1038/s41556-020-0474-3

Secretariat

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