Gunma University

関東がん専門医療人養成拠点

1st International Symposium of MEXT Program
"Fostering Health Professionals for Changing Needs of Cancer"

Genomic Medicine

Kanto Academic Alliance for Fostering Cancer Professionals

February 17, Sat 10:00～17:00
ROSE HALL
(Maebashi Chamber of Commerce and Industry)

PROGRAM

Welcome address

10:30～10:35 **Prof. Yasuki ISHIZAKI**
(Dean, Gunma University Graduate School of Medicine)

Session I. Cancer Genomic Medicine

Moderator: Hisahiro MATSUBARA
(Graduate School of Medicine, Chiba University)

10:35 ~ 11:15

Implementation of "Clinical Sequencing" in Cancer Genome Medicine in Japan

Dr. Takashi KOHNO
(Division of Genome Biology, National Cancer Center Research Institute/ Division of Translational Research, Exploratory Oncology Research & Clinical Trial Center (EPOC), National Cancer Center, JPN)

11:15 ~ 11:50

Genome Sequencing Analysis for Cancer Research and Precision Medicine

Dr. Hidewaki NAKAGAWA
(Laboratory for Genome Sequencing Analysis, RIKEN Center for Integrative Medical Sciences, JPN)

11:50 ~ 12:50 Lunch

Session Ⅱ. Toward Further Progress：Omics Analysis and Bioinformatics

Moderator: Prof. Masahiko NISHIYAMA
(Gunma university Graduate School of Medicine)

12:50 ~ 13:30

Identification of Novel Therapeutic Targets for Cancer Based on the Omics Cancer-Assciated Fibroblasts: Tumor Allies and Foes

Dr. Andrei TURTOI
(Tumor Microenvironment and Resistance to Treatment, Institute of Cancer Research of Montpellier, FRA)

13:30 ~ 14:10

Innovative strategies to identify and validate new OMICs biomarkers with high translational potential for diagnostic, prognostic and treatment in oncology

Prof. Vincent CASTRONOVO
(Laboratory of Metastases Research, GIGA-CANCER, Liege University, BEL)

14:10 ~ 14:50

The dynamic cerebrospinal fluid proteome and a perspective on a new class of biomarkers

Prof. Jacques COLINGE
(Cancer Bioinformatics and System Biology, , Institute of Cancer Research of Montpellier, FRA)

14:50 ~ 15:00 Coffee Break

Guidance Session for Students : Meet the Experts

15:00 ~ 16:55

Student attendance will be separated into 5 groups and rotate 5 stations to directly ask something to 5 invited speakers in order to be a specialist of Cancer Genomic Medicine. Each invited speakers will give advices and supervise to students from a view point of each special field.

Closing Remarks

16:55～17:00 **Prof. Nobuhiro OHKOHCHI**
(Project Director/ Graduate School of Comprehensive Human Science,
University of Tsukuba)

Takashi Kohno, Ph.D

Position: Chief, Division of Genome Biology, Research Institute
Chief, Division of Translational Genomics, Exploratory Oncology
Research and Clinical Trial Center (EPOC)
National Cancer Center, Japan

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EDUCATION

Kyoto University, School of Pharmacy, Kyoto, Japan (1985-1989)
Kyoto University, Graduate School of Pharmacy, Kyoto, Japan (1989-1991)
Tokyo University, Graduate School of Medicine, Tokyo, Japan (1991-1995)

WORK EXPERIENCE

Researcher, Biology Division (Dr. Yokota Lab)
National Cancer Center Research Institute (1995-2000)
Section Head, Biology Division (Dr. Yokota Lab)
National Cancer Center Research Institute (2000-2010)
Chief, Division of Genome Biology
National Cancer Center Research Institute (2011-present)
Chief, Division of Translational Genomics
EPOC, National Cancer Center (2013-present)

CERTIFICATION

Doctor of Philosophy, Tokyo University (1995)

RESEARCH INTEREST

Cancer genome medicine

Dr. Takashi Kohno is currently a Chief in Division of Genome Biology of National Cancer Center Research Institute, Japan. Dr. Kohno graduated from Kyoto University in 1989. He received PhD from Tokyo University. From 1995, he has studied lung cancer genetics and genomics in National Cancer Center. His representative research product is the finding of RET fusion in lung adenocarcinoma and its translation to lung cancer clinic. He is also a Chief of Division of Translational Research, Exploratory Oncology Research and Clinical Trial Center, National Cancer Center Research Institute. His research area includes genomics, genetics (polymorphisms), and cancer genome medicine.

Implementation of “Clinical Sequencing” in Cancer Genome Medicine in Japan

Takashi Kohno
Division of Genome Biology, National Cancer Center Research Institute
Division of Translational Genomics, Exploratory Oncology Research and Clinical Trial Center, National Cancer Center

In oncology, actionable mutations (alterations) in cancer-associated genes are critical in terms of the selection of therapeutic approaches. Next-generation sequencing (NGS) of tumor sample DNA (i.e., clinical sequencing) can guide clinical management by providing diagnostic or prognostic data, and facilitating the identification of potential treatment regimens, such as molecular-targeted and immune checkpoint blockade therapies. In the U.S., a variety of multi-gene panels have been developed and implemented for this purpose. In Japan, several academic institutions have now performed detailed investigations of the feasibility and value of clinical sequencing, and cancer societies have issued consensus clinical practice guidelines for NGS-based tests. These efforts will facilitate the implementation of cancer genome medicine in Japan.

1) Kohno T et al. KIF5B-RET fusions in lung adenocarcinoma. Nat Med, 2012.
2) Yoh K et al. Vandetanib in patients with previously treated RET-rearranged advanced non-small-cell lung cancer (LURET): an open-label, multicentre phase 2 trial. Lancet Respir Med, 2017.
3) Tanabe et al. Comprehensive screening of target molecules by next-generation sequencing in patients with malignant solid tumors: guiding entry into phase I clinical trials. Mol Cancer, 2016.
3) Kohno T. Implementation of "Clinical Sequencing" in cancer genome medicine in Japan. Cancer Sci, 2018, in press.

Hidewaki Nakagawa, MD, PhD

1991	Osaka University, School of Medicine (M.D.)
1991	Osaka University Hospital, General Surgery, Resident
1992	Osaka University Hospital, ICU/ Anesthesiology, Resident
1993	National Osaka Hospital, GI surgery and breast surgey, Resident
1996	Osaka University, Graduate School of Medicine (Ph.D. 2000)
1999	The Ohio State University, Human Cancer Genetics Program, Postdoctoral fellow
2003	Assitant Professor / Associate Professor, Human Genome Center, Institute of Medical Science, The University of Tokyo
2008	Laboratory Head, Laboratory for Biomarker Development, RIKEN Center for Genomic Medicine
2013 -	Laboratory Head, Laboratory for Genome Sequencing Analysis, RIKEN Center for Integrative Medical Sciences
2015 -	Program Officer of Biobank/Genomic Medicine project in AMED

Dr. Hidewaki Nakagawa graduated from Osaka University School of Medicine in 1991, and he completed training in clinical oncology of GI & breast cancers and critical care medicine as a surgeon. He obtained his PhD in 2000 from Osaka University for genomic research of hereditary colon cancer. After four years postdoctoral training of colon cancer genomics at the Human Cancer Genetics Program, The Ohio State University, USA, he returned to Japan as an assistant/associate professor at Institute of Medical Science, The University of Tokyo, where he was dedicated to therapeutic target screening for pancreatic and prostate cancers. In 2008, he moved to RIKEN as a team leader of genomic medicine. His recent research focuses on cancer genomics by whole genome sequencing and cancer biomarker development using next-generation sequencing. He has been working for cancer genome sequencing analysis of liver cancer and GI cancers as one of the PIs of ICGC /TCGA project. His main interest is genome-based personalized medicine and cancer patient care.

Genome Sequencing Analysis for Cancer Research and Precision Medicine

Hidewaki Nakagawa
RIKEN Center for Integrative Medical Sciences

Cancer is essentially a “disease of the genome” which develops and evolves with the accumulation of a variety of mutations in the background of germline variants, and some driver mutations such as EGFR, HER2, and BRCA1/2 were successfully targeted for treatment. Explosive advances of next-generation sequencer (NGS) and computational analyses handling massive data enable us to comprehensively analyze cancer genome profiles in research and clinical levels, such as targeted sequencing for hundreds of genes, whole exome sequencing (WES), RNA sequencing (RNA-Seq), and eventually whole genome sequencing (WGS) or cell-free DNA sequencing. These approaches combined with mathematical analysis and other -omics analysis can clarify the underlying carcinogenesis and cancer immunology and achieve molecular sub-classification of cancer, which facilitates discovery of genomic biomarkers and personalized cancer medicine. I present recent technical approaches for cancer genome sequencing and the future direction of cancer genome sequencing, and discuss its utility and limitation of an analysis platform and mutation interpretation for cancer genomics and cancer precision medicine.

Dr. Turtoi Andrei

Team Leader
"Tumor Microenvironment and Resistance to Treatment"
Institut de Recherche en Cancérologie de Montpellier/
Inserm U1194, Montpellier, France

EDUCATION

01.04.2008	**PhD** (Faculty of Biology / Department of Genetics, Technical University Dresden, Germany.)
2004	**Dipl. Ing.** (Faculty of Chemical Engineering/ University of Applied Sciences, Aachen, Germany.)
2003	**B.Eng.** (Faculty of Chemical Engineering/ University of Applied Sciences, Aachen, Germany.)
1999	**International Baccalaureate (IB)** (United World Colleges, Pune, India.)

PREVIOUS POSITIONS

07.2016 – 09.2016	**Invited Lecturer (Assistant Professor)** Department of Molecular Pharmacology and Oncology, Graduate School of Medicine, University of Gunma, Maebashi, Japan.
2015 – 2016	**FNRS Scientific Collaborator (Televie Fellowship)** Faculty of Medicine/ GIGA-Cancer, Metastasis Research Laboratory, University of Liege, Liege, Belgium.
05.2015 – 09.2015	**Invited Lecturer (Assistant Professor)** Department of Molecular Pharmacology and Oncology, Graduate School of Medicine, University of Gunma, Maebashi, Japan.
2012 – 2015	**FNRS Charge de Recherché** Faculty of Medicine/ GIGA-Cancer, Metastasis Research Lab University of Liege, Liege, Belgium.
2009 – 2012	**Principal Investigator** Faculty of Medicine/ GIGA-Cancer, Metastasis Research Laboratory, University of Liege, Liege, Belgium.
2008 – 2009	**Post Doctoral Fellow** Faculty of Sciences/ Department of Chemistry, Mass Spectrometry Laboratory, University of Liege, Liege, Belgium.
2005 – 2008	**PhD Fellow** Institute of Medicine, Laboratory of Radiation Biology, Forschungszentrum Jülic Germany.
2003 – 2004	**Research Fellow** Department of Marine Chemistry, Alfred Wegener Institute for Polar and Marine Research, Bremerhaven, Germany.

Cancer-Assciated Fibroblasts: Tumor Allies and Foes

Andrei Turtoi
Institut du Cancer Montpellier, Montpellier 34090, France;
INSERM U1194, Montpellier 34090, France;
Institut de Recherche en Cancérologie de Montpellier, Montpellier 34090, France;
Université Montpellier, Montpellier 34298, France;

Cancer associated fibroblasts are the major component of the tumor microenvironment & a rich source of growth factors, pro-angiogenic molecules and matrix proteins. In contrast to for example macrophages, CAF are almost exclusively regarded as pro-tumorigenic elements and as such they have been proposed as eligible tumor targets. Unfortunately, CAF-directed targeted therapies have thus far not produced the desired anti-tumor effects. These have either showed only modest tumor control or, surprisingly, have induced tumoral progression. Emerging evidence suggest that our simplistic picture of CAF is not correct and that these cells may also have intrinsic tumor-defensive properties. Future studies of tumor microenvironment and notably CAF will thus inevitably relay on single cell approaches, enabling a context and spatially-dependent observation of this highly heterogeneous cell population. In the present talk I will touch upon past and present works supporting such differentiated picture of CAF as well as present some newest research data from our lab.

Vincenzo CASTRONOVO

Professor
Faculty of Medicine, University of Liège

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Tour de Pathologie, +4, Bât. B23 - B-4000 Liège
Tél. : +32 (0) 4 366 2479 - e-mail : vcastronovo@ulg.ac.be

Education

Medical Doctor, Surgery and obstetrics, University of Liège, 1983 – Summa Cum Laude.
PhD in biomedical sciences, University of Liège, 1987 – Summa Cum Laude.
Agrégé de l'Enseignement Supérieur, University of Liège, 1992 – Summa Cum Laude.
Board-Certified in Obstetrics and Gynecology, University of Liège, 1993 – Summa Cum Laude.

University career

Head of Metastases Research Laboratory, University of Liège (Since 1992).
Supervisor of Gynecologics-Obstetrical Department. University of Liège (1993-1998).
Maître de Conférences. University of Liège (1994-1998).
Founder and director of the MetastasesResearch Laboratory (1992-to date)
Maître de Recherches (Fonds National de la Recherche Scientifique (1994-1998).
Medical Director of the Centre Anti-Cancer. (1995-2003).
Director of the Center of Experimental Cancer Research (CRCE). University of Liège (2002-2007).
Professor (Full time). Faculty of Medicine, University of Liège (2005-2010).
Head of GIGA-Cancer. University of Liège (2008-2011).
Full Professor (Biology). Faculty of Medicine, University of Liège (Since 2011).
Member of the Royal Belgian Academy of Medicine.

Innovative strategies to identify and validate new OMICs biomarkers with high translational potential for diagnostic, prognostic and treatment in oncology

Vincent Castronovo[1], Andrei Turtoi[1], Brunella Costanza[1] and Masahiko Nishiyama[2]
Metastasis Research Laboratory, GIGA Cancer, University of Liège, Liège, Belgium
Department of Molecular Pharmacology and Oncology,
Gunma University Graduate School of Medicine, Maebashi, Gunma, Japan

Biomarker discovery is a crucial step for cancer early diagnosis, prognosis, prediction of therapy response and specific effective targeted therapies, particularly in the field of oncology. The discovery of biomarkers that are readily accessible through the circulating blood and are selectively overexpressed in pathological tissues has become a major research objective. This group of molecules has a high potential to serve as a tool for imaging and targeted cancer therapy approaches. In this therapeutic concept, specific cancer proteins are reached by intravenously administered ligands that are coupled to cytotoxic drugs, able to induce cancer destruction while sparing normal tissues. Current high-throughput proteomic analysis allows for the identification of a high number of proteins that are differentially expressed in the cancerous tissues. However, such approaches provide no information regarding the accessibility of the biomarkers and, therefore, the possibility for these discovered proteins to be targeted. To bypass this limitation, which clearly slows the discovery of such biomarkers, we have developed, applied and validated innovative technologies to efficiently identify accessible antigens from clinically relevant samples. Another challenge in the biomarker field is the identification of diagnostic and prognostic biomarkers from early lesions, measurable in liquid biopsies. Fresh human material of high quality is required for biomarker discovery but is often not available when it is totally required for clinical pathology investigation. Hence, all OMICs studies are done on residual and less clinically relevant biological samples. We have developed an innovative, simple, and non-destructive, procedure named EXPEL that uses rapid, pressure-assisted, interstitial fluid extrusion, preserving the specimen for full routine clinical pathology investigation. In the meantime, the technique allows a comprehensive OMICs analysis (proteins, metabolites, miRNAs and DNA). As proof of concept, we have applied EXPEL on freshly collected human colorectal cancer and liver metastases tissues. We demonstrate that the procedure efficiently allows the extraction, within a few minutes, of a wide variety of biomolecules holding diagnostic and prognostic potential while keeping both tissue morphology and antigenicity unaltered. Our method enables, for the first time, both clinicians and scientists to explore identical clinical material regardless of its origin and size, which has a major positive impact on translation to the clinic. Our technology opens a new era for biomarkers discovery and will have a major impact on translational research. We trust that this method meets the emerging concept of precision medicine where cancer diagnosis and treatment are tailored to the individual patient characteristics.

Jacques Colinge, PhD,

Professor
IRCM, ICM, and Faculty of Medicine University of Montpellier
Montpellier, France

Research Career

Ph.D. in Mathematics, University of Geneva, Switzerland

1998-2000	Bioinformatician & Scientist I, Serono Pharmaceutical Research Institute, Geneva
2000-2005	Head of Mass Spectrometry Bioinformatics and Parallel Computing, GeneProt Inc., Geneva
2005-2006	Professor of Bioinformatics, Upper Austria University of Applied Sciences
2006-2014	Head of Bioinformatics, CeMM, Vienna, Austria
2009-	Habilitation & Adjunct Professor in Bioinformatics, Technische Universität Graz
2014-	Full Professor University of Montpellier & Team Leader at IRCM
2014-	Adjunct PI, CeMM, Vienna

Research Interests

Systems and network biology method development applied to cancer and immunology
Personalized cancer therapy
Computational proteomics

The dynamic cerebrospinal fluid proteome and a perspective on a new class of biomarkers

Jérôme Vialaret[1], Christophe Hirtz[1], Maxence Ory[2],
Guillaume Gras Combe[3], Luc Bauchet[3], Marine Girard[1], Audrey Gabelle[1,4],
Sylvain Lehmann[1], Jacques Colinge[2,5]

[1]CHRU de Montpellier, Université de Montpellier and INSERM U1183, IRMB, Laboratoire de Biochimie Protéomique Clinique, Montpellier, France
[2]IRCM, Institut de Recherche en Cancérologie de Montpellier, INSERM U1194, Montpellier, France
[3]Service de Neurochirurgie, CHRU de Montpellier, hôpital Gui de Chauliac, Montpellier, INSERM U 1051 and Université de Montpellier, Montpellier, France
[4]Centre Mémoire de Ressources et de Recherche Languedoc-Roussillon, Département de Neurologie, CHRU de Montpellier, hôpital Gui de Chauliac, Montpellier, France
[5]ICM, Institut du Cancer de Montpellier, Montpellier, France

Intravenous administration of stable isotope labeled amino acid (13C6-leucine) to humans recently made it possible to study the metabolism of specific biomarkers in cerebrospinal fluid (CSF) using targeted mass spectrometry (MS). We have applied an unbiased, large-scale approach to obtain hundreds of leucine-containing peptides in parallel using high-resolution MS. Advanced signal processing and mathematical modeling techniques allowed us to determine the rates of synthesis and clearance of more than 200 proteins in the CSF. Large-scale measures obtained from one individual have been confirmed by targeted measures for a dozen of proteins in 4 patients.

These unpublished results pave the way to the study of proteome dynamics to unravel novel biomarkers witnessing metabolic differences, abnormal protein turnover or deregulated fluxes between biological compartments, e.g. CSF and blood, in diseases. Our results demonstrate that this new field of proteomic investigation can be conducted in human patients and biological fluids but the technique is obviously applicable to animal models and solid tissues with adaptations.

Gunma University Graduate School of Medicine

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