第１５３回

東北大学加齢医学研究所

集談会

プログラム

153rd IDAC Biannual Meeting Program

日時：令和２年１月 31 日（金曜日）13:00～

場所：加齢医学研究所

スマート・エイジング研究棟１階　国際会議室

January 31, 2020,13:00~ Center for Smart Aging Research 1F, IDAC

共催：東北大学加齢医学研究所

Institute of Development, Aging and Cancer, Tohoku University

東北大学加齢医学研究所研究会同窓会

Society of Institute of Development, Aging and Cancer, Tohoku University

13:00－　Opening remarks　Dr. Ryuta Kawashima

第 27 回加齢医学研究所研究奨励賞授与式・受賞記念講演

27th IDAC Young Investigator Award Ceremony and Lecture

13:00－13:15　Ceremony　Dr. Ryuta Kawashima

13:15－13:35　Lecture　Chair: Dr. Kozo Tanaka

Functional analysis of BRCA1: centrosome regulation and DNA repair activity

Department of Cancer Biology, Institute of Development, Aging and Cancer, Tohoku University

Yuki Yoshino

Tumor suppressor BRCA1 contributes to the maintenance of genome stability through DNA repair by homologous recombination (HR) and centrosome regulation. BRCA1 dysfunction causes DNA repair deficiency and centrosome amplification resulting in the accumulation of mutations and chromosome instability.

We recently identified novel BRCA1-interacting proteins OLA1 and RACK1. Abnormal expression of these proteins induced centrosome amplification in mammary tissue-derived cells.

OLA1 formed a multimeric complex with BRCA1 and BARD1. When the formation of the complex was deranged by mutations in BRCA1, BARD1 or OLA1, centrosome number was increased, suggesting that the BRCA1/BARD1/OLA1 complex contributes to centrosome regulation.

RACK1 localized to centrosomes and directly bound to BRCA1, BARD1, and OLA1. We identified two BRCA1 mutants, R133H and E143K, deranged binding to RACK1, localization to centrosomes and centrosome regulating activity. Besides, RACK1 knockdown caused abnormal centrosomal localization of BRCA1 and abrogated centriole duplication. These data suggest that RACK1 contributes to BRCA1 localization to regulate centrosome duplication.

We developed an assay system to evaluate cellular HR activity named ASHRA (Assay for Site-Specific HR Activity). In this system, DNA double-stranded breaks are created in a locus of interest by CRISPR/Cas9 system and a marker sequence is knocked-in through HR. The efficiency of the knock-in of the marker sequence is quantified by real-time PCR as an index of HR activity. This assay could evaluate HR activity at any region in the genome, will provide quantitative data of HR activity, and will be useful to predict the sensitivity to anti-cancer agents, such as PARP inhibitors and DNA damaging agents.

13:35－13:40 *break*

13:40－14:40 Sessions 1～4 Chair: Shota Endo

1、Discovery of a novel PET tracer for imaging astrogliosis in the brain

Ryuichi Harada[1, 2], Aiko Ishiki[1], Naoki Tomita[1], Shozo Furumoto[3], Kazuhiko Yanai[2], Yukitsuka Kudo[1], Nobuyuki Okamura[4], Christopher C Rowe[5], Villemagne Victor[5], Hiroyuki Arai[1]

[1] Department of Geriatrics and Gerontology, Institute of Development, Aging and Cancer, Tohoku University

[2] Department of Pharmacology, Tohoku University Graduate School of Medicine

[3] Cyclotron and Radioisotope Center, Tohoku University

[4] Division of Pharmacology, Tohoku Medical and Pharmaceutical University

[5] Department of Molecular Imaging & Therapy, Austin Health, Melbourne, Australia

2、CTLA4-Ig therapy attenuates bronchiolitis obliterans after mouse intrapulmonary tracheal transplantation model through possibility of effect LAG-3^{+} Tregs.

Yamato Suzuki, MD, Hisashi Oishi, MD, PhD, Masahiko Kanehira, PhD, Yasushi Matsuda, MD, PhD, Tetsu Sado, MD, PhD, Masafumi Noda, MD, PhD, Akira Sakurada, MD, PhD, Jun-ichi Funahashi, MD,PhD, Yoshinori Okada, MD, PhD

Department of Thoracic Surgery, Institute of Development, Aging and Cancer, Tohoku University

3、Strategy for quantitative detection of extracellular vesicles

Masashi Takao

Department of Project Programs, Institute of Development, Aging and Cancer, Tohoku University

4、A novel mechano-sensitive transcription factor regulates Foxo1 activity in adipose tissue.

Atsushi Kubo[1], Yumi Kawamata[1], Takahiro Kondo[1], Genta Sahara[2], Akihiro Yamada[2], Yusuke Inoue[2], Toshihiko Ogura[1]

[1] Department of Developmental Neurobiology, Institute of Development, Aging and Cancer, Tohoku University

[2] Department of Medical Engineering and Cardiology, Institute of Development, Aging and Cancer, Tohoku University

14:40－14:50 *Coffee break*

14:50－15:50 Sessions 5～8 Chair: Ryutaro Shirakawa

5、Molecular basis of chromosomal instability during aging in mouse primary fibroblasts

Guan Chen, Kenji Iemura, Kozo Tanaka

Department of Molecular Oncology, Institute of Development, Aging and Cancer, Tohoku University

6、Negative feedback loop between Let7 miRNA and PPARalpha via a novel Let7-RNF8-RXR axis controls liver lipid synthesis

Tomoki Yagai[1], Frank J. Gonzalez[2]

[1] Department of Metabolic Bioregulation, Institute of Development, Aging and Cancer, Tohoku University

[2] Laboratory Chief, Laboratory of Metabolism, National Cancer Institute, National Institutes of Health

7、Intervention study of the effect of maintaining cognitive function by brown rice diet

Yuji Takano, Masatoshi Ukezono, Yasuyuki Taki

Joint Research Division for Nutrition & Cognitive Health (Toyo Rice Corp.), Smart-Aging Research Center, Tohoku University

８、**The inhibitory role of Ig-like receptor gp49B on murine osteoclast differentiation**

Karin Ono, Mei-Tzu Su, Shota Endo, and Toshiyuki Takai
Department of Experimental Immunology, Institute of Development, Aging and Cancer, Tohoku University

15:50－16:00　*break*

16:00－16:30　Sessions 9～10　　Chair:Fang Zhenzhou

９、**Effects of NRF2 Activation on Aging Phenotypes of Salivary Glands**

Sisca Meida Wati, Daisuke Matsumaru, Hozumi Motohashi
Department of Gene Expression Regulation, Institute of Development, Aging and Cancer, Tohoku University.

１０、**Applications of Synthetic Nanobodies to Biochemical Studies.**

Kota Goto,Ryutaro Shirakawa, Hisanori Horiuchi
Department of Molecular and Cellular Biology, Institute of Development, Aging and Cancer, Tohoku University

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一般口演について
発表時間１２分，討論３分とします。時間厳守にてお願いします。
座長は研究員会委員の集談会コンテスト係が行ないます。

16:30－16:35　*break*

16:35－17:15　Special lecture by new professor

Chair : Dr. Hozumi Motohashi

RNA modomics in human physiology and diseases

Department of Modomics Biology and Medicine, Institute of Development, Aging and Cancer, Tohoku University

Prof. Fan-Yan Wei

Transcriptional control of RNA expression is vital for cellular homeostasis, and its dysregulation can accelerate aging and cause fatal disease. Recently, accumulating studies are identifying diverse chemical modifications in RNAs from all three domains of life. These discoveries have added a new layer of complexity to RNA biology. However, knowledge on the physiological and pathological functions of these modifications in mammals is very limited. To understand the role of RNA modifications, I have developed 'RNA Modomics (Modification + Omics)' methodology, which enables quantitative and qualitative analysis of entire RNA modifications by mass spectrometry. I have applied this technology to thoroughly interrogate RNA modifications that are related to human diseases including type 2 diabetes and mitochondrial disease. In this seminar, I will introduce my latest research regarding the discovery of novel tRNA modifications and its association with intellectual disability.

Recently, linkage analyses have identified FTSJ1 gene as a novel candidate gene of X-linked intellectual disability (XLID). However, the molecular function and its relevance with XLID has been unknown. Using RNA modomics, I have identified that Ftsj1 is a tRNA modification enzyme, which catalyzes 2'-O-methylation at position 32 and 34 of a subset of cytosolic tRNAs including $tRNA^{Phe}$. Importantly, Ftsj1-deficiency caused a decrease in decoding efficiency specifically at Phe codons, leading to the aberrant translation of genes related to brain function. The aberrant protein translation resulted in profound abnormalities at the electrophysiological, morphological and behavioral properties in Ftsj1 KO mice. There results suggest that Ftsj1-mediated tRNA modification is important for efficient translation at specific codons, which is indispensable for maintaining brain function.

17:15－17:20　Closing remarks　Dr. Hozumi Motohashi

終了後
加齢研実験研究棟 7 階セミナー室（1）におきまして１８時から研究員会主催新年会を開催いたします。皆様、多数ご参加くださいますようご案内いたします。