第１６１回
東北大学加齢医学研究所
161st IDAC Biannual Meeting

集談会

日時：令和6年2月2日（金）13:00～
February 2, 2024,13:00～

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

AGENDA

13:00—	OPENING REMARKS	KOZO TANAKA

第 31 回加齢医学研究所研究奨励賞受賞記念講演

31st IDAC Young Investigator Award Lecture

13:00—13:15	CEREMONY	KOZO TANAKA
13:15—13:20	GUIDANCE FOR Q&A	SHINPEI KAWAOKA
13:20—14:00	LECTURE	CHAIR: FAN-YAN WEI

E3 ligase activity of Aurora A is critical for the regulation of BRCA1-interacting protein OLA1 to promote centrosome maturation

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

Zhenzhou Fang

Germline mutations in *BRCA1* cause hereditary breast and ovarian cancer. BRCA1/BARD1 functions in a variety of cellular processes, including DNA repair and centrosome regulation. We have identified Obg-like ATPase 1 (OLA1) as a BARD1-interacting protein. OLA1 binds to BRCA1 and BARD1 and localizes to centrosome throughout the cell cycle, whereas its localization decreases in G2 phase. Knockdown or overexpression of OLA1 causes centrosome amplification, suggesting that adequate level of OLA1 expression is important for the regulation of centrosome number. Aurora A is known as a critical kinase that regulates mitotic processes including centrosome maturation. I found a novel role of Aurora A as an E3 ubiquitin ligase in the promotion of centrosome maturation. Aurora A bound to and polyubiquitinated OLA1, targeting it for proteasomal degradation. NIMA-related kinase 2 (NEK2) phosphorylated the T124 residue of OLA1 and increased the binding of OLA1 to Aurora A and OLA1 polyubiquitination by Aurora A, resulting in the reduces centrosomal OLA1 in G2 phase. The kinase activity of Aurora A suppressed OLA1 polyubiquitination by Aurora A. The decrease in centrosomal OLA1 caused by Aurora A-mediated polyubiquitination promoted the recruitment of pericentriolar material proteins in G2 phase. The E3 ligase activity of Aurora A was critical for centrosome amplification induced by its overexpression. These results suggest a dual function of Aurora A as an E3 ubiquitin ligase and a kinase in the regulation of centrosomal OLA1, which is essential for proper centrosome maturation in G2 phase.

LILRB4 promotes cancer progression by regulating MDSCs and impacts the prognosis of non-small cell lung cancer patients

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

Sakiko Kumata

Myeloid-derived suppressor cells (MDSCs) have been shown to express the leukocyte immunoglobulin-like receptor B4 (human LILRB4 (B4)/ILT3, mouse homolog receptor gp49B), suggesting the association between B4 expression and the suppression of cancer immunity. However, the role of B4 in lung cancer progression is poorly understood. We first investigated the impact of B4 expression on MDSCs on lung cancer metastasis using a mouse model. Our results showed that B4 deficiency inhibited metastasis of lung cancer cells, which was accompanied by a reduction of MDSCs in metastatic foci. $B4^{-/-}$ MDSCs from tumor-bearing mice inhibited activation of Treg cells, cancer cell migration, and tumor angiogenesis in *in vitro* experiments. We also examined the B4 expression levels on tumor-infiltrating cells (TICs) in resected samples of 239 non-small cell lung cancer (NSCLC) patients. The group of patients with a high B4 expression level on TICs showed a shorter overall survival (OS) ($p = 0.013$) and relapse-free survival (RFS) ($p = 0.0017$) compared to those with a low B4 expression level. Multivariate analyses identified a high B4 expression as an independent factor for post-operative recurrence, poor OS and RFS. A part of B4 positive cells was found positive for MDSC markers, CD33 and CD14. These results suggest that the signaling through B4 on TICs, including MDSCs, play an important role in cancer progression. We conclude that the B4 expression level on TICs may serve as a predictor for poor prognosis and also it could be a promising therapeutic target in NSCLC patients.

14:00－14:10　COFFEE BREAK

14:10—15:10 SESSION 1 PRESENTATIONS 1-4

CHAIRS: KOKI KAKIZAWA KEISHI SOGA

1. **CHAMP1 heterozygous mutations identified in intellectually disabled individuals; analyzing their effects on DNA double strand break repair pathway choice**

   Yujiro Yoshizaki, Yunosuke Ouchi[1], Yuuki Yoneyama[1], Kozo Tanaka[1],
   Department of Molecular Oncology, Institute of Development, Aging, and Cancer

2. **Graft Evaluation for Safe Lobar Lung Transplantation**

   Sho Murai, Yui Watanabe, Kazunori Ueda, Tatsuaki Watanabe, Takashi Hirama, Hisashi Oishi, Ken Onodera, Hirotsugu Notsuda, Takaya Suzuki, Hiromichi Niikawa, Masafumi Noda, Yoshinori Okada
   Department of Thoracic Surgery, Institute of Development, Aging and Cancer, Tohoku University

3. **Evaluation of age-related neurofunctional changes in mice**

   Takuya Urushihata[1] and Akiko Satoh[1]
   [1]Depertment of Integrative Physiology, Institute of Development, Aging, and Cancer (IDAC), Tohoku University.

4. **Mitochondrial Activities Guide the Pathway Decision in Lineage Commitment of. Megakaryocyte-Erythroid Progenitors**

   Eunkyu SUNG[1], Shohei MURAKAMI[1], Tomoaki, IDA[2], Masanobu MORITA[3], Takaaki AKAIKE[3], Hozumi MOTOHASHI[1]
   [1]Department of Gene Expression Regulation, Institute of Development, Aging and Cancer, Tohoku. University
   [2]Department of Biological Chemistry, Graduate School of Science, Osaka Metropolitan University
   [3]Department of Environmental Medicine and Molecular Toxicology, Tohoku University Graduate. School of Medicine

15:10—15:20 COFFEE BREAK

15:20－16:05 SESSION 2 PRESENTATIONS 5-7

CHAIRS: SHOKI OGATA SHIGERU MATSUDA

5. **Influence of *Citrobacter freundii* on *NINJ2* Expression and Oxaliplatin Resistance in Colorectal Carcinomas**

Reio Ueta, Hiroo Imai, Ken Saijo, Yoshifumi Kawamura, Shuto Kodera, Chikashi Ishioka

Department of Clinical Oncology, Tohoku University Graduate school of Medicine, Sendai, Japan

6. **Nicotinamide-N-methyltransferase regulates lipid metabolism via SAM and 1-methylnicotinamide in the AML12 hepatocyte cell line.**

Mayuko Yoda[1], Rin Mizuno[2], Yoshihiro Izumi[3], Masatomo Takahashi[3], Motonao Nakao[3], Takeshi Bamba[3], Shinpei Kawaoka[1]

[1]Department of Integrative Bioanalytics, Institute of Development, Aging and Cancer (IDAC), Tohoku University

[2]Inter-Organ Communication Research Team, Institute for Life and Medical Sciences, Kyoto University

[3]Division of Metabolomics, Research Center for Transomics Medicine, Medical Institute of Bioregulation, Kyushu University

7 . **Investigating predictors of bleeding events in patients with left ventricular assist devices**

Ryuichi Taketomi

Department of Molecular and Cellular Biology, Institute of Development, Aging, and Cancer

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。

座長は研究員会集談会コンテスト審査員が行ないます。

12 min talk and 3 min Q&A

16:05－16:10　CLOSING REMARKS　HOZUMI MOTOHASHI

集談会終了後、17:15 から研究員会主催新年会を加齢研実験研究棟 7 階セミナー室 1 で開催いたします。

We will have a new year party at 実験研究棟 7 階セミナー室 1 from 17:15. Join us!

東北大学加齢医学研究所集談会に関するガイドライン

【趣旨】

定期開催される東北大学加齢医学研究所集談会(以下、「集談会」という)において、加齢医学研究所同窓会メンバー(以下、メンバーという。)向けに、所属研究者等の日頃の成果を発表いただいておりますが、その中にはメンバー向けのため、公知となっていない研究データ等を発表いただける場合もございます。

ご存じのとおり、研究者のマナーとしまして、不用意に口外しないことを前提に発表いただいておりますが、昨今、ウェブ等で開催することもあり、ＵＲＬをご存じの方は、メンバー以外でもご参会いただけるため、発表者に不利益が生じないよう、守秘義務を講じて開催いただきますようお願いいたします。

注意事項「本集談会を聴講するにあたり、同会において提供又は開示され、若しくは同発表会を通じて知得した一切の情報について秘密に保持すること。

但し、聴講を受ける前に公知であったこと又は自ら正当に保有していたことを証明できる情報、若しくは聴講を受けた後、貴学が公開したことを証明できる情報についてはこの限りではないものとします。」