Cell Signal Unit

Professor Tadashi Yamamoto

Yamamoto unit members are posing Y with their hands.

Abstract

The Cell Signal Unit analyzes the CCR4-NOT complex-mediated gene regulation to study molecular and cellular events that are relevant to and important for maintaining healthy life. Through the studies, Unit explores the cause of various diseases that include cancer, neuronal disorder, immunological diseases, diabetes/obesity, and defects in development at the molecular level. The Unit characterizes both transcriptional and post-transcriptional gene regulation that involves microRNA, long non-coding RNA and RNA binding proteins. The Unit also aims to develop novel methodology of cancer therapy in which anti-apoptotic gene is suppressed via siRNA technology.

1. Staff

- Dr. Hiroaki Sako, Postdoctoral Scholar
- Dr. Lea Picard, Postdoctoral Scholar

- Dr. Haytham Mohamed Aly Mohamed, Postdoctoral Scholar
- Dr. Olga Elisseeva, Visiting Researcher
- Dr. Rieko Ajima, Visiting Researcher
- Dr. Emi Kawamoto, Visiting Researcher
- Dr. Akiko Tamura, Visiting Researcher (May-June)
- Dr. Saori Nishijima, Technical Staff
- Dr. Akiko Nishiyama, Technical Staff (July-)
- Ms. Risa Ishida, Technical Staff
- Ms. Nao Ohmine, Technical Staff
- Ms. Atsuko Sato, Technical Staff
- Ms. Aisulu Maipas, Graduate Student
- Mr. Yuki Tara, Graduate Student
- Ms. Ting-Hua Chen, Graduate Student (Wolf Unit)
- Mr. Hajime Uenishi, Research Intern (March-July)
- Ms. Chisato Umehara, Research Intern (August-October)
- Mr. Tomohiro Hasegawa, Research Intern (September-January)
- Mr. Hironori Kishi, Research Intern (December-March)
- Mr. Ryutaro Tomono, Research Intern (December-March)
- Ms. Eriko Okamatsu, Research Unit Administrator

2. Collaborations

2.1 Physiology and Molecular Cellular Biology of the CCR4-NOT complex

- Description: Analyze physiological and molecular biological roles of the CCR4-NOT complex subunits using gene-modified mice..
- Type of collaboration: Joint research
- Researchers:
    - Keiji Kuba, MD; PhD, Professor, Department of Pharmacology, Kyushu University Graduate School of Medical Sciences
    - Toru Suzuki, PhD, Assistant Professor, Division of RNA and Gene Regulation, The Institute of Medical Science, The University of Tokyo
    - Masahiro Morita, PhD, Assistant Professor, Department of Molecular Medicine UT Health Professor, WPI Premium Research Institute for Human Metaverse Medicine Osaka University

2.2 Role of CNOT9 in mouse embryonic development

- Description: Cnot9 KO mice are embryonic lethal, possibly due to defects occurring in embryonic stem cells (ESC). We will search for genes whose expression is altered in the absence of CNOT9 and molecularly analyze the cause of the alteration.
- Type of collaboration: Joint research
- Researchers:
    - Hiroshi Hamada, PhD, Professor in National Center for Biological Sciences, India

- Rieko Ajima, PhD, Associate Professor, Division of Embryology, National Institute for Basic Biology
- Hemanta Sarmah, PhD, Postdoctoral Fellow, Columbia Stem Cell Initiative, Columbia University Irving Medical Center

2.3 Studies on CNOT variants in neurodevelopmental disorder

- Description: Cnot9 KO mice are embryonic lethal, possibly due to defects occurring in embryonic stem cells (ESC). We will search for genes whose expression is altered in the absence of CNOT9 and molecularly analyze the cause of the alteration.
- Type of collaboration: Joint research
- Researchers:
  - Takanobu Nakazawa, PhD, Professor, Department of Bioscience, Tokyo University of Agriculture

2.4 The neuromuscular junction as a new target for treatment of hereditary motor and sensory neuropathy, Okinawa-type and related disorders

- Description: Cnot9 KO mice are embryonic lethal, possibly due to defects occurring in embryonic stem cells (ESC). We will search for genes whose expression is altered in the absence of CNOT9 and molecularly analyze the cause of the alteration.
- Type of collaboration: Joint research
- Researchers:
  - Yuji Yamanashi, PhD, Professor. Institute of Medical Science, University of Tokyo

3. Activities and Findings

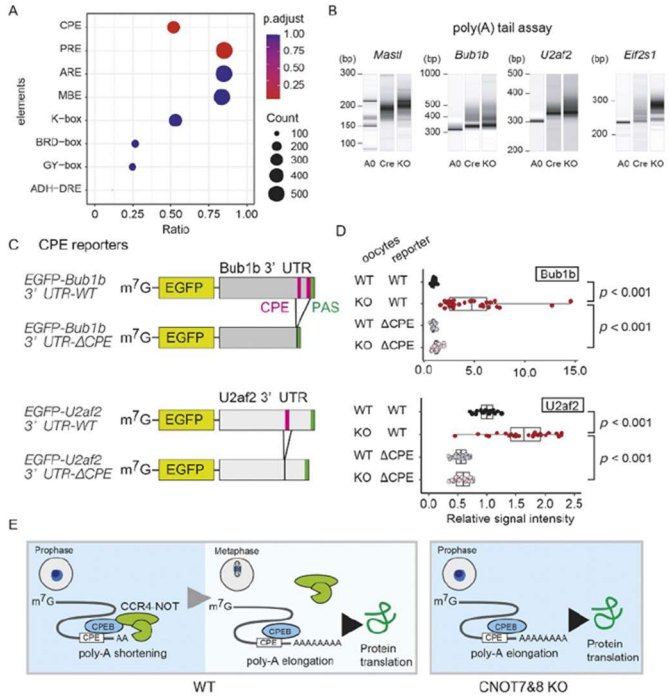
3.1 The CCR4-NOT complex suppresses untimely translational activation of maternal mRNAs, *Development vol 150, issue 21, Nov. 1, 2023*

Abstract

Control of mRNA poly(A) tails is essential for regulation of mRNA metabolism, specifically translation efficiency and mRNA stability. Gene expression in maturing oocytes relies largely on post-transcriptional regulation, as genes are transcriptionally silent during oocyte maturation. The CCR4–NOT complex is a major mammalian deadenylase, which regulates poly(A) tails of maternal mRNAs; however, the function of the CCR4–NOT complex in translational regulation has not been well understood. Here, we show that this complex suppresses translational activity of maternal mRNAs during oocyte maturation. Oocytes lacking all CCR4–NOT deadenylase activity owing to genetic deletion of its catalytic subunits, Cnot7 and Cnot8, showed a large-scale gene expression change caused by increased translational activity during oocyte maturation. Developmental arrest during meiosis I in these oocytes resulted in sterility of oocyte-specific Cnot7 and Cnot8 knockout female mice. We further showed that recruitment of CCR4–NOT to maternal mRNAs is mediated by the 3′UTR element CPE, which suppresses translational activation of maternal mRNAs. We propose that suppression of untimely translational activation of maternal mRNAs via deadenylation by CCR4–NOT is essential for proper oocyte maturation.

Results

Genes with CPE in their 3′UTRs are translationally activated in CNOT7&8 KO oocytes.



(A) Enrichment analysis of cis-regulatory elements on mRNA 3′UTRs of upregulated proteins in CNOT7&8 KO oocytes. mRNA 3′UTRs of genes for which protein expression was upregulated were subjected to enrichment analysis of cis-regulatory elements. The dot plot indicates the number of genes with each cis-regulatory element and its ratio. Adjusted P-value (chi-squared test); CPE: 0.053; PRE: 0.062; others: 1.0. (B) Poly(A) tail assay on the translationally activated mRNAs. Poly(A) tail lengths were analyzed by poly(A) tail assay on indicated genes. A0, amplicon from poly(A) removed samples. (C) Design of CPE reporter mRNAs. Magenta and green regions indicate CPE and polyadenylation signal (PAS), respectively. (D) CPE reporter assay in CNOT7&8 KO GV oocytes. CNOT7&8 KO or WT GV oocytes were injected with EGFP-Bub1b or U2af2-3′UTR-WT or ΔCPE. Each circle indicates relative EGFP signal intensity. Horizontal lines indicate data range. Left, middle and right vertical lines indicate lower quartile, median and upper quartile, respectively. Student's t-test. (E) Graphical summary of the proposed regulatory mechanism of translational activity of maternal mRNAs by the CCR4–NOT complex. The CCR4-NOT complex targets CPE-containing mRNAs to suppress their untimely translational activation by shortening their poly(A) tails.

3.2 microRNAs slow translating ribosomes to prevent protein misfolding in eukaryotes. *EMBO J. Vol 42, issue 18, September 2023*

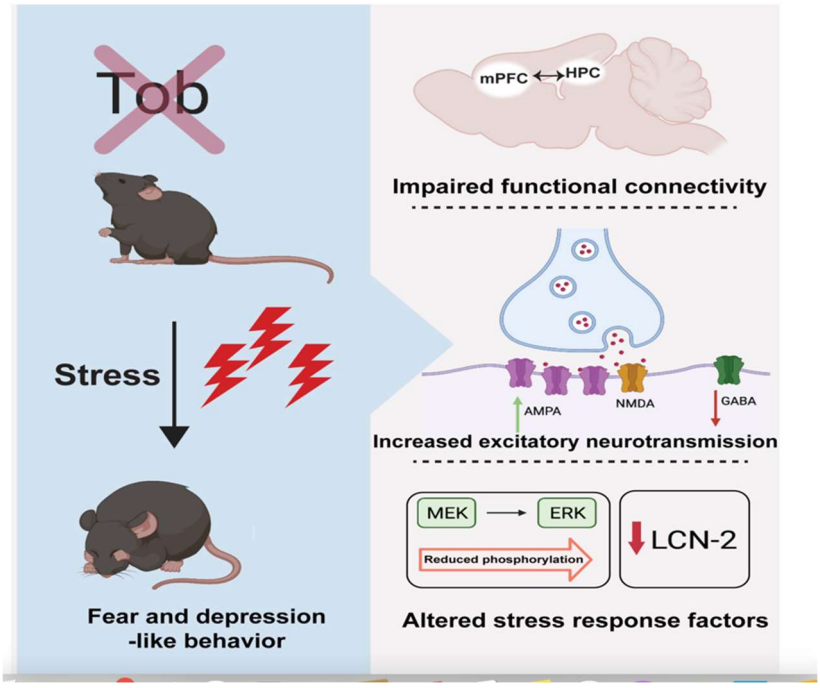
Abstract

Slower translation rates reduce protein misfolding. Such reductions in speed can be mediated by the presence of non-optimal codons, which allow time for proper folding to occur. Although this phenomenon is conserved from bacteria to humans, it is not known whether there are additional eukaryote-specific mechanisms which act in the same way. MicroRNAs (miRNAs), not present in prokaryotes, target both coding sequences (CDS) and 3′ untranslated regions (UTR). Given their low suppressive efficiency, it has been unclear why miRNAs are equally likely to bind to a CDS. Here, we show that miRNAs transiently stall translating ribosomes, preventing protein misfolding with little negative effect on protein abundance. We first analyzed ribosome profiles and miRNA binding sites to examine whether miRNAs stall ribosomes. Furthermore, either global or specific miRNA deficiency accelerated ribosomes and induced aggregation of a misfolding-prone polypeptide reporter. These defects were rescued by slowing ribosomes using non-cleaving shRNAs as miRNA mimics. We finally show that proinsulin misfolding, associated with type II diabetes, was resolved by non-cleaving shRNAs. Our findings provide a eukaryote-specific mechanism of co-translational protein folding and a previously unknown mechanism of action to target protein misfolding diseases.

3.3 TOB is an effector of the hippocampus-mediated acute stress response *Translational Psychiatry. Vol 12, July 19, 2022*

Abstract

Stress affects behavior and involves critical dynamic changes at multiple levels ranging from molecular pathways to neural circuits and behavior. Abnormalities at any of these levels lead to decreased stress resilience and pathological behavior. However, temporal modulation of molecular pathways underlying stress response remains poorly understood. Transducer of ErbB2.1, known as TOB, is involved in different physiological functions, including cellular stress and immediate response to stimulation. In this study, we investigated the role of TOB in psychological stress machinery at molecular, neural circuit, and behavioral levels. Interestingly, TOB protein levels increased after mice were exposed to acute stress. At the neural circuit level, functional magnetic resonance imaging (fMRI) suggested that intra-hippocampal and hippocampal-prefrontal connectivity were dysregulated in Tob knockout (Tob-KO) mice. Electrophysiological recordings in hippocampal slices showed increased postsynaptic AMPAR-mediated neurotransmission, accompanied by decreased GABA neurotransmission and subsequently altered Excitatory/Inhibitory balance after Tob deletion. At the behavioral level, Tob-KO mice show abnormal, hippocampus-dependent, contextual fear conditioning and extinction, and depression-like behaviors. On the other hand, increased anxiety observed in Tob-KO mice is hippocampus-independent. At the molecular level, we observed changes in factors involved in stress response like decreased stress-induced LCN2 expression and ERK phosphorylation, as well as increased MKP-1 expression. This study introduces TOB as an important modulator in the hippocampal stress signaling machinery. In summary, we reveal a molecular pathway and neural circuit mechanism by which Tob deletion contributes to expression of pathological stress-related behavior.

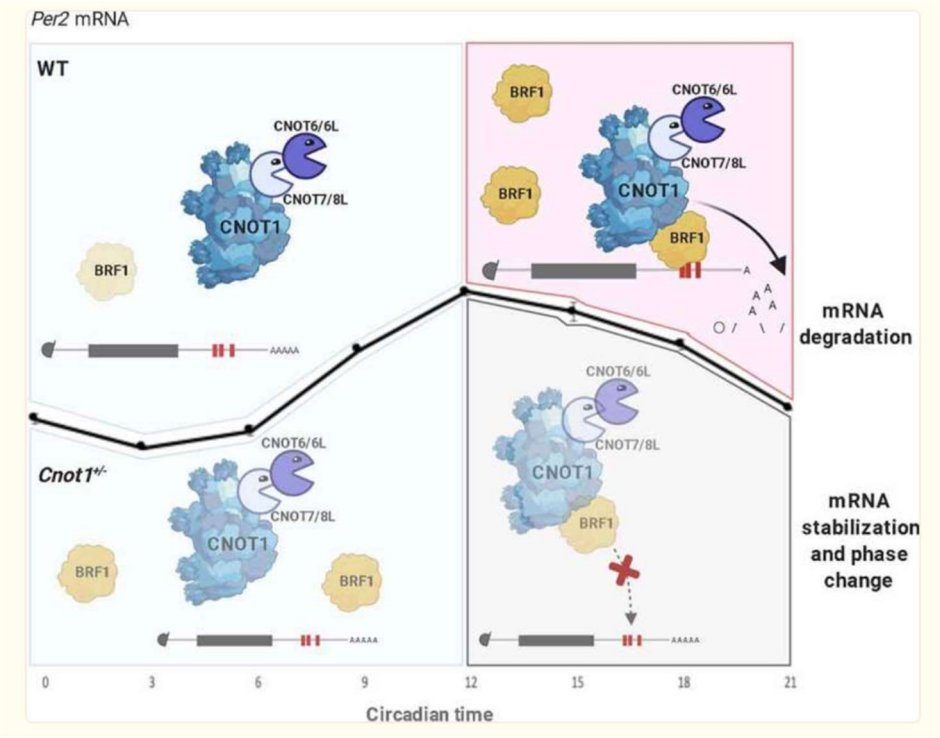


3.4 CNOT1 regulates circadian behavior through Per2 mRNA decay in a deadenylation-dependent manner *RNA Biology, Vol 19, issue 1, 2022*

Abstract

Circadian clocks are an endogenous internal timekeeping mechanism that drives the rhythmic expression of genes, controlling the 24 h oscillatory pattern in behaviour and physiology. It has been recently shown that post-transcriptional mechanisms are essential for controlling rhythmic gene expression. Controlling the stability of

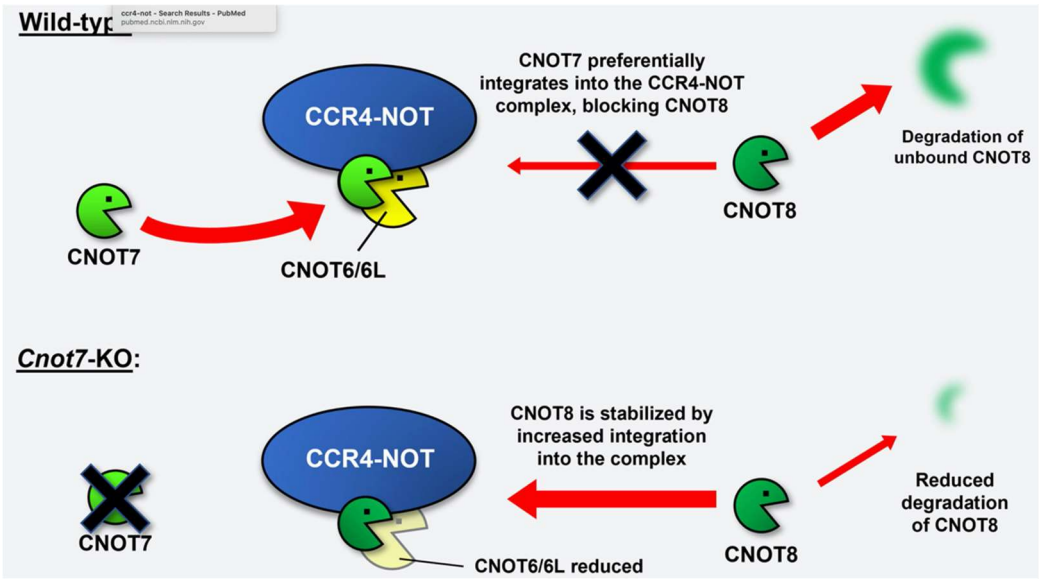
mRNA through poly(A) tail length modulation is one such mechanism. In this study, we show that Cnot1, encoding the scaffold protein of the CCR4-NOT deadenylase complex, is highly expressed in the suprachiasmatic nucleus, the master timekeeper. CNOT1 deficiency in mice results in circadian period lengthening and alterations in the mRNA and protein expression patterns of various clock genes, mainly Per2. Per2 mRNA exhibited a longer poly(A) tail and increased mRNA stability in Cnot1+/− mice. CNOT1 is recruited to Per2 mRNA through BRF1 (ZFP36L1), which itself oscillates in antiphase with Per2mRNA. Upon Brf1 knockdown, Per2 mRNA is stabilized leading to increased PER2 expression levels. This suggests that CNOT1 plays a role in tuning and regulating the mammalian circadian clock.



Proposed model of CCR4-NOT/BRF1 mediated decay of Per2 mRNA.

Suggested model showing that in WT liver, BRF1 levels are lower during the subjective morning and levels increase during the subjective night, when it binds to the 3'UTR region of Per2, destabilizing it by recruiting the CCR4-NOT complex, removing the tail of adenosine bases, and ultimately degrading the mRNA transcript. While in Cnot1+/- livers, BRF1 levels during the subjective night are decreased, and the BRF1/CCR4-NOT complex is not able to bind effectively to Per2 3'UTR

3.6 CNOT7 outcompetes its paralog CNOT8 for integration into the CCR4-NOT. *Journal of Molecular Biology Vol 434, issue 9, May 15, 2022*



Abstract

The CCR4-NOT deadenylase complex is a major post-transcriptional regulator of eukaryotic gene expression. CNOT7 and CNOT8 are both vertebrate homologs of the yeast CCR4-NOT catalytic subunit Caf1. They are highly similar

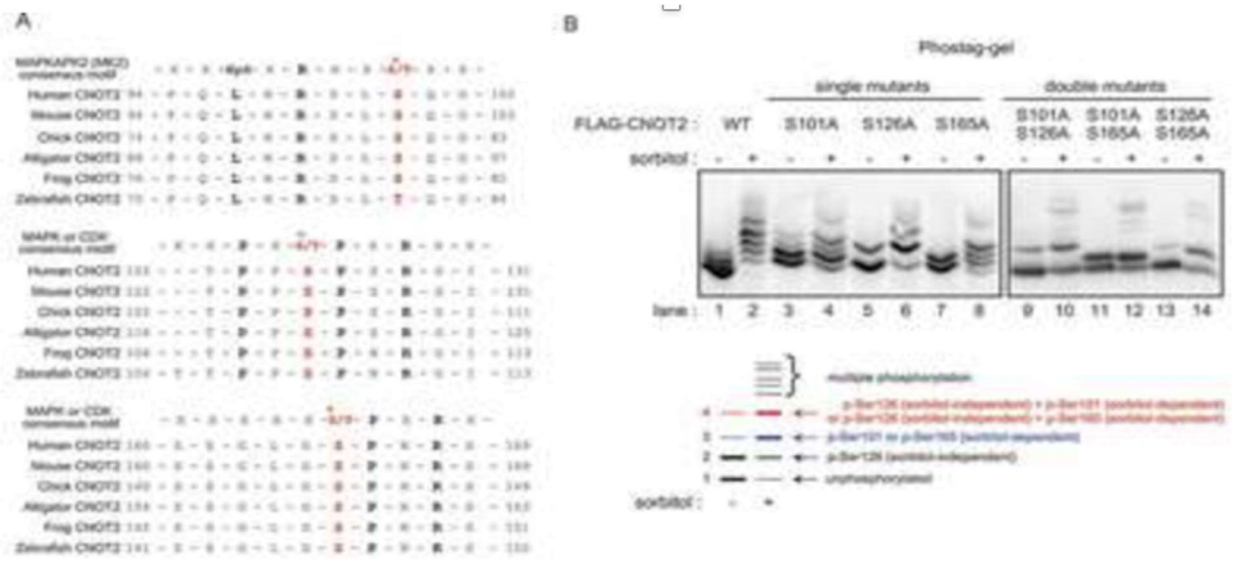
and are sometimes considered redundant, but Cnot7 and Cnot8 knockout mice exhibit different phenotypes, implying distinct physiological functions. In this study, we reveal a non-reciprocal effect of CNOT7 on CNOT8, in which CNOT8 protein is increased in the depletion of CNOT7 without corresponding changes in mRNA levels whereas CNOT7 is not affected by the loss of CNOT8. Cnot8 mRNA may be bound by the CCR4-NOT complex, suggesting that CCR4-NOT might directly regulate CNOT8 expression. Cnot8 mRNA is relatively unstable, but Cnot7 knockdown did not stabilize Cnot8 mRNA, nor did it increase translation. CNOT8 protein was also less stable than CNOT7. CNOT7 showed greater affinity than CNOT8 for the CCR4-NOT scaffold protein CNOT1 and was able to block CNOT8 from binding to CNOT1. Depletion of CNOT7 increased CNOT8 incorporation into the CCR4-NOT complex and stabilized CNOT8. These data suggest that CNOT7 is the dominant paralog in CCR4-NOT and that CNOT7 and CNOT8 protein stability is regulated in distinct ways.

A model of the mechanism by which CNOT8 is increased by CNOT7 depletion. In wild-type cells, CNOT7 preferentially binds to CNOT1 via the MIF4G domain and integrates into the CCR4-NOT complex. CNOT8 is excluded and unbound CNOT8 is degraded by the proteasome. In Cnot7-KO tissue, or in CNOT7-depleted cells, CNOT8 can integrate into the CCR4-NOT complex, which stabilizing it and protecting it from degradation. However, the increased integration of CNOT8 into the CCR4-NOT complex fails to fully compensate for loss of CNOT7 in terms of recruiting CNOT6 and CNOT6L due to the weaker interaction between CNOT8 and CNOT6/6L.

3.6 Regulation of CCR4-NOT complex deadenylase activity and cellular responses by MK2-dependent phosphorylation of CNOT2. *RNA Biology Vol 19, issue 1, 2022*

Abstract

CCR4-NOT complex-mediated mRNA deadenylation serves critical functions in multiple biological processes, yet how this activity is regulated is not fully understood. Here, we show that osmotic stress induces MAPKAPK-2 (MK2)-mediated phosphorylation of CNOT2. Programmed cell death is greatly enhanced by osmotic stress in

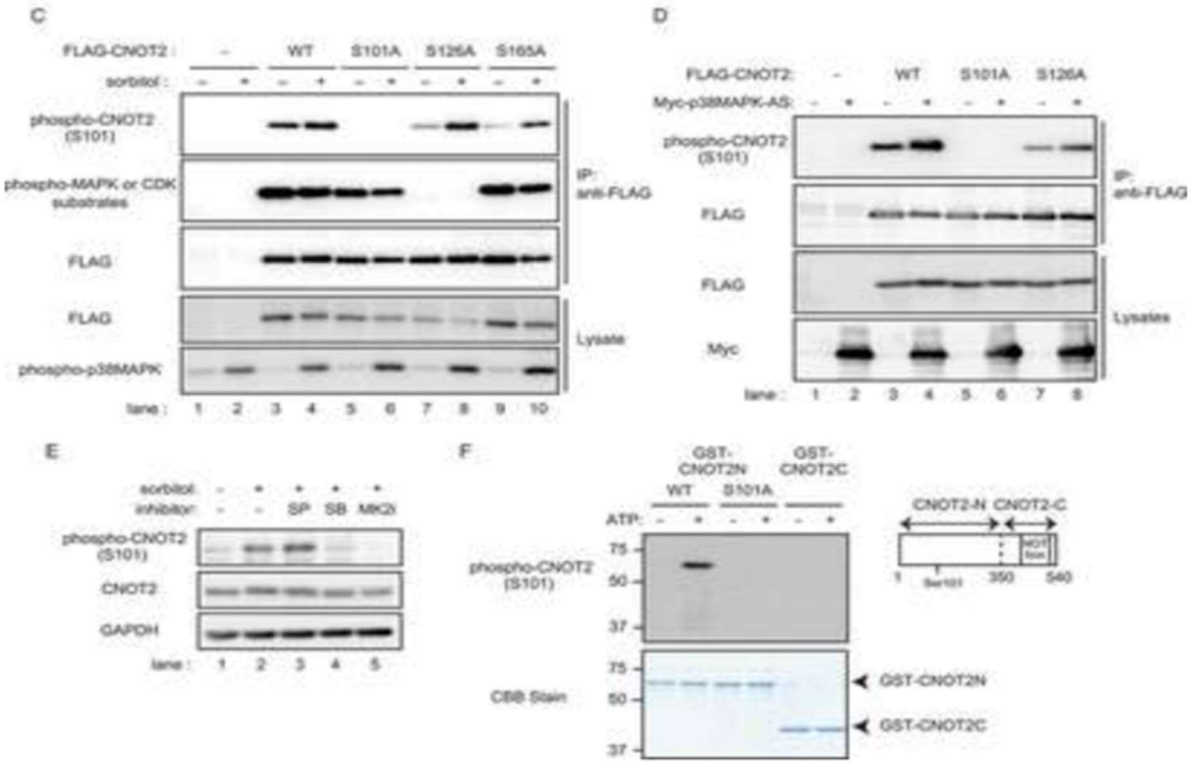


CNOT2-depleted cells, indicating that CNOT2 is responsible for stress resistance of cells. Although wild-type (WT) and non-phosphorylatable CNOT2 mutants reverse this sensitivity, a phosphomimetic form of CNOT2, in which serine at the phosphorylation site is replaced with glutamate, does not have this function. We also show

that mRNAs have elongated poly(A) tails in CNOT2-depleted cells and that introduction of CNOT2 WT or a non-phosphorylatable mutant, but not phosphomimetic CNOT2, renders their poly(A) tail lengths comparable to those in control HeLa cells. Consistent with this, the CCR4-NOT complex containing phosphomimetic CNOT2 exhibits less deadenylase activity than that containing CNOT2 WT. These data suggest that CCR4-NOT complex deadenylase activity is regulated by post-translational modification, yielding dynamic control of mRNA deadenylation.

A key finding

Osmotic stress-induced, MK2-dependent phosphorylation of CNOT2 at Ser101.



In (A) alignment of CNOT2 amino acid sequence in various organisms and the consensus sequence for MK2, MAPK or CDK substrates. Asterisks indicate putative phosphorylation sites. (B) HEK293T cells transfected with vectors expressing the indicated CNOT2 constructs were treated with (+) or without sorbitol (-). Cell lysates were immunoprecipitated using anti-FLAG antibody. The anti-FLAG immunoprecipitates were analyzed by Phos-tag SDS-PAGE, followed by immunoblotting using anti-FLAG antibody. A schematic representation of immunoblot images in CNOT2 WT treated with (+) or without sorbitol (-) is shown at the bottom. (C) HEK293T cells transfected with vectors expressing the indicated CNOT2 constructs were treated with (+) or without sorbitol (-). Cell lysates were immunoprecipitated with anti-FLAG antibody. Immunoprecipitates (IP) and lysates were analyzed by immunoblot. Anti-FLAG antibody detects exogenously expressed CNOT2. Immunoblots for phosphor-p38MAPK was used to monitor the presence of osmotic stress-induced response (bottom). (D) HEK293T cells were transfected with the indicated constructs. Cell lysates were immunoprecipitated using anti-FLAG antibody. Ips and lysates were analyzed by immunoblot. Anti-FLAG antibody wand anti-Myc antibody detect exogenously expressed FLAG-CNOT2 and Myc-p38MAPK-AS (constitutively active p38MAPK), respectively. (E) HeLa cells were treated with inhibitors for 30 min anf then treated with sorbitol for an additional 30 min. Cell lysates were analyzed by immunoblot. SP: SP600125 (JNK inhibitor), SB: SB203580 (p38MAPK

inhibitor), MK2i; (MK2 inhibitor). (F) An invitro kinase assay was performed by incubating recombinant MK2 and indicated CNOT2 fragment in the absence (-) or presence (+) ATP. Reaction products were analyzed by immunoblot using phosphor-CNOT2 S101 antibody (upper) and CBB staining (lower). A schematic representation of CNOT2 fragments is shown on the right.

4. Publications

4.1 Journals

1. Sako H., Youssef M., Elisseeva O., Akimoto T., Suzuki K., Ushida T., Yamamoto T., microRNAs slow translating ribosomes to prevent protein misfolding, *The EMBO Journal* (2023) doi:https://doi.org/10.15252/embj.2022112469 (Published online: July 26, 2023)
2. Soeda S., Oyama M., Kozuka-Hata H., and Yamamoto T., The CCR4-NOT complex suppresses untimely translational activation of maternal mRNAs, *Development* (2023) 150 (21) doi:10.1242/dev.201773 (Published online: Oct. 18, 2023)
3. Li H., Tamura R., Hayashi D., Asai H., Koga J., Ando S., Yokota S., Kaneko J., Sakurai K., Sumiyoshi A., Yamamoto T., Hikishima K., Tanaka K. Z., McHugh T. J., Hisatsune T., Silencing dentate newborn neurons alters hippocampal excitatory/inhibitory balance and impairs impulse inhibition and cognitive flexibility, *Science Advances*, (2023) Vol 10, Issue 2 doi:10.1126/sciadv.adk4741 (Published online: Jan. 10, 2024)

4.2 Books and other one-time publications

Nothing to report

4.3 Oral and Poster Presentations

([NOTE] *Seminars and workshops by OIST faculty/unit members (either with or without other speakers), either at OIST or at other institutions than OIST, should be included in the 4.3 Oral and Poster Presentations.

1. Picard, L., Hashimoto, E., Yamamoto, T., *An evolutionary overview of the CCR4-NOT complex and adjacent proteins*, A recipe for scientific synergy -Series 4- “Advancing biotechnology through multidisciplinary approaches”, Osaka, Japan, May 29 (2023)
2. Yamamoto, T., *Physiology of gene expression regulation by CCR4-NOT deadenylase complex,* A recipe for scientific synergy -Series 4- “Advancing biotechnology through multidisciplinary approaches” Osaka, Japan, May 29 (2023)
3. Picard, L. Hashimoto, E., Yamamoto, T., *Evolutionary insights into the impact of viral infections on the metabolism of mRNAs by the CCR4-NOT complex and associated proteins*, EMBO Workshop: Eukaryotic RNA turnover and viral biology, Brno, Czech Republic, June 20-23 (2023)
4. Tara, Y., Yamamoto, T., *mRNA turnover mediated by RNA modification for maintenance of pancreatic β cell homeostasis*, 24th Annual Meeting of the RNA Society of Japan, Naha, Okinawa, Japan, July 5-July 6 (2023)
5. Yamamoto, T., Special Seminar *"A modality of gene regulation mediated by the CCR4-NOT deadenylase complex"*, 24th Annual Meeting of the RNA Society of Japan, Naha, Japan, July 5 (2023)

6. Sako, H., *microRNAs slow translating ribosomes to prevent protein misfolding*, System Biology seminar, Osaka University, Osaka, Japan, August 25 (2023)
7. Maipas, A., Kono, K., Yamamoto, T., *Suppression of DNA Damage-Induced Senescence in Non-Small Cell Lung Cancer: The Protective Role of CNOT3 via p53-p21 Downregulation*, Biology of Cancer: Microenvironment & Metastasis, CSHL, NY, USA, September 19-23 (2023)
8. Yamamoto, T., *Modalities of gene regulation mediated by the CCR4-NOT deadenylase complex*, The 29th Easit Asia Joint Symposium, Cheonan-si, Chungcheongnam-do, S Korea, October 24-27 (2023)
9. Picard, L. Hashimoto, E., Yamamoto, T., *Evolutionary insights into the impact of viral infections on the metabolism of mRNAs by the CCR4-NOT complex and associated proteins*, 10th CCR4-NOT meeting, Fukuoka, Japan, November 13-15 (2023)
10. Yamamoto, T., *Journey of CCR4-NOT from meiosis to gastrulation*, 10th CCR4-NOT meeting, Fukuoka, Japan, November 13-15 (2023)
11. Picard, L. Yamamoto, T., *Exploring the interplay between m6A methylation and CCR4-NOT during IAV infection*, OIST-KEIO Showcase Talk Series 5, OIST, Okinawa, Japan, November 16 (2023)
12. Sako, H., *microRNAs slow translating ribosomes to prevent protein misfolding*, OIST-RIKEN meeting, OIST, Okinawa, Japan, November 16 (2023)
13. Sako, H., *microRNAs slow translating ribosomes to prevent protein misfolding*, The 13th Signal Network Meeting, Kanazawa, Japan, November 24-25 (2023)
14. Yamamoto, T., Soeda, S., *Modalities of CCR4-NOT-mediated gene regulation CCR4-NOT が制御する遺伝子発現制御機構*, The 13th Signal Network Meeting, Kanazawa, Japan, November 24-25 (2023)
15. Sako, H., *microRNAs slow translating ribosomes to prevent protein misfolding*, OIST-Kyudai Joint Symposium Series 1: Bio-Inspired Wonders and Energy Innovations, OIST, Okinawa, Japan, February 29 (2024)
16. Mohamed, H., Yamamoto, T., *CCR4-NOT Complex Regulation of Gene Expression and its Role in Animal Physiology*, OIST x iTHEMS workshop series - Will We Find Answers? Exploring the Mysteries of the Universe and Life - Series 1 | Cosmic ray and Life project |, OIST, Okinawa, Japan, March 6 (2024)

5. Intellectual Property Rights and Other Specific Achievements

Nothing to report

6. Meetings and Events

([NOTE] You can include the following in "6. Meetings and Events":
(1) Seminars and workshops by guest speaker(s)
(2) Seminars and workshops by guest speaker(s) and OIST faculty member(s)/unit member(s)

6.1.1 A novel extrinsic apoptosis pathway regulated via the p53-p53PAD7-Hippo-YAP/TAZ axis.

- Date: April; 5, 2023
- Venue: OIST Campus Lab3
- Speaker: Dr. Rieko Ohki (National Cancer Center Research Institute)

6.1.2. T cell senescence inducing inflammaging.

- Date: April 12, 2023
- Venue: OIST Campus Lab3
- Speaker: Dr. Takashi SAITO (RIKEN, Center for Integrative Medicines)

6.1.3. Exacerbating role of ILC3s in deficits in social behavior in immunodeficiency.

- Date: June 28, 2023
- Venue: OIST Campus Center building
- Speaker: Dr. Michio MIYAJIMA (Japan Science and Technology Agency (JST), PRESTO (Sakigake) researcher)

6.1.4. A ribonuclease involved in glucose signaling in yeasts?.

- Date: December 26, 2023
- Venue: OIST Campus Center building
- Speaker: Professor Marc Lemaire (Universite Claude Bernard, Lyon, France)

6.1.5. Role of c-Myc on the ROS inducer cytotoxicity in cancer cells

- Date: January 31, 2024
- Venue: OIST Campus Lab3
- Speaker: Dr. Nobumoto Watanabe (RIKEN, Center for Sustainable Resource Science)

6.1.6. EHE – Epithelial Hemangio-Endothelioma, cancer driven by fusions of YAP or TAZ oncogenes with genes that encode transcription factors.

- Date: February 7, 2024
- Venue: Online
- Speaker: Dr. Marius Sudol (Icahn School of Medicine at Mount Sinai)

6.1.7. Post-translational modification of Ubc13 during bacterial infection.

- Date: February 14, 2024
- Venue: OIST Campus Lab3
- Speaker: Dr. Minsoo KIM (Kyoto University)

6.1.8. Our attempts to develop VHH antibodies with neutralizing activity against diverse coronavirus mutants and introduction of Japanese vaccine development strategy

- Date: February 21, 2024
- Venue: OIST Campus Lab3
- Speaker: Project Professor Jun'ichiro INOUE (The University of Tokyo)

6.1.9. Signaling in neuromuscular junction (NMJ) formation/maintenance, and NMJ-targeted therapeutics

- Date: February 28, 2024
- Venue: OIST Campus Lab3
- Speaker: Professor Yuji Yamanashin (The University of Tokyo)

6.1.10. Inhibition of SARS-CoV-2 infection by MPRSS2 antibodies

- Date: March 13, 2024
- Venue: OIST Campus Lab3
- Speaker: Dr. Takashi SAITO (RIKEN, Integrative Medical Sciences)

6.1.11. Tumor microenvironments accelerate tumor progression

- Date: March 27, 2024
- Venue: OIST Campus Lab3
- Speaker: Dr. Takeharu SAKAMOTO (Kansai Medical University)

6.2 Something Group for Something on Something (SG2S)

Nothing to report.

7. Other

Nothing to report.